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Abstracts

Acute Liver Failure

Oral Presentations

Abstract # 371

MicroRNA-181c potentially relieved fulminant viral hepatitis by targeting TNF-α

Xi Dong, Wang Ming, Yang Muyang, XuMengyin, Wang Faxi, Ding Wen, Ma Wenwen, Ning Qin

Department and Institute of Infectious Disease, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology. Wuhan, China

Objectives: The relationship between circulating microRNAs (miRNAs) and HBV associated acute-on-chronic liver failure (HBV-ACLF) need to be further investigated. The purpose of our study was to identify the aberrant expression of miRNAs in HBV-ACLF and to investigate its potential role during the progression of HBV-ACLF.
Methods: miRNA expression profile by miRNA microarray analysis was performed on Peripheral Blood Mononuclear Cell (PBMC) obtained from patients with mild chronic hepatitis B (CHB) or HBV-ACLF, respectively. Selected unnormal expressed miRNAs were verified in more clinical samples by quantitative real-time PCR (qRT-PCR). A luciferase reporter assay was conducted to confirm direct target of miR-181c. mmu-miR-181c agomir was delivered by tail vein injection into mouse hepatitis virus-3(MHV-3)-infected BALB/cJ mice to evaluate its interference effect in fulminant viral hepatitis mouse model.
Results: 7 kinds of miRNAs were down-regulated and 9 kinds of miRNAs were up-regulated in the PBMC of HBV-ACLF patients compared with that of patients with mild CHB. Among the deregulated miRNAs, the expression of Hsa-miRNA-181c was significantly down-regulated in HBV-ACLF by qRT-PCR. While serum TNF-α significantly increased in HBV-ACLF. A luciferase reporter assay was conducted to confirm TNF-α was verified as a target of miR-181c. miR-181c significantly improved fulminant viral hepatitis mice survival rate.
Conclusion: These data suggested that miR-181c might have potentially therapeutic potential for the treatment of fulminant hepatitis.

Abstract #689

Amphiregulin alleviated conA induced acute liver injury by anti-apoptosis and interrupting neutrophil infiltration

Wu Qili[1], Chen Jingrou[1], Zhu Yinhong[1], Peng Yanwen[1]

[1]The Biotherapy Center, the Third Affiliated Hospital, Sun Yat-Sen University, Guangzhou, 510630, China

Introduction and objective: Amphiregulin (Areg) has a well-documented protective role in tissue injury, however, its effects on immune-mediated liver injury are still unclear. Here we used concanavalin A (conA) induced acute liver failure (ALF) model to explore the effects of Areg on immune-mediated acute liver injury.
Methods: C57BL/6 mice were administrated with conA at a dose of 20 mg/kg as the hepatitis mice, part of them received 5 μg Areg as the treated mice. Then survival rates were analyzed within 36 h. After 5 h treatment, liver function, hepatic histology and apoptosis of liver tissue were investigated, cytokines levels, chemokines expressions, neutrophil infiltration and activity in livers were also detected.
Results: Our data showed that Areg treatment obviously increased mouse survival rates, markedly alleviated liver damage and improved liver function. Moreover, Areg administration raised the expression of anti-apoptotic proteins Bcl-2 and Bcl-xL, and down-regulated apoptosis molecule Caspase3 in livers. There were fewer neutrophils infiltration, lower MPO activity and less CX3CL1 expression in livers from the Areg treated mice than those from the untreated mice. Interestingly, these changes were concomitant with significantly enhanced IL-22 levels and IL-22-producing T cells in livers, whereas neutralization of IL-22 in vivo completely abolished the hepatoprotective effects of Areg.
Conclusions: Areg treatment revealed direct protective mechanisms against conA induced acute hepatitis, which provides the potential therapeutic strategy for Areg in immune-mediated acute liver injury.

Abstract #1263

A nomogram to predict mortality in patients with hepatitis E virus-related acute liver failure

Hongcui Cao, Jian Wu, Jinfeng Yang, Qiaoling Pan

State Key Laboratory for the Diagnosis and Treatment of Infectious Diseases, National Clinical Research Center for Infectious Diseases, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, 79 Qingchun Rd., Hangzhou 310003, China

Introduction: Timely and effective assessment scoring systems for predicting the mortality of patients with HEV-related acute liver failure (HEV-ALF) are urgently needed.
Objectives: The present study aimed to establish an effective nomogram for predicting the mortality of HEV-ALF patients.
Methods: The nomogram was based on a cross-sectional set of 404 HEV-ALF patients who were identified and enrolled from a cohort of 650 patients with liver failure. To compare the performance with that of the Model for End-Stage Liver Disease (MELD) scoring and CLIF-Consortium-ACLF score (CLIF-C-ACLFs) models, we assessed the predictive accuracy of the nomogram using the Concordance index (C-index), and its discriminative ability using time-dependent receiver operating characteristics (td-ROC) analysis, respectively.
Result: Multivariate logistic regression analysis of the development set carried out to predict mortality revealed that γ-glutamyl transpeptidase (GGT), albumin (ALB), total bilirubin (TBIL), urea nitrogen (UREA), creatinine (CR), international normalized ratio (INR), and neutrophil to lymphocyte ratio (NLR) were independent factors, all of which were incorporated into the new nomogram to predict the mortality of HEV-ALF patients. The AUC of this nomogram for mortality prediction was 0.671 (95% CI 0.602–0.740), which was higher than that of the MELD and CLIF-C-ACLFs models. Moreover, the tdROC and decision curves analysis showed that both discriminative ability and threshold probabilities of the nomogram were superior to those of the MELD and CLIF-C-ACLFs models. A similar trend was observed in the validation set.
Conclusion: The novel nomogram is an accurate and efficient mortality prediction method for HEV-ALF patients.

Abstract # 1421

Laparoscopic single stage management for treatment of concomitant gallbladder stones and common bile duct stones in elderly patients

Barlian Sutedja, Gading Pluit Hospital, Jakarta, Indonesia

Background: Laparoscopic common bile duct exploration (LCBDE) followed by laparoscopic cholecystectomy as a single stage management for treatment of concomitant gallbladder stones and common bile duct stones is an established procedure. However, the outcomes in elderly patients have not been well assessed. To compare the outcome of the single stage procedure in the elderly with the younger patients.
Methods and Material: A retrospective study was conducted for all patients who underwent the procedure, between January 2008 and 2018, in Pluit Hospital and Gading Pluit Hospital in Jakarta. The short-term outcomes of elderly patients in group A ($\geq$ 65 years) were compared with the younger patients in group B ($<$ 65 years). Technique: The clearance of the CBD stones was performed by Trans-cystic or Trans-choledochal approach. In several cases a T-tube was used.
Result: Three hundred and sixty-eight patients were included in this study. The result of group A (N = 114 patients) was compared with group B (N = 254 patients). The pre-operative clinical findings were similar in both groups. The mean operation time (193 vs 183 minutes, p value = 0.83), conversion rate (2.2% vs 1.7%), major complications (7.8% vs 2.3%), retained stones (1.7% vs 1.5%), mortality (1.7% vs 0.3%) and length of the post-operative hospital stays (5 vs 6 days, p value = 0.37), were not statistically significant different.
Conclusion: Laparoscopic single stage management for treatment of concomitant gallbladder stones and common bile duct stones in elderly patients as safe and effective as in younger patients.
Keyword: Gallbladder Stones. Common Bile Duct Stones. Laparoscopic Single Stage Management. Elderly Patients Populations. Laparoscopic Trans-cystic or Trans-choledochal Technique.

Abstract # 1447

The Effect Of*virgin Coconut Oil* (Vco) To The Liver Histopathological Feature Of White Male Wistar Rats (*Rattus Norvegicus*)

Michael Theodore, Edward Imanuel Simon, Dody Taruna, Wahyu Prasasti Mutia Desi

Faculty of Medicine, Hang Tuah University, Surabaya, East Java, Indonesia

Background: *Virgin Coconut Oil* (VCO) is a product that is highly favored and have been widely applied in the everyday lives of society because of its many benefits especially towards the health and fitness of the human body. The benefits that are not only limited to health and fitness but also in other areas tend to increase the frequencies and duration of VCO consumption. As the frequencies and duration of VCO consumption increases, it is suspected that VCO could negatively impact the target organ. The liver is an organ that absorbs, produces and stores nutrient from digestive system. High consumption of saturated fat can increase body weight and total cholesterol serum, and can lead to the accumulation of fat in the liver. The accumulation of fat in the liver can be observed by histopathological examination.
Objective: To find out the effects of *virgin coconut oil* to the liver histopathological feature of white male wistar rats (*Rattus norvegicus*).
Research method: This research is done by doing a laboratorial experimental type research that uses 30 male wistar rats that are divided into 5 groups, which are listed as follows, K(−) or a negative-controlled group which is given standard fooder, P(1) or the first group of rats that are given VCO with a dose of 2 mL/200 g of the rats' total body weight, P(2) or the second group of rats that are given VCO with a dose of 3 mL/200 g of the rats' total body weight, P(3) or the third group of rats that are given VCO with a dose of 4 mL/200 g and P(4) or the fourth group of rats that are given VCO with a dose of 5 mL/200 g of the rats' total body weight. The research design used is *post test only control group*.
Result: Results from Kruskall Wallis test shows a significant difference in the degree of the liver histopathological features between the K(−) group and P(1), P(2), P(3) and P(4) groups.
Conclusion: Administrating VCO with a dose of 2 mL/200 g, 3 mL/200 g, 4 mL/200 g and 5 ml/200 g of the rats' total body weight affect the histopathological degree of the liver.

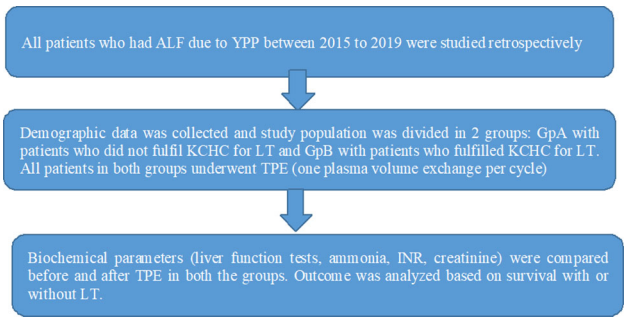
Abstract #1674

Role of therapeutic plasma exchange in acute liver failure due to yellow phosphorus poisoning

Varghese Joy[1], Joshi Vivek[1], Sachan Dipti[2], Malleeswaran Selvakumar[3], Patcha Rajinikanth[4], Nair Harikumar[1], Bollipalli Madhankumar[2], Vij Vivek[4], Venkataraman Jayanthi[5]

[1]Department of Hepatology & Transplant Hepatology, Gleneagles Global Health City, Chennai, India; [2]Department of Transfusion Medicine, Gleneagles Global Health City, Chennai, India; [3]Department of Liver Anesthesia & ICU, Gleneagles Global Health City, Chennai, India; [4]Department of HPB & Transplantation, Gleneagles Global Health City, Chennai, India; [5]Department of Hepatology, Sri Ramachandra Institute for Higher Education & Research, Chennai, India

Introduction: Therapeutic Plasma Exchange(TPE) has been utilized in various liver disorders. There is limited data on efficacy of TPE in patients with acute liver failure (ALF). In Southern India, one of the most common cause of ALF is yellow phosphorus poisoning (YPP).
Objective: To study efficacy of TPE in patients with ALF due to YPP.
Materials and methods: Patients who underwent TPE for ALF due to YPP between 2015 to 2019 in our institute were included in study group. Study population was divided into two groups: Group A (GpA) included patients who fulfilled King's College Hospital Criteria(KCHC) for liver transplantation (LT) and Group B (GpB) with patients who did not fulfil KCHC criteria for LT. TPE was done using OPTIA machine and one plasma volume was exchanged for each cycle. Demographic data was collected. Biochemical parameters (Liver function tests, INR, Ammonia, creatinine) were recorded before and after TPE. Total number of TPE cycles and adverse events during TPE were noted. Outcome was analyzed based on survival with or without LT.
Results: 43 patients underwent TPE for ALF due to YPP. 20 belonged to GpA and 23 belonged to GpB. Both the groups showed significant improvement in biochemical parameters after TPE (Table). Considering survival outcome, all in GpB (100%) survived. In Gp A, 4 underwent LT, 7 survived without LT and remaining 9 died without LT. 7 patients had adverse event such as hypotension and minor allergic reaction which was managed conservatively.
Conclusion: TPE has therapeutic role in patients with ALF due to YPP.



Abstract #1697

Human umbilical cord-derived mesenchymal stem cells alleviate liver fibrosis and acute-on-chronic liver failure in rats

He Yu Lin[1], Meng Zhong Ji[1], Li Rui Ming[1], Wei Zhi Qiang[1], Cheng Bin[1], Liu Guo Hua[1]

[1]Institute of Biomedical Research, Taihe Hospital, Hubei University of Medicine, Shiyan, China

Introduction: Effective treatments for liver fibrosis and acute-on-chronic liver failure (ACLF) are lacking. Human umbilical cord-derived MSCs (hUC-MSCs) have been applied in tissue regeneration and repair, acting through paracrine effect, cell fusion, and actual transdifferentiation.
Objectives: To evaluate the efficacy and safety of hUC-MSCs transplantation in the treatment of liver fibrosis and ACLF.
Methods: Wistar rats were administered with porcine serum (PS) intraperitoneally at a dose of 0.5 mL twice per week for 11 weeks to generate an immune liver fibrosis model. After 11 weeks, rats with immune liver fibrosis were injected intravenously with lipopolysaccharide and D-galactosamine to induce an ACLF model. The rats with liver fibrosis or ACLF were injected intravenously with 2×10^6 hUC-MSCs, 4×10^6 hUC-MSCs, or normal saline (NS) as controls, respectively. Blood and liver tissue samples were taken from all rats for biochemical and histological investigation.
Results: High levels of serum ALT, AST, and total bilirubin (TBIL), prolonged PT, and decreased albumin were displayed in rats with ACLF. Application of hUC-MSCs led to significant decrease in serum TBIL, ALT/AST, PT, while increase in serum albumin. Fibrosis and apoptosis in liver tissues from rats received hUC-MSCs were significantly attenuated. Furthermore, compared with the rats received NS, significant reduction in proinflammatory cytokines (TNF-α, IFN-γ, TGF-β1, IL1β, IL6) and elevated serum levels of hepatocyte growth factor were evidenced in rats received hUC-MSCs.
Conclusion: hUC-MSCs transplantation can improve the liver function and promote the liver repair in rats with ACLF, mediated mostly by paracrine effects leading to inflammation inhibition and hepatocytes regeneration.

Abstract # 2019

Changes and effects of activated protein C in rats with acute liver failure

Lin Shumei, Jia Haijuan, Yang Xueliang, Liu Xiaojing, Chen Yunru, An Xiaocui, Shi Lei, Li Jianzhou, Ye Feng, Zhang Xi

Department of Infection, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, China

Introduction: Liver failure is a serious disease in clinic, which lack of effective treatment. Protein C has anti-inflammatory, anti-apoptotic and protective effect on endothelial barrier.
Objective: To observe the changes of activated protein C in rats with acute liver failure, and to explore its role in the occurrence and development of acute liver failure.
Methods: Fifty-five SD rats were randomly divided into control group, model group and activated protein C intervention group Model of acute liver failure was established with intraperitoneal injection lipopolysaccharide and d-galactose. The intervention group was injected with recombinant human activated protein C 10 min. Serum ALT, AST, activated protein C and TNF-α levels were measured, Pathological changes of liver tissue were observed by HE staining.
Results: Microscopically, rat hepatocytes in both the model group and the intervention group were necrosis, hemorrhage and inflammatory cell infiltration, which aggravating with time. Serum ALT and AST levels in both model group and intervention group were higher than those in control group, and ALT and AST levels in model group were higher than those in intervention group at the same point in time. Activated protein C level decreased rapidly 1 h after modeling and stayed at a low level since then serum TNF-α gradually increased and reached a peak value at 9 h. Serum activated protein C was negatively correlated with TNF-α ($r = -0.5364$, $p < 0.05$).
Conclusion: Activated protein C can reduce hepatocyte damage in rats with acute liver failure and has a protective effect on hepatocytes. The mechanism may be related to the inhibition of TNF-α by activated protein C.

Abstract # 2088

Blood platelet is a vital risk factor to optimize the predictive performance of scorings for short-term mortality in acute-on-chronic liver failure

[1]Zhang Siyu, [1]Nan Yuemin

[1]Department of Traditional and Western Medical Hepatology, The Third Hospital of Hebei Medical University, Shijiazhuang, 050051, China

Introduction: Blood platelet (PLT) has been found associated with the prognostic of patients with acute-on-chronic liver failure (ACLF). However, it's value to optimize the predictive performance of scorings for short-term mortality in patients with ACLF is undefined.
Objective: To evaluate the value of PLT in optimizing the predictive performance of scorings for short-term mortality in patients with ACLF.
Methods: A total of 143 patients with ACLF were enrolled in this study between July 2013 and August 2019. Clinical dates during the golden window period were collected for calculation of model for end-stage liver disease (MELD), MELD-sodium (Na), chronic liver failure consortium-ACLF (CLIF-C ACLF) and Chinese group on the study of severe hepatitis B-ACLF (COSSH-ACLF) scores, respectively.
Results: Among the 143 patients, 72(50.3%) were dead within 28 days, 80 (55.9%) were dead within 90 days. Acute exacerbation of chronic hepatitis B is the predominant cause (n = 100, 69.9%). Cox proportional-hazards (PH) model showed that PLT, age and CLIF-C ACLF were independent risk factors for 28/90 days mortality in ACLF. A novel logistic regression mode (LRM) (0.792 × CLIF − C OFs + 0.025 × Age (years) + 1.512 × ln(WBC) (× 10^9/L) − 0.016 × PLT (× 10^9/L) − 10.260) was fitted with the factors retained in PH model (Hosmer–Lemeshow test: $\chi^2 = 2.372$, p = 0.967).The AUROC values were higher than the other scorings in predicting 28/90-days mortality.
Conclusion: For patients with ACLF in Asian which HBV infection is the predominant cause of underlying chronic liver disease, the predictive value of COSSH-ACLF for short-term mortality is higher than the other scorings. Especially, PLT is a vital risk factor to optimize the predictive performance of scorings for short-term mortality in patients with ACLF.

Table. Independent risk factors of 28-d mortality in patients with ACLF identified by Cox PH

Parameters	B	Wald	Sig.	Exp(B)	95%CI
PLT	-0.009	14.002	0.000	0.991	0.986-0.996
Age	-0.034	7.347	0.007	0.966	0.943-0.991
CLI-C ACLF	0.118	57.094	0.000	1.125	1.091-1.160

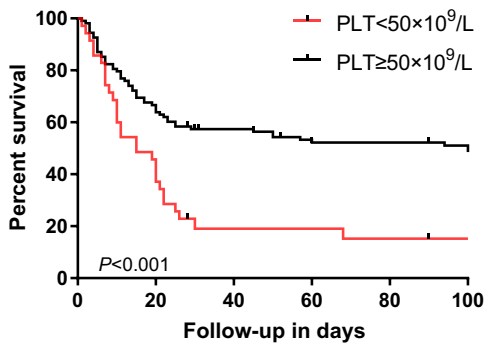


Figure 1. The survival curve stratified on the level of blood PLT.

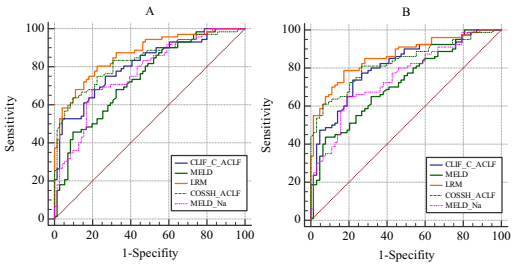


Figure 2. Receiver operating curves (ROC) for the abilities of prognostic models to predict the 28-day(A) and 90-day(B) mortality of patients with ACLF.

Abstract #2184

Differentiation of small hepatocellular carcinomas from small benign nodules in cirrhotic liver on gadoxetic acid-enhanced and diffusion-weighted magnetic resonance images

Byun Jae Ho, Kim So Yeon, Won Hyung Jin, Kim Kyung Won, Shin Young Moon, Kim Pyo Nyun

Department of Radiology, Asan Medical Center, University of Ulsan, Seoul, Republic of Korea

Introduction: Gadoxetic acid enhanced magnetic resonance (MR) imaging offers hepatobiliary phase MR imaging that can provide superior lesion to liver contrast. Diffusion-weighted (DW) MR images offer better results to detect small liver lesions. Then, gadoxetic acid enhanced MR imaging and DW MR imaging can help to differentiate benign lesions from hepatocellular carcinoma (HCC)?
Objectives: To identify imaging characteristics which differentiate small less than 2 cm HCCs from small benign nodules in cirrhotic liver on gadoxetic acid enhanced and DW MR images.
Methods: On gadoxetic acid-enhanced and DW MR images, we analyzed signal intensity of 222 small HCCs and 61 benign nodules (diameter 0.5–2 cm) at each sequence and rim enhancement during portal or equilibrium phases. Univariate and multivariate logistic regression analyses identified predictors of HCC. Combinations of significant MR findings in multivariate analysis were compared with American Association for the Study of Liver Disease (AASLD) practice guidelines.
Results: In multivariate analysis, arterial enhancement (adjusted odds ratio (aOR) = 8.6), T2 hyperintensity (aOR 5.8), and hyperintensity on DW images (aOR 3.8) were significant for differentiating small HCCs from benign nodules. When two or all three findings were applied as diagnostic criteria for differentiating small HCCs from benign nodules, sensitivity and accuracy were significantly higher compared with AASLD practice guidelines (91% vs. 78% and 89% vs. 81%, respectively; each $p < 0.0001$).
Conclusions: On gadoxetic acid-enhanced MR imaging, arterial enhancement and hyperintensity on T2-weighted and DW MR images are helpful for differentiating small HCCs from benign nodules in liver cirrhosis.

Poster Presentations

Abstract # 41

Enhanced ASPP2 promotes liver injury by way of an inflammatory immune regulatory mechanism in acute liver failure

Feng Ren, Xiangying Zhang, Ling Xu, Yuan Tian, Dexi Chen*, Zhongping Duan *

Background and aims: Acute liver failure (ALF), an inflammation-mediated hepatocellular injury process, is a clinical syndrome that results from hepatocellular apoptosis and hemorrhagic necrosis. The apoptosis stimulating protein of p53-2 (ASPP2), a haploinsufficient tumor suppressor, is a pro-apoptotic member of the p53 binding protein family. However, the role of ASPP2 in the pathogenesis of ALF and its regulatory mechanisms remain unclear.

Method: The expression of ASPP2 were analysed using the liver biopsy samples from HBV-related hepatocarcinoma (HCC) patients and ALF patients. ASPP2$^{+/-}$ and ASPP2$^{+/+}$ Balb/c mice were used to examine the effects of ASPP2 on liver injury induced by D-galactosamine(D-GalN)/ lipopolysaccharide (LPS) in vivo. The inflammatory immune mechanism of ASPP2 were also explored in bone marrow-derived macrophages (BMDM) in vitro.

Results: The expression of ASPP2 was significantly upregulated in liver tissue of ALF patients with HBV infection and ALF mice induced by D-GalN/LPS, and significantly down-regulated in HCC patients. Compared with wildtype mice, the ablation of ASPP2 (ASPP2$^{+/-}$) significantly ameliorated the hepatocellular damage, evidenced by reduced serum alanine aminotransferase (sALT and sAST) levels, well-preserved liver architecture compared with controls. The liver protective effect of ASPP2$^{+/-}$ was dependent on an inflammatory immune regulatory mechanism, because ASPP2 is required to regulate liver inflammation by selectively depressing tumor necrosis factor-α (TNF-α) and promoting interleukin-6 (IL-6) in vivo and in vitro, moreover, the luciferase assay results showed that overexpression of ASPP2 could bind to the promoter sequence of TNF-α and IL-6. The molecular mechanistic investigations elucidated that the enhanced ASPP2 promoted liver injury by regulating PPARα-autophagy pathway, because inhibition of PPARα by siRNA abrogated liver protection and decreased autophagy again induced by ASPP2$^{+/-}$.

Conclusion: Our novel findings document the key inflammatory immune regulatory function of ASPP2 in the pathophysiology of ALF, and provide a rationale to target ASPP2 as a refined therapeutic strategy to ameliorate acute liver injury.

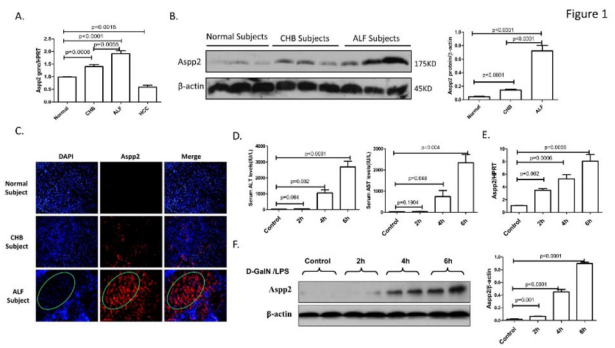


Figure 1 Increased expression of Aspp2 in the liver of ALF

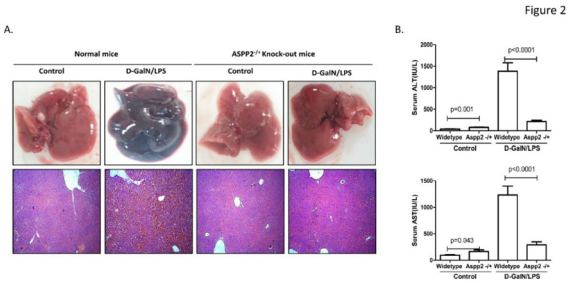


Figure 2 Aspp2 knockdown protects mice from D-GalN/LPS -induced liver injury

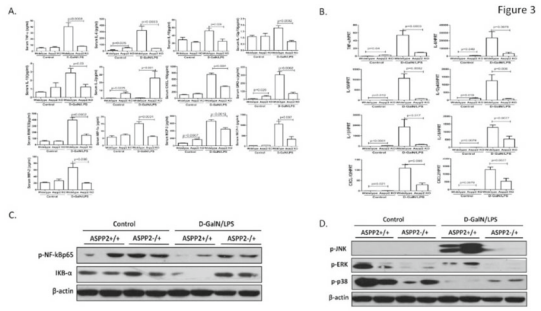


Figure 3 Aspp2 knockdown protects mice from D-GalN/LPS -induced liver injury by suppressing liver inflammation

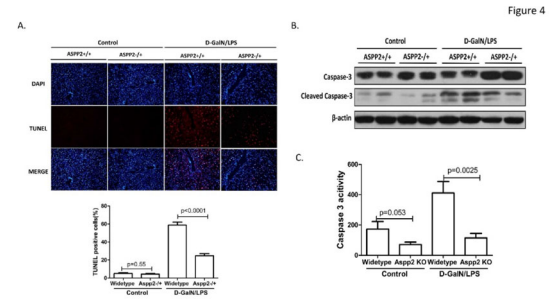


Figure 4 Aspp2 knockdown inhibits hepatocyte apoptosis to protects mice from D-GalN/LPS -induced liver injury

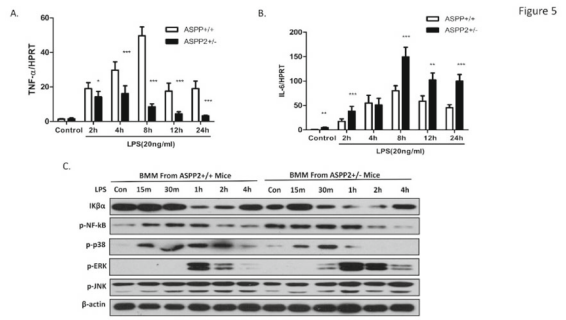


Figure 5 Aspp2 selectively regulates TNF-α and IL-6 expression in macrophage induced by LPS

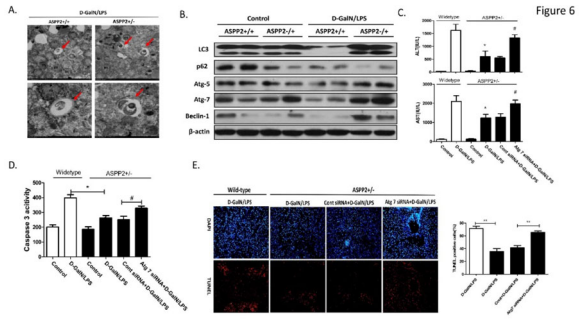


Figure 6 Aspp2 knockdown protects mice from D-GalN/LPS -induced liver injury by promoting autophagy

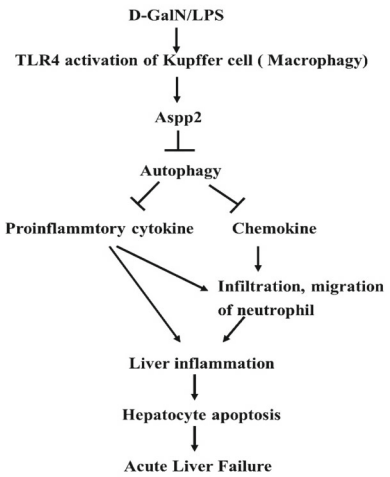


Figure7 A proposed model for the Aspp2-autophagy pathway in acute liver failure

Abstract #158

Unusual complication of hepatitis A

Thendiono Eduward[1]

[1]Internal Medicine department, Siloam Hospital Buton, Bau-Bau, Indonesia

Introduction: Most cases of Hepatitis A virus (HAV) infection is mild and self-limiting disease, nonetheless HAV is potential to have a fulminant course.
Objective: To notify the unusual complication of HAV.
Methods/case description: We report a case of 29-year-old female with a history of one week low grade fever, abdominal discomfort, nausea, vomiting and jaundice. Past medical history was unremarkable. No history of hepatitis vaccination. Physical examination showed tachycardia, icteric sclera, and hepatomegaly. Abnormal laboratory work up showed markedly elevated transaminases (hepatocellular pattern), direct hyperbilirubinemia, and positive anti-HAV IgM. Abdominal ultrasonography suggests acute hepatitis. She was treated as acute Hepatitis A. Hepatoprotector agent (ursodeoxycholic acid, curcuma extract), acetaminophen with acetylcysteine as needed only, and aminofluid® were administered. Two days later, noticed encephalopathy, hypoglycemia episodes, worsening of transaminases and hyperbilirubinemia, thrombocytopenia and coagulopathy which suggests acute liver failure (ALF). Her condition continued to deteriorate despite intensive treatment and inevitably, deceased three days later.
Discussion/results: HAV infection rarely has a fulminant course. The current goal of treatment is to achieve overall metabolic and hemodynamic stability. We applied the same management. However, it failed to deliver. The outcome of HAV infection is mostly determined by the complications. In our case, no vaccination and acute liver failure most probably responsible for poor outcome. Despite of current therapeutic options, liver transplantation is the only therapy proven to improve patient survival in ALF. Unfortunately, this option is not available in our setting.
Conclusion: Although rare, clinicians should be aware of ALF's possibility in acute HAV.

Abstract #191

Progress in HBV related liver failure treatment in China: a large, multicenter, retrospective cohort study

Xiaoxin Wu

Background and aims HBV related liver failure is a complicated syndrome with a high short-term mortality rate. We collected clinical data from a representative sample of the China population from a number of centers, to explore how treatment of HBV related liver failure in the past decade has developed.
Methods Cohort I data were from 2007 to 2011 and cohort II data were from 2012 to 2016. Patients with HBV related liver failure were enrolled retrospectively. Patients of both cohorts were assigned to standard medical therapy (SMT) group (cohort I-SMT; cohort II-SMT) and artificial liver support system (ALS) group (cohort I-ALS; cohort II-ALS). Propensity score matching analysis was used to eliminate the baseline differences between these groups. The short-term (28/56 days) survival rates were compared between the two cohorts.
Results The short-term (28/56 days) survival rate was higher in ALS group than SMT group (60.0% vs 54.8%; 47.5% vs 42.8%, $p < 0.05$, respectively). The short-term (28/56 days) survival rates were higher in cohort II than cohort I (63.2% vs 54.4%; 51.1% vs 41.2%, $p < 0.001$, respectively). After propensity score matching, the short-term (28/56 days) survival rates were higher in cohort II than cohort I for both SMT treatment (60.7% vs 53%; 50% vs 39.8%, $p < 0.05$) and ALS treatment (66.1% vs 56.5%; 53% vs 44.4%, $p < 0.05$). The

short-term (28/56 days) survival rate was higher treated with nucleos(t)ide analogues than without nucleos(t)ide analogues.
Conclusions By analyzing nationwide data from China, we found that treatment for HBV related liver failure has progress in the past decade and that antiviral and ALS treatment can significantly reduce mortality.

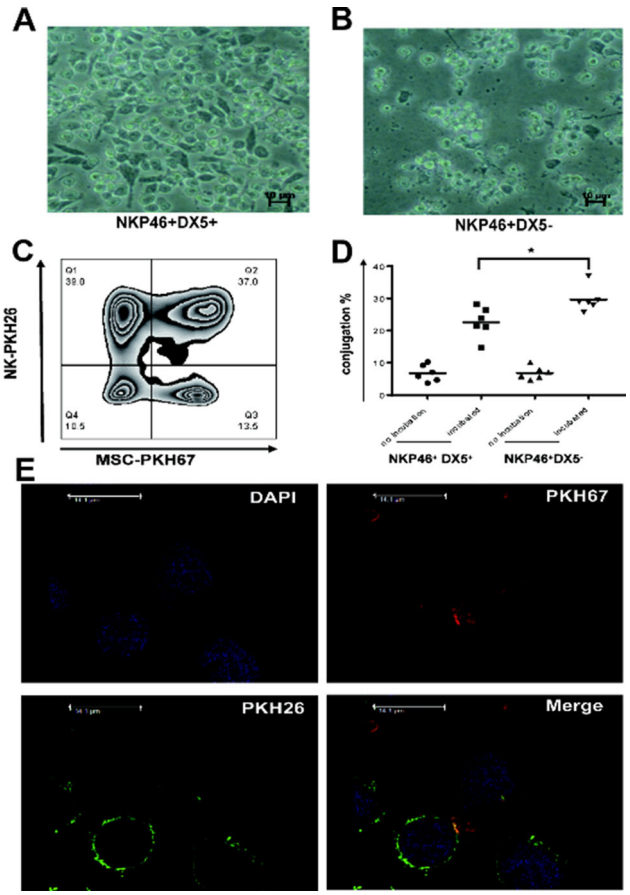
Abstract #552

The crosstalk between mesenchymal stem cells and nature killer cells in rescuing acute-on-chronic liver failure murine

Xiong jing[1,2], Weng weizhen[1,4], Lin dengna[1,2], Xiong shiqiu[3],Gao zhiliang[1,2],Chen junfeng[1],Zhang shaoquan[1],Caohuijuan[1],Gao juan[1,2],Lin bingliang[1,2]

[1]Department of infectious diseases, the third affiliated hospital of Sun Yet-Sen university, Guangzhou, China. [2]GuangDong provincial key laboratory of liver diseases, the third affiliated hospital of Sun Yat-sen university, Guangzhou, China. [3]Cell Biology group, National Measurement Lab, LGC, Cambridgeshire, UK. [4]Department of infectious diseases, the seventh Affiliated Hospital of Sun Yat-sen University, Shenzhen, China

Introduction: Acute-on-chronic liver failure (ACLF) is a severe, life-threatening syndrome with high mortality. Transplantation of Mesenchymal Stem Cells (MSCs) have been shown their efficacy in reducing mortality of ACLF patients in our clinical trials, but the mechanism is not clear.
Objectives: Unveiling the underlying mechanism of action will improve clinical regime of ACLF.
Method: Flow cytometry was applied to characterize natural killer cell (NK) from HBV-ACLF patients and ACLF mouse, and MSC developed in vitro.
An acute-on-chronic liver failure mouse model was established by injection of carbon tetrachloride (CCL4) intraperitoneally. Confocal microscopy was used to investigate cell-cell contact. Hematoxylin and eosin stained specimens and Bromodeoxyuridine incorporated liver tissues were investigated under microscopes. Western blot was used for hepatocellular death assay.
Results: Frequency of peripheral blood NK cells and frequency of NKG2A and KIR3DL1 on NK cells from HBV-ACLF patients were upregulated by MSCs infusion. Frequency of NKG2D, perforin and FasL were suppressed, which correlated with the recovery of liver function. MSCs infusion improved survival rate of ACLF mice efficiently (Log-rank $X^2 = 3.88$, $P < 0.05$), coinciding with hepatitis remission, liver regeneration and NK frequency increase both in blood and liver. Meanwhile, MSCs were proved to promote the proliferation and GM-CSF secretion of $NKP46^+$ $DX5^-$ liver NK cells specifically, which may be owing to their higher cell-cell (MSC-$NKP46^+$ $DX5^-$ liver NK cells) adhesion.
Conclusion: MSCs can rescue the ACLF patient and mouse by regulating NK cell. Promoting $NKP46^+DX5^-$ liver NK cells proliferation and secreting GM-CSF maybe the new machinery of MSCs' efficacy in ACLF.



MSCs conjugated with $NKP46^+DX5^-$ liver NK cells preferentially in vitro. Sorting purified $NKP46^+DX5^+$ (A) and $NKP46^+DX5^-$ (B) liver NK cells from ACLF mice co-cultured with pre-coated MSCs in vitro under 100U/ml IL-2 for 48 hours, One typical result showed from 3 experiments with similar results. (C) Sorting purified $NKP46^+$ $DX5^{+/-}$ liver leukocytes cells from ACLF mice were stained with PKH26, co-cultured with/without PKH67 stained MSCs cell. Representative FACS plot to show NK cells conjugated with MSCs in vitro (PKH26/PKH76 double positive means conjugated cells); (D) conjugation % was assessed via double positive cells, * indicate $P < 0.05$. (E) ell sorter purified $NKP46^+DX5^+$ and $NKP46^+DX5^-$ liver NK cells from ACLF mice were stained by PKH26, added into chamber slides pre-coated with MSCs cells in PKH67, observed by confocal microscope. Above image was from $NKP46^+DX5^-$ liver NK cells. NKP46+DX5+ which showed no immune synapse with MSCs. Data didn't show for clarification.

Abstract #568

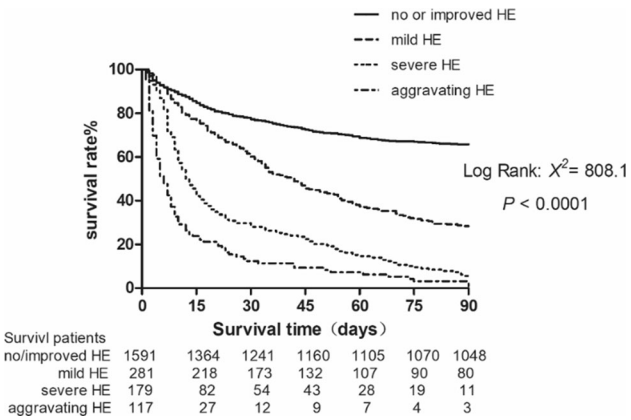
Advanced hepatic encephalopathy is an important determination of mortality in patients with hepatitis B virus related acute-on-chronic liver failure

Weng WeiZhen[1,2], Chen JunFeng[2], Peng XiaoHua[1], Zhang Jing[2], Lin BingLiang[2]

[1]Department of infectious diseases, the seventh Affiliated Hospital of Sun Yat-sen University, Shenzhen, China, [2]Department of infectious

diseases, the third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Introduction: Hepatitis B virus related Acute-on-chronic liver failure (HBV-ACLF) is a life-threatening disease with various complications, among which hepatic encephalopathy (HE) is common. During disease process, whether HE effects the outcome of patients is unclear.
Objectives: To investigate the impact of advanced HE for 90-day mortality in patients with HBV-ACLF.
Methods: In this retrospective study, we identified cases of HBV-ACLF hospitalized from January 2001 to March 2018. Patients' demographics, laboratory results and complications including HE were collected. We defined the new-onset HE and aggravating HE from mild (grade 1-2 HE) to severe (grade 3-4 HE) as advanced HE. Survival was estimated by the Kaplan-Meier method. The Cox regression analysis was used to investigate the effect of advanced HE on the risk of mortality.
Results: A total of 2166 patients were enrolled. Admission HE was observed in 421 (19.44%) patients, among whom mild HE accounted for 84.56% (356/421). During hospitalization, 576 (33.01%) patients occurred advanced HE. In these patients, 281 (48.79%) were new-onset mild HE, 178 (30.90%) were new-onset severe HE, 117 (6.71%) were aggravating HE. The mortality of patients with AHE was 83.85% (483/576), compared with patients without AHE (34.15%, 543/1590). Hazard ratios for AHE were 3.95 (95% CI 3.49–4.47). Furthermore, HRs was 2.61 (95% CI 2.22–3.07) for mild HE, 5.35 (95% CI 4.49–6.38) for severe HE and 9.61 (95% CI 7.80–11.83) for aggravating HE.
Conclusion: As ACLF proceeds, HE may occur or aggravate. Advanced HE increases the risk of 90-day mortality in patients with HBV-ACLF.



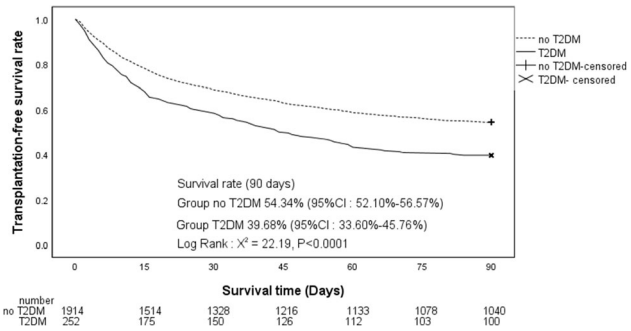
Abstract #569

Type 2 diabetes mellitus heightens the risk of 90-day mortality in patients with hepatitis B virus related acute-on-chronic liver failure

Weng WeiZhen[1,2], Chen JunFeng[2], Peng XiaoHua[1], Xiong Jing[2], Lin BingLiang[2]

[1]Department of infectious diseases, the seventh Affiliated Hospital of Sun Yat-sen University, Shenzhen, China, [2]Department of infectious diseases, the third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Introduction: Hepatitis B virus related Acute-on-chronic liver failure (HBV-ACLF) is a life-threatening disease with high mortality. Some comorbidities effect the prognosis of this disease, whether Type 2 diabetes mellitus (T2DM) for HBV-ACLF is unclear.
Objectives: We aim to investigate the impact of T2DM for 90-day mortality in patients with HBV-related ACLF.
Methods: In this retrospective study, we enrolled hospitalized HBV-ACLF patients from January 2001 to March 2018. Patients' demographics, medical history, treatment, laboratory results including blood sugar, insulin, C-peptide, glycosylated hemoglobin, liver function and comorbidities were collected. Survival was estimated by the Kaplan–Meier method, and evaluated with a stratified log-rank test. The Cox proportional hazard regression analysis was used to investigate the effect of diabetes on the risk of mortality. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated.
Results: A total of 2166 hospitalized ACLF patients were enrolled. 682 (31.49%) patients had at least one comorbidity. 91 (4.2%) patients had two comorbidities while 15 (0.69%) patients had three comorbidities. The most frequent comorbidity was Type 2 diabetes mellitus (252, 11.49%), followed by alcoholic liver disease (191, 8.82%). Type 1 diabetes mellitus was not found. The 90-day mortality in our study group was 47.37% (1026/2166). The mortality of patients with T2DM was 60.32% (152/252), which was higher than patients without T2DM (45.66%, 874/1914, p = 0.00). Univariate hazard ratios for diabetes were 1.51 (95% CI 1.27–1.80, p = 0.00).
Conclusion: T2DM is common in patients with HBV-ACLF. Patients with diabetes increase the risk of 90-day mortality.



Abstract #661

Early terlipressin and albumin treatments improve the outcome of patients with hepatorenal syndrome-acute kidney injury in chronic hepatitis B-related acute-on-chronic liver failure

Chen Guang[1], Chen Tao[1], Guo Wei[1], Wan Xiaoyang[2], Huang Jiaquan[1], Song Jianxin[1], Huang Yuancheng[1], Yang Daofeng[1], Han Meifang[1], Qi Junying[1], Xing Mingyou[1], Wu Liang[1], Qi Junying[1], Ning qin[1,2]

[1]Department of Infectious Diseases, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, Hubei Province, China, [2]Institute of Infectious Disease, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, Hubei Province, China

Background: The mortality in patients with hepatorenal syndrome-acute kidney injury (HRS-AKI) in chronic hepatitis B-related acute-on-chronic liver failure (ACLF) is very high. In previous studies, terlipressin and albumin therapy improved HRS reversal rates, but did not improve survival.
Objectives: To assess the efficiency of the terlipressin and albumin treatment in patients with HRS-AKI in chronic hepatitis B-related ACLF and its impact on the 90-day liver transplantation-free (LTF) survival rate in these patients.
Methods: A retrospective cohort analysis of patients with HRS-AKI in chronic hepatitis B-related ACLF was performed. Baseline clinical

features, HRS reversal rate, and 90-day LTF survival rates were compared in patients treated with or without terlipressin.
Results: A total of 190 patients with HRS-AKI in HBV-ACLF were enrolled in this retrospective study. Of these patients, 132 received terlipressin and albumin treatment, while other patients received standard internal medication (control). The characteristics of the terlipressin and control groups at the initiation of treatment of HRS-AKI were comparable. The HRS reversal rate was higher in the terlipressin group in patients with HRS-AKI stage 1 compared to that in the control group (72.2% vs. 40.0%, $P = 0.037$) and a similar pattern was observed for the 90-day LTF survival rate (27.8% vs. 12.0%, $P = 0.013$). There were no significant differences between the two groups in the overall patients at HRS-AKI stage 2 and 3 for either HRS reversal rate or 90-day LTF survival rates.
Conclusion: Terlipressin and albumin treatment in the early stage of AKI may improve the reversal rate for renal function and survival.

Abstract #665

Mesenchymal stromal cell derived Extract Vesicles promote hepatocyte proliferation in Acute liver failure

Zhang Jing, Gao Juan, Lin Bingliang

Department of Infectious Diseases, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Introduction and objectives: Acute liver failure (ALF) is a severe, life-threatening syndrome with high mortality due to a shortage of effective agency. How to promote hepatocyte regeneration is the key to rescue ALF. Previous studies have confirmed that mesenchymal stem cells (MSCs) derived extract vesicles (EVs) can regulate the proliferation of endogenous cells, but whether it can promote the proliferation of hepatocytes in acute liver failure is unclear.
Methods: To establish the ALF cell model of L02 cell line induced by H_2O_2 and ALF mouse model induced by GalN/LPS, collect and identify MSC-EVs, and co-culture with ALF cells, then detected the proliferation of hepatocytes in ALF cell model by fluorescent label, meanwhile, detected the hepatocytes activity by CCK8. Injected MSC-EVs into ALF mouse by tail vein to evaluate the effect on ALF mouse. To test the molecules and genes of proliferation related pathway by Western Blotting and qPCR.
Results: The MSC-EVs were fused with ALF cell model, and the activity of hepatocytes in ALF cell model was increased. In vivo tracing showed that MSC-EVs were aggregated in liver of ALF mouse. The levels of ALT, AST and TB reduced, and 24-h mortality of MSC-EVs infusion mouse was lower than that in the control group, and the liver inflammatory infiltration, hyperemia decreased, meanwhile, hepatocyte proliferation increased. MSC-EVs could upregulate pAkt and pSer9-GSK3 β, CCND1 and Bcl-2 expression increased, and p53, Bax and cMyc expression decreased.
Conclusion: MSC-EVs can improve the prognosis of ALF by promoting hepatocyte proliferation in vitro and in vivo.

Abstract # 697

Hepatoprotective mechanism of *Aristolochia indica* and *Polygonum bistorta* against liver failure

Deepak Kumar Mittal, Sunita Baroda

Sri Satya Sai University of Technology & Medical Sciences, Bhopal Indore Highway, Pachama, Sehore (M.P.) 466001

The present study was carried out to observe the hepatoprotective effect and antioxidant activity of the aqueous extract of the roots of *Polygonum Bistorta* (PB) (100 mg/kg) and *Aristolochia Indica* (AI) (100 mg/kg) in rats treated with sub chronic exposure of carbon tetrachloride (0.15 ml/kg, *i.p.*). Extract of PB and AI at the tested doses restored the levels liver and kidney function tests with liver homogenate enzymes (glutathione peroxidase, glutathione-*S*-transferase, superoxide dismutase and catalase enzymes significantly. The activities of DNA damage by comet assay and MTT assay significantly recovered the damage towards normal. This study suggests that *Aristolochia Indica* has a more liver protective effect in comparison of *Polygonum bistorta* and against carbon tetrachloride-induced hepatotoxicity and posses antioxidant activities and extracts exhibited moderate anticancer activity towards cell viability at higher concentration.

Abstract #706

Fulminant hepatic failure etiology, clinical manifestations, and outcome: an experience of tertiary care hospital of Karachi, Pakistan

Butt N[1], Khemani H[1], Rai L[1], Soomro SA[1], Channa RH[1], Abbasi A[2]

[1]Gastroenterology Department, Jinnah Postgraduate Medical Centre, Karachi, Pakistan. [2]Medical Unit II, Dow University of Health Sciences, Ojha Campus, Karachi, Pakistan

Introduction: Fulminant hepatic failure (FHF), a term given to the acute liver injury causing sudden deterioration of hepatic function and encephalopathy within eight weeks of appearance of first symptom in a patient having no prior liver disease. It may be caused by toxins, drugs, viruses, or metabolic diseases, with viral hepatitis being the cause in 40–60% cases. In Pakistan, all types of hepatitis viruses are endemic, raising the prevalence up to 70–80%.
Methods: A cross-sectional study was conducted at the Department of Gastroenterology, Jinnah Postgraduate Medical Centre, Karachi, Pakistan from January 2018 till to date. All patients of both gender $\geq$ 16 years were recruited and investigated for acute viral serology, complete blood count, liver function tests, renal function tests, serum creatinine, MELD score parameters and King's college criteria (KCC) parameters.
Results: Total 40 patients were enrolled, out of which 25 (63%) were males and 15 (37%) were females with a mean age of 26.03 ± 9.95 years. Hepatitis E was found to be the most common cause of FHF 21 (51%). Thirty five (88%) of patients died and five patients recovered and were discharged symptom free. Variables i.e. presence of viral hepatitis E, serum creatinine > 2.5 mg/dl, and sepsis were found to have significant association with mortality on linear correlation. Only serum creatinine more than 2.5 mg/dl and development of sepsis were found to predict the outcome after multivariate analysis. The KCC criteria cut off point was reached in a total of 23 patients (out of 40) of which 35 patients died.
Conclusions: The mortality rate of FHF is very high which can be reduced to some extent in a non-liver transplant areas by controlling the risk factors associated with poor outcome.

Abstract # 719

Plasma perfusion combined with plasma exchange improved survival in chronic hepatitis B related acute-on-chronic liver failure patients

Zhongyuan Yang[1], Zhongwei Zhang[1], Qiuyu Cheng[1], Guang Chen[1], Weina Li[1], Ke Ma[1], Wei Guo[1], Tao Chen[1], Qin Ning[1]

[1]Department and Institute of Infectious Disease, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, Hubei Province, China

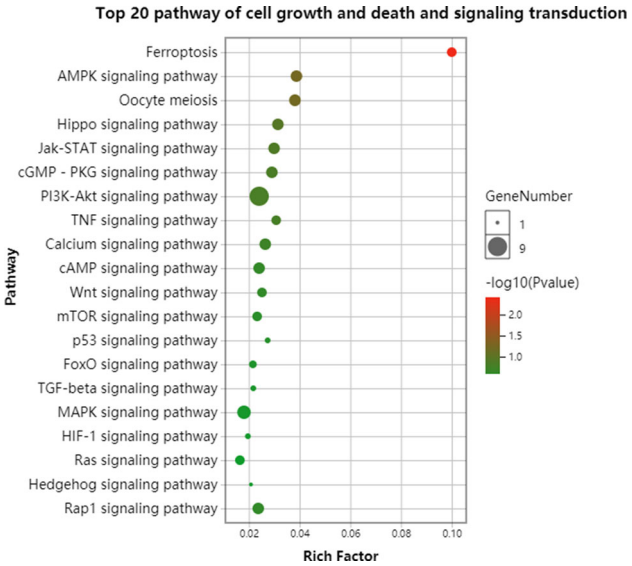
Aims: This study aimed to delineate the indicators for ALSS and evaluate the effectiveness of plasma perfusion combined with plasma exchange (PP + PE) in patients with hepatitis B virus-related ACLF (HBV-ACLF).
Methods: A total of 898 patients with HBV-ACLF in a single center were enrolled retrospectively. Propensity score matching (PSM) was used in case-paired analysis. Hepatic or extra-hepatic organ failures were defined by Chronic Liver Failure-Sequential Organ Failure Assessment (CLIF-SOFA) criteria. Complications included ascites, infection, hepatopulmonary syndrome, hepatorenal syndrome, hepatic encephalopathy and upper gastrointestinal bleeding. Numbers of organ failures or complications were used for risk stratification.
Results: Among all patients, 418 patients received standard medical therapy (SMT) and 480 received PP + PE plus SMT. After one-to-one paired PSM, 293 pairs were enrolled. The PP + PE group showed a significantly lower 28-day transplant-free mortality (TFM) than the SMT group. Furthermore, the PP + PE group displayed a significantly higher cumulative survival rate (CSR) in both 28- and 90-day observation durations. When stratified, patients with two or more organ failures or complications from the PP + PE group showed all observed benefits including significantly lower 28- and 90-day TFM and higher CSR. Moreover, PP + PE treatment significantly increased the resolution of organ failures and complications and ameliorated the development of new organ failures and complications.
Conclusions: PP + PE treatment significantly reversed organ failures and ameliorated the development of new organ failures and complications, thus improving the survival of patients with HBV-ACLF, with superior benefits in patients with two or more organ failures or complications.

Abstract #761

Bone marrow mesenchymal stem cells affect acute on chronic liver failure through hepatocellular exosomes miRNAs

Jing Zhang

Background: Acute on chronic liver failure (ACLF) is a severe hepatopathy syndrome. Human bone marrow mesenchymal stem cells (BMSCs) have been reported to improve the prognosis of ACLF, but the mechanism remains unclear. To explore the role of BMSCs on hepatocyte-to-hepatocyte communication, we used next-generation sequencing (NGS) and bioinformatics to analyze exosomes miRNAs in the hepatocyte microenvironment to identify key genes and signaling pathways that can affect hepatocyte survival.
Methods: This study included normal group, ACLF group and BMSCs treatment group. Primary hepatocytes were isolated from normal or ACLF mice and cultured in vitro. Human BMSCs were co-cultured with ACLF primary hepatocytes. Exosomes were isolated from supernatant and miRNAs sequencing database was established. The target genes were analyzed by GO and KEGG enrichment analysis.
Results: Human BMSCs could reverse the changes of miRNA abundance. In the ACLF group, 44 miRNAs were downregulated, and 88 miRNAs were upregulated. 79 genes were up-regulated and 153 genes were down-regulated. GO enriched 39 differentially expressed genes related to cell proliferation. CXCL5, SOX4, IGF1, Wnt and other genes maybe targets to promote the growth of liver cells. KEGG enrichment annotates pathways associated with cell growth and death. The ferroptosis pathway could be regulated by BMSCs in ACLF hepatocytes.
Conclusion: Human BMSCs can regulate the exosomal miRNAs of hepatocytes in ACLF, which may affect the prognosis of patients. The further study need done to confirm these results and developing new therapeutics methods for ACLF.



Abstract # 1195

Recovery dynamics of intestinal microbiota in CCl_4-treated mice with and without mesenchymal stem cell transplantation

Yanping Xu[1,2†], Hua Zha[1,2†], Qiaoling Pan[1,2†], Jiong Yu[1,2†], Hongcui Cao[†1,2,3*], Lanjuan Li[1,2,3]

[1]State Key Laboratory for the Diagnosis and Treatment of Infectious Diseases, the First Affiliated Hospital, College of Medicine, Zhejiang University, 79 Qingchun Rd., Hangzhou City 310003, China, [2]National Clinical Research Center for Infectious Diseases, 79 Qingchun Rd., Hangzhou City 310003, China, [3]Collaborative Innovation Center for the Diagnosis and Treatment of Infectious Diseases, 79 Qingchun Rd., Hangzhou City 310003, China

Liver injury has caused significant illness in humans worldwide. The dynamics of gut microbiota associated with natural recovery and therapy for CCl_4-treated liver injury remain poorly understood. This study was designed to determine the recovery dynamics of gut microbiota in CCl_4-treated mice with and without mesenchymal stem cells transplantation at 48 h, 1 week (w) and 2 w. MSCs significantly improved the histopathology, survival rate and intestinal structural integrity. The most significant difference of gut microbiota between MSC and CCl_4 was at 48 h, and a range of OTUs associated with health and liver injury for this study were defined at this stage. The gut bacterial communities were determined with significant changes in MSC groups over time, so were for CCl_4 groups. The liver injury dysbiosis ratio (i.e., the abundance ratio of healthy OTUs and diseased OTUs), experienced a decrease in MSC groups and a rise in CCl_4 groups over time, implying the recovery mechanisms of the two

groups were different. A range of OTUs (most assigned to *Clostridiales*, S24-7, *Oscillospira* and *Lachnospiraceae*) and functional categories (e.g., Glycogen phosphorylase, heterodisulfide reductase subunit A and hexosaminidase) were determined differentiating the gut microbiota in MSC groups over time, and the situation was similar for CCl_4 groups over time. The study provided evidence that a range of OTUs and functional categories changed during the recovery dynamics of MSC or CCl_4 groups, which could assist the diagnosis of the status of gut microbiota in the CCl_4-treated cohorts with and without MSCs transplantation.

Abstract #1233

Clinical characteristic of acute on chronic liver failure and acute decompensation of cirrhosis patients in tertiary referal hospital

Kemal F. Kalista

Background: Two disease entities, acute on chronic liver failure (ACLF) and acute decompensation of cirrhosis (ADC) looks similar, hard to differentiate and very often misunderstood. Aim of this study was performed to compare the clinical characteristics of ACLF and ADC patients.
Method: Data of 31 ACLF patient based on APASL and 97 ADC patient who were hospitalized in Cipto Mangunkusumo General Hospital Indonesia were collected.
Result: Most common etiology of CLD in ACLF was HBV (67.7%) and in ADC was Non B&C (35.1%). Most ACLF patients comes with jaundice (35.4%) and ADC patients comes with GI bleeding (40.2%). HBV reactivation and bacterial infection was most common precipitating event in ACLF. ACLF patients admitted with poorer liver function, indicated with higher Child Pugh, MELD score and longer length of stay. Around 80.5% patient in ACLF group comes with APASL-AARC score II & III. Kidney injury, coagulopathy and encephalopathy were more frequently found in ACLF than ADC. GCSF and plasmapheresis were also given to the ACLF group despite antiviral and standard medical therapy (SMT). Mortality rate in ACLF vs ACD was 64.5% vs 44.3% in 28 days and 70.9% vs 47.4% in 90 days. No liver transplantation was done to these patient because of limitation of donor resources.
Conclusion: ACLF patients has poorer condition and liver function lead to higher mortality than ADC patient. Mortality in ACLF group is still high despite of SMT, antiviral, GCSF and plasmapheresis. Wider donour resources should be done to increases the chance of liver transplantation.

Abstract # 1243

Impact of acute insults on the outcomes of 76 patients with acute-on-chronic liver failure 2018–2019

Hasmik Ghazinyan[1], Mher Davidyants[1], Lyudmila Niazyan[1], Lusine Navoyan[2], Ruzanna Safaryan[2], Tatevik Shahinyan[3]

[1]Department of Hepatology, Nork Clinical Infection Hospital, [2]Yerevan State Medical University, [3]"Ecosense" Diagnostic Laboratory

Background: Acute-on-chronic liver failure (ACLF) is clinical syndrome manifesting as acute and severe hepatic derangements with high mortality. The outcome of hepatic decompensation would vary depending on the nature of intervention.
Aims: etiological spectrum of acute insults and outcomes with different acute insults in ACLF patients.
Methods: 76 patients (27 retrospectively and 49 prospectively) fulfilling the criteria of ACLF based on the APASL 2014 consensus recommendations were screened. Investigations included biochemical, serological, virological, instrumental parameters.
Results: Mean age was 46 ± 9 years with a predominance of males (n = 54 [71%]). The predominant acute insult was active alcohol consumption [29 (38.2%)], followed by hepatitis-B-virus (HBV) [17(22.4%)], drug-induced-liver-injury (DILI) [15(19.7%)], autoimmune-hepatitis (AIH) flare [5 (6.6%)], hepatitis A, E and D viruses [2 (2.6%)], respectively and unknown [4 (5.3%)]. Patients with 1 and ≥ 2 organ failures were 17% (13) and 83% (63) respectively. Baseline mean laboratory values: ALT 710.9 ± 1127/17–6612/U/L, WBC 10.4 ± 5.2 /3.54–20/ × 10^3 cells/mm^3, Platelets 156.2 ± 99.1/ 19–462/ × 10^3 cells/mm^3, Serum sodium 134.7 ± 9.4/100–146/ mmol/l, INR 2.1 ± 0.6/1–3/, serum albumin 3.2 ± 0.7/2–5/g/dL, Serum creatinine 2.1 ± 2.4/1–8/mg/dL, MELD 22.1 ± 5/16–34/.
The overall mortality rate was 32.9% (25 patients). The most frequent cause of death were hepatorenal syndrome and hepatic encephalopathy. The mortality in the AIH-ACLF group was the highest [3 (60%)], followed by HBV-ACLF [9 (53%)], DILI-ACLF [5 (33%)], alcohol-ACLF [8 (28%)].
Conclusions: The study demonstrates that active alcohol consumption was and remains the most common cause of acute insult. AIH-ACLF and HBV-reactivation characterized by the highest mortality.

Abstract #1250

Medical treatment for acute liver failure: the efficacy of artificial liver support system

Yusuke Iwata, Hideo Yoshida, Chihiro Shiomi, Hiroyoshi Taniguchi, Syuichi Tange, Koshiro Fukuda, Rintaro Fukuda, Hiroki Ohyama, Hirobumi Suzuki, Shinzo Yamamoto, Yukiko Ito, Ryo Nakata

Department of Gastroenterology, Japanese Red Cross Medical Center, Japan

Introduction: Acute liver failure (ALF) has poor prognosis (the survival rate is around 40%). Indeed, those who do not meet the liver transplant criteria represent high mortality rate. Cooperating with nephrologists, the use of artificial liver support system (ALS) shows benefits among patients with ALF. In our center, plasma exchange (PE) and continuous or online hemodiafiltration (CHDF or OHDF) are performed.
Methods: We retrospectively reviewed 21 cases of ALF, those who were at least once admitted to our center from August 2008 to September 2019, and estimated the efficacy of ALS on their prognosis.
Results: The median age was 43 years old (range 25–78), 13 were male and 8 were female. Nine males and 5 females presented hepatic coma. The backgrounds of ALF consist of 6 alcoholic, 6 viral, 4 drug-induced hepatitis, and 5 others (2 circulatory failure, 1 Wilson disease, 1 HELLP syndrome, and 1 autoimmune hepatitis). Average MELD score was 27.4 in ALF with coma, and 19.1 in ALF without coma. Twelve cases with coma underwent ALS; 6 survived, 3 needed liver transplantation, 3 died (because of infection, gastrointestinal bleeding, and multiple organ failure). Three cases without coma, which presented a tendency of worsening, underwent ALS, and all of them survived. As a result, 60% of those who underwent ALS survived without liver transplantation.
Conclusions: ALS showed relatively good survival rate for ALF patients. However, some cases show less improvement after ALS, and if they do not match the liver transplant criteria, their prognosis is still poor.

Abstract #1300

Acute liver failure caused by mushroom poisoning

Winda A. M. Saragih[1], Muhammad Begawan Bestari[2], Eka Surya Nugraha[2], Nenny Agustanti[2], Dolvy Girawan[2], Yudi Wahyudi[2], Siti Aminah Abdurachman[2]

[1]Department of Internal Medicine. Faculty of Medicine, Universitas Padjadjaran. [2]Division of Gastroenterohepatology, Department of Internal Medicine, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia

Introduction: Over 5.000 species of mushrooms are present worldwide. However, very scarce mushroom species cause poisoning. Clinicians must consider mushroom poisoning in the evaluation of all patients who may be intoxicated by natural substances. Based on onset of toxicity, mushroom poisoning divided in 3 groups, early, late and delayed onset toxicity. Amatoxin containing mushrooms are a rare but significant cause of acute fulminant liver failure.
Case: A 37-year-old male patient was admitted to the emergency room with altered mental status, delirium along with nausea, vomiting, abdomen pain, diarrhea and jaundice. Laboratory showed thrombocytopenia (111.000/μL) and abnormal liver function (AST 669 U/L, ALT 5429 U/L, PT 20.9, aPTT 35.1, INR 1.95, total bilirubin 26.18 mg/dL, direct bilirubin 19.51 mg/dL, indirect bilirubin 6.67 mg/dL and albumin 2.45 g/dL). The patient was admitted to the internal medicine intensive care unit. On the same day patient's son, 14-year-old admitted to pediatric emergency room with the same symptoms. Information from the patient's wife, both of them ate wild mushrooms 24 h before admission. They were tested for Hepatitis A, B and C, both were negative. They were treated in intensive care unit for 7 days. Both of them showed clinical progress with supportive therapy for acute liver failure. Patient and his son discharged from the hospital without complication.
Conclusion: Acute liver disease caused by mushroom poisoning is a rare disease. Early detection and adequate supportive therapy shows good outcome

Abstract #1388

Unusual causes of acute liver failure in a tertiary care center

Anand V. Kulkarni

Background: Acute viral hepatitis and drugs are the leading causes of acute liver failure (ALF). Liver transplant remains the treatment of choice for ALF, but the etiology of liver failure may sometimes change the management and prognostication of ALF patients.
Patients and methods: Consecutive patients over one year who presented as ALF to our tertiary hospital were retrospectively analyzed. The demographics, clinical presentation, treatment given, and the outcome was documented.
Results: Over one year, 49 ALF patients were admitted. The etiology of ALF was Hepatitis E in 14, anti-tuberculous drugs in 9, Hepatitis B in 6, and Hepatitis A virus in 4. The etiology was unknown in 3, Wilson's in 3 (pediatric patients), and acute Budd-Chiari syndrome in one. Nine patients (females-6; mean age—35.45 years) (Table 1) with atypical causes of ALF were admitted during the study period. The etiologies were drugs in 4 patients {Efavirenz (n = 2), Warfarin (n = 1), Vitamin A (n = 1)} and infections in the other 5{Epstein Barr virus (n = 2), Hemophagocytic lymphohistiocytosis (satisfying 6/8 criteria) secondary to Tuberculosis (n = 1) and Herpes simplex virus (n = 1)}. Five patients underwent liver biopsy, which aided in diagnosis. However, the most crucial point which helped in diagnosis was a thorough history taking, clinical examination, and closer look at the complete blood counts/peripheral smear. Four (44.45%) of the nine patients succumbed by day 180.
Conclusions: The management of ALF is dependent on the etiology. A thorough history taking and clinical examination aids in the diagnosis and management of the atypical cases of liver failure.

Parameters	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9
Cause (Indication)	Warfarin (CVT prophylaxis)	Efavirenz (HIV)	Efavirenz (HIV)	Vitamin A (Pancreatitis)	Herpes simplex	EBV	EBV	HLH secondary to TB	Sickle cell hepatopathy
Age (years)	45	30	35	34	43	58	15	30	29
Gender	Female	Female	Female	Male	Female	Female	Female	Male	Male
Symptoms	Cholestatic jaundice	Jaundice	Jaundice and ascites	Jaundice	DRESS (Skin rashes & jaundice)	Jaundice	cholestatic jaundice with infectious mononucleosis	Fever, jaundice, abdominal pain, and loss of weight	Jaundice
Examination	Icterus	Icterus, hepatomegaly	Icterus, hepatomegaly	Skin dryness	Skin rashes, icterus, & hepatomegaly	Icterus	Splenomegaly with lymphadenopathy	Hepatosplenomegaly	Hepatosplenomegaly
Complete blood picture	-	-	-	-	Eosinophilia	-	Atypical lymphocytes	Pancytopenia	Sickle cells
Maximum Bilirubin (mg/dl)	37.1	25.1	29	1.2	15.7	11.1	5.6	4.1	>50
Maximum INR	1.98	3.9	3.49	1.96	2.17	1.99	1.61	>6	1.9
AST/ALT (U/L)	394/253	666/290	363/194	1848/967	1059/1028	337/420	179/127	341/219	67/58
ALP(U/L)	940	210	231	112	285	140	807	406	165
Biopsy	Cholestatic hepatitis with ductopenia	Not done	Not done	Steatosis with prominent Ito cells (PAS stain) in the sinusoids	Portal inflammation with multi-nucleated giant cells. Eosinophilic nuclear inclusions in hepatocytes	Not done	Not done	Granulomatous inflammation	Marked cholestasis with congested sinusoids with sickle-shaped RBCs
Treatment	Supportive	Supportive	Supportive	Steroids	Steroids plus acyclovir	Acyclovir	Steroids plus Acyclovir	ATT+Steroids+ Etoposide	Whole blood RBC exchange plus Plasmapheresis
Outcome at 180 days	Death	Alive	Death	Alive	Alive	Alive	Alive	Death	Death

CVT-cortical vein thrombosis; HLH-Hemophagocytic lymphohistiocytosis; HE-Hepatic encephalopathy;DRESS-Drug Rash with Eosinophilia and Systemic Symptoms; ATT-Anti-tubercular treatment

Abstract #1572

Same subtype but different strains of hepatitis A virus (HAV) causing outbreaks in two districts of one province in Indonesia almost at the same time

Dewi Setyowati[1], Teguh Mubawadi[2], Soetjipto Soetjipto[1,3], Juniastuti Juniastuti[1,3] and Maria Inge Lusida[1,3]

[1]Faculty of Medicine, Airlangga University, Surabaya, Indonesia, [2]Regional Center for Environmental Health and Disease Control of Surabaya, Surabaya, Indonesia, [3] Institute of Tropical Disease, Airlangga University, Surabaya Indonesia

Introduction: Hepatitis A virus (HAV) infection, a major cause of acute hepatitis, poses an important public health problem worldwide. The virus spreads through the faecal-oral route, e.g. ingestion of contaminated food and water or direct contact with an infected person. Indonesia experienced hepatitis A outbreaks almost every year.
Objectives: The present study aimed to analyse molecular epidemiological data from HAV outbreaks in two affected areas, East Java province.
Methods: Serum samples were obtained from 88 individuals with clinical manifestations of acute hepatitis in Lamongan district (n = 54) in January 2018 and Bangkalan district (n = 34) in March 2018. To characterize the HAV wild type strains circulating in two areas, the VP3–VP1 and VP1–P2A junction regions were amplified from all anti-HAV IgM-positive and negative serum samples. A phylogenetic tree was constructed using MEGA X software.
Results: A total of 32 (59.25%) of the 54 individuals from Lamongan and 19 (55.9%) of the 34 participants from Bangkalan were positive for anti-HAV IgM. Twenty six PCR tests were positive in the VP3–VP1 and/or VP1–P2A junction, which were all identified as HAV subgenotype IA. The sequences from Bangkalan were 96% to 99% homology with the sequences from Lamongan. The amino acids of samples from Bangkalan were substituted as K813N in the VP1–P2A junction and M519T in the VP3–VP1 junction, comparing to Lamongan.
Conclusion: The subtype of HAV in the two areas was IA, but they were not originated from the same HAV source, as proven identified by multiple alignment.

Abstract #1827

Characteristic liver injury in adult sepsis patients at tertiary hospital in North Sumatera

Barimbing Morris Lintong[1*], Sopacua Andre[1], Kumalasari Carissa[1], Mardianto[2], Ginting Franciscus[1,3]

[1]Antimicrobial Stewardship Program Haji Adam Malik Hospital, [2]Director of Haji Adam Malik Hospital, Medan Indonesia, [3]Division of Infectious Disease, department of Internal medicine, faculty of Medicine University of North Sumatera Haji Adam Malik Hospital Medan Indonesia

Introduction: Sepsis is a life-threatening condition that can cause organ injury and death. Not much data that explains organ injury that most often occurs in sepsis, especially in liver injury in sepsis patients. The aim of this study was to determine the characteristics of liver injury associated with sepsis.
Methods: A retrospective study. The data collected from the medical record and Hospital Information System period 2016 at Tertiary Hospital in North Sumatera, Indonesia. Sepsis diagnosed based on Survival Sepsis Campaign (SSC) 2012 criteria. Liver injury was defined as a state in which the patient's blood laboratory AST or ALT greater than 41 IU/L and serum total bilirubin of equal more than 2 mg/dl. Shock liver was defined as liver function test with both AST and ALT over 200 IU/L
Result: Totally of 535 Adult patients with sepsis, 404 patients were excluded (data not complete and had a primary liver disease). In this study, the age range 50–59 years (25.2%), predominantly were males (64.8%). There was 133 sepsis patients were analyzed in which 131 (98.5%) sepsis patients were associated with liver injury. Characteristics of liver injury associated with sepsis was dominated by 88.5% hypoalbuminemia (88.5%), followed by hepatic hypoxia 27.4%, cholestasis 19.8%, and shock liver 14.5%.
Conclusion: Liver injury was very high in sepsis patients (98.5%). The most characteristic of liver injury associated with sepsis was hypoalbuminemia followed by hepatic hypoxia, cholestasis, and shock liver.

Abstract #1831

Changes of CLIF-SOFA and MELD score better predict 28-days mortality in patients with EASL-CLIF-ACLF

Han Ah Lee

Aim: We investigated prognostic implications of changes in chronic liver failure-sequential organ failure assessment (CLIF-SOFA) score and model for end-stage liver disease (MELD) score between the onset of European association for the study of the liver chronic liver failure consortium (EASL-CLIF-C) acute-on-chronic liver failure (ACLF) and 7 days after the onset of EASL-CLIF-ACLF.
Methods: Prospective data of 1,765 patients with chronic liver disease were collected in Korean Acute-on-Chronic Liver Failure (KACLiF) study. Among these population, patients developed EASL-CLIF-ACLF were included in this study. Clinical impact of CLIF-SOFA score, MELD score and the changes of each score (ΔCLIF-SOFA and ΔMELD score) on 28-day mortality of patients were evaluated.
Results: 327 patients (74.9% were male) were included. Mean age was 54.7. 313 (95.7%) patients had liver cirrhosis. Alcoholic liver disease was most common cause of chronic liver disease (n = 157, 48.0%). 53 (16.2%) patients died in 28 days. Patients died in 28 days were older, and had higher CLIF-SOFA, ΔCLIF-SOFA, MELD, and ΔMELD score (all $P < 0.05$). On multivariate analysis, higher age, CLIF-SOFA, ΔCLIF-SOFA, MELD, and ΔMELD score were independent predictor of 28-days mortality. Area under curves (AUC) of ΔCLIF-SOFA (0.735) and ΔMELD score (0.748) for 28-days mortality were higher than those of baseline CLIF-SOFA (0.678) and MELD score (0.615). Optimal cut-off values of ΔCLIF-SOFA and ΔMELD score for predicting 28-days mortality were 1.5 and 1.0, respectively.
Conclusions: ΔCLIF-SOFA and ΔMELD score had higher prognostic value in predicting 28-days mortality than baseline CLIF-SOFA and MELD score in patients with EASL-CLIF-ACLF.

Abstract #1914

Diabetes and severity of liver disease are associated with short-term mortality in patients with acute on chronic liver failure

Kang Min Kyu[1], Park Jung Gil[1], Yang Jin Mo[2], Song Do Seon[2], Kim Chang Wook[2], Kim Hee Yeon[2], Lee Sung Won[2], Jun Baek Gyu[3], Yim Hyung Joon[4], Jung Young Kul[4], Lee Han Ah[5], Kim Won[6], Jang Jae Young[7], Jeong Soung Won[7], Kim Sang Gyune[8], Yoo Jeong Ju[8], Yoon Eileen L.? [9], Kang Seong Hee[10], Kim Moon Young[10], Suk Ki Tae[11], Kim Dong Joon[11,] and on behalf of Korean Acute-on-Chronic Liver Failure (KACLiF) Study Group

[1]Department of Internal Medicine, College of Medicine, Yeungnam University, Daegu, Republic of Korea, [2]Department of Internal Medicine, The Catholic University of Korea, Seoul, Republic of Korea, [3]Department of Internal Medicine, Gangneung Asan Hospital, University of Ulsan College of Medicine, Gangneung, Republic of Korea, [4]Department of Internal Medicine, Korea University Ansan Hospital, Korea University College of Medicine, Ansan, Republic of Korea, [5]Department of Internal Medicine, Korea University Anam Hospital, Korea University College of Medicine, Seoul, Republic of Korea, [6]Department of Internal Medicine, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, Republic of Korea, [7]Department of Internal Medicine, Soonchunhyang University Seoul Hospital, Seoul, Republic of Korea, [8]Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, Bucheon, Republic of Korea, [9]Department of Internal Medicine, Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Republic of Korea, [10]Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea, [11]Department of Internal Medicine, Hallym University College of Medicine, Chuncheon Sacred Heart Hospital, Chuncheon, Republic of Korea

Introduction: Bacterial infections are pivotal factors on the aggravation of acute-on-chronic liver failure (ACLF) lead to high 28-day mortality. Diagnostic markers of infection including C-reactive protein (CRP) and procalcitonin (PCT) are useful for detection of early bacterial infection. However, there was limited data of these markers in patient with ACLF.
Objectives: Our study is aim to investigate factors including these two infection marker associated with short term mortality in patient with ACLF.
Methods: We enrolled 196 patients with ACLF (serum bilirubin $\geq$ 5 mg/dL and INR > 1.5) at admission, prospectively. We excluded patients who could not be assessed with CRP (n = 1) and PCT (n = 100) or received liver transplantation (n = 4) within 28 days after admission. A receiver operating characteristic curve analysis was performed to evaluate optimal cut-off value of CRP and PCT for predicting 28-day mortality.
Results: The optimal cut-off value of CRP and PCT to predict 28-day mortality was 0.79 mg/dL and 0.417 ng/mL. Within 28 days, survival of the patients with low PCT ($\leq$ 0.79 mg/dL) was better than those

with high PCT (26.7 ± 0.8 days vs. 24.2 ± 1.1 days, $P = 0.0079$). However, there was no significant difference according to CRP ($P = 0.0661$). On the multivariate analysis, type 2 diabetes (Hazard ratio [HR] 5.086, 95% confidence interval [CI] 1.531–16.897, $P = 0.0079$) and Model for End-stage Liver Disease (MELD) score (HR 1.124, 95% CI 1.056-1.196, $P = 0.0002$) was associated with 28-day mortality.

Conclusion: Diabetes and severity of liver disease are independently associated with 28-day mortality in patients with ACLF.

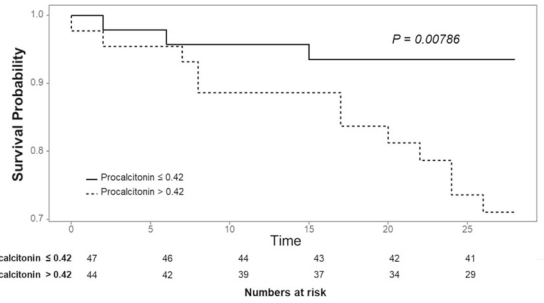


Figure 1. Cumulative survival of patients with Acute on Chronic Liver Failure according to procalcitonin on admission

Table 1. Univariate and multivariate analysis of factors associated with 28-day mortality.

	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Sex	0.600	0.170-2.120	0.4270			
Age	1.030	0.980-1.080	0.3010			
Infection	1.990	0.630-6.250	0.2390			
HTN	1.240	0.160-9.470	0.8320			
DM	3.440	1.090-10.850	0.0350*	5.086	1.531-16.897	0.0079
SIRS	5.660	0.340-94.290	0.2270			
CRP	1.050	0.910-1.200	0.5230			
Procalcitonin	1.030	0.930-1.140	0.5970			
MELD	1.110	1.040-1.170	0.0010*	1.124	1.056-1.196	0.0002

Abstract # 2082

Comparison of performance of NACSELD and CLIF-C diagnostic criteria for predicting short term mortality in ACLF

Arun P

Introduction and aim: Different criteria are applied for the diagnosis of ACLF. The CLIF-C definition incorporates 6 organ failure scores to diagnose ACLF—however it is difficult for bed side calculation. NACSELD is relatively simple to calculate in bedside and incorporates 4 variables only. Our aim is to compare the performance of the two in predicting short term mortality in acute decompensation of CLD

Materials and methods: It is a retrospective cohort study of adult cirrhotic patients admitted with acute decompensation satisfying the APASL criteria for ACLF in a tertiary care centre in South India. The 2 diagnostic criteria were applied to all patients at the time of admission. Evaluated outcome was mortality at 30 day.

Results: Out of the 173 selected patients only 9.8% satisfied NACSELD criteria while 76.3% had ACLF by CLIF-C definition. 15 patients out of 17 by NACSELD criteria died within 1 month and 40 out of 156 patients died in No ACLF group (sensitivity 27.3, specificity 98.3, PPV 88.2 and NPV 95.1). 53 patients out of 132 by CLIF-C criteria died within 1 month (Sensitivity 96.4, Specificity 33.1, PPV 40.2 and NPV 95.1).

Conclusion: ACLF definition by NACSELD has a poor sensitivity in predicting 30 day mortality in ACLF. Meanwhile CLIF-C definition has a good sensitivity and negative predictive value for short term mortality.

Abstract #2131 Bioenergetics defect of CD14 monocytes are associated with early mortality in Human acute liver failure

Dhananjay kumar[1], Ashwani Hidam[1], Jitendra kumar[1], Deepanshu[2] Nidhi[1], Mojahidul Islam[1], Vinendera Pamecha[3], V. Rajan, Rakhi Maiwall [2], Anupam Kumar[1], Shiv K. Sarin[2]

[1]Dept of Molecular and Cellular Medicine, [2]Dept of Hepatology, Department of HPB Surgery; Institute of Liver and Biliary Sciences, India; New Delhi

Background and aims: Increase systemic inflammatory response as a result of massive hepatic injury is associated with development infections & high mortality in ALF though the mechanisms are unclear. We investigated the underlying cellular mechanisms for increased susceptibility to infection & high mortality in ALF

Method: A panel 31 cytokines & growth factor were analysed in ALF (N = 30). Distribution of hepatic macrophages (ALF, N = 10, Healthy (H) = 10), monocytes (ALF N = 15; H = 15) & their phagocytosis was studied by FACS. Mitochondrial respiration and glycolysis were analysed in shorted CD14+ monocyte (ALF N = 18, H = 10) by Agilent-XFe24-analyzer. Expression of glycolysis and TCA pathway gene were done by qPCR.

Results: 21 of 30 ALF patients died or went for liver transplant (non-survivor) and 9 patients showed spontaneous recovery (survivor). Cytokine showed reduction of innate immunity-related cytokines (MCP-3,IL-1β, IL-6, IL-10, & IL-17) in ALF non-survivors. CD68+ macrophage while increased in ALF liver ($p = 0.004$), were deficient in phagocytosis($p = 0.001$) in comparison to healthy. Similarly, the CD14+ monocytes in ALF non-surviver showed reduction ($p = 0.001$) & phagocytosis ($p < 0.001$) in comparison to survivors, suggesting the failure of mono-mac system in ALF non surviver. In comparison to healthy monocyte, the ALF monocyte showed significant decrease in mitochondrial respiration (Fig. 1A),glycolysis (Fig. 1B) & showed decrease expression of enzyme associated with ATP production in glycolysis (PGK1) & TCA cycle (IDH, OGDH) in ALF non surviver, suggesting Bioenergetic failure in ALF. Further analysis of mitochondrial-respiration of monocyte in living-donor-liver-transplant donor before & after surgical resection at D3 & D7 showed significant decrease in mitochondrial-respiration at D3 which recover at D7 with increase in liver mass. these data suggest the loss of hepatic mass adversely affects the energy metabolism of monocytes. In 21Ds of follow-up while 9 patients discharged form ICU & survived 9 died or went for liver transplant. Baseline mitochondrial respiration of monocyte ($p < 0.001$; AUROC = 1) predict the early mortality (21 Ds) in ALF, ALF with OCR less then = 21 pM/min showed increase in mortality (Fig. 1C)

Conclusion: Broad defect in energy metabolism in ALF, lead to a compromise of mono-mac functions & associated with early mortality. Restoring the energy metabolism of monocytes may prevent the secondary infection & mortality.

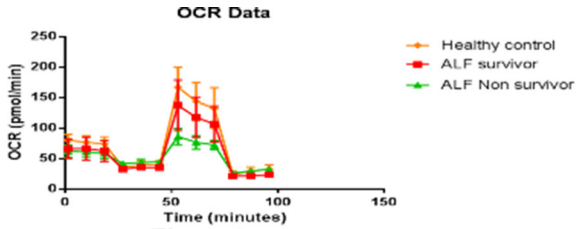


Figure A

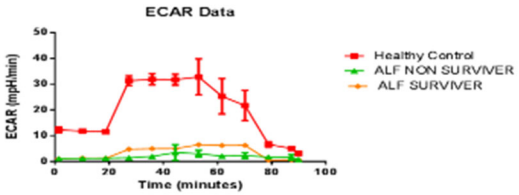


Figure B

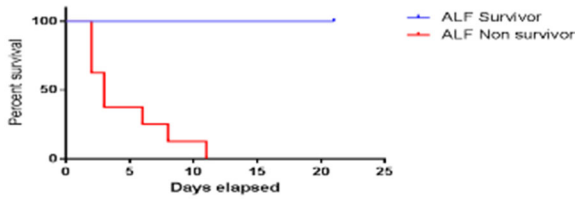


Figure C

Abstract # 2150

Acute liver failure: outcome and prognostic predictors

Mohsin Ali, Jalpa Devi, Amerta Bai, Adil Hassan, Saadat Ali, Muhammad Sadik

Asian Institute of Medical Sciences, Hyderabad

Introduction: Acute liver failure (ALF) is defined as a rapid hepatic dysfunction and encephalopathy in the absence of pre-existing liver disease. Globally, viral hepatitis is responsible for the majority of cases of ALF.
Objectives: This study aimed to determine the etiology, outcome and predictive factors for in-hospital mortality in ALF patients.
Methods: A descriptive study was conducted at the Gastro-Hepatology Department of Asian Institute of Medical Sciences, Hyderabad from May 2018 to September 2019. A total of 31 patients having clinical and biochemical markers suggestive of ALF were included in the study. International Normalized Ratio (INR), sepsis (2 SIRS + confirmed or suspected infection), prognostic scores {King College Criteria (KCC) and Model End-Stage Liver Disease (MELD)} and other prognostic factors were compared.
Results: Thirty-one patients with a mean age of 22 years, 21 (67.7%) were males. Most common etiology was indeterminate 21 (67.7%) while 5 (16.15%) had Hepatitis B and 5 (16.15%) had Hepatitis E. The in-hospital mortality was 19 (61.3%), out of which 14 (73.3%) were males and 12 (38.7%) recovered spontaneously. INR > 5.00 (Mean = 3.12 and 4.02 in both groups respectively, $p = 0.02$), MELD score > 32 (Mean = 29.58 and 33.31 in both groups respectively, $p = 0.049$), KCC 2 or more out of 5 (Mean = 0.83 and 1.31 in both groups respectively, $p = 0.068$), and sepsis ($p = 0.008$) were independently associated with in-hospital mortality.
Conclusion: The in-hospital mortality of ALF was significantly high with raised INR, MELD (> 32), KCC (2/5) and sepsis. Hence, they are poor prognostic factors.

Abstract # 2244

Acute T-cell leukemia presented as acute on chronic liver failure. A case report

Jha[1] Ashish Kumar, Dayal[1] Vishwa Mohan

[1]Department of Gastroenterology, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Bailey Road, Patna, Pin-800014, Bihar, India

Introduction: Hematologic malignancies uncommonly present as acute liver failure or acute on chronic liver failure (ACLF).
Objective: We describe a rare case of a patient who developed ACLF due to acute T-cell leukemia.
Methods: A 19-year-old male presented with jaundice of 3-weeks duration. Evaluation revealed pancytopenia, hyperbilirubinemia (bilirubin 10 mg/dL), transaminesemia (ALT 837 IU/L, AST 210 IU/L), and deranged PT-INR (3.2). Ultrasonography revealed hepatosplenomegaly, ascites and dilated portal veins. Ascites fluid revealed high SAAG ratio without SBP. Work-up for viral hepatitis (HBV, HCV, HAV, HEV, HSV, CMV, EBV), Wilson's disease and autoimmune liver disease were negative. Endoscopy showed mild PHG. Supportive treatment was started, but symptoms did not improved.
One week later, tests showed leukocytosis (24600/cumm). Peripheral blood film showed 43% atypical lymphocytes with 15% blast cells. These cells were positive for T-cell markers cytoplasmic and surface CD3, CD2 and TCRgd; and negative for BCR-ABL t(9:22) assay. Bone marrow and liver biopsy was deferred due to coagulopathy. The patient was diagnosed as ACLF. Acute insult appeared to be caused by acute T-cell leukemia/lymphoma. We didn't found any etiology for chronic liver disease.
Results: Empiric steroid therapy was started. The patient had improvement in his symptoms and liver function tests after 2-weeks.
Conclusions: ACLF due to acute T-cell leukemia/lymphoma is an unusual diagnosis with important implications, as it is a contraindication to liver transplantation.
Keywords: Acute T-cell leukemia; Acute on chronic liver failure; Hematologic malignancies; Liver transplantation

2. Hepatitis B

Oral Presentations

Abstract #146

Baseline M2BPGi level stratifies risks of hepatocellular carcinoma in chronic hepatitis B patients with oral antiviral therapy

Tai-Chung Tseng,[1,2] Cheng-Yuan Peng,[6,7] Yao-Chun Hsu,[11] Tung-Hung Su,[1,2] Chia-Chi Wang,[8,9] Chun-Jen Liu,[1-3] Hung-Chih Yang,[1,5] Wan-Ting Yang,[2] Chia-Hsin Lin,[7] Ming-Lung Yu,[12] Hsueh-Chou Lai,[7] Yasuhito Tanaka,[13] Mindie H. Nguyen,[14] Chen-Hua Liu,[1,2] Pei-Jer Chen,[1-3] Ding-Shinn Chen,[1-3,10] and Jia-Horng Kao[1-4]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan. [2]Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan. [3]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan. [4]Department of Medical Research, National Taiwan University Hospital, Taipei, Taiwan. [5]Department of Microbiology, National Taiwan University College of Medicine, Taipei, Taiwan. [6]School of

Medicine, China Medical University, Taichung, Taiwan. [7]Division of Hepatogastroenterology, Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan. [8]Division of Gastroenterology, Department of Internal Medicine, Taipei Tzuchi Hospital, The Buddhist Tzuchi Medical Foundation, Taiwan. [9]School of Medicine, Tzu Chi University, Hualien, Taiwan. [10]Genomics Research Center Academia Sinica, Taiwan. [11]Division of Gastroenterology and Hepatology, Department of Internal Medicine, E-Da Hospital/I-Shou University, Kaohsiung, Taiwan. [12]Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan. [13]Department of Virology and Liver Unit, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan. [14]Division of Gastroenterology and Hepatology, Stanford University Medical Center, Palo Alto, California, the United States of America

Background and aims: Mac-2 binding protein glycosylation isomer (M2BPGi) is a novel biomarker correlating with liver fibrosis stages. However, little is known about how it predicts risks of hepatocellular carcinoma (HCC) in chronic hepatitis B (CHB) patients receiving long-term antiviral treatment.
Methods: The study contained 2 parts. The first part was to explore whether M2BPGi could be an HCC predictor in 899 CHB patients receiving long-term entecavir therapy. The second part was to validate the findings in an independent cohort of 384 on-treatment CHB patients with more severe liver disease.
Results: In the discovery cohort, there were 64 patients developing HCC within an average follow-up of 7.01 years. Our data showed that M2BPGi level was positively associated with HCC development. When stratifying the patients by an M2BPGi level of 1.73 (the third quartile), the high M2BPGi group was shown to have an increased HCC risk compared to the low M2BPGi group with hazard ratio of 5.80 (95% CI: 3.50-9.60). Furthermore, we found that the M2BPGi level complements PAGE-B score, a well-validated HCC prediction model, to predict HCC development. Lastly, the cutoff was validated in the independent cohort, especially those with an intermediate PAGE-B score.
Conclusions: In CHB patients receiving long-term antiviral treatment, serum M2BPGi level not only serves as an independent HCC predictor but also complements PAGE-B in stratifying HCC risks.

Abstract #204

Elevated testosterone increases the risk of hepatocellular carcinoma in men with chronic hepatitis B and diabetes mellitus

[1,2]Terry Cheuk-Fung Yip, [1,2,3]Grace Lai-Hung Wong, [1,2,3]Henry Lik-Yuen Chan, [1,2]Yee-Kit Tse, [1,2]Lilian Yan Liang, [1,2]Vicki Wing-Ki Hui, [1,4]Hye Won Lee, [2]Alice Pik-Shan Kong, [1,2,3]Vincent Wai-Sun Wong

[1]Institute of Digestive Disease, [2]Department of Medicine and Therapeutics, and [3]State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong; Hong Kong SAR, China. [4]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea

Introduction: Diabetes mellitus (DM) is associated with a doubled risk of hepatocellular carcinoma (HCC) in patients with chronic hepatitis B (CHB). Male sex hormone may play a role in the progression of CHB and DM.
Objectives: We examined the relationship between serum total testosterone and HCC risk in male CHB patients with DM.
Methods: We performed a retrospective cohort study of male CHB patients with DM between 2000 and 2017 using a territory-wide electronic healthcare database in Hong Kong. DM was defined by use of anti-diabetic medications, hemoglobin $A_{1c} \geq 6.5\%$, and/or fasting glucose ≥ 7 mmol/L in two measurements or ≥ 11.1 mmol/L in one measurement.
Results: Of 928 male CHB patients with DM, 83 (8.9%) developed HCC at a median (interquartile range) of 10.7 (6.1–14.6) years. Higher testosterone was associated with an elevated risk of HCC (adjusted hazard ratio [aHR] per 1 SD increase 1.25, 95% CI 1.10–1.43; $P < 0.001$). Upper tertile of testosterone (aHR 2.11, 95% CI 1.14–3.88, $P = 0.017$), but not middle tertile (aHR 0.97, 95% CI 0.47–2.00, $P = 0.928$), was associated with a higher risk of HCC than lower tertile (Figure). The cumulative incidence (95% CI) of HCC at 5, 10 and 15 years was 4.4% (2.5%–7.2%), 12.4% (8.7%–16.7%) and 19.1% (14.2%–24.5%), respectively, in patients in upper tertile of testosterone. By subgroup analysis, the association between testosterone and HCC was stronger in patients aged ≥ 50 years and those not receiving antiviral therapy.
Conclusion: Higher serum testosterone is associated with a higher incidence of HCC in male CHB patients with DM.

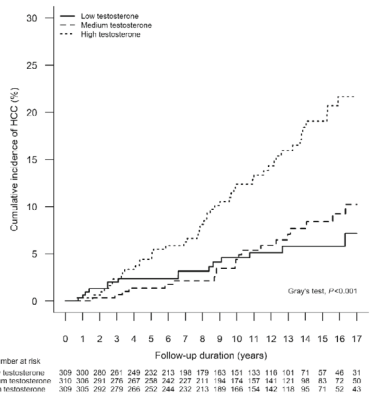


Figure. Cumulative incidence function of hepatocellular carcinoma (HCC) in male chronic hepatitis B patients with diabetes mellitus and different serum total testosterone level at baseline estimated by the Gray's method.

Abstract #213 **24 weeks safety and efficacy of tenofovir alafenamide compared to tenofovir disoproxil fumarate and entercavir in treatment-naive patients with chronic hepatitis B in China**

Wenxiong Xu[1], Yeqiong Zhang[1], Limin Zhen[1], Liang Peng[1]

[1]Department of Infectious Diseases, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Introduction: Tenofovir alafenamide (TAF) was not available in China until November 2018. Little is known about the safety and efficacy of TAF for Chinese chronic hepatitis B (CHB) patients.
Objectives: The aim of this study is to evaluate the safety and efficacy of TAF, compared to tenofovir disoproxil fumarate (TDF) and entercavir (ETV), in treatment-naive patients with CHB in China.
Methods: Chinese treatment naive CHB patients were enrolled in this prospective clinical study. They received anti-HBV therapy of TAF, or TDF, or ETV, according to their willing. Laboratory test results were collected to evaluate the safety and efficacy.
Results: 100 patients were enrolled and finished 24 weeks follow-up. 35 patients received TAF, 31 patients received TDF, 34 patients received ETV. No medicine-related adverse events were observed. At week 4, higher alanine aminotransferase (ALT) and aspartate

aminotransferase (AST) normalization rates were achieved with TAF treatment compared to TDF or ETV. At week 24, the proportions of patients with ALT normalization were higher in patients receiving TAF (81.8%) and TDF (84.2%) than in those receiving ETV (54.5%), the differences in the rates of viral suppression were similar among the three groups (TAF 36.4% vs. TDF 58.8% vs. ETV 50.0%). In terms of renal toxicity, there was no statistical difference among the three groups, and all three drugs were safe to be used.
Conclusions: In CHB patients, 24 weeks of TAF treatment is as safe and effective as TDF and ETV, with high transaminase normalization rate, virological response rate and rare renal function impairment.

Abstract #251

Hepatitis B virus surface antigen specific cytokine secreting T cell responses: an ex-vivo evaluation of antibody non-responders to HBV vaccination

Nessa Afzalun[1], Akther Tahmina[1], Sultana Sharmin[1], Tabassum Shahina[1]

[1]Department of Virology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Introduction: Individual fails to elicit protective antibody response after hepatitis B virus (HBV) vaccination is thought to remain at risk for HBV infection. This non-responsiveness to vaccine is an important concern to achieve the goal of World Health Organization (WHO) global health sector strategy to eliminate viral hepatitis by 2030.
Objective: In this study we aimed to investigate the cellular immunity of vaccine non-responders by analyzing cytokine secreting T lymphocytes on peripheral blood mononuclear cells (PBMCs).
Methods: A total of 25 vaccine good responders (AniHBs $>$ 100 IU/ml), 25 vaccine non responders (AniHBs $<$ 10 IU/ml) and 25 vaccine naïve healthy individuals were recruited after screening for antiHBs antibody test. PBMCs were isolated from heparinized blood following Ficoll-Hypaque density gradient technique and finally suspended in RPMI-1640 supplemented with 10% fetal calf serum (FCS). In vitro cellular immune responses were evaluated using HBsAg specific cell proliferation and Th1 and Th2 specific cytokines secretion assay. Lymphocytes proliferation assay was performed by MTT assay following standard protocol. For in vitro cytokines secretion assay, lymphocytes were cultured in specific cytokine pre-coated 96 well culture plates in presence of rHBsAg and pokeweed mitogen. Interferon gamma (IFN-γ), interleukin (IL)–2, IL-4 and IL-5 secreting T cells were measured by enzyme linked immune spot (EliSpot) assay following manufacturer's protocol.
Results: Relatively poor cell proliferation responses were demonstrated in non-responders ($P < 0.05$) in comparison to good responders and no detectable proliferation were found in vaccine naïve individuals. The overall number of spot forming cell (SFC) for IFN-γ found significantly higher in good responders and non-responders compared to vaccine naïve individuals($P > 0.001$). However, SFC for IL-2, IL-4, and IL-5 were diminished in number ($P < 0.005$) among non-responders than good responders and were comparable to vaccine naïve individuals.
Conclusion: Inadequate antibody response correlates with impaired T helper2 (Th2) cytokines production; conversely, increase frequency of IFN-γ secreting cells may confer their cellular immunity against HBV infection.

Abstract #265

Longitudinal changes in controlled attenuation parameter and body mass index are associated with fibrosis evolution in chronic hepatitis B patients on nucleoside analogue therapy

Hui Rex Wan-Hin[1], Mak Lung-Yi[1], Fung James[1], Wong Danny Ka-Ho[1], Yuen Man-Fung[1], Seto Wai-Kay[1]

[1]Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Introduction: Long-term nucleoside analogue (NA) therapy can lead to fibrosis regression in chronic hepatitis B (CHB) patients, yet fibrosis regression is not universal and metabolic factors may impact the clinical course of CHB.
Methods: CHB patients on NA therapy were prospectively recruited for baseline and 3-year transient elastography. Fibrosis staging was defined according to European Association for the Study of the Liver—Asociacion Latinoamericana para el Estudio del Higado guidelines. Fibrosis progression and regression were defined as increment or decrement of ≥ 1 fibrosis stages from baseline respectively. Steatosis was defined as controlled attenuation parameter (CAP) $\geq$ 248 dB/m.
Results: 404 patients (72.0% male; mean age 58.5 $\pm$ 9.1 years) were recruited. Mean NA treatment duration was 72.3 $\pm$ 43.9 months. Majority of patients had undetectable HBV DNA ($\leq$ 20 IU/mL) at baseline (92.3%) and year 3 (93.9%). Fibrosis regression and progression were observed in 21.8% and 17.8% of patients respectively. Treatment duration, NA type and HBV DNA levels were not predictive of fibrosis evolution. Higher baseline CAP was associated with fibrosis regression in univariate analysis, but was non-significant in multivariate analysis. In a multivariate model of on-treatment factors, serial CAP decrease over 3 years was an independent predictor of fibrosis regression (odds 1.009, 95% CI 1.001–1.016, $p = 0.022$), whereas serial body mass index increase was predictive of fibrosis progression (OR 1.212, 95% CI 1.009–1.456, $p = 0.040$).
Conclusion: Longitudinal changes in CAP and body mass index were predictive of fibrosis evolution during NA treatment, demonstrating the importance of metabolic factors in influencing CHB-related treatment outcomes.

Abstract #283

Influence of IFNAR2 expression on therapeutic effect of pegylated interferon alpha-2b in HBeAg-positive chronic hepatitis B patients

Wenxiong Xu[1], Xiang Zhu[1], Ying Liu[1], Liang Peng[1]

[1]Department of Infectious Diseases, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Introduction: Interferon-encoding gene IFNA2 p.Ala120Thr mutation results in decreased anti-HBV infection ability of interferon. Expression of the interferon receptor IFNAR2 also affect the efficacy of interferon.
Objectives: The aim of this study was to observe the relationship between IFNA2 p.Ala120Thr mutation, IFNAR2 expression and the efficacy of interferon in HBeAg-positive chronic hepatitis B (CHB) patients.
Methods: Naïve HBeAg-positive CHB patients were enrolled. All patients finished IFNA2 p.Ala120Thr mutation detection and received pegylated interferon alpha-2b therapy if mutation was negative. Clinical data and laboratory test results, including IFNAR2 expression, were recorded.

Results: 59 patients were enrolled in the study. IFNA2 p.Ala120Thr gene mutation detections were all negative. 43 patients completed 24 weeks interferon therapy, of whom 18 had good early response, 21 had general early response, and 4 had poor early response. Baseline HBsAg levels were 3.56 ± 0.75 log10 IU/mL in good early response group, 3.82 ± 0.41 log10 IU/mL in general early response group, and 4.83 ± 0.15 in poor early response group (p = 0.001). Baseline IFNAR2 levels were 1.834 ± 1.786 in good early response group, 2.116 ± 1.898 in general early response group and 1.233 ± 1.147 in poor early response group (p = 0.651). 37 patients completed 48 weeks treatment, of which 26 completed 48 weeks interferon monotherapy. There were 8 patients with HBsAg < 20 IU/ml and 15 patients with HBeAg seroconversion.
Conclusions: High baseline HBsAg levels are associated with poor early response. Further study of IFNAR2 expression is needed to find out its effect on interferon therapy.

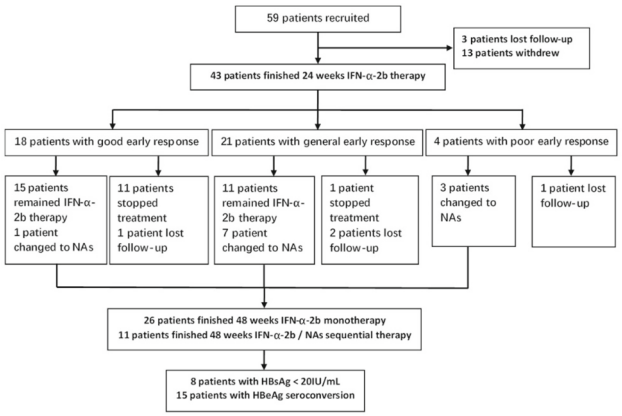


Figure 1 Flow chart of patient recruitment and clinical development.

Abstract #292

Impact of diabetes mellitus on PAGE-B score to exclude hepatocellular carcinoma in chronic hepatitis B patients on antiviral therapy: a territory-wide cohort of 32,150 patients

Terry Cheuk-Fung Yip[1,2], Grace Lai-Hung Wong[1,2,3], Vincent Wai-Sun Wong[1,2,3], Yee-Kit Tse[1,2], Lilian Yan Liang[1,2], Vicki Wing-Ki Hui[1,2], Hye Won Lee[1,4], Henry Lik-Yuen Chan[1,2,3]

[1]Institute of Digestive Disease, [2]Department of Medicine and Therapeutics, and [3]State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong; Hong Kong SAR, China. [4]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea.

Introduction: Diabetes mellitus (DM) is associated with a doubled risk of hepatocellular carcinoma (HCC), and has a rising prevalence among patients with chronic hepatitis B (CHB). The impact on performance of HCC risk scores is unclear.
Objectives: We examined the impact of DM on performance of PAGE-B score among treated CHB patients.
Methods: Adult CHB patients who had received entecavir or tenofovir for at least 6 months in 2005–2018 were identified in Hong Kong. DM was defined by use of anti-diabetic agents, hemoglobin $A_{1c} \geq 6.5\%$, fasting glucose ≥ 7 mmol/L in two or ≥ 11.1 mmol/L in one measurement, and/or diagnosis codes. Performance of PAGE-B score on 5-year HCC prediction was assessed by area under the time-dependent receiver operating characteristic curve (AUROC), and cut-off values of the score were evaluated by survival analysis.
Results: Of 32,150 identified CHB patients, 7388 (23.0%) had DM. At a median (interquartile range) follow-up of 3.9 (1.8–5.0) years, 532 (7.2%) DM patients and 1,000 (4.0%) non-DM patients developed HCC. The AUROC (95% CI) of PAGE-B score to predict HCC at 5 years was lower in DM patients (0.70 [0.67–0.72]) than in non-DM patients (0.79 [0.78–0.81]). 788 (10.7%) DM patients were classified as low HCC risk; their 5-year cumulative incidence (95% CI) of HCC was 1.1% (0.5–2.3%). 6,410 (25.9%) non-DM patients were classified as low HCC risk; their 5-year cumulative incidence (95% CI) of HCC was 0.5% (0.3–0.7%) (Figure).
Conclusion: While PAGE-B score has a lower performance in DM patients, it can identify DM and non-DM patients with low HCC risk.

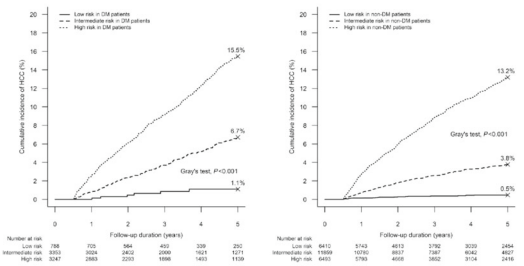


Figure. Cumulative incidence function of hepatocellular carcinoma (HCC) in chronic hepatitis B patients on antiviral therapy with and without diabetes mellitus in different risk groups of PAGE-B score estimated by Gray's method.

Abstract #341

Combination of NA, Peg-IFN alpha-2b and GMCSF enhanced HBsAb production in NA experienced CHB patients (the Anchor A study): an interim analysis

Di Wu[1], Weiming Yan[1], Deming Tan[2], Shifang Peng[2], Yongping Chen[3], Jiaji Jiang[4], Xinyue Chen[5], Xiaoguang Dou[6], Ke Ma[1], Peng Wang[1], Ping Yin[7], Li Sun[8], Meifang Han[1], Qin Ning[*1]

[1]Department of Infectious Diseases, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, [2]Department of Infectious Diseases, Xiangya Hospital, Central South University, Changsha, China, [3]Department of Infectious Diseases, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China, [4]Liver Research Center, First Affiliated Hospital of Fujian Medical University, Fuzhou, China, [5]International Medical Department, Beijing Youan Hospital, Capital Medical University, Beijing, China, [6]Department of Infectious Diseases, Shengjing Hospital of China Medical University, Shenyang, China, [7]Department of Epidemiology and Biostatistics, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, [8]Xiamen Amoytop Biotech Co., Ltd, Xiamen, China

Background: Granulocyte-macrophage colony stimulating factor (GMCSF) has various effects on immune responses and has previously been used as an adjuvant to HBV vaccine to enhance the antibody response. This multicenter, randomized controlled trial (NCT02327416) was to evaluate whether combination of NA, peginterferon alfa-2b (Peg-IFN α-2b) and GMCSF could induce HBsAg loss/seroconversion in patients undergoing long-term NA.
Methods: 249 CHB patients who had received NA > 1 year, with HBsAg < 3000 IU/ml and HBV DNA ≤ 1000 copies/ml, were randomized 1:1:1 to receive ETV for 96 weeks (Group I) or ETV for 48 weeks and Peg-IFN a-2b (180 μg/week) for 96 weeks (Group II) or ETV and intermittent GMCSF (75 μg/day, first 5 days each month) for 48 weeks plus Peg-IFNα-2b for 96 weeks (Group III). Interim data on 249 patients (81 in Group I, 83 in Group II and 85 in Group III) were analyzed.

Results: Baseline characteristics were comparable among treatment groups. At week 96, patients receiving triple combination therapy (NA + Peg-IFN + GMCSF) and patients receiving dual combination therapy (NA + Peg-IFN) achieved higher rates of HBsAg loss than those continuing NA treatment (19.40%, 31.34% and 0%, respectively, $p < 0.001$ for all comparisons vs Group I). There was no significant difference in HBsAg loss rate between Group III and Group II ($p = 0.527$). Rates of HBsAb $\geq$ 10 IU/ml were significantly higher in Group III (32.76%) and Group II (34.43%) than Group I (0%, $p < 0.001$ for all comparisons vs Group I). HBsAg seroconversion was only observed in Group III (20.69%) and Group II (27.87%) ($p = 0.3619$). At week 12 after initiating Peg-IFN, 58 patients in Group III and 47 in Group II had normal or mild elevated ALT levels ($< 2 \times$ ULN), among these subgroup of patients, triple combination therapy induced significantly higher HBsAb positivity rates than dual combination therapy (48.28% vs 29.79%) at week 96. The difference between the two groups and the 95% CI was 18.49% (0.15% to 36.83%), which was statistically significant. Moreover, numerically higher rates of HBsAb > 100 IU/L were observed in Group III than in Group II at week 96 (17.24% vs 8.51%, $p = 0.19$). Both dual and triple combination therapy regimens were generally well-tolerated.

Conclusion: For patients with virological suppression by NA, a combination of ETV and Peg-IFN α-2b therapy with or without GMCSF significantly increases rates of HBsAg loss/seroconversion. GMCSF may enhance the therapeutic effect of Peg-IFN α-2b in terms of HBsAb positivity in those with normal or mild elevated on-treatment ALT levels.

Abstract #394

Continuing besifovir dipivoxil maleate versus switching from tenofovir disoproxil fumarate for treatment of chronic hepatitis B: 192 weeks results of phase 3 trial

Do Seon Song[1], Won Kim[2], Sang Hoon Ahn[3], Hyung Joon Yim[4], Jae Young Jang[5], Yong Oh Kweon[6], Yong Kyun Cho[7], Yoon Jun Kim[8], Gun Young Hong[9], Dong Joon Kim[10], Young Kul Jung[11], Soon Ho Um[12], Joo Hyun Sohn[13], Jin Woo Lee[14], Sung Jae Park[15], Byung Seok Lee[16], Ju Hyun Kim[17], Hong Soo Kim[18], Seung Kew Yoon[19], Moon Young Kim[20], Kwan Sik Lee[21], Young Suk Lim[22], Wan Sik Lee[23], Jin Mo Yang[24], Kwang-Hyub Han[25]

[1]Department of Internal Medicine, Catholic University Medical College St. Vincent, Suwon, Korea, [2]Department of Internal Medicine, Seoul National University College of Medicine, Seoul Metropolitan Government Boramae Medical Center, Seoul, Korea, [3]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, [4]Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea, [5]Department of Internal Medicine, College of Medicine, Soonchunhyang University, Seoul, Korea, [6]Department of Internal Medicine, Kyungpook National University College of Medicine, Daegu, Korea, [7]Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Korea, [8]Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea, [9]Department of Internal Medicine, Gwangju Christian Hospital, Gwangju, Korea, [10]Department of Internal Medicine, Hallym University College of Medicine, Chuncheon, Korea, [11]Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea, [12]Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea, [13]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea, [14]Department of Internal Medicine, Inha University College of Medicine, Incheon, Korea, [15]Department of Internal Medicine, Paik Hospital, Inje University, Busan, Korea, [16]Department of Gastroenterology and Hepatology, Chungnam National University School of Medicine, Daejeon, Korea, [17]Department of Internal Medicine, Gacheon University College of Medicine, Incheon, Korea, [18]Department of Internal Medicine, Soonchunhyang University College of Medicine, Cheonan, Korea, [19]Department of Internal Medicine, Catholic University of Korea, Seoul, Korea, [20]Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea, [21]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, [22]Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, [23]Department of Internal Medicine, Chonnam University Medical School, Gwangju, Korea, [24]Department of Internal Medicine, Catholic University Medical College St. Vincent, Suwon, Korea, [25]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea,

Introduction: Besifovir dipivoxil maleate (BSV) is an acyclic nucleotide phosphonate with a potent antiviral activity against hepatitis B virus (HBV). An antiviral efficacy of BSV for forty-eight week was shown to be comparable to tenofovir disoproxil fumarate (TDF) with improved renal and bone safety.

Objectives: To evaluate the efficacy and safety of BSV in treatment-naïve chronic hepatitis B patients in 192 weeks of the follow-up study.

Method: After 48 weeks of double-blind comparison of BSV to TDF, patients continued to participate in the open-label BSV study. We evaluated antiviral efficacy and drug safety up to 192 weeks for both BSV continuing group (BSV-BSV) and the group switched from TDF to BSV after 48 weeks (TDF-BSV). The primary endpoint was virological response (HBV DNA < 69 IU/mL).

Results: Among 197 patients who received randomized treatments, 170 for 2nd year, 157 for 3rd year and 152 for 4th entered the open-label phase extentional study. Finally, 150 patients completed 192 weeks of follow-up. The virological response rate over 192 weeks was 92.5% in BSV-BSV, 93.1% in TDF-BSV patients ($p = 0.90$). HBeAg seroconversion and ALT normalization rates were similar between the groups. There were no drug resistant mutations to BSV. Bone mineral density and renal function were well preserved in BSV-BSV while those were once worsened and then recovered after switching therapy in TDF-BSV patients.

Conclusion: BSV maintained antiviral efficacy over 192 weeks without any resistance. BSV was also effective for those who have switched from TDF to BSV. BSV was safe and well tolerated.

Abstract #402

Early alteration of TLR2$^+$ monocytes and PD1$^+$CD8$^+$T cells may contribute to virological breakthrough in chronic hepatitis B patients during Peg-IFN-α treatment after NAs cessation.

Da Huang[1*], Di Wu[1], Meifang Han[1], Weiming Yan[1], Qin Ning[1]

[1]Department and Institute of Infectious Disease, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Introduction: A proportion of patients with chronic hepatitis B (CHB) undergoing peg-interferon-α (Peg-IFN-α) treatment developed virological breakthrough (VBT) after nucleoside/nucleotide analogs (NAs) cessation, who were more likely to have poor treatment outcome.

Objective: The aim of this study was to investigate potential immunological mechanisms underlying VBT in such patients.

Methods: 166 NAs-suppressed CHB patients received Peg-IFN-α therapy for at least 48 weeks. Peripheral blood and intrahepatic

immunological indicators were assessed dynamically. HBV DNA levels were evaluated in HepAD38 cell lines after being co-cultured with peripheral blood mononuclear cells pre-treated with TLR2 agonists and anti-PDL1 monoclonal antibody.
Results: 33 out of 166 patients experienced VBT after NAs cessation. Patients with VBT showed a lower $TLR2^+$ monocytes proportion at week 12, an increase in $PD1^+CD8^+$T cells from 12 to 24 weeks, as well as a significant increase in $PD1^+$ HBV antigen-specific $CD8^+$T cells during early 24-week treatment after NAs cessation. Immunofluorescence analysis showed that higher frequencies of intrahepatic $PDL1^+CD68^+$ macrophages and $PD1^+CD8^+$T cells but lower frequencies of $TLR2^+CD68^+$ macrophages were found in VBT patients than those with persistent viral suppression. Moreover, TLR2 agonist and PDL1 blockage resulted in a significant reduction in HBV DNA levels by inducing release of anti-viral cytokines and restoring the function of $CD8^+$T cells.
Conclusion: Early alteration of $TLR2^+$ monocytes and $PD1^+CD8^+$T cells correlated with VBT during Peg-IFN-α treatment after NAs cessation. Diminished TLR2 and enhanced PD1/PDL1 inhibitory pathway may contribute to VBT by inhibiting the functions of mono-macrophages and $CD8^+$T cells.

Abstract #431

Phase 2 Safety and efficacy of oral TLR8 agonist selgantolimod (GS-9688) for 24 weeks in virally-suppressed adult patients with chronic hepatitis B

Gane, Edward J.[1], Zhao, Yang[2], Tan, Susanna[2], Lau, Audrey H.[2], Yang, Jenny C[2], Gaggar, Anuj[2], Subramanian, G. Mani[2], Kottilil, Shyam[3], Tang, Lydia[4]

[1]University of Auckland, New Zealand, [2]Gilead Sciences, Inc, Foster City, California, USA, [3]Division of Clinical Care and Research, Institute of Human Virology, University of Maryland School of Medicine, Baltimore, MD, USA, [4]Division of Clinical Care and Research, Institute of Human Virology, University of Maryland School of Medicine, Baltimore MD, USA

Background: Selgantolimod is an oral small molecule agonist of Toll-like receptor 8 in development for chronic hepatitis B (CHB). We evaluated the safety and efficacy of selgantolimod in CHB patients who were virally suppressed on an oral antiviral (OAV).
Methods: In this multicenter, randomized, double-blind, phase 2 study, 48 patients were enrolled in two cohorts (HBeAg-positive and -negative) evaluating 3.0 mg, 1.5 mg, and placebo (2:2:1) of selgantolimod once weekly for 24 weeks with OAV. Safety assessments included monitoring of adverse events (AE) and laboratory abnormalities. The primary efficacy endpoint was the proportion of patients with $\geq 1\log_{10}$ IU/mL decline in HBsAg levels from baseline at week 24. Secondary endpoints include the proportion of patients with HBsAg and HBeAg loss and changes in pharmacodynamic markers, IL-1RA and IL-12p40.
Results: Baseline characteristics of the 48 patients were similar across groups (table). Grade $\geq$ 3 AEs were observed in 0%, 10%, and 0% of patients treated with 3.0 mg, 1.5 mg, and placebo, respectively, and no tachyphylaxis was observed. One patient (HBeAg-negative, 1.5 mg) achieved the primary endpoint of $\geq 1\log_{10}$ IU/mL decline in HBsAg levels at week 24. One patient (HBeAg-negative, 3 mg) achieved HBsAg loss and another patient (HBeAg-positive, 1.5 mg) achieved HBeAg loss at week 24. Dose-dependent increases in IL-1RA and IL-12p40 in the selgantolimod groups were observed.
Conclusion: Oral selgantolimod is safe, well-tolerated, and induced dose-dependent pharmacodynamic changes in CHB patients. 5% of patients experienced either $\geq 1\log_{10}$IU/mL decline in HBsAg levels or HBsAg loss at week 24. Evaluation of immunologic, antiviral, and pharmacodynamics through week 48 are underway.

	Selgantolimod (GS-9688)		
	3.0 mg	**1.5 mg**	**Placebo**
Characteristic	**n=19**	**n=20**	**n=9**
Baseline Demographics			
Age, years	44 (37-52)	46 (43-52)	48 (41-59)
Male	14 (73.7)	16 (80.0)	6 (66.7)
Asian	11 (57.9)	12 (60.0)	5 (55.6)
HBeAg positive	9 (47.4)	10 (50.0)	5 (55.5)
Baseline HBsAg, $\log_{10}$ IU/mL	3.1 (2.9-3.9)	2.9 (1.9-3.5)	3.2 (3.1-3.7)
Safety parameters			
Grade ≥ 3 AE	0	2 (10.0)	0
AE leading to discontinuation	0	1 (5.0)	0
Grade ≥ 3 lab abnormalities	4 (21.2)	4 (20.0)	1 (11.1)
ALT flare[b]	0	0	0
Pharmacodynamic markers			
IL-1RA concentration ratio, 4 hrs post-dose, Day 1, pg/mL	29.0 (11.7-54.1)	3.0 (2.0-4.6)	1.1 (0.9-1.1)
IL-12p40 concentration ratio, 4 hrs post-dose, Day 1, pg/mL	6.0 (3.9-10.4)	3.0 (1.9-4.4)	0.9 (0.8-1.0)
Median (IQR) by AASLD and Central Lab Criteria			
Abbreviations: OAV, oral antiviral; AE, adverse event; IQR, interquartile range			

Abstract #443

Hepatitis B virus-induced hyperactivation of B cells in chronic hepatitis B patients via TLR4

Jia Bei,[1] Yin Shengxia,[1] Yong Liu,[1] Chao Wu[1]

[1]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China

Background: B cells hyperactivation and function impairment were identified from patients of chronic hepatitis B virus (HBV) infection; however, the underlying mechanism remains unknown. We aim to elucidate the mechanism that are essential for B cell hyperactivation during HBV infection.
Methods: Peripheral CD19+ B cells isolated from 4 HBV patients and 4 healthy volunteers were analyzed by high-through RNA sequencing. Gene-set enrichment analysis for differentially expressed genes (DEGs) between CHB patients and healthy control were analyzed. The expression of B cell activation related genes was further validated by both qPCR and flow cytometry. To further verify the role of TLR4 in B cells activation in vivo during CHB infection, B cells phenotype were determined in hydrodynamic injection (HDI)-based wild type (WT) and TLR4−/− HBV carrier mice, respectively.
Results: 1401 differentially expressed genes were identified from transcriptome-profiles of B cells from CHB patients versus healthy controls. The result indicated that B cells from CHB patients were functional impaired, activation of NF-κB pathway, as well as mitochondrial alteration. The expression of B cell hyperactivation related genes was further verified. Further, in HDI-based-HBV-carrier mice, B cell hyperactivation was observed and TLR4 signaling was activated. In contrast, the ablation of TLR4 failed to induce B cells hyperactivation, and downstream MyD88 and NF-κB were not altered in TLR4−/− HBV carrier mice.
Conclusion: TLR4 pathway play an essential role in B cells hyperactivation in CHB patients, which might serve as a promising target for the restoration of B cell function to treat CHB.

Abstract #510

Hepatitis B virus (HBV) surface antigen (HBsAg) reduction with ISIS 505358 in treatment-naïve chronic hepatitis B (CHB) patients: a phase 2a, randomized, double-blind, placebo-controlled study

Yuen, Man Fung[1], Heo, Jeong[2], Jang, Jeong-Won[3], Yoon, Jung-Hawn[4], Kweon, Young-Oh[5], Park, Sung-Jae[6], Bennett, C. Frank[7], Kwoh, T. Jesse[7]

[1]Queen Mary Hospital, The University of Hong Kong, Hong Kong, [2]Medical Research Institute, Pusan National University Hospital, Busan, Republic of Korea, [3]Seoul St. Mary's Hospital, the Catholic University of Korea, Seoul, Republic of Korea, [4]Seoul National University Hospital, Seoul, Republic of Korea, [5]Kyungpook National University Hospital, Daegu, Republic of Korea, [6]Inje University Busan Paik Hospital, Busan, Republic of Korea, [7]Ionis Pharmaceuticals Inc., Carlsbad, CA USA

Introduction: HBsAg plays a major role in persistent HBV infection. ISIS 505358 (now known as GSK3228836 or GSK836) is a 2´-MOE modified antisense oligonucleotide targeting all HBV RNAs. **Objectives:** The study aim was to evaluate antiviral activity and safety. **Methods:** Patients were treatment-naïve, HBeAg positive or negative, with HBV DNA $\geq 2 \times 10^3$ IU/mL and HBsAg $\geq$ 50 IU/mL. Excluded were patients with liver cirrhosis, HCV, HIV, or HDV coinfection, or ALT or AST $> 5 \times$ ULN. Treatment was administered subcutaneously on Days 1, 4, 8, 11, 15, and 22 with antiviral assessment on Day 29.
Results: At 300 mg GSK836 (n = 12), HBsAg and HBV DNA mean $\pm$ SD changes from baseline were $-$ 1.556 $\pm$ 1.379 (p = 0.001 vs placebo (0.000 $\pm$ 0.112), n = 6) and $-$ 1.655 $\pm$ 1.479 ($p < 0.001$ vs placebo ($-$ 0.001 $\pm$ 0.471)) log10 IU/mL, respectively. Three and 4 patients had HBsAg and HBV DNA reductions $>$ 3.0 log10 IU/mL, where 2/3 and 1/4 were reduced to below the lower limit of quantitation (LLoQ, 0.05 and 20 IU/mL, respectively). One SAE of post-GSK836 treatment ALT flare to 781 U/L (24 $\times$ ULN) occurred in a patient with HBsAg and HBV DNA reductions to $<$ LLoQ. Post-GSK836 ALT flares of 1.7 and 15 $\times$ ULN occurred in two other patients with HBsAg reduction $>$ 3.0 log10 IU/mL. Flares were asymptomatic and self-resolved. The most common adverse events for GSK836 patients (7 of 18) were at injection sites.
Conclusion: Significant inhibitory activity against HBsAg and HBV DNA were observed with 4-week GSK836 treatment. The tolerability and safety were acceptable for proceeding to longer treatment durations. This study was financially supported by GlaxoSmithKline.

Abstract #653

Baseline characteristics could predict the clinical outcome after antiviral therapy in decompensated HBV-related cirrhosis patients

Qi Wang[1], Hong Zhao*[,1], Ligai Liu[1], Changling Luo[1],Yanbin Wang[1], Ting Zhang[1],Yin Fan[1], Rui Ding[1], Jingjing Wang[1], Ying Cao[1], Cheng Cheng[1], Wen Xie[1]

[1]Center of Liver Diseases, Beijing Ditan Hospital, Capital Medical University, 100015 Beijing, China

Objectives: To investigate baseline indicators which could be predictors for re-compensation status and liver-related endpoints events after antiviral therapy in decompensated hepatitis B virus (HBV)-related cirrhosis patients.
Methods: A prospective cohort of patients who were first diagnosis with decompensated ascites from hepatitis B liver cirrhosis were followed up for 48 weeks. Entecavir was given to the all patients at the baseline. Then the patients were divided into two groups according to the decompensation status within 48-week and the baseline characteristics were analyzed.
Results: A total of 95 patients were enrolled and followed up for 48 weeks. The proportion of patients who did not experience decompensation within 48 weeks was 64% (61/95). There were significant differences in age, PLT, ALT, AST, TBIL, DBIL, HDL-C, AFP, MELD, and portal vein width between the two groups ($P < 0.05$). Multivariate logistic regression analysis showed age, PLT, AST, portal vein, and the width is all related to the re-compensation event.
Conclusion: Baseline age, platelet count, AST and portal vein width are effective indicators for predicting re-compensation in patients with decompensated hepatitis B cirrhosis (ascites) for 48 weeks.

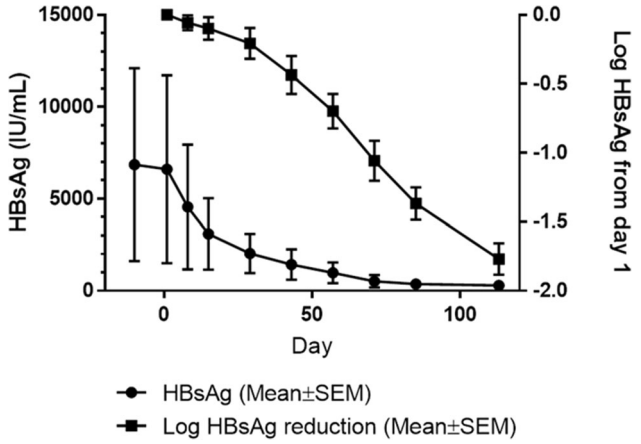
Abstract #763

First clinical experience with RNA interference [RNAi]-based triple combination therapy in chronic hepatitis B (CHB): JNJ-73763989 (JNJ-3989), JNJ-56136379 (JNJ-6379) and a nucleos(t)ide analogue (NA)

Yuen Man-Fung[1], Locarnini Stephen[2], Given Bruce[3], Schluep Thomas[3], Hamilton James[3], Biermer Michael[4], Kalmeijer Ronald[5], Beumont Maria[5], Lenz Oliver[4], Cloherty Gavin[6], Jackson Kathy[2], Ferrari Carlo[7], Lai Ching Lung[1], Liu Kevin Sze-Hang[1], Mak Lung-Yi[1], Wong Danny Ka-Ho[1], To Wai-Pan[1], Ko Kwan-Lung[1], Gish Robert G.[8]

[1]Department of Medicine, The University of Hong Kong, Hong Kong, China; [2]Research & Molecular Development, Victorian Infectious Disease Reference Laboratory, Victoria, Australia; [3]Clinical Development, Arrowhead Pharmaceuticals, Pasadena, CA, United States; [4]Janssen Research & Development, Janssen Pharmaceuticals BV, Beerse, Belgium; [5]Janssen Research & Development, Janssen, Titusville, NJ, USA; [6]Global Scientific Affairs, Abbott Diagnostics, Chicago, IL, United States; [7]Infectious Diseases and Hepatology, University of Parma, Parma, Italy; [8]Hepatitis B Foundation, Doylestown, PA, USA

Introduction: In AROHBV1001, combining the RNAi, JNJ-3989 with a NA in CHB patients achieved additive/synergistic antiviral effects and was well tolerated, so triple-combination therapy may increase functional cure rates after finite treatment.
Objectives: JNJ-3989, JNJ-6379 (class-N capsid assembly modulator [CAM-N]) and NA triple-combination therapy was explored in an additional AROHBV1001 cohort.
Methods: 12 CHB patients received 3 JNJ-3989 doses (200 mg subcutaneously, days [D] 1, 29 and 57) + oral JNJ-6379 250 mg QD for 12 weeks with continued NA treatment. Assessments included safety, qHBsAg, qHBeAg, qHBV-DNA, qHBV-RNA and qHBcrAg levels. Planned follow-up is 1 year.
Results: All patients were Asian (median age 46 years; 8 males; HBeAg 4 positive/8 negative; 7 NA-experienced) and received all planned doses of JNJ-3989 and JNJ-6379 (follow-up 17–64 days). No deaths, discontinuations, serious/severe adverse events (AEs) or clinically-significant vital sign/laboratory findings, and two AEs (mild respiratory infection, not related), were reported. Mean HBsAg (SE) $\log_{10}$ reductions during treatment (Figure) were 1.4 (0.12) (D85, n = 12) and 1.8 (0.11) (D113, n = 7). All patients with $>$ 1000 IU/mL HBV-DNA on D1 (n = 6, 3.7–7.7 $\log_{10}$ IU/mL) had a rapid decline in DNA. Nine patients had quantifiable HBV-RNA (D1, 1.75–7.5 $\log_{10}$ IU/mL); 6 were $<$ limit of quantification by D29. Patients positive (D1) for HBeAg (n = 4) and HBcrAg (n = 8) all had reductions in these parameters.
Conclusion: In the first study to investigate the RNAi (JNJ-3989), CAM-N (JNJ-6739) and NA triple combination in CHB patients, the combination was well tolerated and achieved robust reductions in HBsAg and other measurable viral parameters.



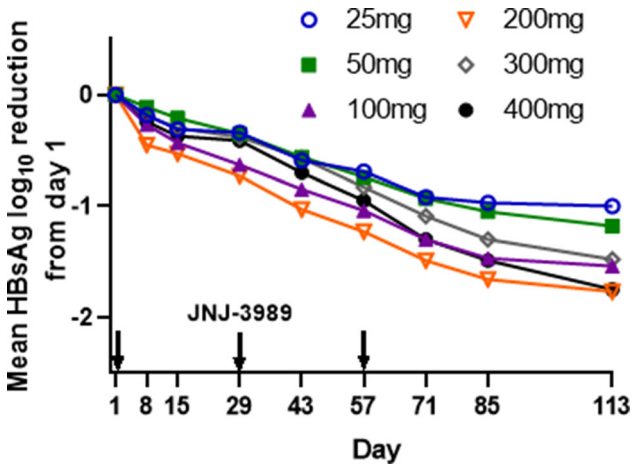
Abstract #777

Dose response with RNA interference (RNAi) therapy JNJ-3989 combined with nucleos(t)ide analogue (NA) treatment in expanded cohorts of patients (pts) with chronic hepatitis B (CHB)

Gane Edward[1], Locarnini Stephen[2], Lim Tien Huey[3], Strasser Simone[4], Sievert William[5], Cheng Wendy[6,7], Thompson Alex[8], Given Bruce[9], Schluep Thomas[9], Hamilton James[9], Biermer Michael[10], Kalmeijer Ronald[11], Beumont Maria[11], Lenz Oliver[10], Cloherty Gavin[12], Wong Danny[13], Schwabe Christian[1], Jackson Kathy[2], Ferrari Carlo[14], Lai Ching Lung[13], Gish Robert G.[5], Yuen Man-Fung[13]

[1]Clinical Services, Auckland Clinical Studies, Auckland, New Zealand; [2]Research & Molecular Development, Victorian Infectious Disease Reference Laboratory, Victoria, Australia; [3]Department of Gastroenterology, Middlemore Hospital, Auckland, New Zealand; [4]Hepatology Clinical Trials, Royal Prince Alfred Hospital, Sydney, Australia; [5]Gastrointestinal and Liver Unit, Monash Health and Monash University, Melbourne, Australia; [6] Department of Gastroenterology and Hepatology, Royal Perth Hospital, Perth, Australia; [7]Linear Clinical Research, Perth, Australia; [8]Department of Gastroenterology St. Vincent's Hospital, Melbourne, Australia; 9Clinical Development, Arrowhead Pharmaceuticals, Pasadena, CA, USA; [10]Janssen Research & Development, Janssen Pharmaceuticals BV, Beerse, Belgium; [11]Janssen Research & Development, Janssen,, Titusville, NJ, USA;[12]Global Scientific Affairs, Abbott Diagnostics, Chicago, IL, USA; [13]Department of Medicine, The University of Hong Kong, Hong Kong, China; [14]Infectious Diseases and Hepatology, University of Parma, Parma, Italy; [15]Hepatitis B Foundation, Doylestown, PA, USA

Introduction: JNJ-3989 silences HBV RNA transcripts from episomal cccDNA and integrated HBV DNA. In AROHBV1001 (phase 2a), JNJ-398 and an NA resulted in: $\geq$ 1 $\log_{10}$ HBsAg reduction; reduction of measurable viral products; was well tolerated.
Objectives: 100–400 mg cohorts were expanded and 2 lower dose cohorts were added.
Methods: HBeAg-positive/-negative, NA-experienced/-naïve CHB pts were enrolled, and received 3 subcutaneous JNJ-3989 doses (25, 50, 100, 200, 300, 400 mg; days 1, 27, 57). Pts started/continued with an NA (day 1) and continued throughout. Safety and viral parameters (HBsAg, HBeAg, HBV DNA, RNA, HBcrAg) were assessed.
Results: No treatment discontinuations or drug-related serious adverse events occurred. At day 113 (typical mean nadir after 3 doses, 56 days after last dose), mean HBsAg (SE) $\log_{10}$ reduction from day 1 (n = 8) was 1.00 (0.18; 25 mg), 1.18 (0.08; 50 mg), 1.54 (0.18; 100 mg), 1.77 (0.18, n = 7, 200 mg), 1.48 (0.11; 300 mg) and 1.75 (0.16; 400 mg) (Figure). 4/8 (25 mg), 5/8 (50 mg), 7/8 (100 mg), 8/8 (200 mg), 8/8 (300 mg) and 8/8 (400 mg) patients achieved $\geq$ 1.0 $\log_{10}$ reduction in HBsAg from day 1 at nadir. For pts with HBsAg > 100 IU/mL (day 1), 2/7 (25 mg), 3/8 (50 mg), 5/7 (100 mg), 6/6 (200 mg), 6/8 (300 mg) and 5/7 (400 mg) achieved HBsAg < 100 IU/mL at day 113. HBV DNA, RNA, HBeAg and HBcrAg declined under treatment.
Conclusion: JNJ-3989 monthly doses, 25–400 mg, with an NA were well tolerated in CHB patients. With 100–400 mg JNJ-3989, 97% of patients (31/32) achieved a $\geq$ 1.0 $\log_{10}$ HBsAg reduction; the 25 mg and 50 mg doses were active but seemed less effective.



Abstract #854

Peg-interferon alpha add-on tenofovir disoproxil fumarate results in more HBsAg decline compared to de novo combination in HBeAg positive chronic hepatitis B naïve patients

Li Jing[1], Gong Qiming[2], Zhang Jiming[3], Qu Lihong[4], Sun Xuehua[5], Zhang Qin[6], Zhang Xinxin[1]

[1]Research Laboratory of Clinical Virology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, [2]Department of Infectious Diseases, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, [3]Department of Infectious Diseases, Huashan Hospital, Fudan University, Shanghai, China, [4]Department of Infectious Diseases, East Hospital, Tongji University, Shanghai, China, [5]Liver Disease Department, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, China, [6]Department of Infectious Diseases, Tongren Hospital Shanghai, Jiaotong University School of Medicine, Shanghai, China

Introduction: Combining peg-interferon alpha (peg-IFNα) with a nucleotide analogue could result in higher rates of HBsAg loss than either therapy given alone.
Objectives: This study aimed to compare the antiviral efficacy between peg-IFNα add-on tenofovir (TDF) therapy and de novo combination therapy in chronic hepatitis B naïve patients.
Methods: 13 de novo combination patients received TDF combination peg-IFNα for 48 weeks then TDF for 48 weeks, matched to 13 patients received TDF alone for 48 weeks and sequentially added on peg-IFNα for 48 weeks by age and sex.
Results: Clinical characteristics at baseline were comparable. At week 48, HBsAg was no difference between two groups, however, from week 48 to week 96, the decrease of HBsAg in add-on group was significantly higher than de novo combination group (p = 0.001).

At week 96, 2 patients in add-on group achieved HBsAg clearance and none in de novo combination group. And a larger proportion of patients in add-on group showed ≥ 1.5 log10 IU/mL reduction of HBsAg level compared to de novo combination group (p = 0.02). The Kaplan-Meier cumulative estimate rates of HBeAg seroconversion and HBeAg loss did not differ significantly between groups. The percentage of patients with HBV-DNA < 20 IU/mL and ALT normalization rate were similar. Side effects were mild and well tolerated.

Conclusion: Compared to de novo combination, the addition of peg-IFNα in TDF-treated one year patients showed more HBsAg decline at 96 weeks and may be an effective strategy for the treatment of HBeAg positive CHB naïve patients.

Abstract #912

Evaluation of the cobas® Plasma Separation Card as a sample type for hepatitis B virus viral load quantification on the cobas® 6800 system

Rando, Ariadna[1], Rodrigo-Velásquez, Fernando[1], Salmerón, Paula[1], Riveiro-Barciela, Mar [2,3], Esteban, Rafael[2,3], Buti, María[2,3], Marins, Ed G[4], Rodríguez-Frías, Francisco[3, 5]

[1]Department of Microbiology, Vall d'Hebron University Hospital, [2]Department of Hepatology, Vall d'Hebron University Hospital, [3]Center for Biomedical Research in Network of Hepatic and Digestive Diseases (CIBERehd), [4]Roche Molecular Systems, Inc. Pleasanton, CA, USA, [5]Liver Pathology Unit, Biochemistry and Microbiology Departments, Vall d'Hebron University Hospital

Introduction: Improving access to diagnostic testing in resource-limited settings is critical to achieving hepatitis elimination goals and expanding coverage in these regions. Alternative sample types, such as the cobas® Plasma Separation Card (PSC), can facilitate the utilization of HBV diagnostic testing by permitting the use of finger-prick blood to prepare dried plasma spots that are stable under high temperature and humidity conditions, allowing for sample transportation without the need of cold-chain.
Objectives: To evaluate PSC performance for HBV viral load (VL) quantification compared to plasma.
Methods: Whole EDTA venous blood from 67 clinical samples (HBsAg positive and HBV VL detected) used to prepare liquid EDTA plasma and PSC samples (PSC: 140 µL of whole EDTA venous blood). PSC plasma spots were eluted (56 °C with Specimen Pre-Extraction Reagent for 10 min at 1000 rpm on a preheated thermo-shaker) and analyzed with liquid plasma EDTA samples using the cobas® HBV Test on the cobas® 6800 system.
Results: VL correlation between PSC and plasma samples was linear (slope = − 1.24, intercept = 0.83, R^2 = 0.89), with mean VL difference of − 1.81 log10 IU/mL (95% CI − 2.22 to − 1.40). Detection with PSC above 1000 IU/mL was 100%.
Conclusion: Demonstration of PSC as an alternative sample type, with linear correlation to plasma VL when tested with cobas® HBV Test, indicating that a correction factor could be applied to better align the PSC and plasma VL. Results support the feasibility of PSC as an alternative sample type for detection and viral load monitoring of HBV.

Abstract #927

Similar hepatic fibrosis in chronic hepatitis B patients with or without fluctuating viremia

Faisal M Sanai[4,5], Ahmad Alhouthali[1], Hamdan Alghamdi[2,3], Feras Badriq[1], Mohammed Mujalled[1], Waleed Khayyat[1], Motaz Attar[1], Basil Bagadeem[1], Alaa M Meer[4], Waleed Alshumrani[3,4], Khalid Albeladi[4], Faisal A Batwa[3,4]

[1]College of Medicine, King Saud Bin Abdulaziz University for Health Sciences – Jeddah; [2]Hepatology Division, Department of Hepatobiliary Sciences and Organ Transplant Center, King Abdulaziz Medical City, Riyadh; [3]King Saud bin Abdulaziz University for Health Sciences and King Abdullah International Medical Research Center, Ministry of National Guard Health Affairs, Riyadh; [4]Gastroenterology Unit, Department of Medicine, King Abdulaziz Medical City, Jeddah; [5]Liver Disease Research Center, College of Medicine, King Saud University, Riyadh, Saudi Arabia

Background/aims: The accurate identification of inactive chronic hepatitis B virus (HBV) carriers from those with active carriers is difficult because of wide and frequent HBV DNA fluctuations. We aimed to assess if fluctuating HBV DNA levels impacted on the presence of significant hepatic fibrosis (Metavir F2-4) in HBeAg-negative chronic HBV patients.
Methodology: Untreated HBeAg-negative patients (n = 175) with fluctuating HBV DNA above or below a level of 2000 IU/mL (n = 50) were included and compared to those without fluctations (n = 125). Hepatic fibrosis (transient elastography, FibroScan®) was correlated with virologic and biochemical profiles of consecutive carriers.
Results: Mean age of the patients was 47.5 ± 12.5 years and 76 (43.4%) were male. HBV DNA fluctuations were frequent and occurred in 28.6% of the overall cohort. Patients with fluctuating viremia had higher $\log_{10}$ qHBsAg (3.2 ± 0.8 vs. 2.8 ± 1.0, $P = 0.009$) and HBV DNA (3.5 ± 0.4 vs. 2.8 ± 1.2, $P < 0.001$) compared to those without fluctuations. Fluctuating viremia patients' qHBsAg $\log_{10}$ (3.2 ± 0.8) was also higher than those with persistently low (HBV DNA < 2000 IU/mL) viremia level (2.6 ± 1.0, $P = 0.001$). Patients with F2-4 were more likely to have higher BMI ($P = 0.033$), AFP (P = 0.012), AST ($P < 0.001$) and ALT levels ($P = 0.021$). Presence of F2-4 fibrosis in those with fluctuating HBV DNA was numerically lower (6%) but not significantly different from those without (15.2%, $P = 0.130$), or from those with persistently low viremia (14.6%, $P = 0.193$).
Conclusions: Fluctuating HBV DNA levels occur frequently but do not distinguish patients with higher prevalence of significant fibrosis. Minor fluctuations of HBV DNA levels are unlikely to be of clinical relevance. Patients with higher qHBsAg levels tend to have greater frequency of fluctuating viremia.

Abstract #960

Compare & correlation between IL-2 & IL-10 after Hepatitis B vaccination in Bangladeshi Patient

Marufa Hossain

Introduction: Hepatitis B virus (HBV) causes chronic infectious which is vaccine preventable where 5%-15% of healthy recipients fail to generate protective levels of antibodies after standard immunization.
Objectives: The present study was designed to compare the expression of host genes, namely IL-2, IL-10 in PBMCs & correlate

AntiHBs with these cytokines among vaccine responders, poor responders, non-responders and unvaccinated individuals.
Methods: This cross-sectional study was conducted between January to December 2012. A total 60 (15 responders, 15 poor responders, 15 non responders and 15 unvaccinated) subjects were enrolled for this study at the Department of Virology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. All data were collected from the vaccinees coming to test for anti-HBs titer 6-8 weeks after receiving hepatitis B vaccine. Data was analyzed by SPSS.
Result: The mean expression of IL-2 gene in responder group was 2.52 ± 0.78 fold, poor responder group 2.21 ± 0.39 fold, non-responder group 1.67 ± 0.41 fold & unvaccinated group 1.00 ± 0.24 fold. The mean expression of IL10 in responder group was 1.53 ± 0.26 fold, poor responder group 1.19 ± 0.32 fold, non-responder group 1.59 ± 0.27 fold, & unvaccinated group 1.08 ± 0.41 fold. Compared with Anti HBs between responder, poor responder and non-responder groups IL-2 production showed a significant positive correlation ($r = 0.675$) & a negative correlation was observed between IL-10 production and Anti HBs response ($r = -0.310$) among these people.
Conclusion: Thus, cytokine production is an important signal to evaluate the outcome of the immune response after vaccination.

Abstract #1009

Management of patients with hepatitis B virus reactivation post-DAA treatment of chronic hepatitis C virus infection in HCV–HBV coinfected patients with pretreatment HBeAg seroconversion and early degree of hepatic fibrosis

Ali A. Ghweil[1], Heba Ahmed Osman[1*], Abeer M. M. sabry[2], Reem E. Mahdy[3] Ashraf Khodeary[4]

[1]Tropical Medicine and Gastroenterology Department, Faculty of Medicine, South Valley University, Qena, Egypt, [2]Internal medicine and Gastroenterology Department, Faculty of Medicine, Helwan University, Helwan, Egypt, [3]Internal medicine Department, Faculty of Medicine, Assiut University, Assiut, Egypt, [4]Clinical Pathology Department, Faculty of Medicine, Sohag University, Sohag, Egypt

Background and aim: Hepatitis C virus (HCV)–HBV coinfection is a significant health problem with rapid progression of liver disease without precise diagnosis and treatment. We aimed in this study to identify if there were any role of HBV antiviral therapy in patients with HBV reactivation after direct-acting antiviral therapy in HCV–HBV coinfected patients.
Methods: A prospective random study was carried out on 140 patients presenting with chronic HCV and chronic HBV coinfection. All patients had pretreatment HBeAg seroconversion, HBV DNA $<$ 2000 IU/mL, normal liver enzymes, and F0/F1 hepatic fi brosis. They treated with sofosbuvir 400 mg and daklatasvir 60 mg once daily for 3 months. All patients underwent pretreatment hepatic fibrosis assessment using Fibro Scan and laboratory investigations: platelet count, liver-function tests, quantitative HCV PCR, HBsAg, HBc IgG, HBeAg, and HBeAb. All patients were followed up at 1, 3, 6, and 12 months from the start of HCV therapy.
Results: The study enrolled 140 HCV–HBV coinfected patients: 55% were F0 and the rest F1. All our patients had negative HCV PCR at 1-month posttreatment and had achieved sustained virologic response with negative HCV PCR 3 months after treatment end. Four patients showed HBV reactivation with raised HBV DNA PCR and liver enzymes. Their mean age was 23.7 ± 2.7 years, and three were male. Regarding patients with HBV reactivation, at 12 months posttreatment they showed significant decreases in liver enzymes, bilirubin, and INR, with increased platelet count ($P = 0.001$), each with undetectable HBV PCR ($P = 0.001$).
Conclusion: HBV–HCV coinfected patients with no/mild hepatic fibrosis, HBeAg seroconversion, and HBV DNA $<$ 2000 IU/mL can complete direct-acting antiviral therapy without HBV antiviral treatment with close monitoring.

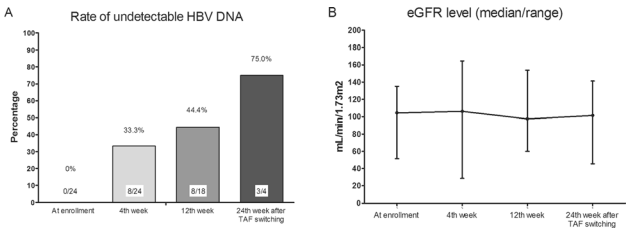
Abstract #1017

Tenofovir alafenamide for chronic hepatitis B patients with advanced fibrosis and partial virologic responses to oral nucleos(t)ide analogues: an interim report

Ming-Lung Yu[1], Ming-Lun Yeh[1], Chi-Yi Chen[2], Pin-Nan Cheng[3], Ming-Jong Bair[4], Jyh-Jou Chen[5], Ching-Chu Lo[6], Chi-Ming Tai[7], Ching-Yang Tsai[8], Kuo-Chih Tseng[9], Chien-Hung Chen[10], Chao-Hung Hung[11], Jee-Fu Huang[1], Chia-Yen Dai[1], Wan-Long Chuang[1]

[1]Hepatitis Center and Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [2]Division of Gastroenterology and Hepatology, Ditmanson Medical Foundation Chia-Yi Christian Hospital, Chia-Yi, Taiwan, [3]Division of Gastroenterology and Hepatology, National Cheng Kung University Hospital, Tainan, Taiwan, [4]Division of Gastroenterology and Hepatology, Taitung MacKay Memorial Hospital, Taitung, Taiwan, [5]Division of Gastroenterology and Hepatology, Chi Mei Medical Center, Liouying, Taiwan, [6]Division of Gastroenterology and Hepatology, St. Martin De Porres Hospital, Chia-Yi, Taiwan, [7]Division of Gastroenterology and Hepatology, E-Da Hospital, Kaohsiung, Taiwan, [8]Division of Gastroenterology and Hepatology, Yuan's General Hospital, Kaohsiung, Taiwan, [9]Division of Gastroenterology and Hepatology, Dalin Tzu Chi Hospital, Chia-Yi, Taiwan, [10]Division of Gastroenterology and Hepatology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, [11]Division of Gastroenterology and Hepatology, Chiayi Chang Gung Memorial Hospital, Chia-Yi, Taiwan

Background/aim: The current study aim to investigate the efficacy and safety of tenofovir alafenamide (TAF) switching for chronic hepatitis B (CHB) patients with advanced fibrosis and partial virological response to other nucleot(s)ide analogue (NUC).
Patients and methods: CHB patients with advanced fibrosis (stage 3 or 4) and under NUC (except TAF) therapy with detectable hepatitis B virus (HBV) DNA for $>$ 52 weeks are enrolled to TAF 25 mg/day for 96 weeks. The objectives are viral suppression, alanine aminotransferase (ALT) normalization and safety.
Results: From Feb. 2019, 24 patients, including 14 (58.3%) with entecavir, 9 (37.5%) TDF and one (4.2%) lamivudine, were enrolled (7 [29.2%] male, median 53 years). The fibroscan demonstrated a mean of 10.6 kPa (6 [25%] cirrhotic). Ten (41.7%) patients were HBV e antigen positive, two (8.3%) had YMDD mutation. The median HBV DNA level declined from 64 IU/mL at enrollment to 28.5 IU/mL at 4th week, 21 IU/mL at 12th week, and undetectable at 24th week, respectively, after TAF switching, with undetectable HBV DNA in 8/24 (33.3%), 8/18 (44.4%), and 3/4 (75.0%) patients (figure 1A) and rate of ALT normalization of 91.7%, 87.5%, 94.4%, and 100%, respectively, after TAF switching. Serum creatinine and eGFR levels were stable after TAF switching (figure 1B). Only mild degrees of adverse events were considered unrelated to treatment.
Conclusion: The preliminary results demonstrated the TAF switching is effective and safe in viral suppression for CHB patients with advanced fibrosis and partial virologic responses to other NUCs.



Abstract #1045

A phase I clinical trial of TLR7 agonist (RO7020531) in Chinese healthy subjects

Luk Andrea[1], Tryatni Miriam[2], Glavini Katerina[2], Zhao Na[3], Upmanyu Ruchi[4], Racek Tomas[2], Hoppe Steffen[2], Fok Benny[1], Retout Sylvie[2], Grippo F. Joseph[5], Jin Yuyan[6], Zhu Yonghong[6], Jiang Qiudi[6]

[1]Phase 1 Clinical Trial Centre, The Chinese University of Hong Kong, Hong Kong SAR, China, [2]Roche Innovation Center Basel, Switzerland, [3]Roche Pharma Development Shanghai, China, [4]Roche Pharma Development Welwyn, UK, [5]Roche Innovation Center New York, US, [6]Roche Innovation Center Shanghai, China

Introduction: RO7020531, an oral double prodrug of the TLR7 agonist, is in clinical development as part of a curative regimen against chronic hepatitis B. The safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) in Chinese healthy subjects following single and multiple ascending doses (SAD and MAD) of RO7020531 are reported.
Methods: Four SAD cohorts and three MAD (receiving RO7020531 every other day, QOD, for 14 days) cohorts with 10 subjects (8 active, 2 placebo) each were completed. Safety and tolerability were monitored throughout the study. Blood PK and PD samples were collected.
Results: 155 adverse events (AEs) were reported in 49 subjects, 51 of which in 18 subjects were assessed as treatment related. Most of the AEs were mild; 9 subjects experienced moderate AEs; there were no severe AEs. In two MAD cohorts receiving 150 mg, 7 out of 20 subjects experienced pyrexia and were discontinued due to transient asymptomatic lymphopenia, which resolved 24–48 h post dose. The AUC of the active metabolite, RO7011785, increased in a dose proportional manner from 40 to 170 mg. There was no PK accumulation following the QOD dosing. Population PK analyses confirmed no race effect on PK of RO7011785.
Single and multiple doses of RO7020531 resulted in dose-dependent increases in TLR7 response markers (cytokines, chemokines and transcriptional responses) at 100 mg or above, and flu-like symptoms were associated with higher interferon-α levels.
Conclusion: RO7020531 was safe and acceptably tolerated in Chinese healthy subjects in single doses up to 170 mg and multiple doses up to 150 mg QOD.

Abstract #1065

Evaluation of non-invasive diagnostic methods as indicators of fibrosis in patients with chronic hepatitis B

Kadri Atay[1], Yusuf Kayar[2]

[1]Mardin State Hospital, Department of Gastroenterology, Artuklu, Mardin, Turkey, [2]Van State Hospital, Department of Gastroenterology, Van, Turkey

Introduction: Liver biopsy is recommended before antiviral treatment for patients with chronic hepatitis B (CHB). Although liver biopsy is the gold standard procedure, many noninvasive tests have been established for the determining of liver damage. The aim of this study was to evaluate the efficacy of several indirect markers of liver fibrosis (APRI, AP, FIB4, AST/ALT ratio) in patients with CHB
Methods: In total 91 patients with chronic hepatitis B were included. Then patient with CHB infection were divided as a mild and advanced fibrosis and this two groups were compared
Results: The mean age was 39.5 $\pm$ 14.9.The areas under receiver operating characteristic curve in the prediction of significant fibrosis were 0.756, 0.849, 0.742 and 0.825 for APRI, FIB-4, AST/ALT ratio, and AP index and FIB-4 score, AP index were the best indicators for the detection of advanced fibrosis. For FIB 4 and AP index, the cut-off value for the prediction of advanced fibrosis were $\geq$ 1.05 and $\geq$ 3.5 with a sensitivity and specificity of 87%,74% and 62%,75% respectively.
Conclusion: According to the results of our study, FIB 4 score and AP index may be considered as a good indicator for predicting advanced fibrosis in CHB subjects.

Abstract #1120

Fatty liver is common, but did not predict adverse liver and non-liver outcomes in chronic hepatitis B patients

Sui-Weng Wong[1], Wah-Kheong Chan[1], Rosmawati Mohamed[1]

[1]Gastroenterology and Hepatology Unit, Department of Medicine, University Malaya Medical Centre, Kuala Lumpur, Malaysia

Background: Non-alcoholic fatty liver disease (NAFLD) is increasingly common and has been implicated in progression of liver fibrosis and adverse clinical outcomes in chronic hepatitis B (CHB) patients. We aimed to investigate the impact of hepatic steatosis on liver fibrosis and clinical outcomes in CHB patients.
Methods: Consecutive CHB patients who underwent transient elastography between 2013 and 2017 at a tertiary hospital were included in this longitudinal cohort study. Presence of hepatic steatosis was defined as controlled attenuation parameter, CAP $\geq$ 248 dB/m, while advanced liver fibrosis was defined as liver stiffness measurement, LSM $\geq$ 9.4 kPa. Composite clinical events (mortality, malignancy, liver-related complications, cardiovascular events) were evaluated with Kaplan-Meier analysis and Cox proportional hazards regression.
Results: Our study cohort included 614 patients with median follow-up of 45 months. Hepatic steatosis was present in 294 patients (47.9%) and advanced liver fibrosis was present in 127 patients (21.0%). Presence of hepatic steatosis (OR 1.956, 95% CI 1.250–3.060) and diabetes mellitus (OR: 3.507, 95% CI 2.069–5.944) were independently associated with advanced fibrosis. Advanced fibrosis was independently associated with composite events (HR: 2.496, 95% CI 1.352–4.606), liver-related complications (HR: 3.765, 95% CI 1.380–10.271), and mortality (HR: 3.632, 95% CI 1.342–9.826), but not cardiovascular events and malignancy. Hepatic steatosis was not associated with any adverse clinical events.
Conclusion: Advanced fibrosis, not fatty liver remained the strongest predictor for adverse liver and non-liver outcomes in chronic hepatitis B patients.

Abstract #1131

Both hepatitis A and hepatitis D infection may be associated with more advanced liver disease in patients with chronic hepatitis B

Wu Jer-Wei,[1] Tseng Tai-Chung,[1,2] Liu Chun-Jen,[1,2,4] Su Tung-Hung,[1,2] Liu Chen-Hua,[1,2] Chen Pei-Jer,[1,2,4] Chen Ding-Shinn,[1,2,4,5] and Kao Jia-Horng[1-4]

[1]Division of Gastroenterology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan. [2]Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan. [3]Department of Medical Research, National Taiwan University Hospital, Taipei, Taiwan. [4]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine Taipei, Taiwan. [5]Genomics Research Center, Academia Sinica, Taiwan

Background and aims: Acute infection of hepatitis A virus (HAV) causes transient but varying degree of liver damage. In contrast, hepatitis D virus (HDV) only infects patients with chronic hepatitis B virus (HBV) infection, which may cause chronic and persistent liver damage. We aimed to explore whether both hepatropic virus infections were associated with worse outcomes in patients with chronic HBV infection in a cross-sectional study.
Methods: We collected serum and clinical data from 464 patients with chronic HBV infection, including 160, 150 and 154 patients with hepatocellular carcinoma (HCC), cirrhosis and inactive carrier status, respectively. Serum HAV-IgG and anti-HDV were determined retrospectively and seroprevalence rates of both markers were compared among the groups with different clinical stages.
Results: In the inactive carrier group, 106 (68.83%) and 3 (1.95%) patients had exposure to HAV and HDV infection, respectively. We found higher seropositive rates of HAV-IgG in cirrhosis (82.67%) and HCC (99.38%) groups, but not seropositive rates of anti-HDV (4.67% and 3.75% for cirrhosis and HCC respectively). When combining cirrhosis and HCC groups as patients with advanced liver disease, seropositive HAV and HDV were associated with increased risks of advanced liver disease with odds ratio of 15.69 (95% CI 3.25–75.68, $p < 0.001$) and 12.41 (95% CI 1.40–109.95, $p < 0.05$), respectively.
Conclusions: In the cross-sectional case-control study of patients with chronic HBV infection, both exposure to HAV or HDV infection might be associated with an increased risk of cirrhosis and HCC development.

Abstract #1137

Transcriptional response to RO7020531, a novel double prodrug of a toll-like receptor 7 agonist, in whole blood of healthy subjects and chronic hepatitis B patients

Tomas Racek, Klas Hatje, Tony Kam-Thong, Ruchi Upmanyu, Qiudi Jiang, Katerina Glavini, Yonghong Zhu

Background: RO7020531 is a double prodrug of RO7011785, a selective toll-like receptor 7 (TLR7) agonist. It is currently in Phase 1 study and evaluated in healthy volunteers and chronic hepatitis B (CHB) patients.
Method: To characterize the transcriptional response to TLR7 stimulation in CHB patients, we performed paired-end RNA sequencing in whole blood samples of healthy volunteers and virally suppressed CHB patients who received 140, 150 or 170 mg RO7020531 orally every other day (QOD) in NP39305 study. Study subjects with a pharmacodynamic response were selected for differential gene expression analysis using DESeq2. Up- and down-regulation of genes at multiple time points was compared to pre-dose measurements. Based on these results, gene signature enrichment analysis was performed using fgsea.
Results: QOD dosing with RO7020531 led to a strong activation of Type I and Type II interferon responses including the genes with antiviral property (eg. ISG15, CXCL10, DDX60, IFIT and OAS gene family) that peaked at 6 and 12 hours post-dosing. Interestingly, some pathway signatures e.g. antiviral IFN signature or RIG-I like receptor signaling, were still upregulated even 48 hours post dosing. ImmuneSpace signature enrichment analysis indicated that the response to RO7020531 was mainly driven by monocytes and activated dendritic cells.
Conclusion: RO7020531, induced strong transcriptional response in immune subsets of healthy subjects and CHB patients, supporting the further development of RO7020531 as a component of next generation combination regimens for CHB treatment

Abstract #1138

Early priming of immune system with toll-like receptor 7 agonist enhanced the therapeutic effect of HBV class A core protein allosteric modulator in preclinical efficacy model

Zhou-Xue[1], Yu-Youjun[1], Yao-Xiangyu[1], Zhu-Yonghong[1], Young-A. T, Gao-Lu[1]

[1]Roche Innovation Center Shanghai, Shanghai, China; [2] Roche Innovation Center Basel, Basel, Switzerland

Introduction: HBV class A core protein allosteric modulator (CpAM) and toll-like receptor 7 (TLR7) agonist are new types of therapeutic agents being developed for the treatment of chronic hepatitis B (CHB). Combination of them in preclinical efficacy model has demonstrated superior HBsAg reduction than either agent as monotherapy.
Objectives: Here we evaluated the combinations of CpAM with different short-term treatment schedules of TLR7 agonist in a mouse model with recombinant adeno-associated virus carrying HBV genome (AAV-HBV) to explore the optimal dosing regimen potentially maximizing treatment effect in patients.
Methods: During the 8-week treatment period of a daily CpAM dosing, AAV-HBV infected mice received one or two 2-week treatment cycles of TLR7 agonist. Serum samples were collected weekly for the measurements of viral markers.
Results: CpAM monotherapy substantially reduced serum HBV viral markers, but none of the mice had their HBsAg below the lower limit of quantification (LLOQ). Adding a single 2-week TLR7 agonist treatment cycle at different time points all triggered further HBsAg reduction with more robust effects observed in the early administration groups. With the administration of the second 2-week cycle of TLR7 agonist, HBsAg in all treated mice declined to below the LLOQ, and the effect was sustained during the 12-week off-treatment follow-up.
Conclusion: Early priming of TLR7 agonism can enhance the therapeutic effect of CpAM in preclinical efficacy model, suggesting that fine-tuning the dosing regimen of an immune modulator in combination therapy may provide a favorable risk-benefit ratio for CHB patients.

Abstract #1142

The role of interleukin-22 serum level on liver fibrosis level in chronic Hepatitis B infected patient in Mohammad Hoesin Hospital Palembang

Antoridi D[1], Suyata[1], Bakry AF[1], Bardiman S[1], Busro VO[1], Supriyanto I[1], Rahmayani F[1], Irfannuddin[2]

[1]Division of Gastroenterohepatology, Internal Medicine Department, Faculty of Medicine, Sriwijaya University, Mohammad Hoesin Hospital, Palembang, Indonesia, [2]Faculty of Medicine, Sriwijaya University, Mohammad Hoesin Hospital, Palembang, Indonesia

Introduction: Hepatitis B Virus (HBV) infection is the main cause of liver cirrhosis and hepatocellular carcinoma. Proinflamation or anti-inflammation cytokines Involvement on chronic liver disease correlates with liver inflamation, necrosis, fibrosis level, and liver failure. Invention of interleukin-22 (IL-22) has attracted the attention of the researchers with respect to its hepatoprotective and antifibrotic effects. Protective or proinflamatory role of IL-22 in Hepatitis B Virus infection in humans is still unclear.
Method: This study was cross-sectional study with 48 samples of chronic hepatitis b infected patient, divided into 3 groups based on fibrosis level: F0–F1, F2–F3, and F4 group. Laboratory and ultrasonographic examination were done on each group. IL-22 serum levels were measured using quantitative sandwich enzyme immunoassay technique.
Result: From 48 research subjects, the median of IL-22 level was 21 (14.5–58) pg/ml, where mean of IL-22 level based on the level of fibrosis for F0–F1 group was: 24.925 ± 4.4525 pg/ml, F2–F3 group: 21.019 ± 10.2091 pg/ml, and F4 group: 32.213 ± 11.7335 pg/ml. There was no significant correlation between the serum IL-22 levels and fibrosis levels in this study. The significant mean differences of IL-22 serum levels only happened betweenF4 group and F2–F3 group.
Conclusion: In this study there was no role of serum IL-22 levels on liver fibrosis levels in the chronic Hepatitis B infected patient.

Abstract #1202

Tenofovir disoproxil fumarate directly regresses liver fibrosis by inducing hepatic stellate cell apoptosis

Lee sung won[1,2], Kim sung min[1], Hur wonhee[1], Kang byung-yoon[1], Lee hae lim[1,2], Nam heechul[1,2], Yoo sun hong[1,2], Kwon jung hyun[1,2], Jang jeong won[1,2], Yoon seung kew[1,2]

[1]The Catholic University Liver Research Center, Seoul, Korea, [2]Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea

Objectives: The treatment with tenofovir disoproxil fumarate (TDF) results in the regression of liver fibrosis but its underlying mechanism has not been clarified thus far. We aimed to investigate the direct impact of TDF on activated hepatic stellate cells (HSCs) and liver fibrosis.
Methods: In mouse liver fibrosis models induced by thioacetamide (TAA), TDF and entecavir (ETV) were given by oral gavage for 10 weeks. After sacrificing the mouse, collagen deposition in the liver and markers of activated HSC and fibrosis were measured. Then activated HSC cell lines, LX-2 and HSC-T6 were used to evaluate the effect of TDF and ETV on HSCs. After treatment with each antiviral agent, cell viability, morphology, apoptotic feature, apoptosis and anti-fibrosis signaling pathways were determined.
Results: After TDF treatment, fibrotic area, hydroxyproline, α-SMA, Col1α1, and TIMP-1 were significantly decreased in the liver fibrosis mouse model but not after ETV. Apoptotic nuclei were concentrated at the periportal fibrotic area merging on α-SMA stains which indicated the cell death of activated HSCs. In HSC cell lines, viabilities of LX-2 and HSC-T6 were decreased with apoptotic features, and PARP, Caspase-3 were cleaved with inhibition of the anti-apoptotic gene Bcl-xl indicating the apoptosis of HSCs. Inactivation of the PI3K/Akt signaling pathway through inhibition of phosphorylation was observed in association with the anti-fibrotic effects.
Conclusion: TDF directly regresses liver fibrosis by inducing HSC apoptosis. Anti-fibrotic effects of TDF may be considered in the selection of antiviral drug for chronic hepatitis B (CHB) patients and as a therapeutic agent for the treatment of liver fibrosis.

Abstract #1224

HBV induces liver fibrosis through regulating TGF-β1/Nur77 pathway

Li Wen-ting[1], Yin Ming[2], Xiao Hui[1], Yang Liang[1]

[1]Liver Unit, Department of Infectious Disease, Anhui Provincial Hospital, he First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, 230000, Anhui, P.R. China. [2]Intensive Care Unit, Department of Infectious Disease, Anhui Provincial Hospital, he First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, 230000, Anhui, P.R. China

Objective: To investigate the role of TGF-β1/Nur77 in HBV induced liver fibrosis.
Methods: NTCP-Huh7.5.1 was constructed by transfecting pCMV6-NTCP into Huh 7.5.1 cells to explore effects of HBV replication and TGF-β1 expression. LX-2 cells was incubated with TGF-β1 in the presence of Nur 77 gRNA and qPCR was used to observe Nur 77, α-SMA, TIMP-1 and CoL1A1 mRNA expression in LX-2 cell. Our study engaged a co-culture system in the presence of Nur 77 gRNA to observe the relationship between HBV replication and liver fibrosis. HE, Masson's and immunohistochemistry (IHC) staining were used to detect Nur 77 expression in liver tissue.
Results: Western-blot showed that pCMV6-NTCP could express in Huh 7.5.1 cells. NTCP-Huh 7.5.1 cells strongly supported HBV replication. At 3 days after infection, HBV DNA level in supernatant was $5.39 \pm 0.96 \times 10^4$ copies/ml ($P < 0.01$), HBV infection enhanced TGF-β1 mRNA expression in NTCP-Huh 7.5.1 cells (1.94 vs 1.00, $P < 0.01$). At 72 h after TGF-β1 incubation, mRNA expression of Nur77, α-SMA, TIMP-1 and CoL1A1 expression was up-regulated significantly compared to control group ($P < 0.05$), which can be inhibited by Nur77 gRNA ($P < 0.05$). Co-cultured with HBV infected NTCP-Huh 7.5.1 cells for 72 h, mRNA expression of Nur77, α-SMA, TIMP-1 and CoL1A1 expression was up-regulated significantly compared to control group ($P < 0.05$), which can be inhibited by Nur77 gRNA ($P < 0.05$). IHC showed a higher Nur 77 level in severe fibrosis liver ($\geq$ S2) than in mild fibrosis liver ($\leq$ S1).
Conclusions: HBV contributes to liver fibrosis through up-regulating TGF-β1/Nur77 signaling pathway.

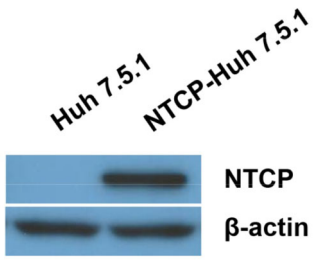


Figure 1 Expression of NTCP in Huh 7.5.1 and NTCP-Huh 7.5.1 cells by Western-blot

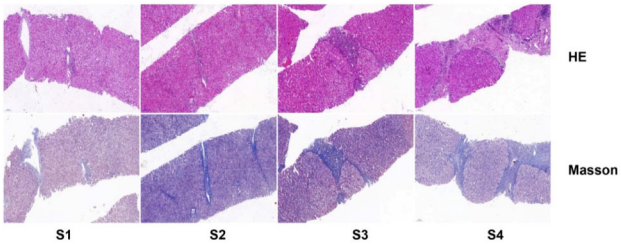


Figure 5 Liver fibrosis stage assessed by HE and Masson staining (×100)

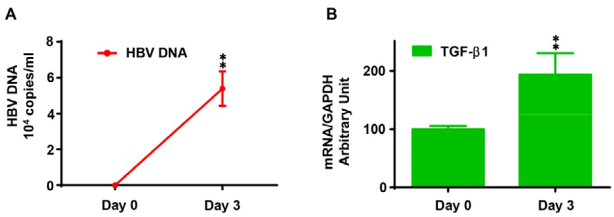


Figure 2 HBV replication and TGF-β1 expression in NTCP-Huh 7.5.1 cells.
· · *P*<0.01

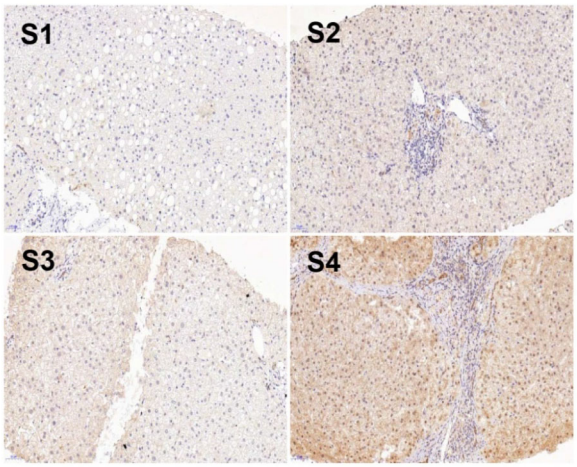


Figure 6 Nur 77 expression in liver tissue by immunohistochemistry **(×200)**

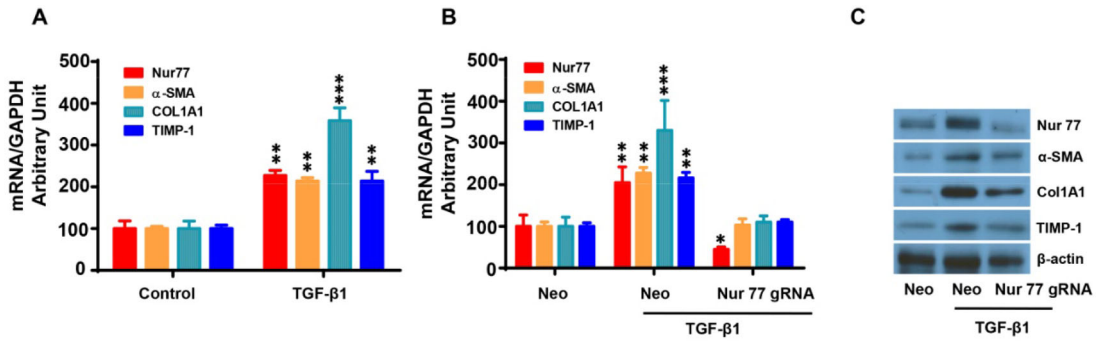


Figure 3 Nur 77 gRNA inhibited TGF-β1 induced LX-2 activation
· *P*<0.05, · · *P*<0.01, · · · *P*<0.001

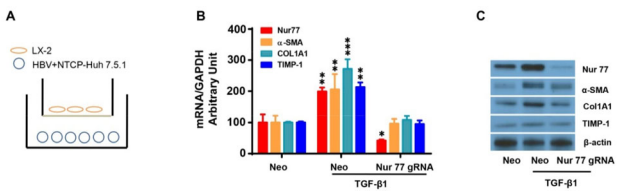


Figure 4 HBV induced LX-2 activation in co-culture system
· *P*<0.05, · · *P*<0.01, · · · *P*<0.001

Abstract #1260

Characteristics and healthcare resource utilisation and costs in chronic hepatitis B (CHB) patients in Japan: a real-world analysis of 11,125 patients

Yotsuyanagi H[1], Yatsuhashi H[2], Kurosaki M[3], Lee E[4], Ng A[5], Brooks-Rooney CT[5], Nguyen MH[6]

[1]Institute of Medical Science, The University of Tokyo, Tokyo, Japan, [2]Nagasaki Medical Center, Nagasaki, Japan, [3]Department of Gastroenterology and Hepatology, Japanese Red Cross Musahino Hospital, Tokyo, Japan, [4]Gilead Sciences Inc., Foster City, California, USA, [5]Costello Medical Singapore Pte Ltd, Singapore, [6]Division of

Gastroenterology and Hepatology, Stanford University Medical Center, Palo Alto, California, USA

Introduction: Recent US and Hong Kong studies reported advancing age, comorbidities and higher healthcare utilization in CHB patients. Data on the characteristics and health economics of CHB from Japan are limited but particularly relevant, given its aging population with 48% of the general population estimated to be ≥ 65 years by December 1, 2019 (http://www.stat.go.jp).
Objectives: To characterize a large cohort of real-world CHB patients in Japan from 2012 to 2016
Methods: Using the Medical Data Vision claims database, we analysed adults with ≥ 1 CHB diagnosis (ICD-10: B18.1) and ≥ 1 HBV test between 01/01/2012–31/12/2016. All-cause healthcare utilization and costs for each patient were summed then divided by the number of patients with ≥ 1 claim in that calendar year to calculate the annual per-patient average.
Results: We analyzed 11,125 patients: mean age and percent of seniors ≥ 65 or ≥ 75 years: 62.0 ± 13.3, 46%, 17% in 2012 and 65.2 ± 13.2, 61%, 24% in 2016. From 2012 to 2016, while cirrhosis (6.9–4.9%) and hepatocellular carcinoma (7.9–4.3%) prevalence decreased, non-liver comorbidities increased (40–52% and 10–15% for solid and hematologic malignancy, 12–18% for osteoporosis, 10–15% for renal impairment). Healthcare utilization and cost also increased, reaching an annual average of 12 outpatient visits and 1.3 million Japanese yen total cost per patient.
Conclusions: The majority of CHB patients in Japan are elderly, had major comorbidities, high healthcare utilization and cost. The management of CHB should include evaluation, monitoring and efforts to reduce non-liver comorbidities.

Table 1. All-cause healthcare resource utilisation of the study population by calendar year

	2012 (N=1,291)	2013 (N=2,253)	2014 (N=4,212)	2015 (N=6,435)	2016 (N=8,556)
Number of patients with at least one inpatient admission (%)	458 (35.5)	784 (34.8)	1,526 (36.2)	2,377 (36.9)	3,089 (36.1)
Mean, per-patient number of inpatient admissions (SD)	0.58 (1.1)	0.60 (1.1)	0.67 (1.3)	0.71 (1.4)	0.70 (1.4)
Mean, per-patient duration of inpatient admissions (SD)	9.3 (24.3)	10.1 (24.4)	9.8 (23.0)	10.9 (25.6)	10.6 (25.2)
Number of patients with at least one outpatient visit (%)	1,150 (89.1)	2,194 (97.4)	4,109 (97.6)	6,281 (97.6)	8,376 (97.9)
Mean, per-patient number of outpatient visits (SD)	7.4 (12.4)	10.6 (13.2)	11.1 (13.2)	11.6 (13.9)	12.0 (14.2)

Table 2. All-cause healthcare costs among the study population by calendar year

Costs (¥)	2012 (N = 1,291)	2013 (N = 2,253)	2014 (N = 4,212)	2015 (N = 6,435)	2016 (N = 8,556)
Mean, per-patient total healthcare costs (SD)	846,178 (1,537,605)	1,045,423 (1,715,049)	1,092,215 (1,640,742)	1,261,248 (1,965,406)	1,332,417 (2,049,712)
Mean, per-patient inpatient costs (SD)	496,755 (1,232,022)	534,012 (1,358,322)	538,055 (1,231,344)	623,209 (1,471,906)	621,894 (1,463,743)
Mean, per-patient outpatient costs (SD)	349,423 (782,989)	511,411 (899,423)	554,160 (930,093)	638,039 (1,155,284)	710,523 (1,283,907)

Abstract #1281

A FIB-4-based risk score predicts hepatocellular carcinoma in patients with chronic hepatitis B

Lilian Yan Liang [1,2], Vincent Wai-Sun Wong [1,2,3], Yee-Kit Tse [1,2], Terry Cheuk-Fung Yip [1,2], Becky Wing-Yan Yuen [1,2], Hye Won Lee [4], Henry Lik-Yuen Chan [1,2,3], Grace Lai-Hung Wong [1,2,3]

[1]Institute of Digestive Disease, [2]Department of Medicine and Therapeutics, and [3]State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong; Hong Kong SAR. [4]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea.

Introduction: Serum fibrosis scores would be useful to define hepatocellular carcinoma (HCC) risk in treatment-naïve chronic hepatitis B (CHB) patients.
Objectives: We aimed to derive and validate a HCC risk score based on serum fibrosis scores to predict HCC in treatment-naïve CHB patients.
Methods: Consecutive treatment-naïve adult CHB patients between January 2000 and June 2018 with serum HBV DNA and at least one fibrosis score (aspartate aminotransferase-to-platelet ratio index [APRI], FIB-4 index, and Forns index) available were identified to form the training cohort. Individual fibrosis score was included in Cox regression model with other parameters to construct a new HCC prediction score. The score was externally validated in an independent treatment-naïve Korean CHB cohort.
Results: 189/15,415 patients (1.2%) in training cohort and 53/4,404 patients (1.2%) in validation cohort developed HCC during a mean follow-up of 5 years. FIB-4 index but not APRI predicted HCC in the training cohort. The newly developed Liang score was composed of 5 parameters—gender, age, albumin, HBV DNA, FIB-4, ranging from 0 to 27. Area under the time-dependent receiver operating characteristic curve of Liang score was 0.77 (95% CI 0.73–0.82), which was significantly higher than FIB-4 index alone (0.70 [95% CI 0.65–0.75]) (P = 0.012). Cut-off value of 8 provided high negative predictive value of 99.8% at 5 years in both training and validation cohorts; patients with Liang score ≤ 8 had a low HCC incidence (≤ 0.2% per year).
Conclusion: Liang score is accurate to predict HCC and useful to exclude low risk groups of treatment-naïve CHB patients.

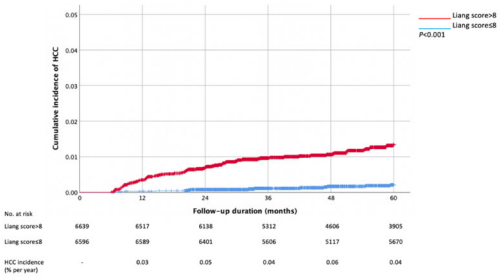


Figure 1. The Kaplan-meier curves of the cumulative incidence of HCC in CHB patients with the new score more and less than 8 in the training cohort.

Abstract #1317

HBV surface antigen loss: A challenging goal that could be predicted

Mohamed Elbasiony[1,2], Ramy Agwa[1,2], Reham Soliman[2,3], Khaled Ghonim[2], Abdelkader Abdelfattah[2], Nader Elmalky[1], Gamal Shiha[1,2]

[1]Internal Medicine Department, Faculty of medicine, Mansoura University, Mansoura, Egypt, [2] Egyptian Liver Research Institute and Hospital (ELRIAH) Mansoura, Egypt, [3]Tropical Medicine Department, Faculty of medicine, Port Said University, Port Said Egypt

Introduction: Seroclearance of hepatitis B surface (HBs) antigen is an infrequent cure during treatment of chronic hepatitis B virus (HBV) patients. It was estimated to be about 1-2% annually in Asian and Western cases. The aim of our study was to assess factors predicting HBV surface antigen loss in chronic HBV e antigen negative patients treated by nucleos(t)ide analogues.
Objectives: Evaluation of baseline predictors for HBV surface antigen loss in chronic HBV patients with negative HBeAg
Methods: A total of 510 HBV e antigen negative patients treated by (lamivudine, entecavir and tenofovir) with a median treatment time of 3.5 years (2.1–4.2 years). HBs antigen level, HBV DNA level, liver stiffness by FibroScan, liver functions tests, complete blood counts

and prothrombin time were assessed at baseline and during follow up visits every 3–6 months.
Results: Out of the 510 treated chronic HBV patients; 34 cases achieved HBs antigen loss. Multivariate regressive analysis showed that HBs antigen levels, HBV DNA levels and liver stiffness measurements were significantly lower in patients achieving HBs antigen loss compared to whom not, with median values of (280 IU/ml, 6580 IU/ml and 6.77 kpa) versus (3772 IU/ml, 8950 IU/ml and 8.45 kpa), with p values of (0.032, 0.003, 0.03) respectively. Interestingly, 30 (88.2%) out of 34 cases with HBs antigen loss had baseline HBs antigen levels below 1000 IU compared to 36 (7.56%) out of 476 cases failed to achieve HBs antigen loss, and there was no cases of cirrhosis (liver stiffness $>$ 16.3 kpa) in HBsAg loss group compared to 11 cases in the group without surface antigen loss. Regarding treatment type in HBs antigen loss group; 19 cases was treated by entecavir and 15 by tenofovir.
Conclusion: Low baseline HBs antigen levels, HBV DNA levels and absence of liver cirrhosis could be considered as predictors of HBsAg loss. HBs antigen level below 1000 IU/ml observed in the majority of patients achieved HBsAg loss.

Abstract #1324

Global and regional burden of hepatitis B virus (HBV) mortality and disability-adjust life years (DALYs), 2015–2019: an analysis of the Global Burden of Disease Study 2019

John W. Ward[1], Lindsey Hiebert[1], Brittney Sheena[2], Angelique Harris[1], Mae Dirac[2], Theo Vos[2]

[1]Coalition for Global Hepatitis Elimination, Task Force for Global Health, Atlanta, GA, USA, [2]Institute for Health Metrics and Evaluation, University of Washington, Seattle, Washington, USA

Introduction: In 2016, WHO set an HBV elimination goal, defined as a 65% reduction in HBV related mortality by 2030. Hepatitis burden of disease data are needed to monitor progress towards this elimination goal.
Objective: To estimate trends in HBV-related mortality and DALYs for 2015–2019
Methods: From GBD 2015-2019, the HBV-related all-age mortality rate from acute HBV, cirrhosis and other chronic liver diseases and primary liver cancer was aggregated globally and for IHME super-regions. Total DALYs were calculated as previously described. Estimates were adjusted based on HBV vaccine coverage specified by country and year with an estimated efficacy of 95%.
Results: From 2015–2019, the global HBV all-age mortality rate remained relatively unchanged from 7.1 to 7.0 (6.2–8.0) per 100,000. Southeast Asia, East Asia, and Oceania region had the greatest DALY burden [7.1 M (6.0–8.4 M]. Globally, DALYs were estimated at 17.3 M (15.2–19.6 M) in 2019. In all, 21 low- and middle-income (LMIC) countries represent 79.8% (95% CI 77.4–82.1) of the global HBV DALY burden. Ten LMIC Asian countries represent 66% of the global burden.
Conclusions: Globally, HBV mortality did not increase from 2015 to 2019. The inclusion of hepatitis B vaccination data will improve the precision in the GBD mortality estimates. HBV DALYs remain high, indicative of the need for HBV testing and treatment particularly in Asian countries with large burdens of HBV disease.

Table 1. Hepatitis-B related mortality rate and DALYs globally and by IHME super-region

	Mortality rate related to hepatitis B (per 100,000), 2015	Mortality rate related to hepatitis B (per 100,000), 2019	Percent change in mortality rate, 2015- 2019 (%)	DALYs due to hepatitis, 2019
Global	7.1 (6.4 – 7.9)	7.0 (6.2 – 8.0)	-1%	17.3 M (15.2 – 19.6 M)
Southeast Asia, East Asia, and Oceania	10.5 (9.3 – 12.0)	11.1 (9.5 – 13.1)	6%	7.1 M (6.0 – 8.4 M)
Central Europe, Eastern Europe, and Central Asia	6.4 (5.3 – 7.8)	6.1 (5.0 – 7.6)	-4%	0.8 M (0.7 – 1.0)
Latin America and Caribbean	2.0 (1.69 – 2.26)	1.1 (1.8 – 2.4)	-46%	0.4 M (0.3 – 0.4 M)
North Africa and Middle East	5.2 (4.0 – 6.7)	5.1 (3.8 – 6.9)	-2%	0.9 M (0.6 – 1.1 M)
South Asia	7.8 (6.8 – 8.8)	7.0 (5.9 – 8.2)	-10%	4.5 M (3.7 – 5.4 M)
Sub-Saharan Africa	7.1 (5.9 – 8.6)	6.5 (5.2 – 7.9)	-9%	2.5 M (2.0 – 3.0 M)

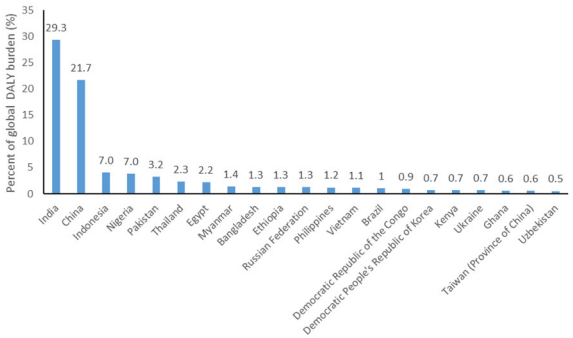


Figure 1. Top 21 low- and middle-income countries for DALYs from acute hepatitis B infection, and HBV related cirrhosis, and liver cancer

Abstract #1359

Histologic fibrosis across the natural course of chronic hepatitis B virus infection: a systematic review and meta-analysis

Wang, Yan[1,2], Lin, Mei-Hong[1,3], Li, Hai-Qiong[1,3], Zhu, Lin[1,3]

[1]Guangdong Provincial Research Center for Liver Fibrosis, Department of Infectious Disease and Hepatology Unit, Nanfang Hospital, Southern Medical University, Guangzhou, China, [2]Biomedical Research Center, Southern Medical University, Guangzhou, China, [3]The Second School of Clinical Medicine, Zhujiang Hospital, Southern Medical University, Guangzhou, China

Introduction: There lack quantitative data on risk of liver fibrosis across natural history of chronic hepatitis B viral infection (CHB).
Objectives: To estimate prevalence of different fibrosis status including non-fibrosis (NF), significant fibrosis (SF), advanced fibrosis (AF), and cirrhosis through the entire CHB natural course.
Methods: We searched Cochrane library, EMBASE, PubMed, SCOPUS, and Web of Science from 1/1/1993 to 9/30/2018 for literatures with histologic data on liver fibrosis in CHB natural course. CHB course was defined based on current criteria for identifying infection phases as recommended by international clinical practice guidelines,[1] including the HBeAg-positive immune-tolerant (P1), HBeAg-positive immune-active (P2), HBeAg-negative immune-inactive (P3), HBeAg-negative immune-reactive (P4), and HBsAg-negative phases (P5). Pooled prevalence rate of different fibrosis status in each phase was obtained from random-effects meta-analyses.
Results: As listed in Table 1, 41 studies with 9,718 participants (21.5-49 age years; 45.5–88.6% male) were included. The prevalence of NF, SF, AF, and cirrhosis was, for HBeAg-positive immune-tolerant phase: 33.8% (95% CI 19.6–47.9), 14.4% (95% CI 8.5–20.3), 2.0% (95% CI 0.1–3.9), and 0.8% (95% CI 0.0–1.6); HBeAg-positive

immune-active phase: 7.5% (95% CI 4.5–10.5), 54.6% (95% CI 46.8–62.4), 30.8% (95% CI 24.1–37.4), and 12.8% (95% CI 8.7–16.9); HBeAg-negative immune-inactive phase: 29.8% (95% CI 13.4–46.2), 20.5% (95% CI 9.7–31.3), 5.7% (95% CI 2.7–8.8), and 3.3% (95% CI 0.4–6.1); and HBeAg-negative immune-reactive phase: 5.9% (95% CI 3.0–8.8), 52.9% (95% CI 40.9–64.9), 33.1% (95% CI 24.3–42.0), and 11.6% (95% CI 7.9–15.3), respectively. There was only one study for HBsAg-negative phase, thus not allowing further meta-analyses.

Conclusion: Fibrosis risk persists through CHB natural course. These data can support risk estimation in clinical practice and investigation of non-invasive diagnosis.

Table 1. Estimated prevalence of fibrosis in CHB natural course

Phase	Pts n.	Studies n.	Basic characteristics				Fibrosis prevalence (%) (95% CI)			
			Age (yrs)	Male (%) (95% CI)	HBV DNA (IU/mL)	ALT (IU/L)	NF	SF	AF	Cirrhosis
P1	987	14	21.5-39.3	60.3 (55.6-65.0)	2.1×10^6-8.3×10^9	21-36	33.8 (19.6-47.9)	14.4 (8.5-20.3)	2.0 (0.1-3.9)	0.8 (0.0-1.6)
P2	4677	23	24.0-41.0	71.0 (67.5-74.4)	1.5×10^5-4.1×10^9	44-226	7.5 (4.5-10.5)	54.6 (46.8-62.4)	30.8 (24.1-37.4)	12.8 (8.7-16.9)
P3	2299	17	28.7-49.0	64.6 (59.7-69.4)	Negative to 7.1×10^5	19.3-40.0	29.8 (13.4-46.2)	20.5 (9.7-31.3)	5.7 (2.7-8.8)	3.3 (0.4-6.1)
P4	1740	16	28.7-48.0	77.6 (73.8-81.4)	10^4-1.3×10^7	50-119.6	5.9 (3.0-8.8)	52.9 (40.9-64.9)	33.1 (24.3-42.0)	11.6 (7.9-15.3)
P5 [a]	15	1	36.0	73.3	Undetectable	Normal	0.0	40.0	20.0	20.0

[a] Without meta-analysis.

Abstract #1373

Association of hepatitis B core antibody with treatment response of chronic hepatitis B patients

Rui Huang[1], Jian Wang[1], Xiaomin Yan[1], Juan Xia[1], Bei Jia[1], Yong Liu[2], Yuxin Chen[2], Zhaoping Zhang[1], Chao Wu[1]

[1]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China, [2]Department of Laboratory Medicine, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China

Introduction: Antibody to hepatitis B core antigen (anti-HBc) is one of the classical serological markers for HBV infection.
Objectives: We aimed to investigate the association of serum anti-HBc with natural history and treatment response in CHB.
Method: 3609 consecutive treatment-naïve CHB patients between January 2010 and May 2019 were enrolled. 281 patients in the immune clearance (IC) phase who were treated by nucleos(t)ide analogues (NAs) and followed for 48 weeks had anti-HBc data. Complete response (CR) was defined as a serum hepatitis B virus DNA < 500 IU/mL and HBeAg seroconversion at the end of 48 weeks NAs treatment.
Results: Anti-HBc level was highest in the HBeAg negative phase (n = 442) (9.9 S/CO) and lowest in the immune tolerant (IT) phase (n = 313) (8.1 S/CO). However, no significant difference of anti-HBc was observed between the immune clearance (IC) (n = 798) (9.2 S/CO) and low replicative (LR) (n = 2053) (9.2 S/CO) phases. At week 48 treatment, 37 (13.2%) of 281 patients with IC phase achieved CR. Patients who had CR after 48 weeks NAs treatment had significantly higher level of baseline anti-HBc as compare with patients who did not achieve CR (11.5 S/CO vs. 10.1 S/CO, $p < 0.001$). Baseline anti-HBc was identified as an independent predictor for CR (OR 1.200, 95% CI 1.002–1.437; $p < 0.05$). The AUROC of anti-HBc at cut-off values of 11.1 S/CO for predicting CR was 0.686 with the sensitivity of 62.16% and specificity of 70.90%.
Conclusion: Baseline anti-HBc level is a useful predictor of NAs therapy efficacy in HBeAg positive CHB patients.

Abstract #1391

The spliceosome factor EFTUD2 promotes IFN-alpha anti-HBV effect through mRNA splicing

Zhu Chuanlong[1], Hu Pingping[1], Tian Anran[1], Xu Ruirui[1], Yuan Hui[1], Cai Jinyuan[1], Li Jun[1]

[1]Department of Infectious Disease, the First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu, China

Introduction: The broadly antiviral cytokine interferon-α (IFNα)'s mechanisms of action against HBV infection are not well understood. We previously identified EFTUD2, a host protein involved in RNA splicing and pre-mRNA processing, as a regulator of IFN's antiviral effects. We hypothesized that EFTUD2 regulates IFN-stimulated genes (ISGs) through mRNA processing and splicing.
Objectives: This study aimed to explore the function of EFTUD2 on IFN-mediated-anti-HBV response.
Methods: We performed EFTUD2 single allele knockout (EFTUD2+/−) model of HepG2.2.15 cells by CRISPR/Cas9 gene editing system. Then we detected HBV biological markers in EFTUD2+/− cells and wild-type (WT) cells after IFNα treatment. Next we performed EFTUD2 protien binding RNA immunoprecipitation-sequencing (RIP-seq) with or without IFNα treatment in HepG2.2.15 cells. Selected gene mRNA variants and their proteins, together with HBV replication, were monitored by qRT-PCR and Western blot. Finally we detected the pre-mRNA of the variant genes.
Results: We observed that IFNα anti-HBV activity were restricted in EFTUD2+/− HepG2.2.15 cells. Then we identified 1636 EFTUD2 binding genes with a greater than 2-fold expression difference between the presence or absence of IFNα in HepG2.2.15 cells. Bioinformatic analysis identified at 12 gene both response to IFNα and negative regulation of viral life cycle. We confirmed there of them have been associated with HBV infection including MxA, OAS1 and PKR. Mechanistically, EFTUD2 single allele knockout abrogated the antiviral activity of IFNα, reduced the expression of IFN-stimulated genes (ISGs) MxA, OAS, and PKR by gene splicing.
Conclusion: EFTUD2 regulates IFNα anti-HBV effect through ISGs pre-mRNAs splicing.

Abstract #1458

The toll-like receptor 8 (TLR8) agonist selgantolimod induces a dose-dependent immune response in chronic hepatitis B patients

Jeffrey Wallin[1], Diana Chen[1], Ondrej Podlaha[1], Sam Kim[1], Ping Cheng Yi[1], Horace Liang[1], Bhawna Poonia[2], Anna Brooks[3], Anuj Gaggar[1], Rod Dunbar[3] and Jenny Yang[1]

[1]Gilead Sciences, Inc.; [2]University of Maryland, [3]University of Auckland

Introduction: An insufficient antiviral response is associated with chronic HBV infection (CHB) and therapeutics designed to promote immune responses are under clinical evaluation. GS-9688 is an oral selective small molecule TLR8 agonist shown to be safe and well-tolerated in CHB patients. Dose-dependent inductions of serum pharmacodynamic (PD) biomarkers (IL-12p40 and IL-1RA) have been observed with GS-9688 treatment in CHB subjects.
Objective: Analyze the effects of GS-9688 on promoting immune responses.
Methods: This Phase 1b study enrolled 4 cohorts (N = 9–10/cohort) of CHB patients (virally suppressed [Cohorts 1, 2, and 5] or untreated viremic [Cohort 4]) randomized 4:1 to receive GS-9688 or placebo to match. In cohorts 1, 2, and 4, patients received once weekly doses of

1.5 mg (Cohort 1) or 3 mg (Cohorts 2 and 4) on Days 1 and 8. Cohort 5 received 4 weekly doses of 3 mg. Peripheral blood mononuclear cells (PBMCs) were collected at baseline and on-treatment and evaluation of their response to HBV by T-cell IFN-γ and B-cell ELISpot when possible. Flow cytometry cell phenotyping, antibody profiling, and cytokines were measured at baseline and on-treatment timepoints.
Results: GS-9688 induced a dose-dependent induction of IL12p70 and IFN-γ, peaking 4 h post-dose and returning to near baseline by 24 h post-dose. Acute phase proteins such as SAA1 and C-reactive protein displayed prolonged upregulation after dosing across all cohorts. ELISpot responses and on-treatment elevation of T cell activation markers were observed in some subjects.
Conclusion: The PD and mechanistic activity of GS-9688 support further evaluation in CHB patients.

Abstract #1472

The impacts of nonalcoholic fatty liver disease on the renal function in patients with chronic hepatitis B

Fang Ji[1], Da-ang Hao[2], Jungui Hao[1], Liping Wang[1], Mingjia Dai[1], Chunyang Li[1], Rui Huang[3], Jian Wang[3], Biao Zhang[4], Longgen Liu[5], Chuanwu Zhu[6], Chao Wu[3], Xuebing Yan [1]

[1]Department of Infectious Disease, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, Jiangsu, China, [2]Department of Infectious Disease, Xuzhou Medical University, Xuzhou, Jiangsu, China, [3]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China, [4]Department of Hepatology, Huai'an No. 4 People's Hospital, Huai'an, Jiangsu, China, [5]Department of Hepatology, Changzhou Third People's Hospital, Changzhou, China, [6]Department of Hepatology, The Fifth People's Hospital of Suzhou, Suzhou, Jiangsu, China

Introduction: Nonalcoholic fatty liver disease (NAFLD) as a hepatic manifestation of metabolic syndrome is linked to chronic kidney disease.
Objectives: We aimed to investigate the impacts of NAFLD on the renal function of chronic hepatitis B (CHB) patients.
Methods: A total of 2508 CHB patients were included in this study and divided into CHB group and CHB-NAFLD group. To reduce the potential baseline differences caused by gender and age, the CHB group and CHB-NAFLD group were matched 1: 1 by propensity score matching (PSM).
Results: 551 (22.0%) CHB patients were diagnosed with NAFLD by abdomen ultrasound. Serum creatinine (Cr) and blood urea nitrogen (BUN) levels were higher in CHB-NAFLD group than in CHB group ($P < 0.001$and $P = 0.021$). However, the estimated glomerular filtration rate (eGFR) did not differ between these two groups ($P = 0.679$). After PSM, there were no significant differences in Cr, BUN and eGFR levels between these two groups ($P = 0.289$, $P = 0.622$ and $P = 0.050$, respectively). In patients with CHB concurrent with NAFLD, Fibrosis-4 (FIB-4) scores correlated with BUN ($P = 0.001$) and eGFR levels ($P = 0.029$). However, HBV DNA levels were not significantly associated with renal function.
Conclusion: In Chinese population, concurrent with NAFLD had no impacts on renal function in CHB patients. However, the renal function may be associated with liver fibrosis, but not HBV DNA levels in CHB patients concurrent with NAFLD (NCT03097952).

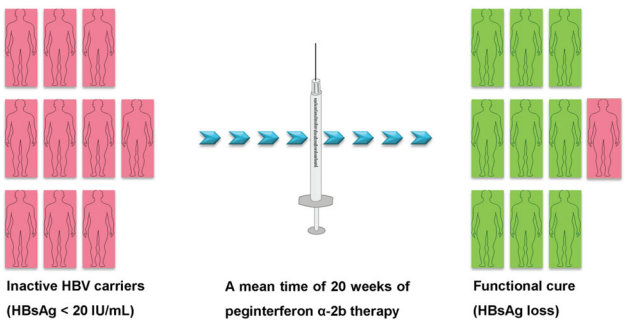
Abstract #1541

High functional cure rate in inactive HBV carriers with extremely low HBsAg levels receiving a short duration of peginterferon α-2b therapy

Zeng Qing-Lei[1,†,*], Yu Zu-Jiang[1,†], Shang Jia[2,†], Xu Guang-Hua[3], Sun Chang-Yu[1], Liu Na[3], Li Chun-Xia[3], Liang Hong-Xia[1], Li Zhi-Qin[1], Pan Ya-Jie[1], Hu Qiu-Yue[1], Li Wei[2], Zhang Da-Wei[4], Wang Fu-Sheng[4,*]

[1]Department of Infectious Diseases and Hepatology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan Province, China; [2]Department of Infectious Diseases, Henan Provincial People's Hospital, Zhengzhou, Henan Province, China; [3]Department of Infectious Diseases, The Affiliated Hospital of Yan'an University, Yan'an, Shaanxi Province, China; and [4]Treatment and Research Center for Infectious Diseases, The Fifth Medical Center of PLA General Hospital, Beijing, China

Introduction: None of the current guidelines recommend antiviral therapy for inactive hepatitis B virus carriers (IHCs), and few studies have reported functional cure in ICHs.
Objective: To investigate the prognosis of treated and untreated IHCs with extremely low hepatitis B surface antigen (HBsAg) levels.
Methods: In this real-world, non-randomized observational study, 16 patients were enrolled in the peginterferon α-2b treatment group and 16 were in untreated control group according to their choices. The primary endpoint was HBsAg loss. The expected treatment duration was 48 weeks, and participants could discontinue therapy at HBsAg loss or at any time during therapy. Adverse events during therapy were reported. The HBV vaccine can be injected after HBsAg loss.
Results: All patients had HBsAg of less than 20 IU/mL. The mean baseline HBsAg levels were 6.6 IU/mL and 5.8 IU/mL in the treated and untreated groups, respectively. Fifteen participants achieved HBsAg loss, five obtained HBsAg seroconversion after undergoing a mean time of 19.7 weeks of therapy in the treatment group, and no one in the follow-up group obtained HBsAg loss during a mean follow-up time of 12.6 months ($P < .0001$). Generally, the therapy was well tolerated. Nine of eleven HBV vaccine-injected HBsAg loss individuals benefitted from vaccine.
Conclusion: An unexpectedly high functional cure rate can be obtained by a short duration of peginterferon α-2b therapy in IHCs with HBsAg less than 20 IU/ml, which indicates that differential or delicacy management of IHCs is considerable. Additionally, HBV vaccine injection is favourable after interferon-induced HBsAg loss.



Abstract #1579

Correlation between status of knowledge and the presence of cirrhosis among hepatitis B patients in Malang Indonesia

Mirza Zaka Pratama[1], Bogi Pratomo[2], Syifa Mustika[2], Supriono[2]

[1]Resident of Internal Medicine, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia, [2]Gastroenterohepatology Division, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia

Introduction: Hepatitis B infection is a major public health concern. Little is known about the knowledge status among hepatitis B patients in Indonesia.
Objective: The aim of this study was to characterize the knowledge status of hepatitis B patients, correlate with the presence of cirrhosis, and identify the sociodemographic determinants.
Methods: This was a cross-sectional study with subjects were 89 hepatitis B patients (63 non-cirrhotic and 26 cirrhotic) in Saiful Anwar General Hospital Malang Indonesia. Subjects were given questionnaire, including 17 question-related hepatitis B across four domain: natural history, transmission, symptoms, and prevention and treatment. Low knowledge status was defined as score below 75%. Sociodemographic determinants: sex, age, race, marital, employment, education, income, and time of diagnosis were recorded. Chi-square and logistic regression was used to estimate the differences between groups.
Results: Low knowledge status was found higher in cirrhotic patients (84.6%vs.25.4%, p = 0000), with lower scores from each domain: natural history (p = 0.000), transmission (p = 0.000), and symptoms (p = 0.000). Low knowledge status correlated with the presence of cirrhosis (OR 16.16 (4.83–54.06), p = 0.000). Unemployment (OR 10.47 (3.89–28.15), p = 0.000), low education (OR 2.92 (1.20–7.15), p = 0.017), low income (OR 8.85 (2.41–32.57), p = 0.000), and diagnosis < 1 year (OR 3.27 (1.30–8.23), p = 0.010) was correlated with low knowledge status.
Conclusion: Low knowledge status towards hepatitis B correlated with the presence of cirrhosis. Employment, education, income, and time of diagnosis was associated with the knowledge status in hepatitis B patients. This finding highlights the need to improve the public knowledge to hepatitis B to prevent the progression into cirrhosis.

Abstract #1588

Comparison of HBV DNA quantitative log in patients hepatitis B with telbivudine therapy compared with tenofovir therapy in saiful anwar general hospital Malang: January 2016–December 2017

Muhammad Imanuddin Nasution[1], Bogi Pratomo[2], Syifa Mustika[2], Supriono[2]

[1]Resident of Internal Medicine, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia, [2]Gastroenterohepatology Division, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia

Introduction: Hepatitis B is a health problem with high endemic in Indonesia. Hepatitis B virus infection is transmitted parenterally, and can be risk of cirrhosis and hepatocellular carcinoma. Detection and quantification of HBV DNA Kuantitatif is a marker of active HBV replication and determines treatment options for hepatitis B. Therefore, in this study will discuss the comparison of HBV DNA Quantitative Log after Telbivudine treatment compared with Tenofovir treatment.
Objective: Find the comparison of HBV DNA Quantitative Log reduction in hepatitis B patients with Telbivudine treatment compared with Tenofovir treatment.
Method: This study was a retrospective analytic observational study in patients treated for hepatitis B in Hepatology Out Patient Clinic Of Saiful anwar general hospital Malang which was followed for two years in January 2016 to December 2017. A total of 34 patients participated and were divided into two groups: Telbivudine treatment (n = 26) and Tenofovir treatment (n = 8). Data collection was carried out at follow-up by way of anamnesis to the family and research subjects with laboratory examinations. Statistical analysis was performed using multiple logistic regression to assess the comparison of HBV DNA Quantitative logs between treatment groups.
Results: The mean age of subjects was 45.91 ± 15.27 years with male sex (65.3%) and female (34.7%), the mean initial SGOT levels were Tenofovir 146 ± 337 IU/L and Telbivudine 86 ± 95 IU/L, Tenofovir HBV DNA baseline 5.05×10^7 IU/mL and Telbivudine 5.59×10^6 IU/mL. The results showed not significant difference in HBV DNA levels between before and after Tenofovir treatment, in 6 months follow-up (OR 95% CI 5.41 [0.83–35.16], p = 0.0770) and 12 months (OR 95% CI 5.39 [0.83–34.99], p = 0.0780). Telbivudine administration showed significant differences in HBV DNA levels between before and after treatment at 6 months follow-up (OR 95% CI 13.69 [4.53–41.40], p = 0.0001) and 12 months (OR 95% CI 13.69 [4.53–41.41], p = 0.0001). Comparison of tenofovir and telbivudine therapy showed no significant difference at 6 months follow-up (OR 95% CI 0.44 [0.10–1.88], p = 0.2690) but significant at 12 months follow-up (OR 95% CI 6.23 [1.39–27.97], p = 0.0170).
Conclusion: Significant differences were obtained between the administration of telbivudine as a treatment for hepatitis B with lower serum HBV DNA levels compared with the administration of Tenofovir at the 12-month follow-up therapy.

Abstract #1619

Ten-year individualized immunoprophylaxis strategy to prevent perinatal transmission of hepatitis B

Chuanwu Zhu[1], Rong Zhang[2], Yongyan Tang[2], Jie yao[2], Ming Li[1], Feng Qian[1], Li Zhu[1], Haiyan Wang[1], Yufang Jia[3], Zhiyun Ding[3], Qian Yu[4], Ji Zhao[4]

[1]Department of Hepatology, The Affiliated Infectious Diseases Hospital of Soochow University, Suzhou, China, [2]Obstetrical Department, The Affiliated Infectious Diseases Hospital of Soochow University, Suzhou, China, [3]Obstetrical Department, Kunshan Hospital of Traditional Chinese Medicine, Kunshan, China, [4]Kunshan Maternal and Child Health Institution, Kunshan, China

Introduction: Immunoprophylaxis approach has been reported with an unsatisfying effective rate in reducing mother-to-child transmission (MTCT) of HBV, and the 5–15% of newborns who are infected despite receiving appropriate neonatal immunoprophylaxis.
Objectives: ten-year individualized immunoprophylaxis strategy was evaluated in preventing MTCT in the study.
Methods: An individualized immunoprophylaxis scheme was administered to the exposed infants. For the women with positive HBeAg or with HBV DNA load ≥ 500 IU/ml, infants received first HBIG 200 IU within 5 minutes of birth, and then the second HBIG 200 IU at day 15 post partum, and hepatitis B vaccine at 1, 2, and 7 months; For those with negative HBeAg and HBV DNA load < 500 IU/ml, infants received HBIG 100–200 IU within 5 minutes of birth, and hepatitis B vaccine at 24 hours post partum, 1 and 6 months.
Results: The data of HBV infected pregnant women and their infants from September 2009 to May 2019 were collected. 2702 cases of women (1568 HBeAg positive and 1134 negative) were enrolled. 19 infants were infected in HBeAg-positive mothers. Of them, 17 were born to women with HBV DNA > 6 log 10 IU/ml. The overall effective rate was 99.3%, the rate was 98.8% in HBeAg-positive mothers, and was 100% in HBeAg-negative mothers. The effective

rate was of no significant difference between natural childbirth and cesarean delivery, and so was between breast-fed and formula-fed infants.
Conclusion: The optimized immunoprophylaxis strategy can remarkably improve the effective rate in preventing MTCT in HBV infected pregnant women.

Abstract #1686

C-terminal truncated middle surface protein of HBV (MHBst) contributes to hepatocarcinogenesis via activating innate immunity by induction of autophagy

Cheng Bin[1], Meng Zhongji[1], Wei Zhiqiang[1], He Yulin[1], Li Ruiming[1], Liu Guohua[1]

[1]Institute of Biomedical Research, Taihe Hospital, Hubei University of Medicine, Shiyan, China

Introduction: HBV can induce hepatocarcinogenesis by eliciting host immune responses against the infected hepatocytes. C terminal truncated small surface protein of HBV have been reported to potentially contribute to hepatocarcinogenesis through its transactivating capacity by epidemiology study. The relationship between MHBst and hepatocarcinogenesis is underdetermined.
Objectives: In this study, a premature stop at codon 167 in the *MHBs* gene was investigated to verify the hypothesize that C terminal truncated S proteins may elicit host immune responses and contribute to hepatocarcinogenesis.
Methods: MHBst167 was expressed in L02 cell line, cell proliferation was analyzed by CCK-8 and High Content Screening (HCS) assay, cell cycle was analyzed by flow cytometry (FCM), epithelial-to-mesenchymal transition (EMT) was analyzed by immunoblotting and immunofluorescence. Activation of NF-κB was detected to analyze the activation of innate immunity by immunoblotting and immunofluorescence. Autophagy was analyzed by immunoblotting and immunofluorescence. Autophagy inhibitor and NF-κB inhibitor were used to analyze the relationship between innate immunity and autophagy induced by MHBst167.
Results: MHBst167 promote L02 cell growth and accelerate cell cycle from S phase to G2 phase. Expression of MHBst167 promoted EMT by suppressing E-cadherin and initiating vimentin. Activation of NF-κB and complete autophagy was induced by MHBst167. Cell growth and accelerated cell cycle were inhibited by autophagy inhibitor and NF-κB inhibitor, respectively. Activation of NF-κB was inhibited by autophagy inhibitor.
Conclusion: MHBst167 could elicit host innate immune responses by activating autophagy, which might contribute to hepatocarcinogenesis.

Abstract #1694

Seroprevalence of hepatitis B infection among health care workers (HCWs) At Dr Kariadi General Hospital

Hery Djagat Purnomo[1], Hesti Triwahyu Hutami[1], Hirlan[1], Didik Indiarso[1],Agung Prasetyo[1], Cecilia Oktaria Permatadewi[1]

[1]Division of Gastroenterohepatology, Internal Medicine, Faculty of Medicine Diponegoro University/dr Kariadi General Hospital, Semarang, Indonesia

Introduction: Hepatitis B virus (HBV) infection is a major public health problem. Riskesdas 2013 showed a decline seroprevalence of HBsAg to 7.1% from 9.4% in 2007. Study conducted by Ministry of Health, Republic of Indonesia among health care workers (HCWs) in Indonesia showed the average HBsAg prevalence was 2.56%. There was just a little survey of HBV seroprevalence conducted to HCWs in Indonesia
Objective: To estimate the seroprevalence of HBV among HCWs at Dr Kariadi Hospital
Methods: This cross sectional study analyze data of HBV screening from HCWs in Dr Kariadi General Hospital that was done in 2018–2019. Data collection consisted of sex, age group, site of work, length of service period and seroprevalence of HBV including hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), hepatitis B core antibody (anti-HBc)
Results: Overall, 1870 HCWs were included in this study, with mean age of 36 ± 11 years and 1166 (62.4%) was female. Site of work consists of administration (4.2%), nonintervention (80.9%), and intervention groups (15.0%). There was 36.7% subject susceptible (all markers negative), 1.6% with current infection (HBsAg positive), 10.7% were considered natural immune (HBsAg negative and anti-HBc positive; anti-HBs positive), and 48.3% subjects have immunity as result of vaccination (only anti-HBs positive). There was a correlation between length of service period with seroprevalence of HCWs ($p < 0{,}001$)
Conclusion: This study reaffirms the need for more intensive screening, vaccination programme, also therapy to HCWs in certain condition, to against HBV infection

Abstract #1736

Hepatitis B virus genome analysis in relation to its pathogenesis

Raihan R[1], Akbar SMF[2], Al Mahtab M[3], Takahashi K[4], Masumoto J[2], Tabassum S[5], Tee KK[6,7], Binti Mohamed R[1].

[1]Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, Department of Microbiology, US Bangla Medical College, Narayanganj, Dhaka, Bangladesh, [2]Department of Pathology, Ehime University Proteo-Science Center, Ehime University Graduate School of Medicine, Toon City, Ehime, Japan, [3]Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, [4]Department of Medical Sciences, Tokyo-Shinagawa Hospital, Shinagawa, Tokyo, Japan, [5]Department of Virology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, [6]Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, [7]School of Healthcare and Medical Sciences, Sunway University, Bandar Sunway, Selangor, Darul Ehsan, Malaysia

Background: Hepatitis B virus (HBV) has infected about 2 billion people and about 291 million are chronically infected. A significant proportion of those infected may progress to cirrhosis of liver (LC) and hepatocellular carcinoma (HCC), therefore, treatment is required for eligible patients to prevent or at least reduce liver disease progression. To date, the majority of chronic HBV-infected patients are diag nosed and it is estimated that only 4.8 million receive anti-HBV therapy. Most developed countries have implemented strategies to prevent and control chronic HBV-infected patients. In contrast, most of the developing and resource-constrained countries, although harbouring more than 80% chronic HBV-infected patients, lack national strategic plan to address this important public health issue. HBV possesses considerable heterogenicity in the viral genome, and HBV genotypes may contribute to the pathogenesis of liver disease progression in those chronically infected. In this study, we investigated the HBV genotype and mutations in HBV genome in Bangladesh, the 9th most populous nation of the world with 5.5% prevalence of CHB.
Design: HBV genotyping was performed in 360 patients. 195 patients were classified into 3 groups [Group 1: HBV DNA < 2000 IU/mL

and ALT persistently less than the upper limit of normal (ULN); Group 2: HBV DNA > 2000 IU/mL and ALT persistently above ULN; Group 3: patients with LC and/or HCC)]. Full genome sequences of 38 isolates were performed. Partial sequencing of additional 73 isolates were accomplished to provide additional insights into the role of these mutations in liver damage.

Results: Three major HBV genotypes were prevalent among a total of 360 Bangladeshi chronic HBV-infected patients (Genotype A—18%, Genotype C—43% and Genotype D—39%). However, HBV genotype A and D were mostly found among patients of Group 1, whereas, genotype C predominates among patients of Group 2 (60.8%) and Group 3 (71.2%). Full genome sequences showed that mutations at T1762/A1764 were significantly higher in patients in Genotype C ($p < 0.001$). The T1762/A1764 mutations predominantly occurred in patients of Group 2 with high baseline HBVDNA and persistently raised ALT levels (60%) and Group 3 with LC or HCC (90%). Patients of Group 3 with HBV genotype C had T1762/A1764 mutations in 93.5% patients. Presence of Genotype C or mutations at T1762/A1764 is associated with 9 times higher risk of developing LC/HCC (OR 9.3, 95% CI 2.0–43.4, OR 9.0, 95% CI 2.3–50.9, respectively).

Conclusions: HBV genotypes C, D and A are prevalent among chronic HBV-infected patients in Bangladesh. HBV genotype C and mutation at T1762/A1764 was associated to the more advanced stages of chronic HBV-infections (CHB, LC, and HCC) with progression of HBV-induced liver diseases.

Abstract #1741

Rapid clearance of hepatitis B virus infection using ribonucleoprotein complexes of CRISPR/Cas9: results of in vitro and in vivo studies

Kostyushev D., Kostyusheva A., Brezgin S., Babin Y., Utkina A., Goptar I., Volchkova E., Chulanov V.

Site-specific CRISPR/Cas9 systems can effectively target hepatitis B virus (HBV) cccDNA for decay, but there are many aspects in CRISPR/Cas9 research that remain challenging for translation into clinical setting, including delivery into the body, limited potency and safety of CRISPR/Cas9. In a previous study we developed an efficient and safe approach for highly specific degradation of HBV cccDNA by CRISPR/Cas9 system from Streptococcus thermophilus [1]. We created ribonucleoprotein complexes (RNPs) of Cas9 protein (StCas9) and in vitro transcribed sgRNAs. StCas9 was generated to contain 6 × his tag for detection using anti-6 × his tag antibodies and nuclear localization signals. Three HBV in vitro cell culture systems were nucleofected by RNPs complexes with different sgRNAs. In vivo, liposome-coated RNP complexes were injected into BALB/C mice 6 hours post hydrodynamic injection of HBV-expressing plasmid. Antiviral activity of CRISPR/Cas9 was analyzed dynamically in vitro and in vivo using PCR (HBV DNA, RNA, cccDNA), immunocytochemistry (anti-StCas9, anti-HBcAg) and quantitative analysis of HBsAg. HBV RNAs were completely cleared whereas HBV DNA and cccDNA dropped by > 99% in 3 days after delivery of RNPs. In addition, small molecule inhibitor of non-homologous end-joining NU7026 (inhibitor of CRISPR/Cas9-mediated cccDNA degradation [2]) prevented cccDNA decay by RNP complexes. In vivo experiments in mice demonstrated 75–80% decline in HBV viral loads in 2 days post RNP injection.

In conclusion, this is the first study which utilized CRISPR/Cas9 RNPs for HBV targeting and for the first time revealed rapid clearance of HBV by CRISPR/Cas9 RNPs.

Abstract #1791

Efficacy and safety of switching to tenofovir alafenamide (TAF) in virally-suppressed chronic hepatitis B patients (CHB) with renal impairment: week 24 results

Chuang Wan Long[1], Huang Yi-Hsiang[2], Lim Young-Suk[3], Gane Edward J.[4], Ahn Sang Hoon[5], Tsang Tak Yin Owen[6], Heo Jeong[7], Hui Aric Josun[8], Elkhashab Magdy[9], Chen Chi-Yi[10], Su Wei-Wen[11], Flaherty John[12], Gaggar Anuj[13], Yee Leland J[14], Sethi Shalini[15], Jump Belinda[16], Mo Shuyuan[17], Jafri Syed-Mohammed[18], Janssen Harry L.A.[19]

[1]Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [2]Division of Gastroenterology & Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, [3]Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Songpa-gu, Seoul, South Korea, [4]Liver Unit University of Auckland, Auckland, New Zealand, [5]Severance Hospital, Seoul, South Korea, [6]Department of Medicine and Geriatrics, Princess Margaret Hospital, Hong Kong Special Administrative Region, Hong Kong, [7]Department of Internal Medicine, College of Medicine, Pusan National University, Division of Gastroenterology and Hepatology, Pusan National University Hospital, Busan, South Korea, [8]Alice Ho Miu Ling Nethersole Hospital, Hong Kong, [9]Toronto Liver Centre, Toronto, Canada, [10]Division of Gastroenterology and Hepatology, Department of Medicine, Ditmanson Medical Foundation Chiayi Christian Hospital, Chiayi, Taiwan[11]Department of Gastroenterology, Changhua Christian Medical Center, Changhua, Taiwan, [12]Gilead Sciences, Foster City, CA, USA, [13]Gilead Sciences, Foster City, CA, USA, [14]Gilead Sciences, Foster City, CA, USA, [15]Gilead Sciences, Foster City, CA, USA, [16]Gilead Sciences, Foster City, CA, USA, [17]Gilead Sciences, Foster City, CA, USA, [18]Division of Gastroenterology and Hepatology, Henry Ford Hospital, Detroit, Michigan, USA, [19]Toronto Centre for Liver Disease, Toronto General Hospital, University Health Network, Toronto, Canada

Introduction: TAF, a tenofovir prodrug, has demonstrated noninferior efficacy to TDF with superior bone and renal safety in virally-suppressed CHB patients with eGFR (by Cockcroft-Gault; $eGFR_{CG}$) ≥ 50 mL/min when switched from TDF.

Objectives: To evaluate the efficacy and safety of switching to TAF in virally suppressed, renally-impaired, CHB patients.

Methods: In this Phase 2 study, renally-impaired CHB patients taking TDF and/or other oral antivirals for ≥ 48 weeks and virally suppressed for ≥ 6 months with HBV DNA < 20 IU/mL at screening were enrolled into 2 cohorts: (1) moderate-severe renal impairment ($eGFR_{CG}$ 15- < 60 mL/min; N = 78) and (2) End Stage Renal Disease ($eGFR_{CG}$ < 15 mL/min; N = 15) patients on chronic hemodialysis . All patients were switched to TAF 25 mg QD for 96 weeks. Co-primary endpoints were proportion with HBV DNA < 20 IU/mL and adverse events (AEs)/lab abnormalities at Week 24. Secondary safety endpoints included changes in hip/ and spine bone mineral density (BMD), and in $eGFR_{CG}$.

Results: All patients on treatment at Week 24 maintained HBV DNA < 20 IU/mL and 88% had normal ALT levels. Relative to baseline levels, switching to TAF from TDF resulted in increases in hip/spine BMD, decreases in bone turnover markers, as well as increases in $eGFR_{CG}$ and decreases in renal tubular markers. TAF was well tolerated with few having Grade 3 or 4 AEs.

Conclusions: In renally-impaired CHB patients, including ESRD patients on hemodialysis, viral suppression was well-maintained, and the bone and renal safety were improved 24 weeks after switching from TDF to TAF.

Abstract #1795

Hepatitis B virus S gene mutation analysis in occult hepatitis B infection in indigenous people of Keerom, Papua, Indonesia

Wibowo DP[1], Turyadi[1,2], Rasyak MR[1], Witanto B[1], Ie SI[1], Maghfira[1], El-Khobar KE[1], Thedja MD[1], Muljono DH[1,2,3]

[1]Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [2]Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [3]Faculty of Medicine and Health, University of Sydney, Sydney, Australia

Introduction: Occult hepatitis B (OBI) is characterized by negative hepatitis B surface antigen (HBsAg) but detectable HBV DNA. Most OBI cases are asymptomatic and represent a source of undiagnosed and untreated HBV infection. OBI maintains the risk of disease development including liver cirrhosis and cancer. In some cases, OBIs are associated with HBsAg mutations.
Objectives: To determine HBsAg mutation patterns in OBI in indigenous people of Keerom, Papua, Indonesia.
Methods: A total of 320 apparently healthy individuals (mean age 34.27 ± 14.65; M/F: 115/205) were tested for HBsAg, anti-HBs, and anti-HBc using ELISA. HBV DNA were detected by nested PCR targeting HBV S gene "a" determinant region, followed by direct sequencing. OBIs were defined as HBsAg-negative but HBV DNA-positive. OBIs' viral genotype and HBsAg mutation patterns were analyzed using MEGA 5.2 and PROVEAN.
Results: HBsAg, anti-HBc, and anti-HBs prevalence was 21.3%, 71.3%, and 21.6%, respectively. Ninety-one (28.4%) have HBV DNA, with 44 (13.8%) HBsAg-positive and 47 (14.7%) HBsAg-negative (OBIs). Most OBIs were HBV/B (65.2%), with remaining 32.6% HBV/C and 2.2% HBV/D. Twenty OBIs have 30 identified HBsAg mutations, with 16 known mutations associated with vaccine and/or immune escape including G145R, found mostly in HBV/C, and T143S in HBV/B. Ten of the remaining 14 HBsAg mutations were identified by PROVEAN as having deleterious effect on HBsAg.
Conclusion: HBsAg mutations affecting its antigenicity and associated with escape mutant were found in OBIs in Keerom, Papua. High OBI incidence in HBsAg-negative population indicates the necessity of using HBV DNA detection for HBV screening.

Abstract #1799

Occult Hepatitis B infection in hepatitis B-vaccinated elementary school children in Kupang, East Nusa Tenggara

El-Khobar K[1], Rasyak MR[1], Kambuno NT[2], Kristina RH[2], Irfan[2], Djuma AW[2], Wibowo DP[1], Turyadi[1], Thedja MD[1], Muljono DH[1,3,4]

[1]Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [2]Kupang Health Polytechnic, Ministry of Health, Kupang, Indonesia, [3]Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [4]Faculty of Medicine and Health, University of Sydney, Sydney, Australia

Introduction: Occult Hepatitis B infection (OBI), characterized by absence of detectable HBsAg, remains a potential threat for HBV transmission especially in endemic areas. The implementation of national Hepatitis B (HB) vaccination in 1997 in Indonesia has reduced overall HBsAg prevalence in children, but the impact of OBI on HBsAg detection has been rarely investigated.
Objectives: To determine the prevalence and molecular characteristics of OBI in HB-vaccinated elementary school children in Kupang, East Nusa Tenggara.
Methods: We screened 230 children (5-12 years old; male: 114) with HB vaccination record for HBsAg, anti-HBs, and anti-HBc. From 36 HBsAg-positive and/or anti-HBc-positive samples, HBV DNA was amplified by nested PCR, directly sequenced for genotype/subtype determination and amino acid substitution identification, and further analyzed for antigenicity index alteration.
Results: HBV DNA was detected in 21 (58.3%) HBsAg-positive and 6 (16.7%) HBsAg-negative samples. Seventeen samples were B/*ayw*, 2 were B/*adw*, and the rest were C/*adr*. HBsAg amino acid substitutions were found in the B/*adw* samples (HBsAg-negative-anti-HBs-negative-anti-HBc-positive) with T131N and M133T/S as the most common mutations, while others were G119E/K, C121Y, P127S, A128T, Q129P, and D144A. These mutations altered HBsAg antigenicity index of respective samples.
Conclusions: OBI was found even in children with documented HB vaccination, with more HBsAg mutations found in OBI samples. This finding emphasized the need for evaluation of hepatitis B vaccination including catch-up immunization on school children to ensure the protection against HBV infection. Mutational pattern associated with HBsAg detection failure warrants further investigation in this endemic region.

Abstract #1801

Impact of treatment with tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF) on hepatocellular carcinoma (HCC) incidence in patients with chronic hepatitis B (CHB)

Lim Young-Suk[1], Chan Henry LY[2], Ning Qin[3], Kao Jia-Horng[4], Chuang Wan-Long[5], Izumi Namiki[6], Fung Scott[7], Dr Shalimar[8], Flaherty John[9], Mo Shuyuan[10], Gaggar Anuj[11], Yee Leland J[12], Jump Belinda[13], Hou Jin Lin[14], Seto Wai Kay[15]

[1]Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Songpa-gu, Seoul, South Korea, [2]Department of Medicine and Therapeutic, The Chinese University of Hong Kong, Hong Kong; [3]Department of Infectious Diseases, Tongji Hospital, Tongji Medical College, Wuhan, China, [4]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan; Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, [5]Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [6]Department of Gastroenterology, Musashino Red Cross Hospital, Tokyo, Japan; [7]Toronto Centre for Liver Disease, Toronto General Hospital, University Health Network, Toronto, Ontario, Canada; [8]Department of Gastroenterology and Human Nutrition, All India Institute of Medical Sciences, New Delhi, India; [9]Gilead Sciences, Foster City, CA, USA, [10]Gilead Sciences, Foster City, CA, USA, [11]Gilead Sciences, Foster City, CA, USA, [12]Gilead Sciences, Foster City, CA, USA, [13]Gilead Sciences, Foster City, CA, USA, [14]Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, Guangdong, China, [15]Department of Medicine, The University of Hong Kong, Hong Kong, wkseto@hku.hk.

Introduction: Potent antiviral treatment can reduce HCC incidence in CHB patients. In Phase 3 studies, TAF has shown antiviral efficacy similar to TDF, with higher rates of ALT normalization and no resistance.
Objectives: To evaluate the potential impact of TDF or TAF treatment on HCC incidence in CHB patients in the ongoing Phase 3 studies.

Methods: 1632 CHB patients with HBV DNA ≥ 20,000 IU/mL and ALT > 60 U/L (males) or > 38 U/L (females) were randomized (2:1) to TAF 25 mg or TDF 300 mg QD for up to 3 years, followed by open-label TAF through Year 8. HCC was assessed by regular hepatic ultrasonography introduced after Week 96 and throughout by local standards of care. Standardized incidence ratio (SIR) for HCC was calculated for observed cases relative to predicted risk using the REACH-B model.
Results: Through 5 years of follow-up, HCC occurred in 1.0% and 1.9% of patients taking TAF and TDF, respectively. Median time to HCC onset was 104 weeks (TAF 173, TDF 81 weeks). With treatment (TAF or TDF), HCC incidence was significantly reduced (SIR) [95% CI] 0.42 [0.27–0.64]. For TAF-treated patients, a significant risk reduction was seen SIR [95% CI] 0.35 [0.19–0.62]. With TDF, there was a reduction in incidence, but it did not achieve statistical significance SIR [95% CI] 0.55 [0.30–1.02].
Conclusion: In CHB patients receiving TAF or TDF through 5 years, the incidence of HCC was reduced when compared to expected HCC incidence as determined by the REACH-B model.

Abstract #1803

Existence of hepatitis B surface protein mutations and other variants: Demand for hepatitis B infection control in Cambodia

Ko Ko[1], Kazuaki Takahashi[1], Shintaro Nagashima[1], Chikako Yamamoto[1], Ork Vichit[2], Aya Sugiyama[1], Tomoyuki Akita[1], Masayuki Ohisa[1], Chuon Channarena[1], Shafiqul Hossain Md[3], Bunsoth Mao[4], Junko Tanaka[1]

[1]Department of Epidemiology, Infectious Disease Control and Prevention, Hiroshima University Graduate School of Biomedical and Health Sciences, Japan, [2]National Immunization Programme, Ministry of Health, 151-152 Kampuchea Krom Avenue, Phonm Penh, Cambodia, [3]Expanded Programme on Immunization, World Health Organization Country Office, Cambodia, [4]University of Health Sciences, 73 Monivong Boulevard, Phnom Penh, Cambodia

Objectives: This study aimed to detect Hepatitis B virus (HBV) genome sequences and their variants as of nationwide scale using dried blood spot (DBS) samples and to provide up-to-date reference data for infection control and surveillance in Cambodia.
Method: Among 2518 children age 5–7 years and their 2023 mothers participated in 2017 Cambodia nationwide sero-survey on hepatitis B surface antigen (HBsAg) prevalence using multistage random sampling strategy, 95 mothers and 13 children positive to HBsAg were included in this study. HBV DNA was extracted from DBS, then performed polymerase chain reaction. HBV genotypes and potential variants were examined by partial and full length genomic analysis.
Results: HBV DNA positive rate was 3.46% (70/2023) in mothers and 0.48% (12/2518) in their children. Genotype C (80.49%) was abundantly found throughout the whole Cambodia whilst genotype B (19.51%) was exclusively found in regions bordering Vietnam. HBs mutants were found in 24.29% of mothers and 16.67% of children. Full-length genome analysis revealed the homology of 99.62–100% in each mother-child pair. Genotype B was clarified to recombinant genotype B4/C2 and B2/C2. Double (48.39%) and combination mutation (32.26%) were observed in core promoter region of HBV C1 strains.
Conclusion: This study showed the capable of DBS for large-scale molecular epidemiological study of HBV in resource limited countries. Full-genome sequences yield the better understanding of subgenotypes, their variants and the degree of homology between strains isolated from mother-child pairs calls for effective strategies on prevention, control and surveillance of mother-to-child HBV transmission in Cambodia.

Abstract #1813

A model to estimate survival in hepatitis B virus-related acute-on-chronic liver failure based on dynamic changes in objective parameters

Rui Zhou, Ph.D.[1], Chun lin, Xiu-quan Lin, M.D.[2], Zu-xiong Huang, Ph.D.[1], Fang Sun[1], Yong Lin, M.D.[1], Shui-wen Huang, M.D.[1], Hai-bing Gao, M.D.[1], Chen Pan[1]

[1]Department of Liver Diseases, Infectious Disease Hospital, MengChao Hepatobiliary Hospital, Fujian Medical University, Fuzhou, china, [2]Department of Chronic Disease Prevention, Fujian Center for Disease Control and Prevention, Fuzhou, china

Objective: We aimed to develop a survival model for patients with HBV-related ACLF based on dynamic changes in the values of objective parameters.
Methods: This analysis was based on 714 patients (derivation cohort and validation cohort) with HBV-related ACLF who were hospitalized for more than 7 days in Mengchao Hepatobiliary Hospital of Fujian Medical University. Multivariable proportional hazards models and corresponding risk scores were created based on demographic characteristics and dynamic changes in the values of objective parameters. The validity of the new model was compared with the Model for End-stage Liver Disease (MELD).
Results: The survival model incorporated age, international normalized ratio (INR), Δ INR, Δ platelet (PLT) count, and levels of serum albumin (ALB), ΔALB, serum total bilirubin (TBIL), serum natrium (Na^+), serum alpha-fetoprotein (AFP), and Δ serum creatinine (Cr). The area under the curve (AUC) for the new model (0.791) was superior to that for MELD (0.579). The optimal cutoff for the new model was − 4.98, with a sensitivity of 80.6% and specificity of 72.4%.
Conclusion: The new model for predicting the survival of patients with HBV-related ACLF based on dynamic changes in the values of objective parameters was valid and superior to the MELD scoring system.

Abstract #1814

Spontaneous mobilization of bone marrow-derived stem cells and prognosis of patients with acute-on-chronic hepatitis B liver failure

Lin Chun

Aim: The aim of the study was to assess spontaneous mobilization of BMSC expressing the antigen CD34+ in acute-on-chronic hepatitis B liver failure (ACHBLF) and its relation to the prognosis.
Methods: By analyzing clinical data, blood biochemistry, hepatitis B virology index and peripheral blood CD34+ cell counts of patients with ACHBLF, chronic hepatitis B, and carriers with chronic HBV, the difference of CD34+ cell counts among the three groups was discussed. The influencing factors of CD34+ cell counts of patients with ACHBLF were analyzed.
Results: The results showed that the influences of ALT, ALT/AST, AFP, AMY, TG, CHE, INR and WBC on mobilization of bone marrow-derived stem cells and prognosis of patients with ACHBLF were statistically significant. 30 deaths (45.5%) were among patients with ACHBLF. The average CD34+ cell count of the death group was

0.36(1.63)/μl which was lower than 2.71(3.17)/μl in the survival group, and the differences were of statistically significance. Grouping median of CD34+ cell counts, survival analysis showed that the survival rate of the group which CD34+ cell counts were higher than 1.855/μl was higher than the group which CD34+ cell counts were lower than 1.855/μl.
Conclusions: The control group of liver failure was more active than chronic hepatitis B group and chronic HBV group in spontaneous mobilization of bone marrow-derived stem cells. ALT, ALT/AST, AFP, INR, AMY, TG, CHE and WBC were the influencing factors in spontaneous mobilization of bone marrow-derived stem cells. Levels of spontaneous mobilization of bone marrow-derived stem cells were related with prognosis.

Abstract #1817

The effects of granulocyte colony-stimulating factor on the marrow-derived stem cells mobilization and prognosis in patients with HBV-related acute-on-chronic liver failure

Lin Yong

Background and objective: To investigate the effects of granulocyte colony-stimulating factor (G-CSF) on the marrow-derived stem cells mobilization and prognosis in patients with hepatitis B virus related acute-on-chronic liver failure (HBV-ACLF) by random control.
Methods: First, 140 patients with HBV-ACLF were divided into a control group and a treatment group randomly. Patients in the control group received the comprehensive physical treatment; patients in the treatment group received the comprehensive physical treatment and G-CSF. Next, compare the differences of maximum CD34+ cell count and prognosis between two groups. Then adopt *t* test or non-parametric test, Chi-square test or Fisher exact test to examine results and use Survival Analysis on prognostic difference according to different data.
Results: The study was completed with 66 patients of the control group and 60 patients of the treatment group. The maximum CD34+ cell count of the treatment group [3.0(1.45)/μl] was higher than the control group [1.86(2.58)], and the difference was statistically significant ($Z = -2.385$, $P = 0.017$). The results of Survival Analysis showed that the area under the curve (AUC) was larger than the control group with a higher survival rate, and the difference was equally statistically significant (Log Rank = 4.101, P = 0.043).
Conclusion: G-CSF can enhance the marrow-derived stem cells mobilization in HBV-ACLF patients and improve survival rate.

Abstract #1863

Serum MIP-3α predicts disease progression of hepatitis B-related acute on chronic liver failure

Xin Jiaojiao[1], An Zhanglu[1], Li Jiang[1], Liang Xi[1], Li Jiaqi[1], Li Jun[1]

[1]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine. 79 Qingchun rd., Hangzhou, 310003. China.

Introduction: Acute liver dysfunction on the basis of chronic hepatitis B is the main type of acute on chronic liver failure(ACLF). COSSH-ACLF criteria is a effective tool in diagnosis and staging of HBV-ACLF, and the expression level of macrophage inflammatory protein 3α (MIP-3α) is positively correlated with the severity of ACLF. This study intent to further clarify the expression characteristics of MIP-3α in different stages of disease progression.
Objectives: We selected 422 patients with HBV aetiology from the COSSH study open cohort: chronic hepatitis B (CHB, n = 99), liver cirrhosis (LC, n = 104), acute-on-chronic hepatic dysfunction (ACHD, n = 81), and ACLF (n = 138). Normal healthy volunteers were enrolled as controls (NC, n = 98). Relevant clinical data were collected.
Methods: The expression level of MIP-3α in serums from 520 subjects were detected by enzyme-linked immunosorbent assay (ELISA).
Results: The expression of MIP-3α was significantly increased in ACHD (23.59 ± 73.05 pg/ml) and ACLF (142.48 ± 282.63 pg/ml) groups, compared with the NC(0.65 ± 5.53 pg/ml), CHB (1.41 ± 4.18 pg/ml) and LC (2.39 ± 1.26 pg/ml) groups ($P < 0.01$), and there was also a significant difference between ACHD and ACLF groups ($P < 0.001$). In addition, we found that the MIP-3α expression level of 4 patients in the ACHD group was particularly high, further analysis showed that 3 of 4 patients developed into ACLF in 1 month.
Conclusion: The expression of MIP-3α was related to the development of HBV-ACLF,and might be useful as a novel biomarker for early diagnosis of HBV-ACLF, which will provide theoretical support for clinical HBV-ACLF intervention and reduction of incidence rate.

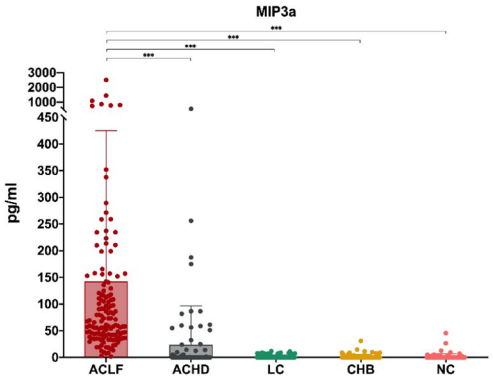


Fig 1. MIP-3α expression levels in different stages of disease progression

Abstract #1865

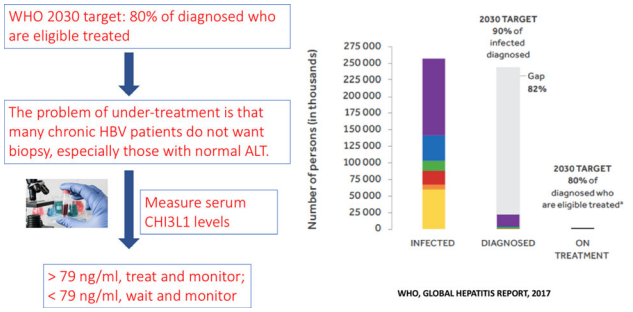
CHI3L1 as a non-invasive marker for effective selecting of chronic HBV patient with normal ALT levels but with advanced liver fibrosis for treatments

Lin Biaoyang[1-3], Liu Yunhua[4], Qian Yunsong[5], Longgen Liu[6], Shengjun Wu[7], Zhang Hongfei[8]

[1]Dept. of Urology, University of Washington School of Medicine, Seattle, WA, USA, [2]Systems Biology, Zhejiang-California International Nanosystems Institute (ZCNI), Zhejiang University, Hangzhou 310058, Zhejiang, China, [3]Proprium Biotech USA LLC, Seattle, WA, USA, [4]Department of Liver Diseases, The Second Hospital of Yunnan Province, Kunming 650000, Yunnan Province, China, [5]Department of Liver Diseases,Ningbo No.2 Hospital, Zhejiang Province, China, [6]Department of Liver Diseases,the Third People's Hospital of Changzhou, 300 North Lanling Rd, Changzhou 213001, Jiangsu, China, [7]Dept. of clinical laboratories, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou 310020, China, [8]Center for Liver Diseases, Changfeng Hospital of Jumei Medical group, Beijing

Introduction: WHO has mandated a goal for reaching 80% treatment rate for eligible HBV patients by 2030. However, the current treatment rate for eligible HBV patients is only about 8% worldwide due to lack of effective and noninvasive means to identify those eligible patients.

Objectives: To test the utility of using CHI3L1 for the identification of occult ongoing liver fibrosis for those chronic HBV patients with normal ALT levels.
Methods: Serum CHI3L1 levels were measured by the ELISA kit with CFDA approval and CE mark status from Proprium Biotech Co. Ltd (Hangzhou, China).
Results: We found that 20 of 61 (46.5%) chronic HBV patients with biopsy-confirmed fibrosis stage > 2 or inflammation > 2 and normal ALT have CHI3L1 level greater than 79 ng/ml, which was previously established to identify fibrosis stage > 2 for HBV patients. Furthermore, we identified 10 naïve chronic patients (no prior antiviral treatments) with CHI3L1 > 79 ng/ml but normal ALT (< 40), and subjected them to entecavir treatments. Nine of the 10 patients showed reduced CHI3L1 levels at week 12. Finally, we recruited 405 patients who underwent antiviral treatment and measured the CHI3L1 in 2-3-month intervals. 73.09% showed improved fibrosis (CHI3L1 reduced > 5 ng/ml), 7.16 showed stable fibrosis and 19.75% still showed progressive fibrosis, which await longer antiviral treatments.
Conclusion: CHI3L1 is a non-invasive surrogate serum marker for effectively identifying chronic HBV patient with normal ALT levels but with occult ongoing liver fibrosis passing stage 2 for starting antiviral treatments.



Abstract #1918

The changes of the degree of liver fibrosis and its correlation with duration of therapy in chronic hepatitis B patients, Sanglah General Hospital Denpasar

NWW Dharmesti[1], IDN Wibawa[2], IK Mariadi[2], G Somayana[2]

[1]Resident: Internal Medicine Department, School of Medicine Udayana University/ Sanglah General Hospital, Denpasar, Bali, Indonesia, [2]Division of Gastro-Entero-Hepatology, Internal Medicine Department, School of Medicine Udayana University/ Sanglah General Hospital, Denpasar, Bali, Indonesia

Introduction: Liver fibrosis was regarded as irreversible since long time ago, until recent evidences persistently showed regression of fibrosis if the underlying causes of liver injury could be eliminated. Fibrosis reversibility in patient with chronic Hepatitis B is expected after treatment with antiviral, hence make this event as one of therapeutic goal in treating patients with chronic Hepatitis B.
Objectives: This study is aimed to evaluate the change of degree of liver fibrosis in our patient treated at Gastro-Hepatology outpatient clinic Sanglah General Hospital, also its correlation with duration of therapy.
Methods: This is a retrospective observational (analytic cross-sectional) study involving patients with chronic Hepatitis B infection treated at Gastro-Hepatology outpatient clinic Sanglah General Hospital from January 2016 until May 2019. Degree of liver fibrosis is evaluated using transient elastography (TE), we compare the degree of fibrosis before and after starting antiviral therapy. We also evaluate, whether degree of liver fibrosis after treatment has a correlation with the duration of therapy. Inclusion criteria are patient age > 18 years old, without co-infection of Hepatitis C and HIV, and have complete data of liver fibrosis before and after starting therapy with antivirus.
Results: This study enrolled total of 78 patients with chronic Hepatitis B, we found initial mean of liver fibrosis is 14.66 kPa ± 13.33 (3.3–75.0) and mean of 9.27 kPa ± 7.05 (3.4–37.0) after starting therapy, this difference is statistically significant using Wilcoxon test ($p < 0.01$). The mean duration of therapy in month is 14.18 ± 10.15 (1–38). We found significant correlation between duration of therapy with change in degree of liver fibrosis after therapy (r = − 0.258, p 0.02).
Conclusion: Antiviral therapy in chronic Hepatitis B gives significant improvement in degree of liver fibrosis, as compare to fibrosis before therapy. Improvement of liver fibrosis has significant correlation with duration of therapy.

Abstract #1921

Hepatitis B virus infection profile in Enggano Island, Bengkulu, Indonesia

Wibowo DP[1], Rasyak MR[1], Turyadi[1,2], Ie SI[1], Witanto B[1], El-Khobar K[1], Thedja MD[1], Muljono DH[1,2,3]

[1]Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [2]Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [3]Faculty of Medicine and Health, University of Sydney, Sydney, Australia

Introduction: Hepatitis B virus (HBV) infection remains a global health problem with high rates of mortality and morbidity. Adequate HBV epidemiological data is needed in Indonesia, as an archipelago country with high HBV endemicity, to improve current HBV preventive and curative strategies. Currently, there is limited data on the HBV infection profile among population in the outermost islands of Indonesia.
Objectives: To investigate HBV serological profile in Enggano Island, Bengkulu, one of the outermost islands of Indonesia.
Methods: A total of 399 plasma samples were collected from apparently healthy subjects (mean age 37.2 ± 16.9; 64.7% female) from Enggano Island, Bengkulu, following individual informed consent. HBV serological markers, HBsAg, total anti-HBc, and anti-HBs were tested by ELISAs. Data on serological profile, age, and gender were then analyzed by SPSS.
Results: Total HBsAg, anti-HBc, and anti-HBs prevalence were 4.5%, 39.1%, and 26.6%, respectively. More than half of the subjects (55.4%) were still susceptible to HBV infection, while the remaining subjects could be categorized as: isolated anti-HBs (5.3%), HBV-infected (acute/chronic) (4.6%), immune due to past HBV infection (20.8%), and isolated anti-HBc (14%). There was no significant difference in HBV seroprevalence between genders. HBsAg prevalence were not associated with age, however both anti-HBc and anti-HBs prevalence increased gradually according to age ($p < 0.001$).
Conclusion: Moderate HBsAg with high anti-HBc prevalence was found in Enggano Island. Increasing trends of anti-HBs and anti-HBc might reflect the occurrence of horizontal transmission. Protecting susceptible individuals and improving HBV management and care are necessary to reduce further HBV transmission.

Abstract #1960

Association of LAIR-1 expression on peripheral blood T cells with clinical-virological characteristics and T cell cytokines production in untreated chronic hepatitis B Patients

Gu Yurong[1], Bi Yanhua[2], Chen Lubiao[1], Gu Lin[2], Li Jing[2], Wei Huan[2], Huang Yuehua[1,2]

[1]Department of Infectious Diseases, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China., [2]Guangdong Provincial Key Laboratory of Liver Disease Research, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Introduction: Inhibitory receptors including PD-1, CTLA-4, TIM-3 plays an important role in T cell immunity on chronic hepatitis B (CHB) patients. However, little is known about the expression of inhibitory receptor leukocyte-associated immunoglobulin-like receptor-1 (LAIR-1) on T cells in CHB patients.
Objectives: To study the expression of LAIR-1 on T cells in different phases of CHB and its correlation with clinical-virological characteristics and cytokine production.
Methods: 320 CHB patients in different phases and 17 healthy donors were enrolled. LAIR-1 expression and cytokine production of T cells were tested by flowcytometry.
Results: The LAIR-1 expression in T cells were significantly lower in IA (immune-active) than IT (immune-tolerant), IC (inactive-carrier), GZ (gray-zone) patients and healthy controls. LAIR-1 expressions on CD4+ T and CD8+ T cells showed significantly negative association with HBV-DNA load ($r = -0.1397, -0.1491$, $p = 0.0128, 0.0078$, respectively) and were lower in HBeAg+ patients than HBeAg− ($p < 0.05$). In addition, LAIR-1 expressions on total T, CD4+ and CD8+ T cells were all found negatively associated with liver inflammation ALT levels and Fibroscan values ($p < 0.05$). Interestingly, the results showed that LAIR-1 expressions on T cells had negative correlations with pro-inflammatory cytokines IL-2+, IFN-γ+ and TNF-α+ produced by total T, CD4+ and CD8+ T cells ($p < 0.05$).
Conclusion: LAIR-1 levels on T cells were associated with virology, liver inflammation and fibrosis variables and T cells pro-inflammatory cytokines production, which suggest LAIR-1 might play an important regulatory role in the HBV induced T cell immune-pathogenesis in CHB patients.

Abstract #2025

The outcomes of dose reduction in patients with chronic hepatitis B infection who had renal impairment after treatment with tenofovir disoproxil fumarate

Monson Saritwetworakun[1], Supot Nimanong[1]

[1]Division of Gastroenterology, Department of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: Tenofovir disoproxil fumarate (TDF) is the first line treatment for patients with chronic hepatitis B (CHB) infection. However, TDF can induce renal dysfunction, including acute kidney injury (AKI) and hypophosphatemia, which leads to dose reduction or discontinuation and switch to more expensive drugs such as entecavir and tenofovir alafenamide. We aimed to evaluate the outcomes of dose reduction strategy in patients with CHB infection who had renal impairment after treatment with TDF.
Methods: This retrospective cohort study included patients with CHB who had reduced dose of TDF due to rising of serum creatinine (sCr) or hypophosphatemia (serum phosphorus < 2.5 mg/dL) at Siriraj Hospital from January 1, 2012 to December 31, 2018. Patients were excluded if they had prior chronic kidney disease (eGFR < 60 ml/min/1.73 m^2), hypophosphatemia, co-infection with HCV or HIV, concomitant hepatocellular carcinoma, or AKI from other causes. The baseline characteristics and laboratory data were collected. The outcomes measured the improvement of renal dysfunction and HBV virological breakthrough after dose reduction of TDF. The independent prognostic factors were identified.
Results: The prevalence of renal dysfunction in patients with CHB, receiving TDF was 12%. A total of 182 patients were enrolled, 71.4% were men and the mean age was 57 years. There were 35.7% with HBeAg positive, 10.4% with cirrhosis (mostly Child A). The median duration of TDF use before dose reduction was 46.7 months. The number of patients with rising sCr, hypophosphatemia and both were 85.2%, 3.9% and 10.9% respectively. The mean change of rising sCr was 0.19 ± 0.14 mg/dl and the mean decrease in eGFR was 16.48 ± 11.16 ml/min/1.73 m^2. There were only 19.2% of patients who had AKI (sCr increased more than 0.3 mg/dl). Three month after dose reduction of TDF, there were 78.9% of patients with improved eGFR and 62.9% of patients with complete recovery of hypophosphatemia. Interestingly, 4.4% of patients had virological breakthrough after dose reduction of TDF. The median level of AST and ALT were 24 (21–98) and 19 (16–56) IU/ml respectively, and none of them had jaundice. After multivariate analysis, the predictors of absence of renal improvement after TDF dose reduction were statin use (OR 4.64, 95% CI 1.84–11.72, P 0.001) and eGFR less than 60 ml/min/1.73 m^2 (OR 2.61, 95% CI 1.001–6.82, P 0.05).
Conclusions: The prevalence of renal dysfunction in patients with CHB infection, treated with TDF was 12%, most of them had mild rising of serum creatinine. Dose reduction strategy is effective without clinical significant HBV reactivation. The risk factor of non-recovery of renal impairment were statin use and eGFR less than 60 mL/min/1.73 m^2.

Abstract #2039

Serum HBV pregenomic RNA is associated with NK cell immunity in treatment-naïve chronic hepatitis B

Gu Yurong [1], Huang Zexuan[2], Li Xiaoyan[1], Liao Chunhong[2], Bi Yanhua[2], Huang Yuehua[1,2]

[1]Department of Infectious Diseases, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China, [2]Guangdong Provincial Key Laboratory of Liver Disease Research, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Introduction: As a new hepatitis B virus (HBV) biomarker, little is known about the role of HBV pregenomic RNA (pgRNA) in nature killer (NK) cell immunity.
Objectives: To identify the relationship between serum HBV pgRNA and NK cell immunity in chronic hepatitis B (CHB) patients.
Methods:323 treatment-naïve CHB patients were enrolled. Serum HBV pgRNA was detected by a reverse transcription-polymerase chain reaction. NK cells were tested by flow cytometry. Serum cytokines were measured by Luminex multiplex platform.
Results: Serum HBV pgRNA was found positively associated with Fibroscan value, HBV-DNA and HBsAg titers by both of univariate and multivariate linear regression analysis ($P < 0.05$), and positively associated with liver inflammation (AST and ALT) by only univariate linear regression analysis ($P < 0.001$). Although serum HBV pgRNA was found negatively correlated with frequencies of NK, NKdim and NKT cells, except for NK^{bright} cells ($B = 3.957$, $P < 0.001$), it was positively correlated with TNF-α^+ produced by NK, NK^{dim} and NKT cells ($P < 0.05$). Furthermore, serum HBV pgRNA was found negatively correlated with exhaustion marker LAIR-1 expression on NK,

NK^{dim} and NKT cells ($P < 0.05$) and negatively correlated with NK cell inhibitory cytokine PGE2 in serum ($P = 0.002$). Serum HBV pgRNA showed positive correlation with the expression of NKP44 on NK and NK^{dim} cells ($P < 0.05$). However, no significant correlation was found between HBV pgRNA and NKG2A, NKG2D on these cells.

Conclusion: This study showed that that serum HBV pgRNA had association with NK cell related immunity, indicating that HBV pgRNA might play a positive role in activating NK cell immunity.

Abstract #2056

GIV improves HBV particles assembly via enhancing endosomal trafficking and blocking autophagy degradation

Wei Zhiqiang[1], He Yulin[1], Cheng Bin[1], Li Ruiming[1], Meng Zhongji[1]

[1]Institute of Biomedical Research, Taihe Hospital, Hubei University of Medicine, Shiyan 442000, Hubei province, China

Introduction and objectives: Hepatitis B virus particles are thought to be secreted from hepatocytes through multivesicular bodies (MVB), however the upstream mechanisms of HBV particle assembly are unknown. We previously reported that the expression of Gα-interacting vesicle-associated protein (GIV), which is involved in multiple vesicle transports, dynamically changes at different stage of chronic HBV infection. The aim of this study was to investigate the role of GIV in HBV replication.

Methodology: HBV replication and expression were evaluated in HepG2.2.15 and Huh7 cells lines. Cellular membrane trafficking systems including autophagy and endosome were investigated to study the mechanism of GIV's action on HBV replication.

Results: HBV infection inhibited GIV expression, which modulates the formation of endosome and autophagosome. However, GIV overexpression significantly enhanced HBV replication, and endosome formation, but inhibited autophagosome formation. In addition, GTPase dynamin-2 (one of the effectors of GIV), CLTC and Rab5A, which are the critical proteins in endocytosis, had similar effects like GIV on HBV replication. Furthermore, blocking endocytosis can cause HBsAg accumulating in the endoplasmic reticulum (ER), which triggers ER stress and autophagic degradation of HBV antigens, and prevents HBV core particles from entering MVB. Otherwise, GIV and its another effector GTPase Gαi3 decreased autophagosome formation through enhancing insulin induced Akt/mTOR pathway. In contrast to the results of GIV silencing, Gαi3 silencing increases HBV replication, suggesting that GIV-regulated HBV replication is Gαi3 independent.

Conclusion: GIV enhanced HBV replication by increasing endosome formation, suggesting that endocytosis plays an important role in HBV replication.

Abstract #2062

An immuno-clinic model for early detection of chronic hepatitis B patients needing antiviral therapy

Gu Yurong[1], Li Xiaoyan[1], Chen Lubiao[1], Gu Lin[2], Lian Yifan[2], Huang Yuehua[1,2]

[1]Department of Infectious Diseases, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China, [2]Guangdong Provincial Key Laboratory of Liver Disease Research, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

Introduction: Immune pathogenesis is the main mechanism inducing liver injury in chronic hepatitis B (CHB). However, immune model to predict disease progression is lack.

Objectives: To develope an immuno-clinic model (ICM) that could detect the CHB patients who would turn into the antiviral therapy recommendation in 2 years.

Methods: Expression of 97 immune features of T and nature killer (NK) cells in blood was measured by flowcytometry. An ICM_{CHB} was constructed using LASSO Cox regression model in 158 CHB patients of training cohort. 68 patients were included for validation.

Results: Principal component analysis (PCA) by the 97 immune features in training cohort showed highly consistent with classification by antiviral therapy criteria of 2018 American Association for the Study of Liver Diseases. Then using LASSO model, we established an ICM_{CHB} based on 6 out of 97 immune features and 3 clinic features: CD3_CD107a+, CD3_CD127+, CD8_perforin+, NK-perforin+, NKbright, NKbright-TNF-α+, AST, HBV-DNA and fibroscan value. Through receiver-operator characteristic (ROC) curve analysis, the area under the curve (AUC) of the ICM_{CHB} to classify patients who would turn into the antiviral therapy recommendation in 2 years were 0.968 (95% CI 0.935–0.992), sensitivity and specificity were 0.951 and 0.903 respectively in the training cohort. In the validation cohort, the AUC, sensitivity and specificity of the ICM_{CHB} were 0.836 (95% CI 0.716–0.955), 0.841 and 0.724 respectively.

Conclusion: ICM_{CHB} could effectively identify the CHB patients who would turn into the antiviral therapy recommendation in 2 years, indicating ICM_{CHB} might be a useful tool for instructing antiviral therapy in advance.

Abstract #2072

The contrary characteristics of Tim-3 on T and NK cells in treatment-naïve patients with chronic hepatitis B

Li Jing[2], Gu Yurong [1], Li Xiaoyan[1], Liao Xialin[2], Huang Zexuan[2], Bi Yanhua[2], Huang Yuehua[1,2#]

[1]Department of Infectious Diseases, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China, [2]Guangdong Provincial Key Laboratory of Liver Disease Research, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

Introduction: Immune response mediated by T and nature killer (NK) cells plays an important role in chronic hepatitis B (CHB). As an immunoregulatory molecule, the characteristics of T cell immune globulin-and mucin-domain contain in gmolecule-3 (Tim-3) on T and NK cells are unknown.

Objective: To identify the association of Tim-3 on NK and T cells with clinical-virological features and cytokines production in treatment-naïve CHB patients.

Method: 337 CHB patients in different phases and 17 healthy donors were enrolled. Tim-3 expression and cytokine production were tested by flowcytometry.

Results: The expressions of Tim3 on total T, CD4+ T and CD8+ T cells were significantly higher in IA (immune-active) phase than IT (immune-tolerant), IC (inactive-carrier), GZ (gray-zone) phases and healthy controls, while Tim3 on NK, NK^{dim} and NK^{bright} cells was higher in the IT and IC phases which had normal aminotransferase levels. Tim3 expressions on T and subset cells were found positively associated with liver inflammation (ALT, AST and TBIL), fibrosis (Fibroscan value and APRI score) and virological features (HBV-DNA, HBsAg titers and pgRNA). In contrast, Tim3 expressions on NK and subset cells were negatively associated with above clinical-virological features. Interestingly, Tim3 expressions of CD8+ T cells were positively correlated with inflammatory cytokines TNF-α+

production, however, Tim3 expressions of NK, NK^{dim} and NK^{bright} cells showed negative association with cell inflammatory cytokines production.
Conclusion: Tim-3 expression on T cells and NK cells showed contrary characteristics with liver inflammation, fibrosis, virus features and immune cytokines, indicating its different immune roles on different cells in CHB.

Abstract #2123

Anti HBc positivity: should we ignore it? Challenges in managing HBV reactivation in panhypopituitarism

Khan Ahsan Habib[1], Alam Md Shahinul[2], Mustafa Md Golam[3], Mukit Abdullah Al[4], Mahtab Mamun Al[5]

[1]Senior Resident, Department Of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, [2]Associate Professor, Department Of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, [3]Associate Professor, Department Of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, [4]Senior Resident, Department Of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, [5]Chairman & Professor, Department Of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Hepatitis B reactivation is the reappearance or rise of Hepatitis B Virus (HBV) DNA in the serum of patients with past or chronic HBV infection. Reactivation can occur in a variety of clinical settings, usually in the context of an immunosuppressed state or immunosuppressive therapy. There are certain conditions where an individual may require lifelong maintenance corticosteroid therapy. In such conditions, HBV flares or reactivation is not uncommon. Although the HBsAg positive patients or those having Occult HBV Infections are usually properly evaluated prior to initiation of lifelong immunosuppressive therapy, those who are Isolated Anti HBc (IAHBc) positive are quite often ignored. Hepatitis B core antibody (Anti HBc) is currently considered as the most sensitive serological marker for a patient's history of HBV infection given its long-term persistence in the bloodstream. When considering IAHBc positive patients requiring long term immunosuppressive therapy, the use of antiviral prophylaxis or preemptive therapy should be taken into consideration after proper evaluation of complete HBV profile in order to prevent disease progression and consequent development of HCC. We report a case of a 45 year old IAHBc positive gentleman, who was diagnosed with Panhypopituitarism requiring long term low dose immunosuppressive steroid therapy, now presented with HBV reactivation. Although HBV reactivation or flares are quite common in patients receiving higher doses of steroids, we report this interesting case where the patient was getting low dose maintenance steroid therapy while being only IAHBc positive and still developed HBV reactivation within a few months.

Abstract #2165

Systematic review with meta-analysis: combination treatment of regimens based on pegylated interferon for chronic hepatitis B focusing on hepatitis B surface antigen clearance

Wit Jeamwijitkul[1], Kanit Bunnag[1], Worayon Chuerboonchai[1], Chutatip Charoenthanawut[1], Pongpan Boonmeeseeprasert[1], Pawinee Saybungkla[2], Supattraphorn Kullapa[3], Sakkarin Chirapongsathorn[4]

[1]Department of Internal Medicine, Phramongkutklao hospital; [2]Computer center, Phramongkutklao hospital; [3]Phramongkutklao hospital library; [4]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Phramongkutklao hospital, Bangkok, Thailand

Background and aims: Current guidelines recommend either a finite course of pegylated interferon (PEG-IFN) or nucleoside/nucleotide analogues (NA) treatment, however patients with chronic hepatitis B infection rarely achieve loss of serum HBsAg. Several new studies shown that PEG-IFN plus NA have better outcome than PEG-IFN alone. This study aimed to perform a systematic review and meta-analysis of randomized controlled trials that have evaluate treatment strategy that compared PEG-IFN plus NA with PEG-IFN monotherapy.
Method: We performed a comprehensive search of several electronic databases—UpToDate, AccessMedicine, Cochrane Library, and PUBMED databases through December 2019, supplemented with a manual search.—using the search terms "hepatitis B" and "humans" and "adults" and "RCTs" and "pegylated interferon" and "combination". Hepatitis B surface antigen clearance rate was the primary outcomes, and we also analyze virological response and biochemical response.
Results: Our analysis included 11 RCTs studies involving 3,136 patients. All studies was differentiated by combination therapy strategies. Most of combination therapy trial was PEG-IFN plus lamivudine (5 studies), others was PEG-IFN plus Adefovir/Entecavir/Tenofovir (2 studies in each group). Analysis was revealed that PEG-IFN combined with adefovir produced better virological outcome than PEG-IFN monotherapy at the end of treatment [RR 0.46 (0.31–0.68)], PEG-IFN combined with tenofovir has significant better HBsAg loss rate than in PEG-IFN monotherapy [RR 0.27 (0.12–0.72)]. Another combination treatment has shown no significant treatment outcome in all respects. No publication bias demonstrate in analysis.
Conclusion: PEG-IFN plus adefovir has better virological outcome at the end of treatment and PEG-IFN plus adefovir has better HBsAg loss rate than PEG-IFN monotherapy. Combination treatment using Peg-IFN with nucleotide analogues (adefovir and tenofovir) may be useful to help patients achieve better outcome than PEG-IFN monotherapy.

Poster Presentations

Abstract #43

Comparison of occult hepatitis B prevalence between blood donors and pre-surgery screened patients

Sevda Aghayeva[1], Alihuseyn Hidayatov[1], Parvana Hajiyeva[2], Hicran Xidirova[3]

[1]Azerbaijan Medical University, Baku Azerbaijan, [2]Azerbaijan Institute of Hematology and Transfusion, Baku Azerbaijan, [3]Medera Hospital, Baku Azerbaijan

Objectives: Anti-HBcIgG is not included in the routine viral hepatitis B screening tests in Azerbaijan, thus, the rates of occult hepatitis B infection is unknown.
Methods: A total of 512 blood donors, (mean age 41.2; 26% females) and 149 preoperatively screened patients (mean age 52.7; 40.9% females) were checked for anti-HBcIgG along with standard HBsAg and anti-HCV tests. HBsAg (−), anti-HBcIgG (+) individuals were additionally screened for anti-HBcIgM, anti-HBs, HBeAg anti-HBe, and HBV DNA viral load. The results were compared.

Results: The prevalence of HBV and HCV was higher in preoperatively screened patients comparing to younger and healthier donors: 2.7 vs 3.3%; 3.5 vs 4% respectively. In HBsAg (−) donor group anti-HBcIgG was detected in 43 (9.3%), of which 7 (16.3%) had low detectable viral load. Among 17 HCV-positive donors, anti-HBcIgG was detected in 10 (37%), of which 2 (20%) showed detectable HBV DNA. Among 138 preoperatively screened patients 16 (11.6%) had positive anti-HBc IgG, 3 (18.75%) showed minimal viral load. Among 6 HCV (+) patients 3 (50%) had anti-HBcIgG; one (33.3%) had countable HBV DNA.
Conclusion: Older age, previous surgeries/blood transfusions are associated with slightly higher rates of positive HBsAg, anti-HCV and anti-HBcIgG. HBV DNA detection rate in patients with positive anti-HBcIgG was the same in both groups.

Abstract #44

Occult hepatitis B infection in patients with elevation of liver enzymes during chemotherapy for GI malignancies

Sevda Aghayeva[1], Alihuseyn Hidayatov[1], Nasimi Qasimov[2]

[1]Azerbaijan Medical University, Baku Azerbaijan, [2]Oncology Clinic of Azerbaijan Medical University, Baku Azerbaijan

Objectives: The presence of occult hepatitis B infection may also be a cause of elevated of liver enzymes during chemotherapy, mimicking toxic liver injury.
Method: A total of 51 patients with newly diagnosed with various GI malignancies and were assigned for chemotherapy ± surgery were followed up by checking liver enzymes during each cycle of chemotherapy. Those who showed elevation of normal pre-treatment liver enzymes were screened for anti-HBcIgG. Patients with positive test result, were further screened for HBV DNA level.
Results: Five (9.8%) patients were positive for anti-HBc antibodies; detectable HBV DNA was observed in 2 (40%) samples. HBV DNA level was 69 IU/ml and 312 IU/ml, respectively. Low viral load (< 2000 IU/ml), was associated with slightly higher mean ALT and AST level (92 vs 81; 86 vs 63 respectively, $p < 0.5$). Fluorodeoxyuridine (5FUDR) for treatment of colorectal liver metastases was associated with the highest elevation of the liver enzymes, mostly after the fourth cycle of chemotherapy administration.
Conclusion: Occult hepatitis B with detectable HBV DNA may cause slightly higher elevation of liver enzymes during chemotherapy treatment than antineoplastic agents alone. Chemotherapy did not provoke reactivation of OBI. Larger sample size and further molecular analysis is needed for the evaluation of patients with OBI.

Abstract # 55

Impact of viral load on liver fibrosis in patients with chronic hepatitis B infection: using transient elastography

Usama M Abdelaal, MD, PhD[1], Mohammed E Mahmoud, MB BCh[1], Ali Taha Ali, MD[1], Amal Khalifa Ahmed, MD[1]

Department of internal medicine, Sohag hospital, Sohag, Egypt

Background and aim: Hepatitis B virus (HBV) infection is a serious global health burden, and a leading cause of chronic hepatitis, hepatic fibrosis, cirrhosis, and hepatocellular carcinoma. In Egypt, the prevalence of HBsAg is of an intermediate endemicity (2–8%). It has been known that the Viral load and degree of hepatic fibrosis are considered independent factors which predict clinical outcomes after persistent HBV infection. However, the exact relationship between viral load and hepatic fibrosis is not well studied. we aimed to explore the clinical impact the viral load on the degree of hepatic fibrosis.
Patients and methods: 60 patients with evident chronic HBV infection were enrolled. Using transient elastography, the patients were divided into 2 groups. Group 1: low fibrosis stage F1–2, and Group 2: high or significant fibrosis stage (F3–F4). Both groups were statistically compared with respect to HBV-DNA viraemia (PCR), clinical, and laboratory investigations.
Results: Higher grades of liver fibrosis on top of CHB were associated with a significant elevation of s. bilirubin ($p = 0.048$) and INR ($p < 0.0001$), and with a significant decrease in s. albumin ($P = 0.01$). Additionally, the viral load was significantly higher in patients with higher grades of liver fibrosis and cirrhosis ($P = 0.03$).
Conclusions: During follow up, an obvious reduction in the viraemia level may indicate a significant hepatic fibrosis in patients with chronic HBV infection. Our results could influence the decisions of liver biopsy or treatment at that point.

Stage (*n.*)	HBV PCR (IU/ml)		
	Mean ± SD	Median (IQR)	Range
F1 (21)	85026±213435	13500 (1331:22700)	424:840000
F2 (9)	1784441±2956297	143000 (18750:1130000)	(1950:7700000)
F3 (17)	1514554±2836027	201000 (2440:751000)	(440:7950000)
F4 (13)	951928±1666222	196000 (6900:739000)	(512:5700000)
Kruskal–Wallis test (χ^2 value) = 8.79 P value= 0.03			

Abstract #56

Comparison of the effect of tenofovir and entecavir on renal function in patients with chronic hepatitis B

Kim Nam Hee[1], Kim Hong Joo[1]

[1]Division of Gastroenterology, Department of Internal Medicine, Sungkyunkwan University Kangbuk Samsung Hospital, Seoul, Korea

Introduction: The effects of nucleos(t)ide analogs on kidney function in patients with chronic hepatitis B (CHB) are controversial. We aimed to compare the effects on renal function for tenofovir (TDF) and entecavir (ETV) in CHB patients.
Methods: We performed a retrospective cohort study of 357 consecutive treatment-naïve patients with CHB who were treated with TDF or ETV between January 2006 and March 2016. To assess renal function more accurately in the normal range, we used the recently validated, Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula to calculate the estimated glomerular filtration rate (eGFR).
Results: Two hundred one (56.3%) and 156 (43.7%) patients received TDF and ETV treatment, respectively. Clinically significant and persistent decrease in eGFR was noted in 26 (12.9%) and 7 (4.5%) patients in TDF and ETV treatment arm, respectively (p = 0.006). Advanced age, TDF treatment, presence of LC at baseline, higher baseline $\log_{10}$HBV-DNA level, and occurrence of hepatocellular carcinoma (HCC) and disease progression (PD) during antiviral treatment were significantly associated with the occurrence of clinically significant and persistent decrease in eGFR by univariate analyses. Multivariate analyses showed that TDF treatment (odds ratio [OR] 3.36, 95% confidence interval [CI] 1.38–8.13, p = 0.008), presence of LC at baseline (OR 4.22, 95% CI 1.88–9.47, $p < 0.01$), and higher baseline $\log_{10}$HBV-DNA level (OR 1.58, 95% CI 1.16–2.15, p = 0.004) were significant and independent contributors to clinically significant and persistent decrease in eGFR.
Conclusions: TDF treatment adversely impacted the renal function in patients with CHB compared to ETV treatment.

Abstract #58

Case report: HBV flare under tenofovir treatment

Sila Akhan[1], Murat Sayan[2], Müge Deniz[1], Emre Bayhan[1]

[1]Kocaeli University Medical Faculty Infectious Diseases and Clinical Microbiology, Kocaeli, Turkey, [2]Kocaeli University PCR Unit, Kocaeli, Turkey and Yakin Dogu University, Deneysel Sağlık bilimleri Araştırma Merkezi (DESAM) Lefkoşa, KKTC

Introduction: A 28-year-old male patient was referred to our outpatient clinic when hepatitis B virus was detected while investigating the cause of infertility in Urology clinic. Resistance development is no longer an important problem since drugs with a high genetic barrier are used to treat chronic hepatitis B infection. We present the problem caused by decreased sensitivity to tenofovir caused by adefovir resistance patern in our previously untreated naive patient. It has also a public problem with causing a S gene mutation.
Methods: We found HBsAg+, anti-HBs−, antiHBc IgM−, anti-HBc IgG+, HBeAg+, anti-HBe−, anti-HCV−, anti-HIV−, HDV RNA−, HBV DNA 170000000 IU/mL. Although it seems to be an immunotoleran phase with normal ALT levels, we performed a liver biopsy because of a family history and evaluated according to the modified Knodell scoring system as grade: 4 stage: 3. We begin to treat the patient with tenofovir at April 2018. HBV DNA was found to be 17600 IU/mL at the end of the first month of treatment and 20400 IU/mL at the end of the third month. At 6th month of treatment HBV DNA was increased to170000000 IU/mL. Simultaneous ALT was 52, AST 36. After performing resistance profile we add entecavir to the therapy.
Antiviral resistance analysis was made in Kocaeli University by the Sanger dideoxy sequencing method as follows; oligonucleotides (forward primer: 5′-TCG TGG TGG ACT TCT CTC AAT T-3′/reverse primer: 5′-CGT TGA CAG ACT TTC CAA TCA AT-3′) were used for the HBV pol gene amplification. There are the PCR reactions: 95 °C–10 min. for 35 cycles and then 95 °C–45 s, 60 °C–45 s, finally 72 °C–45 s. The primers concentration was 0.3 mM. The amplicon size was 740 bp. A drug resistance tool that was Genafor/arevir (http://coreceptor.bioinf.mpi-inf.mpg.de/) used on the interpretation of HBV resistance mutations.
Results: HBV DNA pol gen was isolated from the patient's blood and rtN236T was identified as one of the primary drug resistance mutations that could explain nonresponse to the nucleoside (t) id analogue treatments, suboptimal response or viral rebound. This mutation leads to resistance to adefovir, an acyclic phosphonate, but also to reduce susceptibility to TDF. This is not a direct mutation for TDF, but acyclic phosphonate mutations in TDF treatments should be carefully monitored and switch or add on approaches should be performed accordingly. On the other hand, due to the structural characteristics of the HBV genome, the pol / S gene is overlapping. Therefore, developing nucleosis (t) id analogue mutations cause amino acid changes in the S gene. In our patient, rtN236T mutation, which reduces the sensitivity of TDF, does not cause overlapping mutations in the S gene. The sP120T and sC124R mutations detected in the S gene are not of this nature. However, these include escape from HBV vaccine, HBIg treatment and diagnostic tests.
Conclusion: Therefore, careful monitoring of pol/S gene overlapping mutations in the treatment of nucleosis (t) id analogs of hepatitis B is important and necessary for public health. Also we have to be aware for TDF reduced susceptibility and clinical flares even not a direct TDF mutation was found.

Abstract #67

Self-assessment of mental and emotional health, perceptions of disease of patients with Hepatitis B

Woo Shi Min[1], Teo Pek Siang Edmund[2], Chia Pei Yuh[2], Lee Hwei Ling[2], Ekstrom Victoria[2], Xin Xiaohui[2], Chow Wan Cheng[2], Kumar Rajneesh[2]

[1]Yong Loo Lin School of Medicine, National University of Singapore, Singapore. [2]Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore

Introduction: Chronic Hepatitis B (CHB) is a cause of liver cirrhosis and cancer with prevalence of hepatitis B being 3.6% in Singapore.
Objectives: We aim to characterize the physical, mental and emotional health, perception of the disease burden, perception of care received, extent of knowledge on disease and information seeking behaviour of Hepatitis B patients.
Methods: 326 patients with Hepatitis B were recruited at Singapore-General-Hospital. A questionnaire was conducted that explores perception of CHB disease burden, own health, extent of knowledge on the disease and information seeking behaviour.
Results: There were 54.9% females, mean age 58.4 ± 12.9 years, with 97.9% Chinese. 46.6% had tertiary education. 29.4% of participants used Chinese language while remaining used English. More-than 50% rated their health as good while 94.8% perceived the disease as serious. 76.4% were concerned about liver disease, 93.9% understood reasons for blood tests and 96.3% felt that regular screening is effective at detecting liver disease at an early stage. 94.8% found it safe and 66% found it affordable. Across all education groups, 93.9% felt satisfactory on care received and 94.5% had significant confidence in their doctor's competence. Notably, despite the language barriers in our multi-racial society, 92% were able to understand doctor instructions. On information seeking, patients preferred to get information from televisions or newspapers compared to public talks.
Conclusion: Patients' perception of their health appears to be good and they value screening practices. Gastroenterologists delivered information in an understandable and professional manner, showed concern through interactions regardless of language and education level barriers.

Abstract #75

Efficacy of double-dose hepatitis B vaccination in HIV-infected patients

Yıldırım Çiğdem[1], Erdem Hüseyin Aytaç [1], Akyol Deniz [1], Sertöz Şaziye Rüçhan[2], Işıkgöz Taşbakan Meltem[1], Gökengin Ayşe Deniz [1], Pullukçu Hüsnü [1]

[1]Ege University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Izmir, Turkey, [2]Ege University Faculty of Medicine, Department of Clinical Microbiology, Izmir, Turkey

Introduction: In this study it was aimed to compare the efficacy of single-dose versus double-dose hepatitis B vaccination in HIV-infected patients in a tertiary-care educational university hospital.
Methods: Patients who were admitted to in our center for performing single-dose or double-dose hepatitis B vaccine between January 2017 and March 2019 were evaluated retrospectively. The anti-HBs antibody levels of patients were analyzed. Anti-HBs level above 10 IU/L were considered to be seropositive. Statistical analysis was performed

via Chi square test with IBM SPSS statistics 25.0 and a p value < 0.05 was considered significant.

Results: The study included 90 participants [81male (90%), 9 female (10%); mean age: 37.76 ± 10.11 years]. Demographic features, HIV-viral loads, CD4 counts and antiHBs antibody levels were shown in table 1. In terms of age, gender, antiretroviral therapy (ART) and detectable HIV RNA level had no statistical difference between seropositive and unresponsive groups ($p > 0.05$). Although there was no statistically significant difference between the two groups in terms of CD4 count, the mean CD4 level was 591 in the seropositive group and 534.4 in unresponsive group. The anti-HBs antibody response was 68.7% in single-dose of vaccine group and 87% in the double-dose vaccine group ($p = 0.071$).

Conclusion: In HIV infected people, the response to hepatitis B vaccine is lower than non-HIV infected people according to our results. In terms of dual infections, seronegative patients should be vaccinated for hepatitis B. A double-dose of hepatitis B vaccination is routinely recommended in HIV infected people.

		Anti-HBs level>10IU/L	Anti-HBs level<10 IU/L
Mean age	37,76 ± 10,11	37,29 ± 9,86	39,04 ± 10,88
Gender	Male (81)	58 (71,6%)	23 (28,4%)
	Female (9)	8 (88,9%)	1 (11,1%)
CD4 count	>200 (86)	63 (73,3%)	23 (26,7%)
	<200 (4)	3 (75%)	1 (25%)
HIV RNA level	Detectable (39)	27 (69,2%)	12 (30,8%)
	Undetectable (51)	39 (76,5%)	12 (23,5%)
ART	(+) (80)	60(75%)	20(25%)
	(-) (10)	6(60%)	4(40%)
Vaccination schedule	Double-dose (0-1-6.months)	20(87%)	3(13%)
	Single-dose (0-1-6. months)	46 (68,7%)	21(31,3%)

Abstract #81

Higher risk of hepatocellular carcinoma progression in the population of untreated immune-tolerant phase chronic hepatitis B patients: an evidence based case report

Alessa Fahira[1], Irsan Hasan[2]

[1]Faculty of Medicine, Universitas Indonesia, Jakarta, [2]Hepatobilier Division, Internal Medicine Department, Cipto Mangunkusumo National General Hospital, Jakarta

Introduction: Hepatitis B infection is a major health problem worldwide, currently occurring in 350–400 million people. If not treated properly, hepatitis B infection may progress into chronic hepatitis B (CHB)—which may be developed into hepatocellular carcinoma (HCC). The first phase of CHB, the immune-tolerance (IT) phase, is marked with minimal necroinflammation activity and lower risk in the development of a more chronic liver condition, hence antiviral therapy is not recommended. Recent studies, however, show that there is apparently histological activity and immune specific response towards HBV, accompanied by extensive clonal expansion of hepatitis in the IT phase, hence questioning its risk for the development of HCC. This evidence-based case report is meant to comprehensively review the effect of antiviral treatment in IT-phase CHB patients from available studies.

Method: Pubmed, ProQuest, Cochrane, Scopus, Sciencedirect and EBSCOhost were comprehensively searched for systematic review and cohort prognostic researches studying the impact of anti-virals treatment for CHB patients in IT-phase. Three studies were selected and critically appraised. Data were then summarized descriptively.

Results: The three studies included in this study were retrospective cohort studies. One study stated that the treated IT-phase group had significantly reduced the risk for HCC (HR, 0.234; log-rank $P = 0.046$), compared to the untreated IT-phase group. One study found that the untreated IT phase is associated with a significantly higher risk of HCC (HR 2.54; 95% CI 1.54 to 4.18; $p < 0.001$) compared to the treated immune-active (IA) phase group. The last study stated a higher adjusted hazard ratio (aHR) of the UIT in predicting HCC risk was 2.327 (95% CI 0.475–11.391; $p = 0.297$) if compared to the IA group.

Conclusion: While studies show apparent results regarding the treatment of CHB patients in the IT-phase and its benefit in reducing the cumulative incidence of HCC, its clinical advantage is soon to be discovered. The results were inconclusive, and the initiation of treatment in CHB patients within the IT-phase cannot yet be recommended until further research.

Abstract #127

Comparison of vitamin D levels naive treated and inactive carriers with chronic hepatitis B

Berna Bozca[1], Ayşegül Koç[2]

[1]Infectious Diseases and Clinical Microbiology MD, Afyonkarahisar State Hospital, Turkey, [2]Physical Medicine and Rehabilitation MD, Afyonkarahisar Parkhayat Private Hospital, Turkey

Background: Our study aimed to assess the in-vitro relationship between HBV production and vitamin D signalling pathway and to explore the associated mechanism.

Method: Four hundred and sixty-seven (467) patients with CHB presented to the Afyonkarahisar State Hospital in Afyonkarahisar, Turkey from March 2016 to february 2019 were included in the study. The patients were divided among three groups (Table 1). All the samples used in this study were collected during autumn and winter.

Results: The results are shown in table 2.

Conclusion: Whether low vitamin D levels are the cause or the result of certain diseases, including chronic viral liver diseases, is not clear. Many clinical trials and meta-analyses have strongly linked vitamin D deficiency with liver fibrosis progression, regardless the aetiology of chronic liver disease, with unclear causality relationship whether liver morbidity, affects vitamin D synthesis or the vitamin deficiency and is the contributor in the development of liver pathology. In our study, we found a similar trend, however, but it was not significant. Additionally, amongst the Turkish population, the level of vitamin D3 has been reported to be generally lower than the mean global value. That means, Turkey has a problem of vitamin D deficiency that seems to be on a national base and may not be directly related to certain diseases. So, because our samples were taken from a Turkish population, the results may be influenced by this issue. We believe that vitamin D3 has other effects on the HBV specific immune responses, which have not yet been recognized. But, further studies are needed.

Table 1. Definition of the different groups included in this study

Group	Defining characteristics
Inactive carrier (n=265)	Negative HBeAg and positive HBeAb, undetectable or low levels HBV DNA (<2000 IU/mL) by PCR-based assays, repeatedly normal ALT levels, and no fibrosis
Treated (n=202)	Receipt of anti-viral therapy (tenofovir) for at last 1 year, at the dose of 245 mg daily, within at least 6 months before analysis of the vitamin D3 levels, and regardless of HBeAg or HBeAb status
Control (n=162)	Healthy individuals without any viral hepatitis and liver diseases or cancer history , no vitamin D3 supplementation or taking of multi-vitamins during the past 3 months

Table 2. Comparison of clinical and biochemical features of HBV patients and healthy controls

	Inactive carrier (n=265)	Treated (n=202)	Control (n=162)	
Sex F(%) M(%)	117(44) 148(56)	80(40) 122(60)	63(39) 99(61)	p>0,05
Age(years)	48,9±9,47	54,25±4,48	50,93±15,23	p>0,05
ALT, IU/L	22,00±9,03	28,95±19,01	23,21±6,21	P<0,001
AST, IU/L	23,2±8,54	29,41±12,18	29,7±6,13	P<0,001
PLT, 10^5	2,31±0,64	1,98±1,03	3,14±0,61	p>0,05
Vitamin D3, ng/Ml F M	22,88±20,71 45,28±31,40	20,62±21,82 33,42±34,47	23,14±31,08 50,98±33,79	p>0,05
BMI (kg/m²)	28,55±2,18	26,36±3,46	27,68±4,47	p>0,05
HBV-DNA (IU/mL)	563,17±488,26	1586103,7±1126688,4	-	P<0,001

Abstract #135

The results of tenofovir alafenamide treatment in patients with chronic hepatitis B virus infection

Tuvshinbayar N.[1,2], Amaraa R.[1], Burmaajav B.[2], Gegeebadrakh B.[1], Enkhtuvshin D.[3], and Baatarkhuu O[3]

[1]Department of Gastroenterology, State Second Central Hospital, Ulaanbaatar, Mongolia. [2]"Ach" Medical University, Ulaanbaatar, Mongolia. [3] Department of Infectious Diseases, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia

Introduction: Worldwide, an estimated two billion people have evidence of HBV infection, and approximately 240 million have CHB. In this study, a representative group of Mongolian adults was tested for hepatitis B virus (HBV) in 2017. The latest data shows that 11.1% of mongolian adult population are infected with HBV.
Goal: Evaluate the efficacy and safety of tenofovir alafenamide treatment in patients with chronic hepatitis B.
Materials and methods: The clinical trials have evaluated TAF in HBeAg-positive and HBeAg-negative chronic HBV patients. The trials have similar design and randomized, single blind, non-inferiority studies. The primary efficacy endpoint was the proportion of patients with HBV-DNA < 29 IU/ml at weeks 24 and 48. Other prespecified efficacy endpoints were the proportion of patients with HBsAg seroconversion to antiHBs at weeks 24 and 48.
Results: The primary efficacy endpoint, an HBV-DNA < 29 IU/ml at weeks 48 and was achieved by 251 (79.9%) of 314 patients receiving TAF, which was non-inferior to the 113(74.8%) of 151 patients receiving TDF who had an HBV-DNA < 29 IU/ml. After 48 weeks of treatment, patients receiving TAF hed significantly smaller reductions in bone mineral density (BMD) compared with patients receiving TDF. At weeks 48, median changes in eGFR were significantly smaller in the TAF recipients compared with the TDF recipients.
Conclusion: TAF treatment has the same efficacy as TDF treatment. However, TAF treatment demonstrates more safety profile compared with TDF treatment. Patients receiving TAF had a significantly smaller median decrease in eGFR, by Cockcroft–Gault equation, than patients receiving TDF.

Abstract #164

Clinical outcomes of chronic hepatitis B patients who switched from entecavir or tenofovir disoproxil fumarate to tenofovir alafenamide

Eiichi Ogawa[1], Hideyuki Nomura[2,3], Makoto Nakamuta[4], Norihiro Furusyo[1], Toshimasa Koyanagi [5], Kazufumi Dohmen[6], Aritsune Ooho[7], Takeaki Satoh[8], Akira Kawano[9], Eiji Kajiwara[10], Kazuhiro Takahashi[11], Koichi Azuma[12], Rie Sugimoto[13], Hiromasa Amagase[14], Masami Kuniyoshi[15], Yasunori Ichiki[16], Chie Morita[17], Masaki Kato[18], Shinji Shimoda[19], and Jun Hayashi[3]

[1]Department of General Internal Medicine, Kyushu University Hospital, Fukuoka, Japan, [2]The Center for Liver Disease, Shinkokura Hospital, Kitakyushu, Japan, [3]Department of Internal Medicine, Haradoi Hospital, Fukuoka, Japan, [4]Department of Gastroenterology, Kyushu Medical Center, Fukuoka, Japan, [5]Department of Medicine, Fukuoka City Hospital, Fukuoka, Japan, [6]Department of Medicine, Chihaya Hospital, Fukuoka, Japan, [7]Department of Hepatology, Steel Memorial Yawata Hospital, Kitakyushu, Japan, [8]Center for Liver Disease, Kokura Medical Center, Kitakyushu, Japan, [9]Department of Internal Medicine, Kitakyushu Municipal Medical Center, Kitakyushu, Japan, [10]Kajiwara Clinic, Kitakyushu, Japan, [11]Department of Medicine, Hamanomachi Hospital, Fukuoka, Japan, [12]Department of Medicine, Kyushu Central Hospital, Fukuoka, Japan, [13]Department of Gastroenterology, Kyushu Cancer Center, Fukuoka, Japan, [14]Amagase Clinic, Kitakyushu, Japan, [15]Department of Gastroenterology, Kyushu Rosai Hospital, Kitakyushu, Japan, [16]Department of Internal Medicine, JCHO Kyushu Hospital, Kitakyushu, Japan, [17]Department of Internal Medicine, JR Kyushu Hospital, Kitakyushu, Japan, [18]Department of Medicine and Bioregulatory Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, [19]Department of Medicine and Biosystemic Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan,

Objectives: Tenofovir alafenamide (TAF) has been approved for the treatment of chronic hepatitis B (CHB). Unfortunately, there is little data regarding switching from entecavir (ETV) or tenofovir disoproxil fumarate (TDF) to TAF. The aim of this study was to evaluate the effectiveness and safety of switching to TAF in a real-world setting.
Methods: This multicenter, cohort study included 323 consecutive CHB patients who switched to TAF after previous treatment with ETV or TDF for over 2 years. Virological/laboratory response and kidney function were evaluated for the 48 weeks after switchover.
Results: In the ETV to TAF group (n = 192), the HBV DNA suppression (< 20 IU/mL) rate at week 48 was significantly increased, from 75.5 to 96.4% (P < 0.001). The rates of ALT normalization (< 30 U/L) and HBV DNA suppression were also significantly increased, from 62.0 to 78.6% (P < 0.001). For patients with chronic kidney disease (CKD) (eGFR < 60), serum creatinine (sCr) and eGFR levels at week 48 were almost the same as baseline (sCr + 0.004 mg/dL, eGFR + 0.40 mL/min). In the TDF to TAF group (n = 131), almost all patients (97.7%) had achieved HBV DNA suppression at week 48. The rates of ALT normalization (< 30 U/L) and HBV DNA suppression increased, from 67.2 to 76.3% (P = 0.06). For CKD patients (eGFR < 60), sCr and eGFR levels at week 48 were significantly improved (sCr − 0.06 mg/dL, eGFR + 3.70 mL/min) (P < 0.001) compared to baseline.
Conclusion: Patients who switched to TAF in a real-world setting continued to achieve improvements in both ALT normalization and HBV DNA suppression at week 48.

Abstract #168

High risk of clinical relapse in HBV-infected patients after stopping prophylactic antiviral therapy for rituximab-containing chemotherapy

Wei-Yuan Chang[12], Yen-Cheng Chiu[6], Fang-Wei Chiu[7], Yao-Chun Hsu[11], Tai-Chung Tseng[1,2], Pin-Nan Cheng[6], Sheng-Shun Yang[7-10], Ding-Shinn Chen[5], and Jia-Horng Kao[1-4]

[1]Division of Gastroenterology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, [2]Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan, [3]Department of Medical Research, National Taiwan University Hospital, Taipei, Taiwan, [4]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan. [5]Genomics Research Center, Academia Sinica, Taiwan. [6] Department of gastroenterology and hepatology, National Cheng Kung University Hospital, Tainan, Taiwan, [7]Division of Gastroenterology & Hepatology, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, [8]School of Medicine, Chung Shan Medical University, Taichung, Taiwan, [9]Rong Hsing Research Center for Translational Medicine, National Chung Hsing University, Taichung, Taiwan, [10]Ph.D. Program in Translational Medicine, National Chung Hsing University, Taichung, Taiwan. [11]Division of Gastroenterology and Hepatology, Department of Internal Medicine, E-Da Hospital/I-Shou University, Kaohsiung, Taiwan, [12]Division of Gastroenterology, Department of Internal Medicine, National Taiwan University Hospital Hsin-Chu Branch, Hsin-Chu, Taiwan.

Background and aims: Prophylaxis treatment with nucleos(t)ide analogue (NA) is mandatory for hepatitis B surface (HBsAg)-positive patients receiving chemotherapy containing rituximab, which is a potent B cell-depleting agent. However, little is known about whether withdrawal of prophylactic NA is associated with a high risk of clinical relapse after completing rituximab-containing chemotherapy.
Methods: We retrospectively analyzed 77 non-cirrhotic HBsAg carriers with hematological malignancies who received rituximab-containing chemotherapy. All of them received either prophylactic entecavir or tenofovir therapy, which had been extended for 6 months or more after discontinuation of the anti-tumor therapy (extended NA therapy). We explored their risks of HBV clinical relapse and HBV-associated liver decompensation after stopping NA.
Results: There were 25 (32.5%) patients developing clinical relapse and most of events occurred within 1 year (20/25; 80.0%). Our data showed that higher pre-treatment HBV viral load (> 2000 vs < 2000 IU/ml), was associated with an increased risk clinical relapse (HR: 3.47, 95% CI 1.56–7.73, p = 0.002). To be noted, eleven (14.29%) patients developed HBV-associated hepatic decompensation after stopping NA treatment and two of them died from subsequent hepatic failure.
Conclusions: In conclusion, there are high risks of clinical relapse or liver decompensation after stopping prophylactic NA therapy in non-cirrhotic HBV carriers receiving rituximab-containing chemotherapy for hematological malignancies. A higher pre-treatment HBV viral load is associated with risks of these hepatic events.

Abstract #192

Serial change in liver stiffness by point shear wave elastography during tenofovir therapy in antiviral treatment-naïve patients with chronic hepatitis B: three-years follow up

Byung Ik Kim,[1] Kyungjin Ko,[1] Won Sohn, Hong Joo Kim,[1] Yong Kyun Cho[1]

[1]Division of Gastroenterology, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea

Introduction and objectives: This study aimed to evaluate a change of liver fibrosis using shear wave elastography (SWE) in patients with chronic hepatitis B (CHB) receiving antiviral treatment.
Methods: A total of 127 treatment-naïve patients with CHB were treated with tenofovir as an initial therapy. Liver stiffness was measured using pSWE (Elastography Point Quantification; ElastPQ®) every 6 months. The changes of liver stiffness (kilopascals, kPa) during antiviral treatment in chronic hepatitis B were analyzed.
Results: The enrolled patients underwent pSWE at 6, 12, 18, 24, 30, 36 and 42 months during tenofovir treatment, respectively. Median liver stiffness values were decreased from 7.36 kPa (95% CI 8.33–6.38) at baseline to 5.83 (95% CI 6.55–5.09), 5.45 (95% CI 6.12–4.79), 5.16 (95% CI 5.93–4.39), 4.93 (95% CI 5.80–4.06), 4.95 (95% CI 5.58–4.31), 4.58 (95% CI 5.03–4.13) and 4.14 (95% CI 4.50–3.79) kPa at 6, 12, 18, 24, 30, 36 and 42 months after tenofovir treatment. A significant decrease in liver stiffness was observed at 6, 12, 18, 24, 30, 36 and 42 months, respectively compared with the outcomes of pretreatment ($P < 0.05$). A decrease in liver stiffness was observed in both HBeAg positive and negative. There was no significant difference in a decrease of liver stiffness during tenofovir therapy between HBeAg positive and negative ($P > 0.05$).
Conclusion: Liver stiffness by pSWE was improved during tenofovir treatment in patients with CHB. Oral antiviral treatment has a crucial role to improve liver fibrosis as well as to suppress viral replication in patients with CHB.

Abstract #194

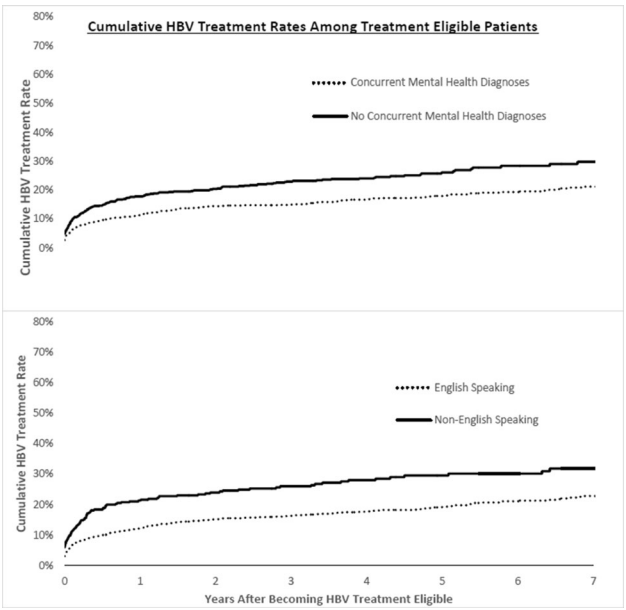
Non-english speaking immigrants with hepatitis B virus (HBV) had higher HBV treatment rates, whereas patients with concurrent mental health diagnoses had lower HBV treatment rates

Robert J. Wong[1], Mamta K. Jain[2], George Therapondos[3], Bolin Niu[4], Onkar Kshirsagar[5], Mae Thamer[5]

Division of Gastroenterology and Hepatology, Alameda Health System-Highland Hospital, Oakland, CA USA, [2]Division of Infectious Diseases, University of Texas Southwestern Medical Center, Dallas, TX, USA, [3]Multi-Organ Transplant Institute, Ochsner Health System, New Orleans, LA, USA, [4]Division of Gastroenterology and Hepatology, MetroHealth Medical Center, Case Western Reserve University, Cleveland, OH, USA, [5]Medical Technology and Practice Patterns Institute, Bethesda, MD, USA

Introduction: Immigrant status and concurrent mental health disorders (MHD) are important under-investigated factors affecting the hepatitis B virus (HBV) care cascade.
Objectives: To better understand the impact of these factors on contributing HBV care, we aim to evaluate disparities in HBV treatment by primary language and presence of MHD among a large diverse HBV cohort.

Methods: We retrospectively evaluated HBV adults (diagnosed with ICD-9/10 coding and laboratory data) across four urban safety-net heath systems from January 1, 2010 to December 31, 2015, with follow-up through 2018. We determined HBV treatment eligibility using AASLD guidelines. Comparison of HBV treatment rates was performed using chi-square testing among treatment-eligible patients. Adjusted multivariate Cox proportional hazards models evaluated predictors of receiving HBV treatment. Statistical significance was met with $p < 0.05$.
Results: Among 5,157 HBV patients (54.7% men, 22.3% Asian, 77.7% non-Asian, 25.8% cirrhosis, 14.2% HIV), 24.6% were non-English speaking, 48.0% had a diagnosis for MHD. Among treatment-eligible HBV patients, non-English speaking immigrants were significantly more likely to receive HBV treatment than English-speaking patients (36.1% vs. 23.7%, adjusted relative risk (ARR) 1.63, 95% CI 1.24–2.13, $p < 0.001$). Concurrent MHD demonstrated a trend towards lower likelihood of receiving treatment (22.8% vs. 29.8%; ARR 0.81, 95% CI 0.65–1.01, $p = 0.06$).
Conclusion: Among an ethnically diverse multi-center HBV cohort, non-English speaking immigrants had significantly higher HBV treatment rates. Lower rates among HBV patients with concurrent MHD is concerning. Better understanding of the contributing source of these lower treatment rates is needed to develop targeted quality improvement programs to improve HBV care.



Abstract #199

The role of eLIFT score as a non-invasive method in determining the level of liver fibrosis in Turkish hepatitis B patients

Ferzan Aydin, Hatice Rizaoglu Balci, Zanyar Akkuzu, Serkan Yaras, Osman Ozdogan, Enver Ucbilek, Fehmi Ates, Orhan Sezgin, Engin Altintas

Mersin University School of Medicine, Gastroenterology, Mersin, Turkey

Aim and background: Liver biopsy is the gold standard method for detecting liver fibrosis in patients with hepatitis B, but many tests have been developed as a non-invasive method for detecting liver fibrosis. The aim of this study was to compare eLIFT score with FIB4 and APRI scores in the detection of liver fibrosis in hepatitis B patients.
Methods: Six hundred and forty-nine CHB patients who underwent liver biopsies and age, sex, AST, ALT, GGT, PT%, platelet count in Mersin University School of Medicine Gastroenterology Dept. between January 2010 and January 2017 were retrospectively screened. eLIFT, APRI, FIB4 scores were calculated. Liver fibrosis was determined according to the ISHAK score (fibrosis score 0: none, 1-2: mild, 3-4: moderate, 5-6: severe).
Results: The mean age of the patients was 41.66 ± 12.73 (15–77) years. Of the patients, 394 (60.7%) were male and 255 (39.3%) were female. The distribution of patients according to fibrosis levels (none, mild, moderate and, severe) was 16 (2.46%), 385 (59.32%), 186 (28.66%), 62 (9.56%), respectively. Only FIB4 test was found to be statistically significant in patients with mild fibrosis (AUC: 0.646 at 95% CI, $p = 0.0392$, cut off = 0.74). eLIFT, FIB4, and APRI scores were statistically significant to demonstrate moderate fibrosis ($p = 0.0044$; 0.0002; and < 0.0001, respectively) and severe fibrosis ($p = < 0.0001$, < 0.0001 and < 0.0001, respectively).
Conclusion: FIB4 was found to be more sensitive than eLIFT and APRI in demonstrating the level of fibrosis in Turkish Hepatitis B patients.

Abstract #205

Clinical outcome in 96 weeks follow-up after discontinuation of nucleos(t)ide analogues in chronic hepatitis B patients

Wenxiong Xu[1], Ying Liu[1], Xiang Zhu[1], Liang Peng[1]

[1]Department of Infectious Diseases, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Introduction: Virological relapse rate is high in patients with chronic hepatitis B (CHB) after discontinuation of nucleos(t)ide analogues (NAs), but the final clinical outcome remains unclear.
Objectives: The aim of this study was to find out clinical outcomes after discontinuation of NAs and predictors of relapse.
Methods: Patients who met the criteria for discontinuation of NAs according to the recommendations of 2012 APASL guideline were enrolled in this study and discontinued NAs. Clinical data and laboratory test results were recorded at the time of and after NAs discontinuation.
Results: 103 patients were enrolled in the study. 74 patients completed 96 weeks follow-up and none of them developed cirrhosis, liver failure, or hepatocellular carcinoma. 19 patients were HBsAg negative before NAs discontinuation, no relapse occurred. 55 patients were HBsAg positive before NAs discontinuation, they were divided into 4 categories: Category A included 12 patients without virological relapse; Category B included 7 patients who were virological relapse and changed into non-relapse without antiviral therapy; Category C included 10 patients maintained virological relapse; Category D included 26 patients who were clinical relapse and retreated with NAs. In 55 patients who were HBsAg positive before NAs discontinuation, mean age was 28.75 ± 7.19 years in non-relapse group and 38.79 ± 9.15 years in virological relapse group ($p = 0.001$).
Conclusions: There were four clinical outcomes after NAs discontinuation in CHB patients. Negative HBsAg is a predictor for NAs discontinuation without relapse. Age is one of the predictors of relapse for patients remaining HBsAg positive.

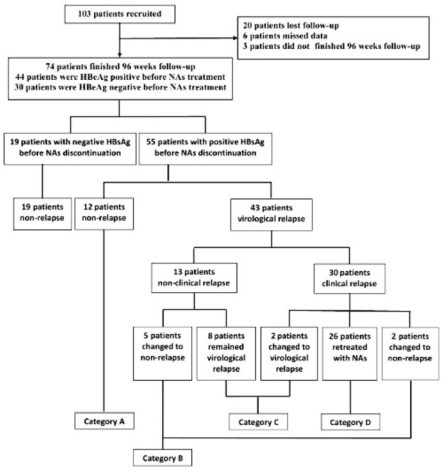


Figure 1 Flow chart of patient recruitment and clinical development.

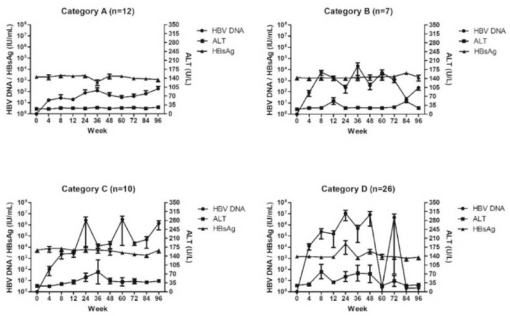


Figure 2 Change of levels of ALT, HBV DNA and HBsAg in four categories from 0 to 96 weeks.

Table 1. Variables associated to virological relapse in HBsAg positive patients

Parameters	non-relapse group (n=12)	virological relapse group (n=43)	F	*p*
Age, year	28.75±7.19	38.79±9.15	12.276	0.001
Male (%)	6 (50.0)	31 (72.1)	/	0.177
Duration of NA treatment, year	4.65±2.17	4.15±1.88	0.617	0.436
Duration of negative HBV DNA maintenance, year	4.22±2.06	3.42±1.28	2.755	0.103
EOT HBsAg, log10(IU/mL)	3.09±0.56	3.03±0.59	0.099	0.754

Abstract #216

An industry-governmental-NGO public health model to treat hepatitis B in Papua New Guinea

Lee, Alice[1], Jackson, Kathy.[2], Mair, Luke[3], Kevin, Bob[4], Gandi, Lily[5], Tarumuri, Olive[5], Hilmers, David[6]

[1]University of Sydney, Concord Repatriation General Hospital, Department of Gastroenterology and Liver services, Hospital Road Concord NSW 2139, Australia, [2]Victorian Infectious Diseases Reference Laboratory, Royal Melbourne Hospital, The Peter Doherty Institute for Infection and Immunity, Victoria, Australia, [3]Doncaster and Bassetlaw Teaching Hospitals, HNS Foundation Trust. Liverpool, United Kingdom., [4] Popondetta General Hospital, Popondetta, Papua New Guinea. [5]Siroga Clinic. New Britain Palm Oil Company, LTD. Popondetta, Papua New Guinea, [6]Departments of Internal Medicine, Pediatrics, and Space Medicine, Baylor College of Medicine, Houston, Texas, USA

Introduction: Over 290 million people worldwide are infected with chronic hepatitis B (CHB) with the highest prevalence in the Pacific Islands. Antiviral treatment has not been accessible in this region until recently. An innovative model of health care delivery to treat CHB, involving industry, government, and NGO's, was recently established in Papua New Guinea (PNG).
Objectives: Using a partnership of industry, government, and NGO's, we sought to initiate the first hepatitis B treatment program in PNG.
Methods: Partners include New Britain Palm Oil LTD (NBPOL), the largest employer in PNG, the Oro Province government, and an NGO, Hepatitis B Free (HBF). Molecular testing is provided by the Victorian Infectious Diseases Research Laboratory (VIDRL). Sero-surveys demonstrated a 15% prevalence of hepatitis B infection in Oro Province. After 6 years of negotiations between partners, funding and donations were received; the importation of tenofovir was approved; and the first patients were placed on therapy. Critical program elements include prevalence surveys, medical training, public education, improved laboratory capacity, and direct patient care.
Results: The first cohort of patients have completed screening with molecular testing, and a group of 100 has been placed on tenofovir. Universal testing in the catchment area is underway. Educational materials in the local language have distributed. Local health care providers have been trained during in-person and teleconference sessions. However, geographic barriers make outreach problematic. Little is known about rates of co-infection with hepatitis D. Local belief systems are often difficult to overcome.
Conclusions: Despite many obstacles, the program is succeeding, demonstrating the potential of collaborations between industry, NGO's, and government in low income countries to combat diseases such as CHB.

Abstract #261

Acute hepatitis C virus superinfection among patient with chronic hepatitis B virus and delta co-infection: A case report

Marine Karchava[1,2,3], Ekaterine Dolmazashvili [1,2], Lali sharvadze[1,2,4], Tengiz Tsertsvadze [1,2,4]

[1]Infectious Diseases, AIDS and Clinical Immunology Research Center, [2]Hepatology Clinic-Hepa, [3]Petre Shotadze Tbilisi Medical Academy, [4]Ivane Javakhishvili Tbilisi State University

Superinfection with hepatitis C among hepatitis B (HBV) and Delta virus (HDV) co-infected patients is rare and is a diagnostic challenge. We report a case of acute HCV superinfection among long term chronic HBV/HDV patient. He was a 38-years-old intravenous drug user, diagnosed in 2014. His liver aminotransferase activity was normal (ALT 41 U/l, AST 32 U/l), fibrosis score was 5.7 kPa. HBV DNA and HDV RNA VL were < 6 IU/ml and 1,540,000 cop/ml, while HBsAg was 750 Iu/ml respectively. Autoimmune hepatitis was ruled out and no other comorbidities were found at that time. Patient was followed up for more than 5 years and no treatment was administered due to the stabile liver conditions. In 2019, he was admitted to the hospital with jaundice, weakness, fatigue and abdominal pain. His laboratory finding indicated acute HCV superinfection based on the following criteria: Anti HCV positive, HCV RNA VL—21478000 Iu/ml, ALT—2760 U/l, AST—918 U/l, GGTP—350 U/l, total bilirubin—118 U/l. HBV DNA was < 6 IU/ml and HBsAg 56 Iu/ml and liver fibrosis score was 15.0 kPa. Patient was followed up for 3 month intervals until the final improvement. As of October 2019, HCV and HDV RNAs, as well as HBV DNA were undetectable, liver aminotransferase activity was normal, HBsAg was

undetectable, HBsAg AB > 250 Iu/ml and liver fibrosis score was 5.0 kPa. This case represents rare clinical event about possibility of clearance from long-term chronic HBV and HDV infection due to the self-limited acute hepatitis C superinfection.

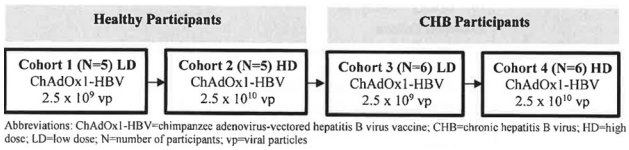
Abstract #262

ChAdOx1-HBV therapeutic vaccine: Phase 1 study results in healthy volunteers and patients with chronic hepatitis B

Eleanor Barnes[1], Paola Cicconi[1], Senthil Chinnakannan[1], Tamsin Cargill[1], Tom Evans[2], Mariem Charafeddine[2], Linda Kelly[2], Chris Ellis[2], Elizabeth Eagling-Vose[2], Sarah Sebastian[2], Clare Nelis[3], Pedro Folegatti[4]

[1]Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom, [2]Vaccitech ltd, Oxford, United Kingdom, [3]S-Cubed Biometrics ltd, Abingdon, United Kingdom, [4]The Jenner Institute, University of Oxford, Oxford, United Kingdom

Background: Chronic Hepatitis B (CHB) infection is mainly due to the persistence of viral integrated or episomal hepatitis B (HBV) DNA and to dysfunctional and depleted T-cell responses. Functional cure characterized by sustained loss of HBsAg will likely require a combination of antiviral and immune modulatory therapies. Therapeutic vaccination is a promising approach to restore T cell immunity in chronic infections and cancers. Vaccination using a non-replicating viral vector, Chimpanzee Adenovirus Oxford 1 (ChAdOx1), has been safe and highly immunogenic in clinical studies across various indications. This is the first study to evaluate the safety, tolerability, immunogenicity and efficacy of ChAdOx1-HBV in healthy participants and CHB patients.
Methods and results: The primary objective is to evaluate the safety of ChAdOx1-HBV vaccine single doses of 2.5×10^9 and 2.5×10^{10} vp in a stepwise dose escalation schedule, first in 10 healthy participants and then in 12 CHB patients virally suppressed with antiviral therapy. The secondary objectives will include the evaluation of ChAdOx1-HBV immunogenicity, clade cross-reactivity and the impact on the HBV biomarkers. Changes in intrahepatic immunology will be measured in CHB patients undergoing liver fine needle aspirates.
Conclusion: An effective adaptive immune response will likely be required to achieve HBV functional cure. Vaccination with ChAdOx1 has been shown to induce CD4+ and CD8+ responses in multiple clinical studies in indications other than HBV. This study evaluates the safety of and immunogenicity of ChAdOx1-HBV therapeutic vaccine in healthy volunteers and CHB patients. Available study results will be presented at the meeting. This study is the first step towards the development of a therapeutic prime-boost vaccination regimen in combination with antiviral agents.



Abstract #267

Timing of antiviral treatment initiation does not affect the survival of chronic hepatitis B related hepatocellular carcinoma

Vicki Wing-Ki Hui[1], Vincent Wai-Sun Wong[1,2], Yee-Kit Tse[1,2], Terry Cheuk-Fung Yip[1,2], Henry Lik-Yuen Chan[1,2], Stephen Lam Chan[3], Grace Lai-Hung Wong[1,2]

[1]Department of Medicine and Therapeutics, [2]Institute of Digestive Disease, and [3]Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong

Introduction: Antiviral treatment is known to improve survival in patients with chronic hepatitis B (CHB)-related hepatocellular carcinoma (HCC). Whether the timing, i.e. before or after HCC diagnosis, of starting antiviral treatment impacts on survival remains unclear.
Objectives: To compare the effect of nucleos(t)ide analogues (NA) treatment initiated before or after HCC diagnosis on survival.
Methods: A territory-wide cohort study was conducted using the database managed by Hospital Authority, Hong Kong. HCC treatments, NA use and laboratory parameters were retrieved. The primary endpoint was overall survival. A 3-month landmark analysis was used to evaluate the primary outcome in patients with NA treatment before (i.e. pre-HCC NA) or within 3 months after (i.e. post-HCC NA) their first HCC treatment (i.e. baseline).
Results: 3093 CHB patients (2,626 NA-treated before baseline and 467 NA-treated within 3 months after baseline) with HCC, receiving at least one type of HCC treatment were included in the analysis. At a median follow-up of 26.4 (IQR 12.–48) months, death occurred in 1147 (43.7%) subjects in the pre-HCC NA group, and in 203 (43.5%) subjects in the post-HCC NA group; the median survival was 30.7 months and 32.3 months, respectively. The median NA treatment duration was 9.4 (IQR 1.3–37.1) months before HCC treatment. Post-HCC NA treatment was associated with improved survival, as compared to pre-HCC NA or no NA group.
Conclusion: It is never too late to initiate NA treatment, even after HCC diagnosis, as it would still improve patient survival.

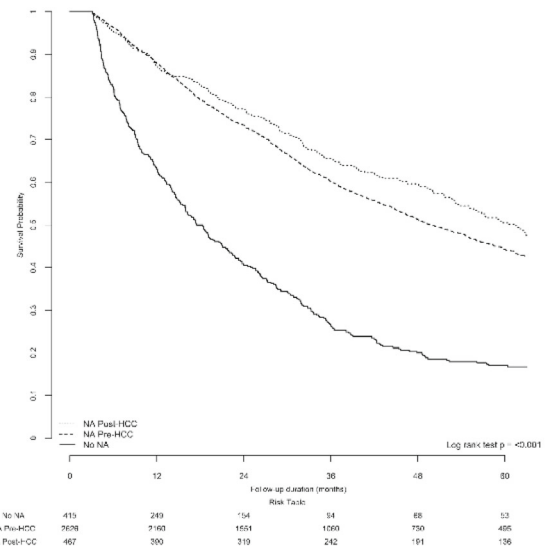


Figure: Kaplan-Meier curve of overall survival.

Abstract #269

Entecavir resistance

Llewelyn J[1], Gane E[1]

[1]New Zealand Liver Transplant Unit, Auckland City Hospital

Introduction: Entecavir monotherapy for chronic hepatitis B is associated with a low rate of resistance in nucleoside-naïve patients (1% after five years of treatment), but a high rate in lamivudine-refractory patients (50% after 5 years).
Objectives: Our aim was to investigate the unusually high numbers of observed possible primary entecavir resistance in our diverse population.
Methods: All 593 patients who had received or are currently receiving entecavir were entered into our Excel spreadsheet. Data were collected from electronic health records for documented previous antiviral therapies, duration of treatment, ethnicity, age and e-antigen status. 38 patients had no clinical data available for over 2 years and were therefore excluded, leaving 555 patients in total.
Results: 13 patients (2.3%) were deemed to have entecavir resistance, and nine (1.6%) were nucleoside-naïve (median age starting entecavir 49 years and median duration six years). Six nucleoside-naïve patients had confirmatory resistance testing, while three were changed to tenofovir disoproxil on clinical grounds. Our computed Kaplan–Meier curve estimated a cumulative resistance rate of 1.3% and 4.4% at five and ten years, respectively.
Conclusion: Entecavir remains a potent antiviral agent in patients with chronic hepatitis B, but results from our audit suggest a higher rate of primary entecavir resistance compared to the reported literature. Our cohort had 37 different nationalities, with prior antiviral therapy sometimes difficult to definitively exclude. Careful medication history is required when assessing patients for the first time, to enable the successful long term suppression of their hepatitis B viral load.

Abstract #274 **12 weeks safety and efficacy of tenofovir alafenamide compared to tenofovir disoproxil fumarate and entercavir in treatment naive patients with HBV-ACLF**

Wenxiong Xu[1], Yeqiong Zhang[1], Limin Zhen[1], Liang Peng[1]

[1]Department of Infectious Diseases, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Introduction: Tenofovir alafenamide (TAF) was not available in China until November 2018. Little is known about the safety and efficacy of TAF for Chinese patients with hepatitis b virus related acute-on-chronic liver failure (HBV-ACLF).
Objectives: The aim of this study is to evaluate the safety and efficacy of TAF, compared to tenofovir disoproxil fumarate (TDF) and entercavir (ETV), for Chinese treatment-naive patients with HBV-ACLF.
Methods: HBV-ACLF patients were enrolled in this prospective clinical study. They received anti-HBV therapy of TAF, or TDF, or ETV, according to their willing. Laboratory test results were collected to evaluated the safety and efficacy.
Results: 88 patients were enrolled in the study and finished 12 weeks follow-up. 33 patients received TAF, 23 patients received TDF, 32 patients received ETV. No medicine-related adverse events were observed. The baseline characteristics of the three groups were similar and comparable. At 8 weeks of treatment, TAF group had the highest HBV DNA undetectable rate (50%) and the least creatinine increase ($-$ 6.69 $\pm$ 11.17 μmol/L), while TDF group acted the opposite. At 12 weeks of treatment, TAF group showed a decrease in creatinine level ($-$ 7.63 $\pm$ 8.03 μmol/L), compared to TDF group (5.20 $\pm$ 17.29 μmol/L) and ETV group (3.00 $\pm$ 8.94 μmol/L), $p = 0.032$.
Conclusions: TAF treatment for HBV-ACLF patients is safe and effective in 12 weeks treatment. Virological and biochemical response of these three drugs tend to be similar, but TAF may benefit to renal function. All above results still need to be further verified.

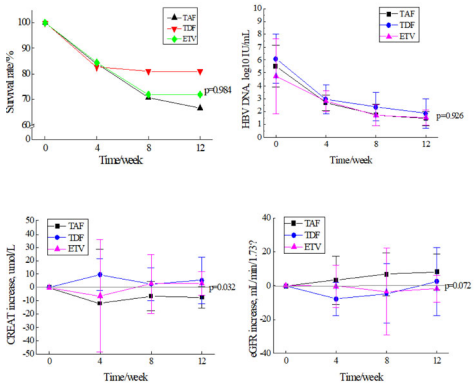


Figure 1 Comparison of survival rate, HBV DNA, creatinine increase and eGFR increase in three groups.

Abstract #279

Secular trend of antiviral treatment uptake in patients with chronic hepatitis B: a territory-wide study of 135,395 patients from 2000 to 2017

Jimmy Che-To Lai[1], Vincent Wai-Sun Wong[1,2], Terry Cheuk-Fung Yip[1], Becky Wing-Yan Yuen[1], Vicki Wing-Ki Hui[1], Yee-Kit Tse[1,2], Henry Lik-Yuen Chan[1,2], Grace Lai-Hung Wong[1,2]

[1]Department of Medicine and Therapeutics and [2]Institute of Digestive Disease, The Chinese University of Hong Kong, Hong Kong

Objectives: World Health Organization calls for a reduction of chronic viral hepatitis incidence and mortality of 90% and 65%, respectively, by 2030. Antiviral treatment is the key to reduce mortality. Nonetheless, the uptake of antiviral treatment for patients with chronic hepatitis B (CHB) has been suboptimal. We aimed to determine the secular trend of treatment uptake in the territory wide CHB cohort in Hong Kong from 2000 to 2017, and the factors for no treatment despite fulfilling treatment criteria.
Methods and results: CHB patients under public clinics and hospitals were identified through the Clinical Data Analysis and Reporting System of the Hospital Authority. The treatment indications were defined according to the Asian-Pacific guidelines published at the time of patients' first appearance in 4 periods: 2000–2004, 2005–2009, 2010–2013 and 2014–2017. 135,395 CHB patients were included; 1493/12472 (12.0%), 7416/43426 (17.1%), 10129/46559 (21.8%), 8051/32938 (24.4%) patients fulfilled treatment criteria in the four periods, respectively. The treatment uptake rate increased with time: 35.1%, 43.4%, 59.6% and 67.4% respectively. High fibrosis indices (APRI, FIB-4 and Forns indices) appeared to be the main driver for treatment indication in non-cirrhotic patients, with over 90% fulfilling treatment criteria due to high fibrosis indices alone. Of those fulfilling treatment criteria by high fibrosis indices, less than 60% of patients (25.2%, 36.0%, 45.2% and 57.6% respectively) had antiviral treatment initiated. Normal platelet count (odds ratio 0.42, $p < 0.001$) was the independent factor associated with not initiating antiviral treatment in patients fulfilling treatment criteria.
Conclusions: Treatment uptake rates have been increasing over time. Patients who did not receive antiviral treatment even if they fulfilled the treatment indication tended to have less advanced liver disease but

the importance to identify patients with significant liver fibrosis should be emphasized.

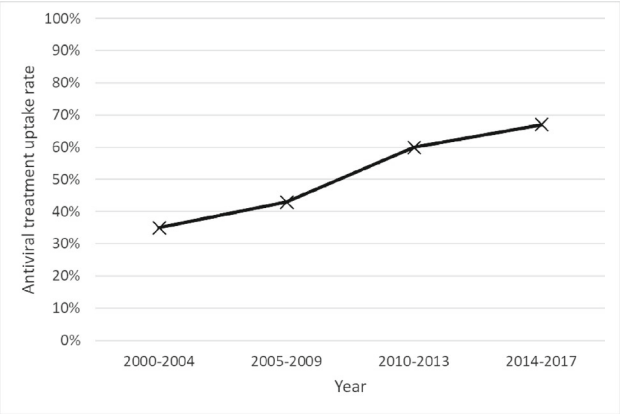


Figure 1. Change in antiviral treatment uptake rate over time in CHB patients fulfilling treatment criteria

Abstract #315

HBsAg seroclearance after anti-viral treatment for chronic hepatitis C in patients with hepatitis B and hepatitis C coinfection: case series

Kim Youngnam[1], Yoo Kideok[1]

[1]Department of Internal Medicine, Cheju Halla General Hospital, Jeju, Korea

Introduction: Hepatitis B virus (HBV) and hepatitis C virus (HCV) coinfection is a complex clinical entity that has an estimated worldwide prevalence of 1–15%. In Korea, The prevalence of HBV coinfection in Chronic hepatitis C (CHC) patients was 2.37%. The progression of disease is faster in HBV-HCV coinfected patients compared to patients with monoinfection. Hepatocellular carcinoma development also tends to have higher rate in coinfections. Here we report 4 cases of HBsAg seroclearance after anti-viral .treatment for chronic hepatitis C in HBV-HCV coinfected patients.
Case: Patients were included from March 2007 through March 2012 who visited Cheju Halla General Hospital. Total number of 601 patients with CHC were included. Twenty-four out of 601 CHC patients were positive for HBsAg. Of these, seven CHC predominant patients were underwent peginterferon alfa with ribavirin treatment. HCV genotype 2a was the most common (42%). The overall sustained virologic response rate was 14% in all patients. One of the 7 patients was positive for HBeAg, and six patients had negative for HBeAg with undetectable HBV DNA level. Four patients had obtained HBsAg seroclearance after treatment for chronic hepatitis C. All patients who had obtained HBsAg seroclearace had a low HBsAg titer, negative for HBeAg, undetectable HBV DNA level.
Conclusion: We experienced 4 cases of HBsAg seroclearance after peginterferon alfa with ribavirin treatment in patients with chronic hepatitis C predominant chronic hepatitis B and C coinfection.

Abstract #324

Evaluation of alinity m and cobas 8800 hepatitis B virus (HBV) and hepatitis C virus (HCV) viral load assays

Dominik Duelli[1], Dan Toolsie[1], Wai Bing Mak[1], John Karavitis[1], Jay Mukherjee[1], Tatsuya Nakasatomi[1], Brian Erickson[1], Danijela Lucic[1], Shihai Huang[1]

[1]Abbott Molecular, Inc., 1300 E Touhy Ave., Des Plaines, IL 60018-3315, USA

Background: Treatment guidelines recommend the use of viral load assays as treatment indicators. Currently there are several fully automated commercially available HBV and HCV viral load assays. These assays differ in their design features, analytical performance characteristics and platform automation. This study compared performance of the two recently approved assays across broad distribution of genotypes.
Methods: Assay performance was evaluated across clinical samples from HBV genotypes A-H and HCV genotypes 1–5. Comparison between assays was evaluated by assessing: assay correlation, mean bias between assays, bias standard deviation, percentage of samples with < 1.0 Log IU/mL difference and percentage of samples > 1.0 Log IU/mL difference.
Results: Study results are summarized in the table below.
Conclusions: Clinical assessment of the recently approved Alinity m HBV and HCV assays demonstrated good correlation and performance versus cobas 8800 assays across broad distribution of genotypes. Correlation coefficient for the HBV assay was 0.99 and 0.95 for the HCV assay. The observed mean bias between the two HBV and HCV assays (Alinity m-cobas 8800) was 0.09 and − 0.23 log IU/mL, respectively.

Number of samples	Alinity m - cobas 8800 HBV assay (N=125)	Alinity m – cobas 8800 HCV assay (N=124)
R^2	0.99	0.95
Mean Bias (Log IU/mL)	0.09	-0.23
Bias Standard Deviation (Log IU/mL)	0.28	0.30
% Samples Different by < 1.0 Log IU/mL	100	98.4
% Samples Different by > 1.0 Log IU/mL	0.0	1.6

Abstract #327

Response to hepatitis B vaccination in patients receiving immunosuppressive or biological agents

Hüsnü Pullukçu[1], Figen Yargucu Zihni[2] Seichan Chousein Memetali[1], Çiğdem Yıldırım[1], Hüseyin Aytaç Erdem, Tansu Yamazhan[1] Meltem Işıkgöz Taşbakan[1]

[1]Ege University Medical School Department of Infectious Diseases, [2]Ege University Medical School Department of Internal Medicine

Background: Patients with rheumatic diseases are in risk groups because of the usage of highly effective immunosuppressive agents in recent years. In many international sources and immunization guides (guidebooks), there are recommendations against diseases that can be prevented by vaccination. In real life, it may be hard to perform standard (convenient) vaccination schemes in cases (situations) like (such as) disease activity, emergency treatment need (requirement), fail to reach vaccine. In this study, hepatitis B vaccination efficiency was reviewed in patients who were directed from the Outpatient Clinic of the Rheumatology Department for routine immunization program.
Materials and Methods: This study took place at the Vaccination Outpatient Clinic of the Department of Infectious Diseases, at Ege University Hospital from January 2017 to April 2019. The response of HBV vaccine administered at 0, 1–6 month intervals, in patients who may need immunosuppressive treatment and with negative HBsAg and anti-HBs were evaluated. Vaccinated patients with an hepatitis B surface antibody titre more than 10 mIU/mL were considered as seropositive.

Results: This study was conducted by the enrolment of 35 patients (mean age 49.46 ± 11.05 minimum 25, maximum 69 years of age, 15 male and 20 female)
Of 35 patients, 12 were rheumatoid arthritis, 4 pemphigus vulgaris, 4 systemic lupus erythematosus, 3 multiple sclerosis, 3 Behçet's disease, 2 scleroderma, and one for each ankylosing spondylitis, dermatomyositis, ulcerative colitis, Sjögren's disease, alopecia areata, IgA nephritis, and autoimmune hepatitis. Hepatitis B surface antibody titre was higher than10 mIU/mL in 18 patients, and the other hand 17 patients (48%) were non-responders.
Conclusion: Although the small number of patients in our study, the decrease in vaccination response rates is remarkable in patients where immunosuppressive therapy cannot be postponed due to disease activity. These patients should be screened at the time of diagnosis and right after, immunization should be started. Patient-based vaccination schemes should be established for them.

Abstract #388

ALT normalization after entecavir and tenofovir correlated with reduction of development for HCC

Sehwa Kim[1], Min-jin Lee[1],Young-Sun Lee[1], Ji Hoon Kim[1], Yeon Seok Seo[1], Hyung Joon Yim[1], Jong Eun Yeon[1], Soon Ho Um[1], Kwan Soo Byun[1]

Department of Internal Medicine, Korea University College of Medicine, Seoul, South Korea

Introduction: Recently, the use of potent antiviral agents has made it possible to effectively reduce liver disease related events such as hepatic encephalopathy, variceal bleeding, ascites, and Hepatocelluar carcinoma (HCC) in patients with chronic hepatitis B.
Objectives: The aim of this study was to determine whether there is a relationship between normalized alkaline phosphatase (ALT) resulting from the use of antiviral agents and the occurrence of liver disease related events.
Methods: From 2007 to 2018, we studied 427 patients treated with entecavir or tenofovir at Korea University Guro Medical Center. The patients divided into ALT normal group and ALT abnormal group after 1 year of antiviral treatment. The ALT normal level is 34 for men, 30 for women in the Korean Association for the Study of the Liver (KASL) standard, and 35 for men and 25 for women in the American Association for the Study of Liver Diseases (AASLD) standard. Liver related disease included HCC, hepatic encephalopathy, variceal bleeding, and ascites.
Results: The baseline characteristics of 427 patients median age was 50 (IQR 42–57), median value of AST was 78 (IQR 47–135), ALT was 88 (IQR 45–178), HBV DNA(IU) was 2,190,000 (IQR 170,000–36,815,316 IU), and AFP was 7.05(IQR 3.325–26.025). The 67% of all patients were male and 33% were female. The 61.4% of patients used entecavir and 46.4% of patients used tenofovir. The people who used both drugs sequentially were 7.5%. Patients with HBeAg-positive were 54.8% and patients with anti-HBe Ab positive were 50.8%. Overall survival in ALT abnormal group was lower than ALT normal group after 1 year of antiviral treatment without statistical significance (Log rank test, $P = 0.201$ in the KASL standard and $P = 0.265$ in the AASLD standard). The cumulative incidence of HCC in normal ALT group was significantly lower than abnormal ALT group (Log rank test, $P < 0.001$ in both the KASL and AASLD standard). The incidence of Liver disease related events in the two group was not significant. (Log rank test, $P = 0.333$ in the KASL and $P = 0.428$ in AASLD standard).
Conclusions: ALT normalization after 1 year of entecavir and tenofovir treatment is correlated with reduction of development for HCC, but not overall survival and development of liver disease related events. Patients who failed to normalize ALT after 1 year of entecavir and tenofovir treatment should be observed more carefully for development of HCC.

Abstract #404

Chronic hepatitis B management in clinical practice in Fuzhou Province, China: retrospective cross-sectional analysis of electronic medical record data

Meng Xing[1], Liu Sen[1], Dong Jane[1] and Gillespie Iain Andrew[2*]

[1]GSK Institute for Infectious Diseases and Public Health, Beijing, China, [2]GSK Value Evidence & Outcomes, London, UK

Introduction: There have been few published reports on the treatment rate of chronic hepatitis b virus (HBV) infection in real-world practice in China. This study is the first to review a large regional Chinese electronic medical record (EMR) database in the HBV area (GSK-sponsored study 208571).
Objectives: To describe the characteristics of HBV patients overall and by the treatment status in a cross-sectional review of an EMR database.
Methods: A cohort of chronic HBV infection patients in the National Health Medical Big Data Platform (Fuzhou) Regional Database (covering 37 hospitals) was identified in 2017 through diagnostic and laboratory codes/values. An algorithm, developed to reflect international treatment guidelines, was applied to stratify patients into treatment-status groups (treated, indicated-but-not-treated or not-indicated-not-treated), utilizing demographic, clinical (cirrhosis, fibrosis) and biochemical (HBsAg, HBeAg, DNA, ALT) characteristics.
Results: In total, 21,614 chronic HBV infection patients were identified. The peak age distribution was between 25 and 50 years (65.71%); 68.6% were male. Co-infection was rare (0.04% with HIV/HCV; 1.77% with HDV). Liver fibrosis, cirrhosis and hepatocellular carcinoma was observed in 13.40%, 11.96% and 0.81% respectively. Half (49.56%) were treated (nucleos(t)ide analogues (NUCs) 99.91%; interferon-based 0.07%, NUC/IFN combinations 0.02%). Among 21,050 patients evaluable by our algorithm, 50.06%, 14.61% and 35.33% were treated, indicated-but-not-treated and not-indicated-not-treated, respectively.
Conclusion: Data from this large Chinese EMR database demonstrated a substantial number of patients (15%) did not receive therapy despite meeting treatment criteria, signifying the need to better understand the barriers to treatment. Complete analyses of the dataset will be subject to future reports.

Abstract #416

Management of obstructive jaundice due to gallstone suspected of having hepatitis B flare

Windradi C[1], Maimunah U[2], Pongbulaan A[1]

[1]Resident of Internal Medicine Department, Universitas Airlangga, Surabaya, Indonesia, [2] Division of Gastroenterology & Hepatology, Internal Medicine Department, Universitas Airlangga, Dr. Soetomo General Academic, Surabaya, Indonesia

Introduction: Obstructive jaundice, yellow discoloration of the skin and mucous membranes due to increased serum bilirubin level, is one of serious problem in gastrointestinal system. Therefore, prompt diagnosis and early treatment is urgently needed.

Case illustration: A 53 yo male came with chief complaint yellow discoloration of the skin and nausea. Neither fever or abdominal pain is remarked. Physical examination did not reveal any hepatomegaly and splenomegaly. His abdominal ultrasound showed intra hepatic bile duct dilatation and proximal common bile duct duet to distal common bile duct obstruction. Magnetic resonance cholangiopancreatography described choledocolithiasis with left and right intra hepatic bile duct dilatation, common hepatic duct, and common bile dct. There are multiple stones distal to the common bile duct with cupping sign distal to the common bile duct. Perioperative evaluation showed positive HbsAg and increased of liver function test. Her HBV DNA was 1.78×10^7 copies/mL and HbeAg negative. He was treated with ursodeoxycholic acid, N-acetylcysteine and lamivudine prior laparoscopy surgery. There is improvement on liver function test remarked.
Discussion: Jaundice may present asymptomatic or acute illness. The concomitant hepatitis B infection could confound diagnosis jaundice. Ultrasound can be useful as non invasive diagnostic tools to exclude intra or extra hepatic obstruction. MRCP has High sensitivity and specificity for identifying gallstones anywhere. there's no contraindication in preoperative evaluation.

Abstract #424

Pisagor cohort: tenofovir alafenamide real life data in hepatitis B

Mustafa Kemal Ãtelen

Introduction: The aim of this study was to evaluate the effectiveness and reliability of the use of tenofovir alafenamide (TAF) in the South Anatolia of Turkey.
Material-Methods: This retrospective-multicenter study was a cohort of 480 adult patients (mean age 47.40 ± 14.57). The data collected at $t = 0$, $t = 3$ months, and $t = 6$ months of treatment were analyzed. Chi-square, Mann Whitney-U, Friedman, Wilcoxon, Cochran's Q, and McNemar tests were used.
Results: Our findings showed that 79.6% of patients were HBeAg negative and 86.5% of the patients had Tenofovir disoproxil (TDF) experience. The most common reasons for the initiation of TAF treatment were use of drugs affecting bone mineral density (BMD) (42.9%) and osteoporosis (22.3%). From $t = 0$ months to $t = 6$ months, TAF patients experienced with TDF showed a significant improvement in GFR, hip-spine T score and phosphor level (p 0.05). Concerning LDL and cholesterol, no statistically significant difference was observed from $t = 0$ months to $t = 6$ months for this group. Side effects were reported by 5.7% of patients in the 3rd month and 7.1% in the 6th month, with the most common being hair loss (1%).
Discussion: TAF is seen as an effective and safe alternative to the long-term risks of TDF, which include nephrotoxicity, and decreased bone density risk, especially in patients with comorbidity. In our study, the increase in T score of BMD, phosphor, and GFR in the 6th month measurements after TAF treatment supports the literature.

Abstract #428

Normalon-treatment ALT could achieve antiviral outcomes not inferior to evaluated-treatment ALT in patients with HBeAg-positive chronic hepatitis B

Mingxing Huang[1a], Jian Liu[1a], Zongping Han[2a], Ruihong Liu[3a], Xuan Zhu[1], Pengyuan He[1a], Wentao Luo[1], Zhijie Xu[1], Jingxian Shu[4] Zhe Zhu[5,] Xinhua Li6*, Jinyu Xia1*

[1]Department of Infectious Diseases, 5th Affiliated Hospital, Sun Yat-Sen University. Zhuhai, 519000, China. [2]Department of Clinical Nutrition, 5th Affiliated Hospital, Sun Yat-Sen University. Zhuhai, 519000, China. [3]United SYSU The Fifth Affiliated Hospital -BGI, Department of Experimental Medicine, Guangdong Provincial Engineering Research Center of Molecular Imaging, Fifth Affiliated Hospital, Sun Yat-sen University, Zhuhai, 519000, China. [4]Department of Pharmacy. 5th Affiliated Hospital, Sun Yat-Sen University. Zhuhai, 519000, China. [5]Department of Medicine, Division of Regenerative Medicine, University of California, San Diego, School of Medicine, La Jolla, CA, USA. [6]Department of Infectious Diseases, 3th Affiliated Hospital, Sun Yat-Sen University. Guangzhou, 510630, China

Objectives: To evaluate the differences of antiviral outcomes between normal on-treatment ALT and evaluated-treatment ALT in patients with HBeAg-positive chronic hepatitis B (CHB).
Methodology: Retrospective studies were adopted to compare the antiviral outcomes of HBeAg-positive CHB patients with normal ALT, mildly (1–2ULN) and moderately elevated (above 2ULN) ALT, who were confirmed for antiviral treatment by liver biopsy.
Results: A total of 145 patients were recruited and followed up for 336 weeks. The virological response rate in the normal ALT group at 24 weeks was lower than that in the elevated ALT group (26.3% versus 30.9% versus 36.9%, respectively, P = 0.022), but in the long-term, there was no significant difference between these groups (92.1% versus 88.1% versus 98.4% at week 336, respectively, P = 0.065); The serological negative rate of HBeAg increased year by year, but there was no significant difference between these groups also (39.5% versus 40.5% versus 47.7% at week 336, respectively, P = 0.696). If the ULN was 35U/L for male patients, the virological response rate and the serological negative rate of HBeAg in each group increased year by year. Binary logistic regression analysis found that baseline ALT level was not a predictive value for serological negative conversion of HBeAg (P = 0.203), while age, HBeAg baseline, HBsAg baseline were the predicators.
Conclusion: HBeAg-positive CHB patients with normal ALT could achieve considerable antiviral outcome compared to patients with elevated ALT, thus those who meet the therapeutic condition should be strongly recommended for early antiviral treatment.

Abstract #438

Risk factors of HBV in Mongolia

Badamnachin Batsukh[1,2], Ganbold Sarangua[2], Badarch Gansaikhan[2], Jamyan Ariunbileg[2], Sosorbaram Ariunaa[2], Oidov Baatarkhuu[1,3]

[1]Department of Infectious Diseases, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [2]Department of Hepatology, National Center for Communicable Diseases, Ulaanbaatar, Mongolia, [3]Mongolian Academy of Medical Sciences, Ulaanbaatar, Mongolia

Background: Mongolia introduced HBV vaccination into routine immunization schedules for newborns and children under1 year of age in 1991, which substantially decreased the incidence of HBV infection.
Objectives: To study risk factors of HBV transmission.
Methods: The study was conducted 200 patients with acute HBV infection, treated in Mongolia from 2015–2017.
Results: The mean age of the patients were 26 ± 6.4, of those 57.5% were males and 42.5% were females and 41% were married. 17(8.5%) were vaccinated, 116 were unvaccinated and 67(33.5%) they don't know whether they were vaccinated or not. 99(49.5%) survey

participants were born before 1991, 87(43.5%) were born between 1992–1997 and 14(7%) were born since 1997. A specially developed questionnaire was used to determine the risk factors for HBV infection (last six months). In the serology test, 178(89%) were HBsAg and anti-HBcIgMboth positive and 22(11%) wereHBsAg positive and anti-HBcIgM negative.
Conclusion: HBV vaccination is effective method for preventing HBV infection. Most common risk factors of HBV infection are household and sexual contacts of people with HBV and having multiple sexual partners.

Risk factors	n	%
Multiple sexual partners	105	52.5%
History of dental surgery	32	16%
Tattoo	22	11%
History of hospitalization	81	40.5%
Surgical procedures	26	13%
Acupuncture	22	11%
Piercing	14	7%
Shares toothbrush with others	18	9%
Family member with HBV infection	39	19.5%
Shares razor with others	28	14%
Shares nailclipper with others	170	85%

Abstract #450

Clinical profiles and treatment patterns of patients with HBV-related liver cirrhosis in China

Kong Yuanyuan[1], Wei Wei[1], Shan Shan[2], Ma Hong[2], Ou Xiaojuan[2], Xu Xiaoyuan[3], Duan Zhongping[4], Hou Jinlin[5], Wei Lai[6], You Hong[2], Jia Jidong[1,2], CR-HepB Group

[1]Clinical Epidemiology and EBM Unit, Beijing Friendship Hospital, Capital Medical University; National Clinical Research Center for Digestive Diseases, Beijing 100050, China, [2]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China, [3]Peking University First Hospital, Beijing, 100034, China, [4]Beijing Youan Hospital, Capital Medical University, Beijing, 100069, China, [5]Nanfang Hospital, Southern Medical University, Guangzhou, 510515, China, [6]Beijing Tsinghua Changguang Hospital, Beijing 102218, China

Introduction: Chronic infection of hepatitis B virus (HBV) is the predominant cause of cirrhosis and hepatocellular carcinoma (HCC) in China. To facilitate real-world clinical study of chronic HBV infection, we established a nation-wide hospital-based registry system, China Registry of Hepatitis B (CR-HepB) in June, 2012.
Objective: To analyze the clinical profiles and treatment patterns in patients with HBV-related cirrhosis in real world clinical setting.
Methods: We respectively retrieved the information on demographic, medical history, virology, biochemistry and hematology, as well as diagnosis and treatment information from patients with HBV-related liver cirrhosis enrolled in CR-HepB.
Results: As of Sep 30, 2019, 53 tertiary or secondary hospitals across China had participated in this registry. A total of 5263 patients with HBV-related liver cirrhosis were included in the study, including 2013 (38.2%) patients in compensated status, 2752 patients (52.3%) with decompensated status and 498 patients (9.5%) unspecified. With the evolution of time: the age at diagnosis of cirrhosis was gradually increased in patients with hepatitis B; the HBeAg positive rate decreased, and the HBVDNA detection rate decreased. The percentage of first-line antiviral drugs (entecavir or tenofovir) treated patients increased, up to now reaching 92.8%.
Conclusion: This study provides real-world information on the clinical features and evolution of treatment pattern in patients with HBV-related liver cirrhosis in China.

Abstract #451

No resistance to tenofovir alafenamide (TAF) detected through 144 weeks of treatment in patients with chronic hepatitis B from China

Jinlin Hou[1], Yu Chen[2], Gregory Camus[3], Hongmei Mo[3], John F Flaherty[3], Anuj Gaggar[3], Hong Tang[4], Qing Xie[5], Qin Ning[6]

[1]Nanfang Hospital, Southern Medical University, Guangzhou, China, [2]Beijing YouAn Hospital, Capital Medical University, Beijing, China, [3]Gilead Sciences, Foster City, CA, United States, [4]West China Hospital, Sichuan University, Chengdu, China, [5]Shanghai Ruijin Hospital, Shanghai Jiao Tong University, Shanghai, China, [6]Tongji Hospital, Tongji Medical University, Wuhan, China

Introduction: In the Phase 3 studies GS-US-320-0108 (HBeAg-negative) and GS-US-320-0110 (HBeAg-positive), TAF has shown non-inferior efficacy to TDF through Week 144.
Objectives: Conduct ongoing annual resistance surveillance in CHB patients participating in 2 studies in China through 144 weeks of TAF or TDF treatment.
Methodology: HBV polymerase (pol)/reverse transcriptase (RT) population sequencing was done for patients with $\geq$ 24 weeks of treatment with HBV DNA $\geq$ 69 IU/mL at Week 144 or at early discontinuation (ED). Sequence changes from Baseline at Week 144/ED are reported. Phenotypic analysis was performed for adherent subjects with virologic breakthrough (VB), and those with emergent conserved site substitution(s), or polymorphic substitutions detected in $>$ 1 patient.
Results: Through Week 144, 9 of 214 (4%) and 5 of 98 (5%) subjects in the TAF and TDF groups, respectively, qualified for viral sequencing. Overall, of the 14 subjects who qualified for sequencing, 6 were unable to be sequenced, 3 had no change in pol/RT from baseline, 4 had unique polymorphic site substitutions, and 2 had unique conserved site substitutions in pol/RT. Three subjects in the TAF group, all with VB, and two subjects in the TDF group, one with VB and one with a conserved site change, met the criteria for phenotypic analysis. In vitro phenotyping results will be presented.
Conclusion: Consistent with non-China results, in China, small and similar percentages of patients across TAF and TDF groups qualified for resistance analysis. No genotypic resistance was detected through 3 years of TAF treatment.

Abstract #456

Dynamic changes of IP-10, IL-10, TNF-α, and MIP-1B serum levels in chronic HBV-Infected patients undergoing nucleos(t)ide analogues treatment

Xiang-An Zhao[1], Juan Xia[2], Jian Wang[2], Yong Liu[3], Yuxin Chen[3], Rui Huang[2], Chao Wu[1,2]

[1]Department of Gastroenterology, Northern Jiangsu People's Hospital, Clinical Medical College of Yangzhou University, Yangzhou, Jiangsu, China; [2]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China; [3]Department of Laboratory Medicine, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China

Introduction: Past studies have found that interferon-g-inducible protein-10 kDa (IP-10), interleukin (IL)-10, tumor necrosis factor (TNF)-α and macrophage inflammatory protein-1β (MIP-1b) would be involved in immune reactions in response to HBV infection.

Objectives: This study aimed to explore whether IP-10, TNF-α, IL-10 and MIP-1b can predict treatment outcome in CHB patients.
Method: A total of 74 CHB patients, including 6 inactive carriers (IC), 24 immune tolerance patients (IT), 35 HBeAg-positive CHB (EPH) and 15 of HBeAg-negative CHB (ENH), were enrolled in this study. In addition, 10 healthy donors were enrolled as controls. Serum IP-10, TNF-α, IL-10 and MIP-1b level were assayed by Luminex. 35 EPH received anti-viral therapy with nucleoside analogues were followed-up for 5 years.
Results: IP-10 and IL-10 levels were increased in the CHB patients at different immune status when compared to healthy people. While, TNF-α and MIP-1B makes no difference. Through correlation analysis, it was found that IP-10 and IL-10 expression were positively correlated with ALT. Besides, IP-10 expression was positively correlated with copies of HBV DNA. After antiviral treatment, serum IP-10 and IL-10 levels were significantly reduced. Through follow-up of 2 years, 3 years and 5 years, it was found that the level of IL-10 was declined at both baseline and 12 weeks after treatment. In addition, the rate of IP-10 were significantly higher in patients from HBe serconversion group than HBe untranslated group.
Conclusion: Our study revealed that serum IL-10 and IP-10 levels in CHB patients was significantly increased, and closely monitoring changes of serum IL-10 and IP-10 levels can predict antiviral treatment outcomes.

Abstract #474

Assessment of fibrofast; (FIB-5) versus FIB-4 index for the differentiation between non-significant and significant fibrosis in patients with chronic hepatitis B

Khaled Metwally[1], Maha Elsabaawy[1], Mohamed Abdel-Samiee[1], Wessam morad[2], Nermine Ehsan[3] and Eman Abdelsameaa[1]

[1]Hepatology and gastroenterology department, National Liver Institute, Menoufia University, Egypt. [2]Community and Preventive Medicine Department, National Liver Institute, Menoufia University, Egypt. [3]Pathology department, National Liver Institute, Menoufia University, Egypt

Introduction: Chronic Viral Hepatitis B disease is a major health problem in the world. The FIB-4 index is a non-invasive test for the assessment of liver fibrosis, and could be used to avoid liver biopsy. FIB-5 was developed using five routine laboratory tests (ALT, AST, alkaline phosphatase, albumin and platelets count) for the detection of significant hepatic fibrosis in patients with chronic hepatitis B. The aim of this study was to compare the performance characteristics of FIB-5 and FIB-4 to differentiate between non-significant and significant fibrosis.
Methods: A cross-sectional study included 176 chronic HBV patients. All liver biopsies were scored using the METAVIR system. Both FIB-5 and FIB-4 scores were measured and the performance characteristics were calculated using the ROC curve.
Results: for the differentiation between non significant fibrosis and significant fibrosis were: At a cutoff level 1.28 PPV 41.4% and specificity 48% for FIB-4 while at a cutoff level 7.08 PPV 98.8% and specificity 98% for FIB-5 respectively.
Conclusion: FIB-5 score at the new cutoff is superior to FIB-4 index for the differentiation between non-significant and significant fibrosis.

Abstract #487

Profile of hepatitis B in Morocco: experience of university service

F. Lamarti,[1] I. Benelbarhdadi,[1] S. Zertiti,[1] C. Berhili,[1] N. Lagdali,[1] M. Borahma,[1] FZ. Ajana[1]

[1]Department of medicine C, Hospital IBN SINA, Mohammed V University, Rabat-Morocco

Introduction: Infection with the hepatitis B virus(VHB)remains a major public health problem. Our objective is to determine virological profile of patients with VHB through a university series, the main co-morbidities, the factors predicting their occurrence, the efficacy of the analogues: virological response and tolerance.
Methods: Prospective study including all patients with HVB. Virological and biological assessment and regular follow-up at week12, week 24, 12 months and surveillance of clinical tolerance and virological response.SPSS22.0was used. Hepatic steatosis (HS) was associated and the main predictors of its occurrence by chi-square were studied. Statistically significant variable = $p < 0.05$.
Results: 88patients with HBsAg. Sex ratio H.F 0.87. Average age 38.6 ± 10.9 years. Discovery of HBsAg was fortuitous: blood donation in 86.4%. 3 patients pregnant at the time of screening. Contamination: non-medical care in 22.7%, blood transfusions 17.04%, surgery 12.5%, 1 accident of exposure to blood, unspecified in 45.4%. Chronic hepatitis with HbeAg (+) in 3.4%, chronic infection (CI) with HbeAg (−) in 59.09%, chronic hepatitis with HbeAg (−) in 34%, non-serious acute hepatitis in 2 patients and fulminant in 1.3patients had occult hepatitis. Co-infection with HVC in 3 patients. No cases of co-infection with Delta virus. Fibroscann in 20%, FibroTest in 5%and liver biopsy in 75%. F3–F4 in 9.09%, F2 in 22.7% and F0–F1 in 68.18%. 40% of patients had HS: the predictive factors during HVB in univariate analysis: age > 30, high BMI, diabetes and hypertriglyceridemia. Factors related to the virus (AgHbe status, the average level of viral DNA) were statistically insignificant ($p = 0.14$, $p = 0.27$).Tenofovir 300 mg. day in 96.5% and Entecavir 0.5 mg day in 3.4%. Virological response in 98.8%. Seroconversion Hbs at 12 months in 2 patients. 1 presented a virological rebound under Tenofovir. The side effects of tenofovir with hypophosphoremia and decrease creatinine clearance in 2patients switched to Entecavir.
Conclusion: The virological profile of HVB was dominated by CI HbeAg (−). SH in VHB appears to be associated with host metabolic factors and not the effect of the virus. Our study confirmed the almost constant > 98% efficacy of virologic response of analogues and should lead to enhanced screening before the advanced liver fibrosis stage.

Abstract #499

Clinical progression to hepatocellular carcinoma and mortality in chronic hepatitis B patients under antiviral therapy: real-world experience and analysis

Seong Jun Park[1], Sung Hyeok Ryou[1], Hyun Jae Lee[1], Hyun Deok Shin[1], Suk Bae Kim[1], Il Han Song[1]

[1]Division of Hepatology, Department of Internal Medicine, Dankook University College of Medicine, Dankook University Hospital, Cheonan, Korea, Republic of

Introduction: Chronic hepatitis B virus (HBV) infection is a main cause of hepatocellular carcinoma(HCC) and liver-related mortality. Currently, global practice guidance recommends entecavir, tenofovir

disoproxil fumarate, or tenofovir alafenamide for the first line oral antiviral therapy in chronic hepatitis B(CHB) patients.
Objectives: The present study tried to investigate real-world data on clinical progression to HCC and mortality in CHB patients under antiviral therapy.
Methods: We retrospectively recruited 347 CHB patients who received entecavir or tenofovir for more than 48 weeks based on medical database of Dankook University Hospital. Kaplan-Meier curve was used to estimate the development of HCC and overall/liver-related mortality, and Cox's regression analysis was used to identify clinical, biochemical, and virological factors relevant to HCC development and mortality.
Results: Eighteen patients developed HCC during median follow-up period of 134 (68–214, 25–75 percentile) weeks. One-, two-, three-, and five-year cumulative incidence rates of HCC were 0.31%, 2.28%, 3.40% and 11.17%, respectively. Accompanying cirrhosis (P = 0.0019) and platelet count (P = 0.028) were independent risk factors affecting the development of HCC. Eight patients died during follow-up period. Liver-related mortality at 1-, 2-, 3-, and 5-years was 0%, 0.79%, 0.79%, and 3.56%, while overall mortality was 0%, 1.18%, 1.73%, and 5.28%, respectively. Accompanying cirrhosis (P = 0.014), platelet count (P = 0.021), and serum albumin(P = 0.045) were significantly associated with liver-related mortality. No significant difference of HCC and mortality was noted between the CHB patients treated with entecavir or tenofovir.
Conclusion: Accompanying cirrhosis, platelet, and albumin were significant risk factors related to the development of HCC and mortality in CHB patients under antiviral therapy.

Abstract #519

Characterization of nucleos(t)ide analogue resistance mutations among treatment naïve chronic hepatitis B Minangkabau ethnic patients

Suryadi Syam[1], Nasrul Zubir[2], Arnelis[2], Saptino Miro[2], Julius[2]

[1]Department of Internal Medicine Pariaman Hospital, Indonesia, [2]Department of Internal Medicine dr. M. Djamil Hospital/Medical Faculty Andalas University, Padang, Indonesia

Introduction: Minangkabau ethnic is unique because differences in genotypes and subtypes of hepatitis B virus (HBV) compared to other ethnic groups in Sumatra. Resistance of nucleos(t)ide analogue (NA) treatment in patients with chronic hepatitis B (CHB) caused by mutations in the reverse transcriptase region HBV associating to the determination of HBV genotypes and subtypes.
Objectives: To understand the characterization of mutation and the relationship between NA resistance mutations against its genotypes in treatment-naïve CHB Minangkabau ethnic patients
Methods: This study was an observational study with cross sectional study design. Sequencing of DNA fragments with ABI Prism 310 genetic analyzer. NA mutations, genotypes, subgenotype, and subtypes then analyzed.
Results: There are 33 subjects (28 men and 5 women), with a mean age 46.1 ± 10.39 years, genotype C 25 (75.8%) and genotype B 8 (24.2%) subjects. NA mutations found in 31 (93.9%), namely the putative mutation 65.9% and 34.1% pretreatment mutations. Putative mutation analysis demonstrated lamivudine resistance occurs 21 (77.8%), adefovir 3 (11.1%), the combination of lamivudine and adefovir resistance 2 (7.4%) and a combination of lamivudine resistance, adefovir and entecavir 1 (3.7%) subjects. There was no relationship between the incidence of mutations with the type of genotype (p = 0.568). But there were significant differences statistically between lamivudine resistance compared with the genotype C and genotype B (p = 0.002), as well as adefovir resistance (p = 0.02).
Conclusion: Among treatment-naïve CHB Minangkabau ethnic patients was found putative mutation and pretreatment mutation. Further research is needed to know the clinical response and virologic response of treatment with NA.

Abstract #637

Secular trend of treatment uptake in patients with chronic viral hepatitis: a territory-wide study of 120,279 patients with data from HADCL from year 2000 to 2017

Grace Lai-Hung Wong[1,2], Yee-Kit Tse[1,2], Becky Wing-Yan Yuen[1,2], Terry Cheuk-Fung Yip[1], Vincent Wai-Sun Wong[1], Henry Lik-Yuen Chan[1,2], Pong-Chi Yuen[3]

[1]Department of Medicine and Therapeutics, [2]Institute of Digestive Disease, The Chinese University of Hong Kong, and [3]Department of Computer Science, Hong Kong Baptist University, Hong Kong.

Background: World Health Organization (WHO) calls for the reduction of chronic viral hepatitis (CVH) incidence and mortality of 80% and 65% respectively by year 2030. Antiviral treatment is the key to reduce mortality. Nonetheless, the uptake of antiviral treatment for CVH is generally suboptimal. We aimed to determine the secular trend of treatment uptake in the territory-wide CVH cohort in Hong Kong from year 2000 to 2017 with data retrieved from the Hospital Authority Data Collaboration Lab (HADCL).
Methods: This was a territory-wide retrospective observational cohort study in Hong Kong. We identified CVH patients through HADCL based on laboratory data of viral markers, diagnosis codes and the drug record of antiviral treatment for chronic hepatitis B and/or C.
Results: 120,279 CVH patients were included; 33,4278, 39,408, 29,961 and 17,483 were identified in year 2000–2004, 2005–2009, 2010–2013 and 2014–2017 respectively. In patients with chronic hepatitis B, the treatment uptake rate increased with time: 3.1%, 11.2%, 22.5% and 32.0% respectively (Table). In patients with chronic hepatitis C, the treatment uptake rate increased with time: 0.8%, 0.9%, 4.7% and 8.9% respectively (Table).
Conclusions: Treatment uptake rates have been increasing over time, but remained < 50% and < 10% in patients with chronic hepatitis B and C respectively.

Abstract #654

Differences ın microrna expression ın chronic hepatitis B patients with liver fibrosis classified based on traditional Chinese medicine syndromes

Shi-Meijie[1], Xiao-Huanming[1], Xie-Yubao[1], Jiang-Junmin[1], Zhao-Pengtao[1], Cai-Gaoshu[1], Li-Yingxian[1], Li-Sheng[1], Zhang-Chaozhen[1], Cao-Minling[1], Chen-Qubo[1], Tan-Zhijian,Gao-Hengjun[2*], Chi-Xiaoling[1*]

[1]Guangdong Provincial Hospital of Chinese Medicine, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou510120, China, [2]National Engineering Center for Biochip at Shanghai, Shanghai201203, China

Introduction: Many microRNAs (miRNAs) have been proved to be correlated with liver fibrosis in chronic hepatitis B (CHB) patients.

However, no data revealed that miRNAs could be potential markers for distinguishing TCM syndromes in CHB-fibrosis patients.
Objective: To find whether miRNA expression is significantly different in different TCM syndromes in CHB-fibrosis patients.
Methods: A total of 18 CHB-fibrosis patients and 12 patients without fibrosis were enrolled, including 9 CHB-fibrosis patients with syndrome of Ganyu Pixu Xueyu (liver stagnation, spleen deficiency and blood stasis) and 9 patients with syndrome of Qixu Xueyu (deficiency of qi, blood and blood stasis). Agilent miRNA Microarray was done in liver specimens of these patients first. Then QRT-PCR was performed to validate the miRNA microarray results.
Results: Compared to patients without fibrosis, 145 miRNAs were up regulated and 124 were down regulated in CHB-fibrosis patients. Approximately 7 miRNAs were differentially expressed between these two TCM syndromes. According to RT-qPCR data, 5 miRNAs were confirmed to be up regulated (miR-139-3p, miR-148b-3p, miR-18a-5p, miR-24-1-5p, miR-654-3p) in patients with syndrome of Qixu Xueyu compared to that with syndrome of Ganyu Pixu Xueyu. Gene Ontology and pathway analysis implicated that molecular mechanisms might be quite different between these two syndromes, while the Qixu Xueyu syndrome is more dangerous than Ganyu Pixu Xueyu syndrome in the process of liver fibrosis.
Conclusion: miRNAs expression is different in different syndromes in CHB-fibrosis patients. Therefore,miRNAs could be potential markers for distinguishing TCM syndromes in CHB-fibrosis patients.

Abstract #659

Screening of hepatitis B surface antigen among pregnant women living in Peri-urban Yangon, Myanmar

Htut, Hnin Nandar[1], Min, Myat Sandi[2], Richards, Adam[3], Whelan, Rachel[2], Shein, Htun Aung[1], Htoo, Eindra[2], Win, Su Yee[1], Kyi, Khin Pyone[4], Swe, Win Win[5], Thura Si[2]

[1]B.K.Kee Foundation, Yangon, Myanmar, [2]Community Partners International, Yangon, Myanmar, [3]University of California at Los Angeles, United States of America, [4]Myanmar Liver Foundation, Yangon, Myanmar, [5]Liver Unit, North Okkalapa General Hospital, Yangon Myanmar

Introduction: In Myanmar, the country with the highest estimated rate of perinatal Hepatitis B virus (HBV) infection in Southeast Asia, availability of HBV surface antigen (HBsAg) testing during antenatal care (ANC) is challenging. The B.K.Kee Clinic in peri-urban Yangon is conducting a pilot program to coordinate with public facilities to expand access to antenatal HBsAg screening and HBV treatment to support elimination of perinatal HBV transmission. The prevalence of chronic HBV among adults was estimated to be 12.3% in Yangon, though few data were from a non-representative survey and were not disaggregated for women of reproductive age. This analysis aimed to estimate the prevalence of chronic HBV among pregnant women and HBsAg screening coverage in the project area in the first-year of implementation.
Method: The prevalence of chronic HBV among pregnant women was calculated using results of rapid HBsAg test offered to pregnant women attending ANC at BKKee Clinic and the seven public health facilities in the project area from October 2018 to September 2019. The expected number of pregnancies in the pilot project area was calculated using population figures and crude birth rates from the 2014 census.
Results: 3.1% (n = 177/5791) of screened pregnant women tested positive for HBsAg. Antenatal HBsAg screening coverage was estimated to be 92.1% (n = 1269/1378 expected pregnancies).
Conclusion: The prevalence of chronic HBV among pregnant women in peri-urban Yangon is lower than estimated by previous studies. It is possible to achieve high coverage of perinatal HBV screening by coordinating across providers in NGO and public sectors.

Abstract #662

Poor linkage to care for patients living with hepatitis B virus (HBV) infection in a high-income country. How can we do better?

Horsfall E[1], Anwar A[2], Moyes C[2], Lampen-Smith A[2], Hay S[2], Cunningham C[3], Gane E[1]

[1]New Zealand Liver Transplant Unit, Auckland City Hospital, Auckland, New Zealand, [2]Hepatitis Foundation of New Zealand, Whakatane, New Zealand, [3]Research Centre for Māori Health & Development, Massey University, Wellington, New Zealand

Introduction: The Hepatitis Foundation of New Zealand (HFNZ) provides a free national hepatitis B virus (HBV) surveillance programme for New Zealanders living with HBV. However, most HBV-related hepatocellular carcinomas are diagnosed at an advanced stage in patients not participating in this programme.
Objectives: To determine the overall prevalence of HBV in New Zealand, including patients not recruited into the HFNZ surveillance programme, in order to inform on unmet needs in New Zealanders living with HBV.
Methods: Demographic, clinical and virologic characteristics were collected for all HBV cases on HFNZ surveillance database. Deprivation index was also calculated. Overall HBV prevalence was derived by applying ethnicity-based prevalence rates (Māori 5.6%; Pacific Islander 7.3%; Asian 8.9%) to the 2018 NZ Census age-adjusted population data.
Results: In 2018, an estimated 93,604 New Zealanders are living with HBV, of whom only 18,000 are under active follow up by HFNZ. Most are Asian (49%), Māori (20%) or Pacific Islanders (17%). More than half reside within the Auckland region, reflecting the ethnic diversity of this city. Although the South Island holds more than 15% of the HBV population, less than 3% of those in active follow-up reside there. Over half (57%) of the HBV population fall into the highest levels of deprivation.
Conclusion: HBV burden in New Zealand is high but less than 20% have been recruited into the national surveillance programme, reflecting low awareness, diagnosis rate and linkage to care. New approaches are needed to engage the at-risk ethic minority population who suffer from the highest level of deprivation.

Abstract #677

HBV-specific CXCR5^{+}CD8^{+}T cells are partially exhausted but more functional in a mouse model of chronic hepatitis B virus infection

Li Zhang,[1] Qian Zhang,[1] Xichen Pang,[1] Xiaoqing Liu,[1] Hong Ren,[1] Peng Hu[1]

[1]Department of Infectious Diseases, Institute for Viral Hepatitis, The Key Laboratory of Molecular Biology for Infectious Diseases, Chinese Ministry of Education, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China

Introduction: CD8^{+}T cells are functional exhausted in chronic HBV infection. While studies have shown that CD8^{+}T cells expressing C-X-C motif chemokine receptor 5 (CXCR5) possess potent antiviral function.

Objectives: This study aimed to discuss the functional status of HBV-specific $CXCR5^+CD8^+$T cells in a mouse model of chronic hepatitis B virus (HBV) infection.
Methods: Male C57BL/6J mice was hydrodynamically injected with pAAV-HBV1.2 plasmids. The frequencies and phenotypes of splenic HBV-specific $CXCR5^+$ and $CXCR5^-CD8^+$T cells were detected through flow cytometry. Meanwhile, the splenic lymphocytes were isolated and stimulated by HBc-derived peptides overnight and then the cytokine secretion of HBV-specific $CXCR5^+$ and $CXCR5^-CD8^+$T cells were assessed.
Results: The frequency of HBV-specific $CXCR5^+CD8^+$T cells increased from day 7 to day 14, and then decreased at day 28 and day 56 after transfection. The levels of ICOS, PD1, CD40L and TIM3 were significantly higher in HBV-specific $CXCR5^+CD8^+$T cells than in HBV-specific $CXCR5^-CD8^+$T cells at each timepoint except expression of PD1 at day 14. In addition, the secretion of IL-21, IFN-γ and TNF-α were significantly higher in $CXCR5^+CD8^+$T cells than in $CXCR5^-CD8^+$T cells at each timepoint. However, the expression of the four surface molecules and secretion of IL-21 and IFN-γ declined initially in HBV-specific $CXCR5^+CD8^+$T cells after plasmid injection and then tended to increase.
Conclusions: HBV-specific $CXCR5^+CD8^+$T cells possess a stronger cytotoxic function in spite of they are partially exhausted in chronic HBV infection. However, in the early stage of infection, this effect is limited, which may lead to chronic infection.

Abstract #690

All-cause mortality and liver-related death following entecavir, tenofovir disoproxil fumarate or lamivudine therapy among treatment-naïve chronic hepatitis B patients in British Columbia, Canada

Mawuena Binka[1], Younathan Abdia[1,2], James Wilton[1], Zahid A. Butt[3], Maryam Darvishian[4], Stanley Wong[1], Amanda Yu[1], Sofia Bartlett[1,2], Dahn Jeong[1,2], Emilia Clementi[1,2], Prince Adu[1,2], Margo Pearce[1,2], Maria Alvarez[1], Eric Yoshida[5], Alnoor Ramji[5], Jason Wong[1], Mel Krajden[1,6], Naveed Janjua[1,2]

[1]British Columbia Centre for Disease Control, Vancouver, Canada, [2]School of Population and Public Health, University of British Columbia, Vancouver, Canada, [3]School of Public Health & Health Systems, University of Waterloo, Canada,[4] BC Cancer Research Centre, Vancouver, Canada, [5]Department of Medicine, Division of Gastroenterology, University of British Columbia, Vancouver, Canada, [6]Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada

Introduction: Conflicting information exists about the relative impact of entecavir (ETV), tenofovir (TDF) and lamivudine (LAM) on the long-term survival of chronic hepatitis B (HBV) patients.
Objective: We assessed the association between ETV, TDF or LAM therapy and all-cause/liver-related mortality among chronic HBV patients in British Columbia, Canada.
Methods: Treatment-naïve HBV-positive individuals within the BC Hepatitis Testers Cohort initiating ETV, TDF or LAM and receiving only one of these drugs on or before Dec 31, 2017 were included in this study. To account for differing baseline profiles, treatment groups were matched 1:3:3 by common referent propensity score matching with ETV as the reference group. The effect of ETV, TDF, and LAM therapy on all-cause and liver-related mortality from treatment start until Dec 31, 2018 was assessed with multivariable Cox proportional-hazards models, accounting for the competing mortality risk for liver-related death.
Results: 2,464 matched participants initiated ETV (n = 352), TDF (n = 1056) and LAM (n = 1056). These individuals were predominantly East Asian (63.4%). Relative to TDF, the ETV group was at greater risk of both all-cause (adjusted hazard ratio [aHR] 2.01, 95% CI 1.20–3.35) and liver-related mortality (aHR 2.57, 95% CI 1.11–5.94). Differences in mortality risk for LAM and TDF treatment groups were not statistically significant (aHR: All-cause 1.39, 95% CI 0.83–2.33; Liver-related 1.02, 95% CI 0.41–2.54).
Conclusion: Among treatment-naïve chronic HBV patients, the risk of all-cause mortality and liver-related death post-treatment initiation was higher with ETV relative to TDF and LAM. This finding is noteworthy warrants further study given the potential future implications for HBV therapy.

Abstract #701

Exosomes with miRNAs transfer anti-HBV activity mediated by the interferon from macrophage to HBV-infected hepatocyte

Wenyu Wu, Di Wu, Jie You, Xiaoping Luo, Meifang Han, Qin Ning

Introduction: Interferon alpha (IFN-α) has proven to be clinically effective in the treatment of chronic hepatitis B (CHB) due to its capability to reduce the levels of hepatitis B surface antigen (HBsAg) and hepatitis B virus (HBV) covalently closed circular DNA (cccDNA). However, the underlying mechanisms are not well defined.
Objectives: Research the anti HBV mechanisms of exosome threated with IFN.
Methods: Combine the pegylated IFN-α (PegIFN-α) treated patients' exosomes and the IFN-α-treated cell lines exosomes, research the mechanism of exosomes anti HBV treated with IFN.
Results: Exosomes in serums from PegIFN-α treated patients and the culture supernatants of IFN-α-treated THP-1 derived macrophages exhibited distinct anti-HBV activities including the suppression of supernatant HBsAg, hepatitis B e antigen (HBeAg), and HBV DNA levels as well as intracellular HBV cccDNA in HBV related cell lines. Notably, microRNA sequencing revealed that PegIFN-α treatment upregulated specific miRNAs within the exosomes that could partially inhibit HBV replication and transcription through exosome mediated transfer. The luciferase reporter assay confirmed that miRNA reduced pregenomic RNA (pgRNA) and polymerase mRNA levels by binding to the nucleotides of HBV genomic sequence.
Conclusions: exosomes can transfer IFN-α-related miRNAs from macrophages to HBV-infected hepatocytes, thereby suppressing HBV replication and expression.

Abstract #747

Comparison of the patients using lamivudine, entecavir and tenofovir according to the apri and fib-4 scores which are predicted to be markers of liver fibrosis

Ertugrul Guclu

Introduction: Histopathological examination is the gold standard for the assessment of liver fibrosis in chronic hepatitis B (CHB) infection. However, it is an invasive and painful procedure.
Objectives: We aimed to evaluate the efficacy of treatment by comparing the APRI and FIB-4 scores in patients with hepatitis B patients who had lamivudine, entecavir and tenofovir treatments.
Methods: This retrospective study was conducted in a tertiary hospital between 2008 and 2015. CHB patients who treated with

lamivudine, entecavir, and tenofovir were evaluated with noninvasive fibrosis scores.
Results: In total, 199 patients included in the study, 48 of them had lamivudine, 46 had entecavir, and 105 had tenofovir therapies. There was no significant difference between the three treatment groups in terms of gender and age ($p > 0.05$). No significant difference was found between the three groups in terms of ALT normalization over the years ($p > 0.05$). HBeAg seroconversion developed in 5/36 (13.5%) cases and there was no significant difference between the three groups ($p > 0.05$). For lamivudine, entecavir and tenofovir groups, there was a significant difference between the baseline and the first year APRI, FIB-4 index values ($P < 0.001$). Graphically a plateau was seen for the APRI score after first year and a plateau seen for the FIB-4 score after the second year.
Conclusion: According to our results, tenofovir and entecavir were more effective than lamivudine in the regression of fibrosis. Additionally, after the first year entecavir was found to be more effective than the other two drugs.

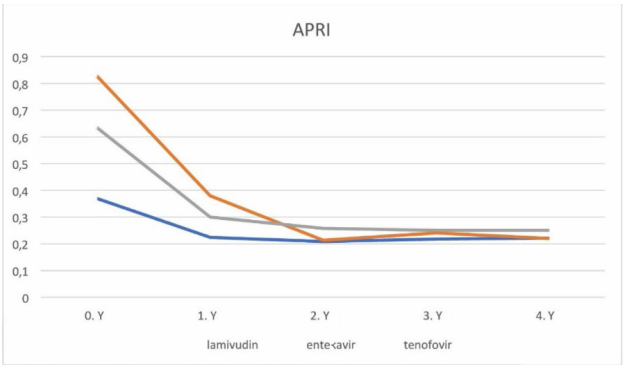


Figure 1: APRI Score Change by Years

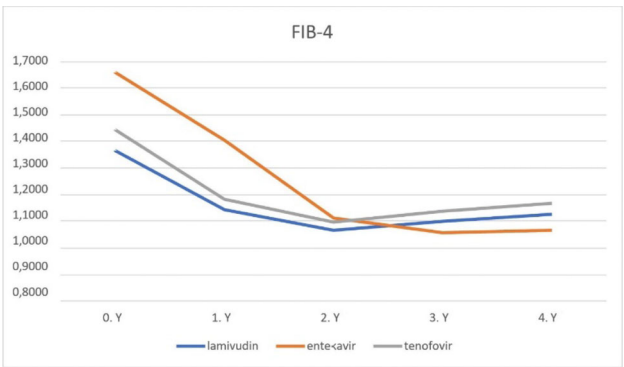


Figure 2: Fib-4 Score Change by Years

Abstract #748

Suboptimal response, elder and comorbidity are decisive elements for choosing tenofovir alafenamide (TAF): a real-world study in southwest of China

Qian Zhang[1], Xiaoqing Liu[1], Peng Hu[1]

[1]Department of Infectious Diseases, Institute for Viral Hepatitis, The Key Laboratory of Molecular Biology for Infectious Diseases, Chinese Ministry of Education, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China

Introduction: Tenofovir alafenamide (TAF), a new nucleotide analogue (NA), provides sustained viral suppression and improves renal and bone safety in chronic hepatitis B (CHB) patients.
Objectives: This study aimed to discuss the application of TAF in CHB patients with complex baseline conditions.
Methods: It involved 147 CHB patients with TAF therapy from January to July, 2019.Relevant data were obtained from patients' records.
Results: Of these patients, 76 were NAs-experienced, and 71 were treatment-naive. 8.8% patients were over 60 years old. Comorbidities included low phosphorus (0.7%), diabetes (3.4%), spontaneous fracture (0.7%), vitamin D deficiency (1.4%), gout (0.7%) and kidney damage (3.4%). The percentage of the advanced liver disease in the NAs-experienced and naive patients were 26.3% (20/76) and 18.3% (13/71) respectively. The percentage of the NAs-experienced patients whose viral load $\leq$ 1000 copies/ml was 63.3%. 40% of the patients developed hypophosphatemia or decreased eGFR, most of them were NAs-experienced (blood phosphorus < 1.0 mmol/L, eGFR < 90 ml/min). Among the NAs-experienced patients: 46.1% were ETV-based treatment, 36.8% were TDF-based treatment, and 19.7% used other low barrier resistance drugs. High incidence rates of alanine aminotransferase normalization and virologic suppression were shown at weeks 12 and 24 in NAs-experienced and naive patients.
Conclusion: Currently, TAF-based treatment is mainly used in patients with comorbidities, elder, suboptimal response to the prior NA regimens, hypophosphatemia or eGFR reduction. In the real word, complicated baseline conditions are important factors in choosing of TAF in the southwest of China.

Abstract #791

Survey on hepatitis B vaccination coverage among mongolian healthcare workers

Nyamsuren Naranzul[1], Altangetrel Enkhjargal[2], Badrakh Burmaajav[3,6], Tsoggerel Nandintsetseg[2], Munkhtur Tselmeg[2], Ganbold Sarangoo[4], Oktyabr Azzaya[5], Oidov Baatarkhuu[1,6]

[1]Department of Infectious Diseases, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [2]Academy of Medical Professionals, Ulaanbaatar, Mongolia, [3]Ach Medical University, Ulaanbaatar, Mongolia, [4]Department of Hepatology Laboratory, National Center for Communicable Diseases, Ulaanbaatar, Mongolia, [5]City Health Authorities, Ulaanbaatar, Mongolia, [6]Mongolian Academy of Medical Sciences, Ulaanbaatar, Mongolia

Introduction: Mongolia has a large burden of viral hepatitis, especially chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, which are associated with cancer and cirrhosis. The occupational risk for transmission of HBV, HCV and HIV among healthcare workers (HCWs) is well recognized.
Objectives: To define HBV vaccination coverage among Mongolian healthcare workers.
Methods: This is a cross-sectional hospital based survey which will be conducted among healthcare workers to evaluate HBV vaccination coverage and KAP towards to the HBV infection and vaccination. In total, 1200 health care workers were attended to the survey.
Results: More than half of survey respondents were had full 3 doses of HBV vaccination. About 4.5% of them had infected with

HBV. About 64.0% of them were health workers who are currently working at risk position and most of them had contact with blood, blood products and other body fluids, as well as the risk of needle-stick injuries. 40.0% of respondents who had full doses of HBV vaccination and 56.9% of them had immune due to natural infection. Whereas, 16.7% of respondents who did not received full doses of HBV vaccination were had immune due to natural infection. In general, 1 of 2 respondents had immune due to natural infection.

Conclusion: The HBV vaccination coverage among health workers are relatively sufficient. However, already infected percentages of among health workers are high in Mongolia.

Abstract #797

The immunogenicity of healthcare workers of hepatitis B vaccination in Mongolia

Nyamsuren Naranzul[1], Altangetrel Enkhjargal[2], Badrakh Burmaajav[3,6], Tsoggerel Nandintsetseg[2], MunkhturTselmeg[2], Ganbold Sarangoo[4], Oktyabr Azzaya[5],Bayanjargal Jargalmaa[2],Oidov Baatarkhuu[1,6]

[1]Department of Infectious Diseases, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [2]Academy of Medical professionals, Ulaanbaatar, Mongolia, [3]Ach Medical University, Ulaanbaatar, Mongolia, [4]Department of Hepatology Laboratory, National Center for Communicable Diseases, Ulaanbaatar, Mongolia, [5]City Health Authorities, Ulaanbaatar, Mongolia, [6]Mongolian Academy of Medical Sciences, Ulaanbaatar, Mongolia

Introduction: A safe working environment for healthcare workers should include the offer of HBV immunization not only for their protection, but also to prevent transmission from HCWs to patients. The immunogenicity of a two-dose HBV vaccine course would be estimated to provide more than 75% sero-protection.

Objectives: To define immunogenicity of Hepatitis B vaccination among health workers in Mongolia.

Method: This is a cross-sectional hospital based survey which will be conducted among healthcare workers to evaluate HBV vaccination coverage and KAP towards to the HBV infection and vaccination. Statistical analysis was done by using an SPSS-21 and conducted relevant statistical tests. In total, 1200 health workers were responded to this survey. 3 main laboratory serological tests was performed among survey participants HBsAg, Anti-HBc total, and Anti-HBs.

Results: The protection level of the subjects was 57.6% $>$ 100 mIU/ml, 24.8%, 11–100 mIU/mL and 17.6%, 0–10 mIU/mL. The mean of Immune due to natural infection level was 459.71 $\pm$ 392.95 mIU/ml and immune due to HBV vaccination level was 516.20 $\pm$ 412.68 mIU/ml. In relatively, high percentage of health workers who are working less than 5 years were had immune due to vaccination. Whereas, 62.7% of health workers who had immune due to natural infection were working in health facility more than 6 years.

Conclusion: On hepatitis B vaccination efficacy done in Mongolia, of the vaccinated HCWs, 57.6% >100 mIU/ml, 24.8%, 11–100 mIU/mL and 17.6%, 0–10 mIU/mL.

Abstract #808

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) as a rare extra-hepatic manifestation of chronic hepatitis b infection: a case report

Ian Huang[1], Rudi Supriyadi[1], Eka Surya Nugraha[2], Muhammad Begawan Bestari[2]

[1]Division of General Internal Medicine, Department of Internal Medicine, Hasan Sadikin General Hospital, Universitas Padjadjaran, Bandung, Indonesia, [2]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Hasan Sadikin General Hospital, Universitas Padjadjaran, Bandung, Indonesia

Introduction: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is scarcely reported as an extra-hepatic manifestation of Hepatitis B virus (HBV) infection. We reported a case of CIDP in a patient with chronic-active HBV infection that gradually improved after the administration of a nucleoside analogue.

Case Report: A 44-year-old male with chronic HBV infection admitted to the hospital with gradual muscle weakness and paraesthesia in all extremities. The patient was slightly icteric, with normal bowel and bladder function. The HbeAg was positive and serum HBV-DNA levels were 1.65×10^5 IU/ml. Nerve Conduction Studies was conducted and showed demyelinating peripheral axonal lesion in both sensory and motoric nerves. Cerebrospinal fluid (CSF) analysis revealed albuminocytologic dissociation, with polyclonal gammaglobulinemia in serum protein electrophoresis. The patient was given oral lamivudine, intravenous steroids, and oral calcium with vitamin D supplementation. His muscle strength recovered significantly after 6 weeks and returned to normal in 24-week follow-up visit. According to the current literature, neurological manifestations of chronic HBV infection may occur in up to 5% patients. However, CIDP associated with HBV infection was rare, and to the deep of our knowledge only 5 cases were reported previously.

Conclusion: CIDP is a rare extra-hepatic manifestation of chronic HBV infection. Administration of nucleoside analogue and CIDP standard treatments may not only prevent further worsening of the condition, but also lead to a gradual recovery of neurologic function.

Abstract #819

A real-life study (RWS) of long-term outcomes after discontinuation of NUC monotherapy, PEG IFN-α monotherapy and their combo-therapy in patients with HBeAg-positive chronic hepatitis B (CHB)

Yuming Wang[1,2], Guangyu Huang[3], Jie Xia[1], Zehui Yan[1], Xuelan Zhao[2]

[1]Institute for Infectious Diseases, Southwest Hospital, Army Medical University, Chongqing, China, [2]Public Health Hospital of Southwest University , Chongqing, China, [3]The Fourth Affiliated Hospital Zhejiang University School of Medicine, Yiwu, China

Introduction: Anti-HBV drugs mainly include nucleotide analogues (NUCs) and interferons-α (IFN-α), particularly PEG IFN-α. At present, there are three types of antiviral treatment strategies, NUCs monotherapy, IFN-α monotherapy and combo-therapy with NUCs plus IFN-α. However, so far, few studies on long-term outcomes after these three treatment strategies after discontinuation of the drugs have been carried out and reported.

Aim: To compare the long-term outcomes after discontinuation of NUC monotherapy, PEG IFN-α monotherapy and combo-therapy in patients with HBeAg-positive chronic hepatitis B (CHB).

Material and methods: HBeAg-positive CHB patients with ideal endpoint or satisfactory endpoint who had discontinued NUCs monotherapy, PEG IFN-α monotherapy and combo-therapy with NUCs plus PEG IFN-α (when PEG IFN-α was used for at least 24 weeks) for more than 48 weeks. The ideal endpoint was defined as HBsAg loss with/without HBsAb seroconversion, and satisfactory endpoint was defined as HBeAg seroconversion. After discontinuation of treatment all patients were evaluated at least once every 3 months for alanine aminotransferase (ALT), HBV markers and HBV DNA levels. The outcomes, including sustained serologic and virologic response and relapse, were evaluated during long-term follow-up for at least 48 weeks. Sustained response was defined as a sustained off-therapy serologic, virologic and biochemical response. Serologic relapse was defined as off-therapy HBsAg positive conversion or HBeAg positive reversion. Virologic relapse was defined as off-therapy HBV DNA levels > 2000 IU/mL in at least two determinations more than 4 weeks apart.

Results: A total of 626 patients were enrolled, including 342 patients with NUCs monotherapy (56 patients with ideal endpoint and 286 patients with satisfactory endpoint), 118 patients with PEG IFN-α monotherapy (67 patients with ideal endpoint and 51 patients with satisfactory endpoint) and 166 patients with combo-therapy (120 patients with ideal endpoint and 46 patients with satisfactory endpoint). In satisfactory endpoint patients, there were no significant differences among NUC monotherapy group, PEG IFN-α monotherapy group and combo-therapy group in serologic relapse rate. But in satisfactory endpoint patients, NUC monotherapy group was significantly higher than PEG IFN-α monotherapy group ($P = 0.0069$) and combo-therapy group ($P = 0.0008$) in virologic relapse rate, respectively. In ideal endpoint patients, there were no significant differences among NUC monotherapy group, PEG IFN-α monotherapy group and combo-therapy group in serologic relapse rate and virologic relapse rate. However, during the follow-up period, some patients had a transient relapse, including 5 serologic relapse patients with satisfactory endpoint (5/17, 29.41%) and 19 virologic relapse patients with satisfactory endpoint (19/95, 20.0%), and 6 serologic relapse patients with ideal endpoint (7/18, 38.9%). Three patients with ideal endpoint were found to have transient viral rebound. There were no significant differences among the baseline characteristics (gender, HBV genotype, age, or ALT level) or between the patients with relapse and sustained-response.

Discussion: Through a large serious cohort follow-up study, we have again demonstrated that satisfactory endpoint in patients with NUC monotherapy is more likely to have virologic relapse compared to those in patients with PEG IFN-α monotherapy and their combo-therapy. As for ideal endpoint, there is no significant difference among above-mentioned three groups, which suggests that this endpoint is stable due to immune-response from the host. Also, in ideal endpoint patients, serologic relapse other than virologic relapse was more common seen, suggesting that host immune responses more often induce viral suppression other than in expression of serum markers. Finally, our study has demonstrated that transient serologic and virologic relapse were seen in patients with ideal and/or satisfactory endpoint, which suggests that current definitions for treatment relapse are not completely reliable. So, the definitions on relapse remain to be studied further.

Conclusion: Through the large serious cohort follow-up study, we have found that ideal endpoint patients are more difficult to relapse than satisfactory endpoint patients, but the overall effect is good. And current definitions for treatment relapse remain to be studied further.

Table. Relapse in three groups after discontinuation of anti-viral therapy

Group	Number of cases	Satisfactory endpoint		Ideal endpoint	
		Serologic-relapse	Virologic-relapse	Serologic-relapse	Virologic-relapse
Group A (NUC monotherapy)	342	4.20% (12/286)	30.07% (86/286)	10.7% (6/56)	1.79% (1/56)
Group B (PEG IFN-α monotherapy)	118	7.84% (4/51)	11.76% (6/51)	5.97% (4/67)	0% (0/67)
Group C (combo-therapy)	166	2.17% (1/46)	6.52% (3/46)	6.67% (8/120)	1.67% (2/120)
P value		A vs. B *P*=0.2592; A vs. C *P*=0.5115	A vs. B *P*=0.0069; A vs. C *P*=0.0008	A vs. B *P*=0.3377; A vs. C *P*=0.3554	A vs. C *P*=0.2721; B vs. C *P*=0.9563

Abstract #820

A real-life study (RWS) of long-term follow-up comparison for the standard and broaden ideal endpoints in patients with chronic hepatitis B (CHB)

Xuelan Zhao[1], Yuming Wang[1,2], Guangyu Huang[3], Jie Xia[2], Zehui Yan[2]

[1]Public health hospital of Southwest University, Chongqing, China, [2]Institute for Infectious Diseases, Southwest Hospital, Army Medical University, Chongqing, China, [3]The fourth Affiliated Hospital Zhejiang University School of Medicine, Yiwu, China

Introduction: Currently, the standard ideal endpoint was defined as HBsAg loss with/without HBsAb seroconversion after drug withdrawal. But previous studies in patients with natural HBV clearance have found that some patients may present with extremely low HBsAg level, i.e., weak positive HBeAg (< 10 COI), and HBeAb does not appear all the time, which was called broaden ideal endpoint in this study. Clinically, it is found that not all the patients who achieve functional cure after antiviral therapy reach the standard ideal endpoint. This may be due to some limitation on current HBV-M detection.

Aim: It is necessary to compare the long-term effects of the standard and broaden ideal endpoints through follow-up after drug withdrawal, to finally determine the ideal endpoints in line with clinical treatment practice.

Material and methods: HBeAg-positive CHB patients with standard or broaden ideal endpoint who had discontinued antiviral therapy for more than 24 weeks. The standard ideal endpoint was defined as HBsAg loss (< 0.05IU/mL) with/without HBsAb seroconversion, and broaden ideal endpoint was defined as the condition with very low HBsAg levels (< 1 IU/ml), weak positive HBeAg (< 5 COI), or persistent absence of HBeAb. After discontinuation of treatment all patients were evaluated at least once every 3 months for alanine aminotransferase (ALT), HBV markers and HBV DNA levels. The outcomes, including sustained serologic, virologic response and clinical relapse, were evaluated during long-term follow-up for at

least 24 weeks. Sustained response was defined as a sustained off-therapy serologic, virologic and biochemical response. Serologic relapse was defined as off-therapy HBsAg positive or HBeAg positive reversion. Virologic relapse was defined as off-therapy HBV DNA levels > 2000 IU/mL in at least two determinations more than 4 weeks apart. Clinical relapse was defined as off-therapy virologic relapse and ALT $> 2 \times$ ULN, but ALT elevation caused by other factors should be excluded.

Results: A total of 353 patients were enrolled, including 221 patients with standard ideal endpoint and 132 patients with broaden ideal endpoint. There was no significant difference between the two groups in serologic relapse rate ($P = 0.5845$) and virologic relapse rate ($P = 0.9025$), respectively. There was no significant difference between the two groups in clinical relapse rate ($P = 0.1788$). There was no significant difference between the two groups in serologic and virologic relapse ($P = 0.9025$). Interestingly, all patients with virologic relapse in standard and broaden ideal endpoint were accompanied by serologic relapse. In standard and broaden ideal endpoint patients, the serologic relapse was significantly higher than virologic relapse. However, transient viral rebound occurred in 3 patients with standard ideal endpoint and 4 patients with broaden ideal endpoint, respectively. One patient with virologic relapse and clinical relapse in standard ideal endpoint achieved standard ideal endpoint through retreatment, and the course of treatment was shorter. And 2 patients with virologic relapse and clinical relapse in standard ideal endpoint were still in treatment follow-up. There were no significant differences among the baseline characteristics (gender, HBV genotype, age, or ALT level) or between the patients with standard and broaden ideal endpoint.

Discussion: Through a large serious cohort follow-up study, we have demonstrated that patients with standard ideal endpoint had fewer relapse compared to patients with broaden ideal endpoint in serology and virology, but there was no statistical difference. The virologic relapse in patients with standard and broaden ideal endpoint were often accompanied by serologic relapse. In patients with standard and broaden ideal endpoint, serologic relapses other than virologic relapses are more common seen, suggesting that host immune responses more often induce viral suppression other than in expression of serum markers. So, when standard ideal endpoint is difficult to be reached through current treatment, the ideal endpoint can be broadened appropriately.

Conclusion: Current standard ideal endpoint may be replaced by our broaden endpoint.

Table 1. Comparison of the baseline characteristics in patients with standard and broaden ideal endpoints

	Standard endpoint (n=201)	Broaden endpoint (n=117)
Gender	M: F=145: 76	M: F =84: 48
Age	35.4(17-67)	35.8 (18-65)
Baseline of treatment		
ALT	77.5 ± 16	79.6 ± 17
HBV DNA (IU/mL)	7.35±0.47	7.39±0.43
Therapies		
NUC monotherapy	23.9%(48/221)	21.4%(28/132)
PEG IFN-α monotherapy	28.5%(63/221)	30.8%(44/132)
combo-therapy with NUCs plus PEG IFN-α	49.8%(110/221)	47.9%(60/32)
Period of treatment (month)	30（7-96）	37（6-108）
History of drug resistance during treatment	14	9
History of relapse/rebound after discontinuation	3	4

Note: There were no statistically significant differences in gender, age, ALT and HBV DNA between the two groups ($P > 0.05$). The lower limit of HBV DNA detection was 50 IU/ml.

Table 2. Comparison of outcome after discontinuation of standard and broaden ideal endpoints in HBeAg positive patients

Group	Cases	Serologic relapse	Virologic relapse	Serologic relapse+ Virologic relapse	Clinical relapse
Standard endpoint(A)	221	8.14% (18/221)	1.36% (3/221)	1.36% (3/221)	1.36% (3/221)
Broaden endpoint(B)	132	9.85% (13/132)	1.52%(2/132)	1.52%(2/132)	0%(0/132)
Total	353	8.78%(31/353)	1.41%(5/353)	1.41%(5/353)	0.85%(3/353)
P value		A vs. B *P*=0.5845	A vs. B *P*=0.9025	A vs. B *P*=0.9025	A vs. B *P*=0.1788

Note: Transient viral rebound occurred in 3 patients with standard endpoint and 4 patients with broaden endpoint, respectively.

Abstract #824

Complex etiology of jaundice in the case of hepatitis B reactivation: case report

Anna Szymanek-Pasternak[1,2], Wojciech Szymański[1,2], Sylwia Serafińska[1,2], Kamila Zielińska[1,2], Justyna Janocha-Litwin[1,2], Krzysztof Simon[1,2]

[1]Department of Infectious Diseases and Hepatology, Wroclaw Medical University, Wroclaw, Poland, [2]1st Department of Infectious Diseases, Regional Specialistic Hospital, Wroclaw, Poland

Here we present the case of 85-years old male who reactivated hepatitis B virus (HBV) infection during chemotherapy for mantle cell lymphoma. Before treatment he was known to be only anti-HBc antibodies positive (HBs antigen-negative, serum HBV DNA-negative) and his liver enzymes were normal. After six courses of mini CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine and prednisolone) he developed hepatitis with elevated liver enzymes: alanine aminotransferase (ALT) − 593 IU/L, aspartate aminotransferase (AST) − 795 IU/L, alkaline phosphatase (ALP) − 292 IU/L, gamma-glutamyl transferase (GGT) − 265 IU/L, positive HBs antigen, positive anti-HBs antibodies, as well as positive HBe antigen and positive anti-HBe antibodies, HBV DNA of 6×10^6 IU/ml and bilirubin 3.3 mg/dl. He received treatment with entecavir 0.5 mg daily. 2 weeks after antiviral treatment initiation his liver enzymes declined (ALT − 312 IU/L, AST − 557 IU/L, ALP − 177 IU/L, GGT − 109 IU/L), HBV DNA decreased significantly but bilirubin increased to 31 mg/dl. Contrast CT showed dilated intra- and extrahepatic bile ducts and enlarged, pathological lymph nodes in abdominal cavity, including liver hilum and area around the head of the pancreas. But cholangio-MRI revealed additionally bile stone in the distal part of the common bile duct. The bile stone was removed upon endoscopic retrograde cholangiopancreatography but it did not result in jaundice improvement. Bilirubin decreased only after administration of high dose of intravenous methylprednisolone. This case shows the risk of HBV reactivation during chemotherapy and complex etiology of jaundice.

Abstract #828

Phylogenetic reconstruction of hepatitis B virus genotype A2 in Japan

Hoshino K[1], Ito K[2], Sugiyama M[3], Mizokami M[3]

[1]Department of Infectious, Respiratory, and Digestive Medicine, University of the Ryukyus, Nishihara, Japan, [2]Division of Hepatology and Pancreatology, Department of Internal Medicine, Aichi Medical University, Nagakute, [3]Genome Medical Science Project, National Center for Global Health and Medicine, Ichikawa, Japan

Introduction: Hepatitis B virus (HBV) has been classified into genotypes (A-J) and subtypes based on genetic divergence. While HBV genotype C (HBV/C) and HBV/B are the most prevailing types in Japan, the increasing prevalence of acute infection with HBV/A has been reported recently.
Objectives: To elucidate population dynamics of HBV/A in Japan using molecular evolutionary analyses.
Methods: In this study, 45 patients with acute HBV/A infection from 12 liver centers throughout Japan were enrolled during 2005–2010. Nucleotide sequences in the pre-S1/pre-S2/S region were determined by direct sequencing. Substitution rate was estimated using Bayesian inference. Phylogenetic trees were reconstructed using maximum-likelihood method. To evaluate population dynamics of HBV/A, Bayesian Skyline Plot method was employed using all sequences from acute HBV/A cases in Japan.
Results: Nucleotide sequences were obtained in 37 of 45 serum samples. The mean age of patients was 33.5 years, and most of subjects were men (36/37, 97.3%). The major route of transmission was sexual contact. Phylogenetic analysis showed that all our samples were classified into genotype A2. Additionally, 44 HBV/A2 sequences from Japan were identified in Genbank database. Phylogenetic analysis revealed 4 groups comprised of genomically identical sequences sampled in Japan and other countries. Phylodynamic analysis revealed an exponential increase in effective population size of HBV/A2 in early 2000s.
Conclusion: HBV/A2 spread rapidly among Japanese young population through sexual contacts in early 2000s, which coincided with the second outbreak of acute HBV/A2 cases in the USA

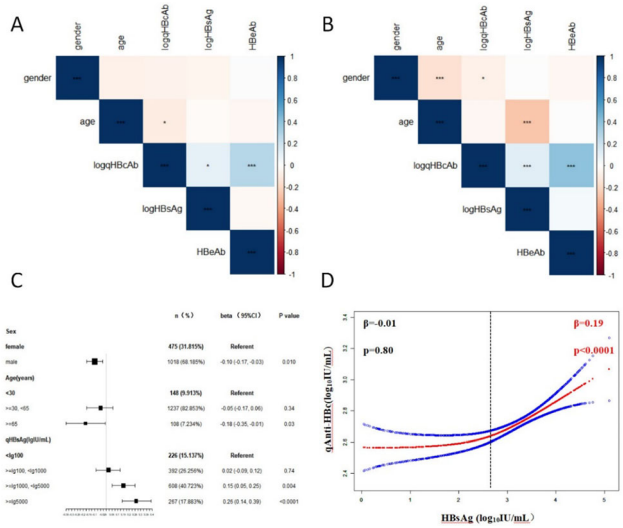
Abstract #829

Association between quantitative hepatitis B virus core antibody levels and surface antigen in chronic low viraemic patients

Li Jing[1], Wei Dong[1], Chen Jia[1], Gong Qiming[2], Zhang Xinxin[1]

[1]Research Laboratory of Clinical Virology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China,
[2]Department of Infectious Diseases, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China

Introduction: Several studies have revealed that baseline quantitative Anti-HBc (qAnti-HBc) could predict the response of antiviral therapy.
Objectives: We performed a cross-sectional study to determine whether the total serum level of qAnti-HBc (immunoglobulins M and G) is associated with hepatitis B surface antigen (HBsAg) in low viraemic chronic HBV infected patients.
Methods: Data were collected from 1493 HBsAg positive patients with HBV DNA $<$ 500 IU/L and quantified qAnti-HBc at RuiJin Hospital, between August 2018 and September 2019. The association between qAnti-HBc and serum virologic markers was systematically analyzed.
Results: The mean qAnti-HBc level was 2.71 $\pm$ 0.69 $\log_{10}$IU/mL, which was higher in HBeAg negative patients of 2.86 $\pm$ 0.71 $\log_{10}$IU/mL than in HBeAg positive patients of 2.41 $\pm$ 0.52 $\log_{10}$IU/mL ($p < 0.001$). The correlation of the qAnti-HBc level and HBsAg was slightly positive in both HBeAg positive patients ($r = 0.10$, $p < 0.05$) and negative patients ($r = 0.13$, $p < 0.001$). Multivariate regression analysis revealed that HBsAg was independent factor associated with qAnti-HBc (beta = 0.10, $p < 0.0001$). Additionally, a nonlinear relationship was observed between qAnti-HBc and HBsAg. The qAnti-HBc level increased significantly only when HBsAg level above 512.86 IU/mL (log HBsAg 2.71) (adjusted beta = 0.19, 95% CI 0.04–0.12, $p < 0.0001$).
Conclusion: In chronic HBV infected patients with low viraemic, serum qAnti-HBc level was closely related to HBsAg in a nonlinear pattern. These findings suggest that monitoring qAnti-HBc level could serve as a useful marker for measuring host immune response against HBV.



Abstract #837 Transfection of polyethylenimine-oligonucleotide complexes reduces HBsAg level in cell cultures

Lin Junyu[1], Li Jing[1], Wei Dong[1], Chen Jia[1], Han Yue[1], Yu Demin[1], Huang Wei[1], Yang Zhitao[2], Zhang Xinxin[1]

[1]Research Laboratory of Clinical Virology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China,
[2]Emergency Department, Ruijin Hospital affiliated to Shanghai Jiaotong University, School of Medicine, Shanghai, China

Introduction: It has been demonstrated that phosphorothioated oligonucleotides (PS-ONs) have a size-dependent inhibition in HBsAg secretion
Objective: Here we demonstrated for the first time that using transfection method to deliver the complexes of polyethylenimine (PEI) with unmodified nucleotides into Human hepatoma cell line AD38 (HepAD38) cells was able to reduce HBsAg in cell culture supernatant.
Method: HepAD38 harboring a replicating HBV genome was employed to test the antiviral effect of oligonucleotide in length of 40 nucleotides (poly-AC repeat-based sequence, 40nt-AC) by transfection with PEI (branchd, MW 25 kDa, 1 μg/μl). 5×10^5 cells per well were seeded in 12-well plate 16 h before transfection.
Results: (A) The complexing of PEI with oligonucleotide was first detected by agarose gel electrophoresis, which indicating that the positive charge on PEI neutralized the negative charge of oligonucleotide to form complexes and thereby hindered the migration of oligonucleotide in the gel. (B) Fluorescence microscope shown that FITC-labeled oligonucleotide could be efficiently transfected with PEI into AD38 cells. (C) Furthermore, the cytotoxicity of PEI/ON complexes was proved to be non-toxic by CCK-8 assay by comparing with blank. (D) PEI/ON complexes significantly reduced HBsAg

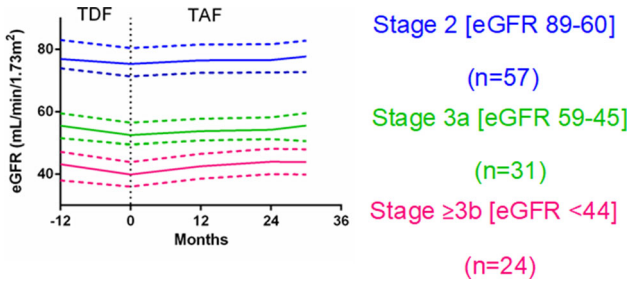
secretion to 59% of the control level in supernatant. However, there were no obvious changes in (E) HBeAg level and (F) HBV DNA.
Conclusion: Transfection of PEI/ON complexes selectively inhibit secreted HBsAg with no cytotoxic effect in AD38 cell culture.

Abstract #874 Tenofovir alafenamide is effective and has superior renal safety in chronic kidney disease (CKD) among Asian patients: real-world study from the canadian hepatitis B network

Scott Fung[1], Mina S. Farag[1,2], Edward Tam[3], Karen Doucette[4], Alexander Wong[5], Alnoor Ramji[6], Brian Conway[7], Curtis Cooper[8], Keith Tsoi[9], Carla S. Coffin[10], Bettina E. Hansen[1,11], Harry L. A. Janssen[1]

[1]Toronto Centre for Liver Disease, Toronto General Hospital, University Health Network, Toronto, Canada; [2]Institute of Medical Science, University of Toronto, Toronto, Canada; [3]LAIR Centre, Vancouver, BC; [4]Division of Infectious Diseases, University of Alberta, Edmonton, AB; [5]Department of Medicine, University of Saskatchewan, Regina, Saskatchewan; [6]Gastroenterology Division, St Paul's Hospital, Vancouver, BC; [7]Vancouver Infectious Diseases Centre, Vancouver, BC; [8]Department of Medicine, University of Ottawa, Ottawa, Ontario; [9]Department of Medicine, McMaster University, Hamilton, Ontario; [10]Division of Gastroenterology and Hepatology, University of Calgary, Calgary [11]Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Canada

Introduction: Tenofovir alafenamide fumarate (TAF), has high plasma stability and fewer renal adverse events compared to tenofovir disoproxil fumarate (TDF) for chronic hepatitis B (CHB).
Objectives: To study the effectiveness and renal safety of TAF in a real-world setting.
Methods: CHB patients from 10 Canadian academic institutions who received TAF (Nucleos(t)ide Analogue (NA)- naïve or experienced) were studied. Kidney function was measured by estimated glomerular filtration rate (eGFR) for chronic kidney disease (CKD) stage. HBsAg kinetics, virologic suppression (HBV DNA < 10 IU/ml), and ALT normalization while receiving TAF at 1 and 2 years were also measured.
Results: Of 175 patients receiving TAF, 133 (84%) switched from TDF, and 30 (17%) were NA-naïve. At TAF start (baseline), mean (SD) age was 52 (13) years, 71 (69%) patients were male and 85% of patients were Asian. Among the Asian subset of patients, majority had HBV DNA < 20 IU/mL (73%), (25%) were HBeAg-positive and mean eGFR was 72.6 (0.28) ml/min. CKD stages at baseline were Stage 1: 37(24%), Stage 2: 57(38%), Stage 3a: 31 (20%), Stage 3b or higher: 24 (16%).
Among the NA switch group, HBsAg significantly declined after TAF (during TAF: (− 0.01 [− 0.01 to − 0.002]; P = 0.009). eGFR increased significantly after TAF (during TAF: + 0.11 [0.01–0.22] per month; P = 0.04; Figure). HBV DNA continued to decline on TAF: − 0.07 [− 0.09 to − 0.06] per month; P < 0.001 vs. pre-TAF: (+ 0.01 [− 0.04 to 0.05]; Abnormal ALT at baseline showed a significant decline after switching (− 1.02 [− 1.03 to − 1.01] ULN per month; P < 0.01). Among patients with stage 2 CKD, eGFR significantly increased after switching (+ 0.20 [0.01–0.41] per month; P = 0.05).
Conclusion: In Asian CHB patients on NA treatment, switching to TAF resulted in further decline in HBsAg, normalization in ALT and maintained virologic suppression. TAF was safe and well tolerated and switching to TAF led to improvement in renal function, particularly in those with stage 2 CKD.



Abstract #913

Evaluation of the cobas® Plasma Separation Card as a sample type for hepatitis B serological testing and viral load quantification

Rando, Ariadna[1], Rodrigo-Velásquez, Fernando[1], Salmerón, Paula[1], Riveiro-Barciela, Mar[2,3], Esteban, Rafael[2,3], Buti, María[2,3], Marins, Ed G[4], Rodríguez-Frías, Francisco[3,5]

[1]Department of Microbiology, Vall d'Hebron University Hospital, [2]Department of Hepatology, Vall d'Hebron University Hospital, [3]Center for Biomedical Research in Network of Hepatic and Digestive Diseases (CIBERehd), [4]Roche Molecular Systems, Inc. Pleasanton, CA, USA, [5]Liver Pathology Unit, Biochemistry and Microbiology Departments, Vall d'Hebron University Hospital

Introduction: Improving access to laboratory-based screening and diagnostic testing in resource-limited settings, where there exist challenges with sample transportation and supply chain management, is critical to achieving hepatitis elimination goals. This goal can be facilitated using alternative sample types, such as the cobas® Plasma Separation Card (PSC).
Objectives: To evaluate PSC performance for HBV serological testing and viral load (VL) quantification compared to plasma.
Methods: Serum, EDTA plasma and PSC samples prepared from whole EDTA venous blood. PSC spotted (140 µL), dried and eluted: VL—56°C Specimen Pre-Extraction Reagent for 10 min, thermoshaker at 1000 rpm; Serology—37 °C, Elecsys universal diluent for 8 h, centrifuged at 3000 rpm for 10 m. Testing: Plasma/PSC VL—cobas® HBV 6800/8800; Serum/PSC serology—Elecsys HBs II and Elecsys anti-HBc (cobas® 8000).
Results: VL correlation was linear (slope = − 1.24, intercept = 0.83, R^2 = 0.89), with mean VL difference of − 1.81 log10 IU/mL (95% CI − 2.22 to − 1.40); detection with PSC above 1000 IU/mL was 100%. Sensitivity for HBsAg was 97.0% (n = 101; 95% CI 91.6–99.4%) and for anti-HBc was 98.9% (n = 94, 95% CI 94.2–100%) when HBsAg positive and 43.8% (n = 23, 95% CI 38.5–80.3%) when HBsAg negative and anti-HBc positive.
Conclusion: PSC demonstrated good correlation and concordance with standard methods, supporting the feasibility of PSC as an alternative sample type for serological screening and viral load monitoring of HBV infected patients in resource-limited settings.

Abstract #921

Management of hepatitis B and C infection during pregnancy by obstetricians

Mustafa Altındiş[1], Hilal Yuvacı[2], Hande Toptan[1], Serhan Cevrioğlu[2], Oğuz Karabay[3]

[1]Sakarya Unv School Of Medicine Department Of Microbiology, Sakarya, Turkey, [2]Sakarya Unv School Of Medicine Dept Of

Obstetrics, Sakarya, Turkey, [3]Sakarya Unv School Of Medicine Department Of Infection Diseases, Sakarya, Turkey

Introduction: In our study, it was aimed to investigate how gynecologists/obstetricians (G/O) manage the intermediate endemic classified chronic hepatitis B and Hepatitis C(HCV)(+) pregnant women in our country.

Methods: Online/digital questionnaire prepared for the management of HBV (+) and/or HCV (+) pregnant women were applied to G/O physicians to determine relevant knowledge, attitudes and behaviors.

Results: Of the total 125 participants, 58.9% were male, 68.5% were specialist physicians, 10.5% were research assistants, 25.0% had 20 years or more professional experience, 86.3% send tests for HBsAg in each pregnancy for all pregnant women and 93.5% had at least one pregnant patient with a positive HBsAg test. It was reported that 85.4% of the physicians informed HBsAg positive pregnant women and other people living in the same household and their sexual partners that they should be tested for hepatitis B. 56.9% routinely ensured that a copy of the pregnant women's HBsAg results was sent before the expected date of delivery to the hospital where delivery will be made and to the pediatrics department where the baby will be admitted. 92.7% of the participants determined the importance of hepatitis B immunoglobulin administration in the first 12 h to prevent perinatal transmission of hepatitis B to babies born to HBsAg positive pregnant women..

Conclusion: When the results of our questionnaire were examined, it was found that there were some deficiencies in subjects such as patient education, case reporting, referral for HBV treatment and disease follow-up in pregnant women infected with HBV.

Abstract #930

Pharmacokinetics of GSK3389404, an Antisense Oligonucleotide (ASO), is Similar in Subjects With Chronic Hepatitis B (CHB) across Asia-Pacific Region

Han Kelong[1], Ito Hiroshi[2], Elston Robert[3], Cremer Jennifer[4], Chen Shuguang[1], Hood Steve[3], Paff Melanie[1], Theodore Dickens[4]

[1]GSK, Upper Providence, PA, United States, [2]GSK, Tokyo Head Office, Tokyo, Japan, [3]GSK, Hertfordshire, UK, [4]GSK, Research Triangle Park, NC, United States

Introduction: GSK3389404 is a liver-targeted (GalNAc-conjugated) ASO designed to reduce hepatitis B surface antigen level. Few studies have examined ASO in Asian subjects.

Objectives: To evaluate and compare GSK3389404 pharmacokinetics in subjects with CHB across Asia-Pacific countries.

Methods: Hepatitis B e antigen positive and negative adult subjects with CHB who were treatment-naïve or on stable nucleos(t)ide regimens received single or multiple subcutaneous injections of GSK3389404 (GSK-sponsored NCT03020745). Plasma concentrations were measured on Day 1 in all cohorts, and on Days 29 and 57 in multiple-dose cohorts.

Results: 64 subjects with evaluable pharmacokinetic data from China (n = 24, Hong Kong included), Japan (n = 21), Korea (n = 12), Singapore (n = 4) and Philippines (n = 3) were enrolled in one of the following cohorts: 30mg single-dose (n = 3), 120mg single-dose (n = 6), 30 mg weekly (n = 6), 60 mg weekly (n = 20), 120 mg weekly (n = 15), and 120 mg biweekly (n = 14). Median time to peak plasma concentration (t_{max}) was 1–4 h across cohorts. Mean plasma half-life was 3–5 h. Half-life and t_{max} were independent from dose levels and consistent with previous studies in non-Asian healthy subjects. No accumulation in plasma concentration was observed following repeat dosing. Increase in AUC and peak plasma concentration (C_{max}) was dose-proportional from 60 to 120mg, but more than dose-proportional from 30 to 60 mg/120 mg. GSK3389404 plasma pharmacokinetic parameters, AUC and C_{max} are similar between subjects from China, Japan, Korea and other Asia-Pacific countries.

Conclusion: Given the similarity of PK among ASOs, plasma PK from any Asia-Pacific country may be used to guide dose selection and study design of ASO in Asia-Pacific region.

Abstract #931

A tool to measure the economic impact of hepatitis B elimination: a case study in Saudi Arabia

Faisal M. Sanai, Abduljaleel Alalwan, Waleed Al-Hamoudi, Faisal Abaalkhail, Naser Almasri, Faleh Z. Alfaleh, Devin Razavi-Shearer, Mohammed Alghamdi, Homie Razavi, Ellen Dugal, Jonathan Schmelzer

Gastroenterology Unit, Department of Medicine, King Abdulaziz Medical City, Jeddah, Saudi Arabia; Department of Organ Transplant and Hepatobiliary Surgery, King Abdulaziz Medical City and King Saud bin Abdulaziz University for Health Sciences, Riyadh; Department of Liver Transplantation and Hepatobiliary-Pancreatic Surgery, Division of Organ Transplant Center, King Faisal Specialist Hospital and Research Center, Riyadh; Department of Gastroenterology, Prince Sultan Military Medical City, Riyadh, Saudi Arabia, [13]Center for Disease Analysis, Lafayette, Colorado, USA; Gastroenterology Unit, Department of Medicine, King Fahad Military Medical Complex, Dhahran, Saudi Arabia

Background: No virologic cure exists for hepatitis B virus (HBV) infection, and existing therapies are designed to control viral replication. We aimed to estimate the national prevalence of HBsAg in 2017 and study the impact of enhanced diagnosis rate and universal treatment administration on HBV-related outcomes in Saudi Arabia.

Materials and methods: A dynamic transmission and disease burden model was developed to estimate the future economic burden of HBV infection. The infected population was tracked by age and gender-defined cohorts; direct costs (healthcare, screening, diagnostics and treatment) and indirect costs (disability-adjusted life years (DALY) and the value of a statistical life year) were calculated. The impact of two intervention scenarios (A: diagnose 90% of infections and treat 80% of high viral load patients by 2030; and B: diagnose and treat all patients by 2022) were compared against the Base Case scenario (no policy action), with near universal vaccination coverage rates held constant. A sensitivity analysis of future treatment cost was also conducted.

Results: In 2017, the prevalence of chronic hepatitis B (CHB) was estimated at 1.7% corresponding to 574,000 infections. The same year, there was an estimated incidence of 490 cases of decompensated cirrhosis, 1500 cases of hepatocellular carcinoma (HCC) and 1740 liver-related deaths (LRD). CHB prevalence was 0.1% among 5-year-olds and $< 0.03\%$ among infants. Disease burden outcomes by 2030, as compared with 2015, were as follows—Base Case: LRDs and HCC incidence were projected to increase by 40% and 60%, respectively. Intervention A: 40% decline in both HCC incidence and LRDs. Intervention B: $> 95\%$ decline in HCC incidence and 90% decline in LRDs. In all scenarios, CHB prevalence among infants and 5-year-olds declined to $< 0.02\%$. Direct costs increase and peak by 2022 in both intervention scenarios due to expansion of treatment and diagnostics. However, these are offset by indirect cost savings, starting immediately in Intervention A and by 2023 in Intervention B. Intervention A is estimated to achieve a positive return on investment (ROI) by 2021 at a treatment price of 10,000 ($2,667) SAR yearly. Intervention B, however, would require a 90% reduction in the unit cost of treatment to achieve a positive ROI by 2030.

Conclusions: Increased diagnosis and treatment rates of HBV would lead to substantial declines in HCC and LRD. This effect would be dramatically enhanced by administering treatment to all HBV cases regardless of viral load and estimated to be cost-effective if treatment prices can be substantially reduced.

Abstract #939

Study of the effect of the interleukin-18 gene (-607C/A) polymorphism on the progression of chronic viral hepatitis B and chronic viral hepatitis B with a delta agent in the Kazakh population

Ilyassova Bibigul

Background: The 8-year experience of the transplant Centre in Almaty has shown that out of 146 recipients 50 had cirrhosis or HCC in the outcome of chronic hepatitis B with Delta agent (CHB + D). The variation in clinical outcome of hepatitis B (CHB) is determined by virological, immunological and host genetic factors. IL-18 plays an important role in the development of chronic inflammatory diseases such as chronic viral hepatitis. SNP in the IL-18 gene promoter at positions - 607 has a critical effect on the activity of the IL-18 gene. It is assumed that the SNPs in the IL-18 gene promoter at positions − 607 have a critical effect on the activity of the IL-18 gene, which leads to different levels IL-18 products. Since IL-18 plays an important role in protecting the host from HBV infection, it is assumed that the difference in the level of its production is associated with the outcome of chronic HBV infection.
Aim: to study the association between SNP of IL-18 gene promoter (− 607C/A) and the progression of CHB and CHB+D in Kazakh population.
Methods*Abstract #939* 244 patients with CHB+D, 248 with CHB and 200 health donors were included to the study. IL18 polymorphism was determined by real-time PCR using the TaqMan allelic discrimination system.
Rresults: The A/A genotype prevailed in the CHB group compare with the group of healthy donors ($p < 0.0001$). The significant relationship was found between the inheritance of genotype A/A (− 607) and viral load in CHB ($p = 0.018$). In CHB the A allele frequency in patients on the different stage of fibrosis was no significant differences ($p = 0.419$).
The A/A genotype prevailed in the group of patients with CHB+D compared with the group of healthy donors ($p = 0.001$). The presence of A/A of the IL-18 promoter genotype (− 607) in the group of patients with viral hepatitis B with a delta agent is statistically significantly associated with the stage of fibrosis (with cirrhosis, the chances of having A/A are 14.73 times higher (95% CI 1.78–122.2). The positive correlation was found between the inheritance of allele A of IL18rs1946518 promoter and the presence of cirrhosis in patients with chronic viral hepatitis B with delta agent ($P = 0.020$), as well as in the general cohort of patients (CHB and CHB+D) ($p = 0.019$)
Conclusion:The inheritance rate of A/A genotype the IL-18 promoter genotype (− 607) was significantly higher in patients with CHB and CHB+D than in the controls in Kazakh population. The inheritance of A/A genotype associated with of viral load of HBV in CHB The progression of fibrosis and the presence of cirrhosis in outcome of CHB+D in the Kazakh population is associated with the inheritance of the A/A genotype and the A allele of the IL-18 promoter (− 607).

Abstract #956

Cessation of nucleos(t)ide analogues therapy in chronic hepatitis B a systematic review and meta-analysis

Yandi Xie

Introduction/objectives: To address the possibility of safe cessation of nucleos(t)ide analogues (NAs) therapy in chronic hepatitis B patients and to identify factors associated with off-NAs virological relapse (VR).
Methods: A published work search was performed in order to identify all published studies including patients who discontinued NAs and were followed for ≥ 12 months. A systematic review and a meta-analysis were performed.
Results: Twenty-six studies involving 2573 patients who discontinued NAs were included. The pooled rate of off-NAs VR was 0.63, being lower in initially HBeAg-positive than HBeAg-negative patients (0.57 versus 0.62, $P = 0.732$). The pooled rates of VR were 0.47, 0.55, 0.61, 0.51, 0.73 and 0.64 at 6, 12, 24, 36, 48 and 60 months after NAs cessation, respectively, being relatively lower in initially HBeAg–positive (0.50, 0.55, 0.69, 0.57, 0.53, 0.68) than HBeAg-negative patients (0.31, 0.45, 0.55, 0.44, 0.48, 0.52) ($P = 0.405$). The pooled rates of hepatitis B surface antigen loss and seroconversion was 0.09 and 0.06, respectively. The pooled rates of VR at 12 months after NAs cessation were significant different between duration of on-NAs virological response ≤ 24 months and >24 months in all patients (0.55 versus 0.41, $P = 0.011$), initially HBeAg-positive patients (0.59 versus 0.41, $P = 0.031$), and initially HBeAg-negative patients (0.53 versus 0.37, $P = 0.025$).
Conclusions: Safe cessation of NAs therapy seems to be feasible in a substantial proportion of CHB patients. On-NAs virological response >24 months reduces the risk of off-NAs VR.

Abstract #976

A Qualitative Study Exploring the Knowledge, Attitudes, and Perceptions on Hepatitis B Virus (HBV) among Rural Communities in Region VI, Philippines

Paluyo, John[1]

[1]Strategy and Research, reach52, Iloilo City, Philippines

Introduction: The burden of hepatitis B virus (HBV) represents a major health challenge for the Philippines. Social enterprise reach52 launched a 6-month program to contribute to better understanding about HBV and improve case detection and diagnosis in rural communities.
Objectives: This study aims to provide baseline information on the current knowledge and attitudes of the general public and diagnosed patients regarding HBV that will inform program design.
Methods: A qualitative study involving in-depth semi-structured interviews among 18 people, 11 from the general public, 5 diagnosed with HBV and 2 with unspecified hepatitis type, conducted in rural communities in Region VI, Philippines.
Results: The results reveal large gaps in hepatitis B knowledge among both the general public and patients. Specifically, there is a lack of awareness about transmission routes; prevention, testing and treatment services; and disease implications. The study also indicates that more capacity is required within the local health system regarding HBV infection management, i.e. there is no standard testing procedures; patients are rarely given counselling pre- and post-diagnosis and are not provided with proper linkage to care.
Conclusion: Efforts to deliver viral hepatitis services to these communities must include an educational component to dispel myths,

correct misinformation, and establish facts to encourage testing, vaccination, and follow-on behaviours. Local health workers would benefit from enhanced training to provide proper information and care to patients.

Abstract #977

Assessment of knowledge, attitude, and practices towards hepatitis B virus (HBV) infection among healthcare workers (HCW) in Region VI, Philippines—Phase 1: Pre-Training

Vargas, Ysabel[1], Paluyo, John[1]

[1]Strategy and Research, reach52, Iloilo City, Philippines

Introduction: The burden of hepatitis B virus (HBV) represents a major health challenge for the Philippines. Social Enterprise reach52 launched a 6-month program to contribute to better understanding about HBV and improve case detection and diagnosis in rural communities.
Objectives: This study aims to assess and identify gaps in knowledge, attitudes, and skills of local healthcare workers (HCWs) in managing chronic hepatitis B.
Methods: Face-to-face structured interviews were carried out with 18 HCWs, six of whom are Rural Health Unit (RHU) staff and 12 are Barangay Health Workers (BHWs), conducted in rural communities in Region VI, Philippines.
Results: Local HCWs displayed some level of knowledge about hepatitis B, however there are significant gaps that need to be addressed, especially among the BHWs. Except from the medical technologists stationed in the RHUs, most of the HCWs have not participated in community screening activities, thus their technical screening and patient management skills are limited. There is also a degree of stigma that was noted among the BHWs that causes apprehension in provision of healthcare services to HBV patients.
Conclusion: There is a need to embed in the training of the HCWs a basic module about hepatitis B to equip them with information about the disease. The training should also involve extensive course on technical screening skills including pre- and post-test counselling, supplemented with a simulation exam to equip them with full skill comprehension required to managing the disease.

Abstract #1029

Distribution of miRNA-146a and miRNA-196a2 Genetic Polymorphism in Chronic Hepatitis B Patients in Indonesian Population

Arfianti Arfianti[1], Djojosugito Fauzia Andrini[2], Ismawati Ismawati[3], Effendi Dasril[4]

[1]Department of Medical Biology, Faculty of Medicine, University of Riau, Pekanbaru, Indonesia, [2]Department of Microbiology, Faculty of Medicine, University of Riau, Pekanbaru, Indonesia, [3]Department of Biochemistry, Faculty of Medicine, University of Riau, Pekanbaru, Indonesia, [4]Department of Internal Medicine, Arifin Achmad General Hospital, Pekanbaru, Indonesia

Introduction: MicroRNA (miRNA) is a short, non-coding RNA that plays an important role in the regulation of gene expression. Aberrant expression of miRNA due to single nucleotide polymorphisms (SNPs) has been associated with risk for liver cancer.
Objectives: This study aimed to examine genetic variants of miRNA-146a (rs2910164) and miRNA-196a2 (rs11614913) in Indonesian patients with chronic hepatitis B (CHB) infection.
Methods: We included 36 CHB, 26 hepatitis B virus [HBV]-positive cirrhosis, and 13 HBV-positive hepatoma. Subjects were recruited in Arifin Achmad General Hospital from March-September 2019. Genetic polymorphisms of miRNA-146a and 196a2 gene were analysed using polymerase chain reaction restricted fragment length polymorphism (PCR-RFLP).
Results: The mean age ($\pm$SD) of study subjects was 45.3 ± 13.3 years (min–max 18–73 years), comprising of 58.7% males and 41.3% females. There was no significant difference in ALT levels between CHB patients but serum albumin was reduced in HBV-positive cirrhosis and hepatoma patients and serum bilirubin was increased in HBV-positive cirrhotic patients compared to CHB patients ($p < 0.05$). Genotype distributions of miRNA-146a in hepatitis B infected patients consisted of 25.3% of GG, 46.7% of GC, and 28% of CC genotypes, while the frequencies of miRNA-196a2 genotypes were 40.3% of CC, 48.6% of CT, and 11.3% of TT. Furthermore, there was no significant difference in frequencies of miRNA-146a and miRNA-196a2 gene polymorphisms between CHB, cirrhosis and hepatoma patients.
Conclusion: This study suggests that miRNA-146a $G > C$ and miRNA-196a2 $C > T$ polymorphisms may not contribute to the development of cirrhosis and hepatoma in Indonesian CHB patients.

Abstract #1034

Knowledge about hepatitis B And C among people attending car free day in medan

Rey, Imelda[1,2]

[1]Department of Internal Medicine, Gastroenterohepatology Division, Universitas Sumatera Utara, Medan, Indonesia, [2]Adam Malik General Hospital, Medan, Indonesia

Introduction: Hepatitis virus B (HBV) and hepatitis C (HCV) become a burden in Indonesia. The better knowledge of HBV and HVC will be important for prevention.
Objective: To analyze the knowledge about HBV and HCV among people attending car free day (CFD) in Medan.
Methods: We performed a survey the knowledge about HBV and HCV by questionnaire among people attending CFD on December 2019 in Medan. Knowledge level were considered low; adequate; and good knowledge for HBV and HCV if respondent gave correct answer $< 50\%$; 50–75% and $\geq 75\%$,respectively.
Results: From total 100 respondent, 75% were female, mean age was 22.1 ± 6.7 years old. Eighty seven percent and 61% respondents knew HBV and HCV were caused by virus, respectively. Regarding transmission, mother to infant and blood transfusion were recognised by 40% and 54% respondents for HBV, and 43% and 57% for HCV, respectively. Meanwhile sexual contact, needle sharing and tattooing were recognized by 48%; 65%; 36% and 53%; 61%; 39% of respondents for HBV and HCV, respectively. The knowledge were 54%; 38% 8%; and 65%; 29%; 6% for low; adequate; and good knowledge for HBV and HCV, respectively. Education, income, gender and marital status were associated significantly with knowledge of HBV, but not with HCV.
Conclusion: There is a low level of knowledge of HBV and HCV among people attending car free day in medan.

Abstract #1038

Long term impact of neonate immunization on hepatitis B in young adult population

Raffaello Wilson Matthew[1], Kurniawan Andree[2], Halim Devina Adella[1], Jodhinata Claudia[1]

[1]Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia

Introduction: Hepatitis B infection was hyperendemic in Indonesia before the implementation of the universal infant hepatitis B immunization program, which first launched in 2001. An estimated 257 million people have chronic HBV infection and 686,000 deaths occur annually due to long-term complications including liver cirrhosis and hepatocellular carcinoma. Exposure later in life can also lead to chronic infection but more frequently results in viral clearance and immunity. A few countries have reported declines in the prevalence of HBV infection following the implementation of infant vaccination program especially Indonesia. There are a few data reported, hepatitis B infection after vaccination in neonates.
Objectives: To know the long-term impact of neonate immunization on hepatitis B in young adult population.
Method: Subjects were recruited voluntarily from one of the medical schools in Indonesia. HBV serology markers included were hepatitis B surface antigen (HBsAg) and antibodies to HBsAg (anti-HBs). The vaccination history in neonates was evaluated during interviews. They were categorized into two groups. One group with undetectable ant-HBs ($<$ 10 IU) and one group as protective ($>$10 IU).
Results: From the questionnaire, 83 students were collected with history of neonatal immunization. 50 students (60%) develop immunity (anti-HBs titer $>$ 10 IU) and 33 students (40%) without immunity (anti-HBs titer $<$ 10 IU). From 50 students with developing immunity, 2 students have a history of positive HBsAg ($p = 0.245$).
Conclusion: Considering around 40% of the students with neonatal immunization have a waning in immunity, we suggest adding one or more booster dose after 15 years.

Abstract #1048

High clinical relapse with low HBsAg clearance after stopping tenofovir or entecavir in chronic hepatitis B, HBeAg negative patients

Sattayalertyanyong Onuma[1], Nimanong Supot[1], Tanwandee Tawesak[1]

[1]Division of Gastroenterology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University

Introduction: Treatment of chronic hepatitis B, HBeAg negative with nucleos(t)ide analogues (NA) has very low rate of HBsAg clearance. Recent studies found that NA stopping will lead to more rapid HBsAg clearance and safe, especially in non-cirrhotic patients.
Objectives: To evaluate the effect of discontinuation of tenofovir (TDF) or entecavir (ETV) in non-cirrhotic chronic hepatitis B, HBeAg negative patients (CHB) on HBsAg clearance and to investigate predictors of virological and clinical relapse (VR, CR) and safety of NAs withdrawal.
Methods: CHB patients who had been treated with TDF or ETV with continued viral suppression $>$ 3 years were included, TDF discontinued (TDF-D), ETV discontinued (ETV-D) groups compared NA continued group NA-continue).
Results: There were 86 patients as shown in Table 1. HBsAg loss found in 3 cases in TDF-D which was not significant from ETV-D. Cumulative VR was found 21 and 2 cases in TDF-D and ETV-D, respectively (Fig. 1). CR was found 14 cases in only TDF-D group within 12 weeks after TDF withdrawal. In TDF-D group, 4 cases had severe ALT flares, 2 required admission and one death (Table 2). Significant predictors of VR and CR were TDF withdrawal and qHBsAg $>$200 IU/mL at the time of withdrawal.
Conclusions: NA withdrawal commonly results in VR and CR, especially TDF. Some result in early and more severe CR leads to hepatic decompensation. HBsAg loss was found in 3 cases in TDF-D group, all of them had low qHBsAg before TDF withdrawal. TDF withdrawal is not advised unless very close monitoring.

Table 1 Baseline characteristics

Variables	Total (n= 86)	Discontinue (n=60)		Continue (n=26) (TDF-14,ETV-12)	*P* value
		TDF-D (n=38)	ETV-D (n=22)		
Age, years (mean± SD)	60.2±10	59.3±10.3	60.3±9.5	61.5±10	0.78
Male sex, n(%)	56 (65.1)	25 (65.8)	14 (63.6)	17(65.4)	0.99
Treatment duration, years (mean±SD)	11.2±3.4	10.9±3.4	11.5±2.7	12.5±3.6	0.23
ALT, U/L (mean±SD)	21.6±8.7	23.1±9.4	21±8.4	20.1±7.7	0.38
HBsAg, log_{10} IU/ml (median(P25-P75))	2.7(1.9-3.3)	2.7(1.8-3.3)	2.6(1.9-3.2)	2.7(2-3.3)	0.96
TE, kPa (mean±SD)	5.6±1.9	5.4±1.4	6±2	5.5±2.5	0.49
Liver fibrosis before treatment (F0:F1:F2) (n)	12:37:11	2:20:3	4:8:5	6:9:3	0.11

TDF, tenofovir; ETV, entecavir; ALT, alanine aminotransferase; TE, Transient elastography

Table 2 Safety profile up to week 24

N(%)	TDF-D	ETV-D	Continue	*P* value
Grade 1	9(23.7)	3(13.6)	0	NS
Grade 2	2(5.3)	0	0	NS
Grade 3	5(13.2)	1(4.5)	0	NS
Grade 4	4(10.5)	0	0	NS
Hospital admission	2(5.3)	0	0	NS
Hepatic decompensation	1(2.6)	0	0	NS
Liver failure	1(2.6)	0	0	NS
Death	1(2.6)	0	0	NS
Total	22(57.9)	5(22.7)	0	<0.001

Grading severity was according to common terminology criteria for adverse event V3 ,2006
TDF, tenofovir isoproxil fumurate; ETV, entercavir; TDF-D, discontinue TDF; ETV-D, discontinue ETV; NS, non-significant
*P <0.05

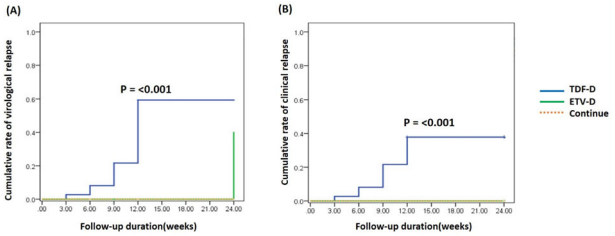


Fig1. Comparison the cumulative rate of virological relapse(A) and clinical relapse(B) between discontinue tenofovir(TDF-D), discontinue entercavir(ETV-D) and continue groups.

Abstract #1049

Association between addition of booster dose and remaining positive hepatitis B immunity in indonesia young adult population

Halim Devina Adella[1], Kurniawan Andree[2], Jodhinata Claudia[1], Raffaello Wilson Matthew[1], Hariyoga Bagus Aldi[1]

[1]Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia, [2]Internal Medicine, Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia

Introduction: Hepatitis B infection is highly endemic in South East Asia. This contagious disease can lead to cirrhosis and even liver cancer. Since 1997, Indonesia has had run Hepatitis B vaccination program which was proven to be effective in preventing horizontal transmission. However, the duration of immunity and the need for booster dose is still debatable.
Objectives: The aim of this study is to know the association between addition of booster dose and remaining positive Hepatitis B immunity.
Methods: A cross-sectional study was done our institution. All subjects were medical students and interviewed for vaccine history assessment. Subjects who had neonatal vaccination were included. Blood sample was taken to evaluate anti-HBs titers. Results were divided into two groups with anti-HBs $\geq$ 10mIU/mL categorized as seroprotective, while anti-HBs $<$ 10 mIU/mL categorized as non-seroprotective.
Results: There were 138 medical students who received neonatal vaccination, consists of 39 (28.2%) males and 99 (71.7%) females. It was found that 55 (39.8%) subjects got a booster dose after neonatal vaccination and 35 (63.6%) subjects were seroprotective. Only 33 (39.7%) from 83 subjects remained immune due to neonatal vaccination. The association between booster dose and remaining seroprotective immunity is statistically significant ($p = 0.010$, OR 95% = 2.652). The mean of anti-HBs titers in both non-boostered and boostered population are 76 ± 198.5 and 282.76 ± 376.6 respectively ($p = 0.001$).
Conclusion: There is an association between addition of booster dose and remaining positive hepatitis B immunity in Indonesia young adult population.

Abstract #1050

The development of Anti-hbs among unvaccinated young adult population in Indonesia

Jodhinata Claudia[1], Halim Devina Adella[1], Hariyoga Bagus Aldi[1], Rafaello Wilson Matthew[1], Kurniawan Andree[2], Yanto Theo Audi[2]

[1]Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia, [2]Internal Medicine, Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia

Introduction: According to Indonesia's national survey on 2013, Hepatitis B infection has the highest incidence rate in Indonesian population with proportional value of 21.8%. Acute infection of Hepatitis B virus (HBV) can cause symptoms or may be asymptomatic. Most individuals that are infected acutely end up with viral clearance state and developed immunity towards HBV infection which indicated by presence of Hepatitis B surface antibody (Anti-HBs).
Objectives: This study aims to find out about hepatitis B exposure and the development of Anti- HBs in young adult population in Indonesia.
Methods: This study is a cross sectional study. Samples were obtained from one of Indonesian medical schools. Blood samples were collected and sent to the laboratory for Anti-HBs assessment. Information regarding vaccination history was taken by interview. We then evaluate Anti-HBs titer value. Individuals with Anti-HBs antibodies $\geq$ 10 IU/L are classified as seroprotective group while individuals with Anti-HBs antibodies $<$ 10 IU/L are grouped as non-seroprotective.
Results: 155 subjects who have never received Hepatitis B vaccine were included. There are 46 (29.6%) male subjects and 109 (70.3%) female subjects. We found that 45 (29%) subjects become seroprotective which means that they had been exposed to acute Hepatitis B infection naturally, whilst 110 (71%) remain non-seroprotective. We also find out that 1 out of 6 individuals with positive family history, 1 out of 2 individuals with blood transfusion history, 5 out of 22 who have undergone surgery developed Anti-HBs.
Conclusion: It is found that 29% of the population had been exposed to Hepatitis B and developed Anti-HBs.

Abstract #1064

Virological and histological characteristics of chronic hepatitis B virus patients with normal serum ALT

Manik abul hayat[1], Tanmoy Saha[1], Momen khan[1], Faroque Ahmad[1]

[1]Hepatology Department, Dhaka Medical College Hospital, Dhaka, Bangladesh

Background: Patients with chronic hepatitis B virus (HBV) infection and persistently normal ALT levels have whether abnormal liver histology or not is crucial for treatment. At present worldwide available most of the guideline recommends treatment depending on serum ALT level, which may miss significant number of liver disease. We studied the ALT, HBV DNA levels, and spectrum of histologic lesions in such patients.
Methods: It was a cross sectional observational study among the chronic hepatitis B virus infected patients presented in the DMCH who shows persistently normal ALT and detected HBV DNA load. Total 104 patients were enrolled in the study and undergone liver biopsy ($n = 104$; hepatitis B e antigen [HBeAg+], 82; hepatitis B e antigen [HBeAg−] 22).
Results: Among 82 HBeAg negative cases, 12 (14%) had moderate and 26 (31%) had mild chronic hepatitis. Among HBeAg positive cases 8 (27%) had moderate and 8 (27%) had mild chronic hepatitis. 62% of HBeAg-positive and HBeAg-negative patients persistent normal ALT had baseline HBV DNA levels of $>$ 3.3 log copies/mL. Serum HBV DNA level and spectrum of histological changes doesn't correlate. 60 (73.1%) HBeAg negative and 14 (63.6%) HBeAg positive patients had Knodell score $>$ 7.
Conclusion: A fair proportion of patients with chronic HBV infection with persistent normal ALT have HBV DNA >3.4 log copies/ml and significant histologic fibrosis in both HBeAg positive and HBeAg negative groups. Use of ALT and HBV DNA levels without resorting to liver biopsy to define "inactive carrier state" in patients may miss histologically significant disease in a proportion of patients.

Abstract #1066

Clinical characteristics and association of microRNA-499 variants with chronic hepatitis B patients in Pekanbaru, Indonesia

Djojosugito Fauzia Andrini[1], Arfianti[2], Ismawati[3], Effendi Dasril[4]

[1]Department of Microbiology, Faculty of Medicine, University of Riau, Pekanbaru, Indonesia, [2]Department of Medical Biology, Faculty of Medicine, University of Riau, Pekanbaru, Indonesia, [3]Department of Biochemistry, Faculty of Medicine, University of Riau, Pekanbaru, Indonesia, [4]Department of Internal Medicine, Arifin Achmad General Hospital, Pekanbaru, Indonesia

Introduction: MicroRNA (miRNA) is a new class of small non-coding RNA which regulates the expression of genes in both physiological and pathological conditions. Single nucleotide polumorphisms (SNPs) in miRNA may contribute to cancer development, including liver cancer.
Objectives: The aim of this study was to determine the clinical characteristics and genetic variants of miRNA-499 (rs3746444) in patients with chronic hepatitis B (CHB) infection.
Methods: A total of 75 patients were enrolled from March to September 2019 in Arifin Achmad General Hospital Riau Province, including 13 hepatocelullar carcinoma (HCC) with Hepatitis B virus (HBV) infection, 25 HBV positive cirrhosis, and 37 CHB patients. miRNA 499 variants were genotyped by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).
Results: The mean age (±SD) of patients was 45.1±13.3 years (min–max, 18–73 years), in which patients with cirrhosis and HCC were much older than those with CHB ($P < 0.05$). There were 41.3% female and 58.7% male patients. Albumin-bilirubin (ALBI) grade 3 and 2 were more frequently found in cirrhotic and HCC than in CHB patients ($p = 0.007$). Distributions of miRNA-499 genotypes were TT (77.3%), CT (21.3%) and CC (1.3%). There was no significant association between miRNA-499 polymorphism with HCC, cirrhotic and CHB patients.
Conclusion: We observed that miRNA-499 C > T variants may not be associated with the progression of HBV-related chronic infection in Indonesian population.

Abstract #1090

The dynamic of liver stiffness in patients with chronic hepatitis B treated with oral antiviral agents in real-life observation

Berak H[1], Opoka-Kegler J[1], Kołakowska-Rządzka A[1], Korczyńska A[1], Platowski A[1], Cholewińska G[1], Marcinkowska E[1], Szymańska-Kotwica B[1], Horban A[1,2]

[1]Hospital for Infectious Disease in Warsaw, Poland, [2]Medical University of Warsaw, Poland

Background: Longitudinal treated with nucleos(t)ide analogues of patients with chronic hepatitis B (CHB) allows not only to obtain biochemical or virological improvement, but also hepatic fibrosis regression, which determine reduction of progression to cirrhosis and HCC occurrence. The aim of this study was to evaluated the regression of hepatic fibrosis through repeated liver stiffness measurement (LSM) using fibroscan, in real-life observation.
Methods: There was retrospectively reviewed 272 CHB patients from Warsaw Hospital for Infectious Diseases. Two FibroScan measurements were taken at different time during each patient's therapy. The first assessment was performed in different time of individual therapy. The mean interval between two Fibroscan (Echosens, France) measurements was 150.4 ± 20.5 weeks. Initial and follow-up average fibrosis was 6.76 ± 3.76 kPa and 7.74 ± 8.50 kPa was respectively. The participants were divided into 4 groups according to the drug taken: Lamivudine (n = 32), Adefovir (n = 32), Entecavir (n = 39) and Tenofovir (n = 169). There were analyzed the differences in F-kPa values between drugs by nonparametric ANOVA and descriptive statistics.
Results: There were no significant differences in F-kPa values according to the kind of antiviral drugs. The average decline of F-kPa value was 1.78 ± 1.8 score was observed in general among 138 patients; in 34% patients treated with ADV, 54% with ETV, 59% with LAM and 51% with TDF. Change in Metavir Scale was observed in 33 patients with decrease of F-kPa value ($p < 0.001$).
Conclusions: In real-life observation, long-term therapy resulted in the improvement of liver stiffness in patients with CHB independently of kind of oral drug.

Abstract #1101

How population pharmacokinetic modeling and exposure-response analysis support RO7049389 recommended phase 2 dose selection in patients with HBV infection

Valérie Cosson[1], Annabelle Lemenuel-Diot[1], Sheng Feng[2], Felix Jaminion[1], Axel Paehler[1], Jing Zhang[3], Man-Fung Yuen[4], Edward Gane[5], Christian Schwabe[5], Tawesak Tanwandee[6], Hugh A. Coleman DO[7], Lingzhi Cao[2], Miriam Triyatni[1], Qingyan Bo[2], Yuyan Jin[2]

[1]Roche Innovation Center Basel, Switzerland, [2]Roche Innovation Center Shanghai, China, [3]Huashan Hospital affiliated to Fudan University, Shanghai, China, [4]The University of Hong Kong, Hong Kong, China, [5]Auckland Clinical Studies, Auckland, New Zealand, [6]Mahidol University, Bangkok, Thailand, [7]Covance, Florida, United States

Introduction: RO7049389 is a small molecule, class A Hepatitis B virus (HBV) core protein allosteric modulator indicated for the treatment of HBV infection. *In vitro* data indicated RO7049389 is actively uptaken into hepatocytes (> 10-fold higher exposure than plasma) by the transporter OATP1B. Potent antiviral effects with a flat dose-response were observed in the Phase 1 study (NCT02952924). Non-linearity of the pharmacokinetics (PK), large PK variability, small sample size, higher plasma exposure in Asians and heterogeneity in patient baseline characteristics, made the ethnic sensitivity assessment and Recommended Phase 2 Dose (RP2D) selection difficult.
Objectives: Using advanced modeling and simulation approach to assess the ethnic sensitivity in PK and support RP2D selection.
Methods: A mechanistic population PK model, simultaneously describing RO7049389 and its metabolite M5, was developed to infer the quantity of RO7049389 in liver and to quantify the ethnicity effect on the plasma and liver exposure using non-linear mixed-effect approach. The exposure-response relationship was quantitatively characterized in the viral kinetic modeling by leveraging observed clinical PK and pharmacodynamics (PD) data (4-week HBV DNA data).
Results: The population PK model indicated a comparable estimated exposure of RO7049389 in liver in Asians and non-Asians despite a higher plasma exposure in Asians. The exposure-response analysis results performed with the viral kinetic model showed that it is the liver exposure driving the HBV DNA decline, with similar relationship between Asian and Non-Asians.
Conclusions: Mechanistic population PK modeling and exposure-response analysis support the same RP2D in Asian and non-Asian patients.

Abstract #1141

Roles of interleukin-21 serum on liver fibrosis level in patient with chronic infection of Hepatitis B virus at Mohammad Hoesin Hospital Palembang

Santoso M. J. [1], Bakry A. F.[1], Bardiman S.[1], Suyata[1], Irfannuddin[2]

[1]Division of Gastroenterohepatology, Internal Medicine Department, Faculty of Medicine, Sriwijaya University, Mohammad Hoesin Hospital, Palembang, Indonesia, [2]Faculty of Medicine, Sriwijaya University, Mohammad Hoesin Hospital, Palembang, Indonesia,

Background: Interleukin-21 (IL-21) is a cytokine derived from T-cells (CD4 +) with a role in the natural and specific immune systems. IL-21 activation occurs through complex pathways involving the Janus kinase (JAK) pathway, Signal Transducer Activator of transcription (STAT), Mitogen-Activated Protein Kinase (MAPK), and Phosphoinositide 3-kinase (PI3K). IL-21 is important in maintaining the number of T-cells (CD8) and triggers the B-cell response which is important for controlling viral load. IL-21 seems to be a double-edged knife in hepatitis B infection, because it has a beneficial effect in the case of acute infection, but worsens liver function during chronic infection.
Method: The study was a paired numerical comparative analysis using the Kruskal Wallis analysis followed by Mann Whitney's post hoc test for the three groups of research subjects. Serum IL-21 examination using quantitative sandwich enzyme immunoassay technique and measured using ELISA READER 680 (Biocard).
Results: The Mann Whitney post hoc test indicate a p value < 0.001 which showed a strong significance between IL-21 levels and the liver fibrosis severity, in subject with mild fibrosis (F0–F1) vs moderate-severe fibrosis (F2–F3), cirrhosis (F4–F1) vs with cirrhosis (F4) and moderate-severe fibrosis (F2–F3) vs cirrhosis (F4).
Conclusions: The results of this study indicate that elevated serum IL-21 levels increase the severity of liver fibrosis, so that serum IL-21 examination can be used as a predictor of the prognosis for the condition of liver fibrosis, but has not been able to replace liver biopsy or fibroscan examination.

Abstract #1154

Liver targeted single stranded (SSO) oligonucleotide RO7062931 is safe and well tolerated in Chinese healthy volunteers (HVs) with similar pharmacokinetic profile to non-Chinese HVs

Sheng Feng[1], Tsang Tommy Cheung[2], Andrea On Yan Luk[3], Sijie LU[1], Ved Pavlovic[4], Cynthia Wat[4], Sudip Das[4], Bernadette Surujbally[4], Miriam Triyatni[5], Joseph F. Grippo[6]

[1]Roche Innovation Center Shanghai, China, [2]Department of Medicine, Queen Mary Hospital, Hong Kong, China, [3]Phase 1 Clinical Trial Center, The Chinese University of Hong Kong, Hong Kong SAR, China, [4]Roche Innovation Center Welwyn, UK, [5]Roche Innovation Center Basel, Switzerland, [6]Roche Innovation Center, New York, USA

Introduction: RO7062931 is an N-acetylgalactosamine (GalNAc) conjugated single-stranded (SSO) with locked nucleic acid (LNA) that is complementary to messenger RNAs (mRNAs) of the HBV genome. Asialoglycoprotein receptor (ASGPR)-mediated hepatocyte uptake results in hybridization with HBV mRNAs, and subsequent RNase H-mediated degradation.
Objectives: To assess the safety, tolerability and pharmacokinetics (plasma and urine) of subcutaneous administration of RO7062931 in Chinese healthy volunteers (HVs).
Methodology: This was a randomized, investigator and subject-blind (sponsor-open), placebo-controlled, Phase 1 single ascending dose (SAD) study conducted at two clinical centers in Hong Kong (NCT03505190).
Results: 41 Chinese HVs were randomized across four dose cohorts, in an 8:2 ratio, to RO7062931 (0.3, 1.0, 2.0 and 4.0 mg/kg) or placebo. One subject was withdrawn and replaced for not fulfilling eligibility criteria. A total of 66 non-serious AEs were reported by 29 (71%) subjects, of which all were mild in intensity except for 2 AEs (presyncope and influenza) of moderate intensity. Most common AEs were influenza (22%), injection site reactions (19.5%) and headache (9.8%). There were no dose related trends in the intensity or nature of AEs, no serious adverse events (SAEs), or withdrawals due to AEs. PK analysis demonstrates that RO7062931 appears rapidly in plasma (peak plasma concentrations after 1.6–2.8 h), and the majority of drug is cleared from plasma within 24–36 h.
Conclusion: RO7062931 was safe and well tolerated in Chinese HVs, with a PK profile that is comparable to that previously reported (AASLD 2019) for non-Chinese HVs.

Abstract #1167

Serum level of interleukine-10 in patient with chronic immune-tolerant hepatitis virus B

Devid Ergan[1], Fuad Bakry[1], Irfannuddin[1]

[1]Department of Internal Medicine, Faculty of Medicine, University of Sriwijaya Palembang, Indonesia

Introduction: Hepatitis B virus (HBV) infection can self-limiting or manifest clinically as chronic immune-tolerant hepatitis B. Interaction between the HBV virus and immune response determines outcome.
Objective: We want to know serum level of interleukin (IL)-10 in patient with chronic immune-tolerant hepatitis B.
Methods: Patients diagnosed with chronic immune-tolerant hepatitis B who came to the Mohammad Hoesin Hospital Palembang on 1 August–31 October 2018 included in this study. Normal person with anti-HBs seropositive were included too. Patients who were taking antiviral drugs, anti-HCV seropositive, suffering from HIV/AIDS, malnutrition, and/or were taking immunosuppressive drugs were excluded. Blood was taken and measured for serum level of IL-10 with the Quantikine® ELISA Human IL-10 HS Immunoassay Reagent kit (R&D Systems, Inc., Minneapolis, USA), The sensitivity of the kit was 0.09 pg/mL. The significance of mean difference in serum level of IL-10 between 2 group was analyzed by the One-way ANOVA statistical test.
Result: There were 17 subjects in the group of chronic immune-tolerant hepatitis B and 17 subjects in normal group. The average serum level of IL-10 were, respectively: 2.22 + 0.48 and 1.02 + 0.12 pg/mL. Statistically, there was significant difference in mean serum level of IL-10 between two groups ($p < 0.001$ and 95% CI (0.88 - 1.50).
Conclusions: Serum level of IL-10 in patient with chronic immune-tolerant hepatitis B was significantly higher than normal.

Abstract #1173

Anti HBs antibody titer in medical professionals: how susceptible are we?

P. Arun,[1] A. R. Venketeshwaran[1]

[1]Institute of Medical Gastroenterology, Madras Medical College, Chennai, Tamil Nadu, India

Introduction: Immune status in health care workers is important since they have a high risk of acquiring HBV infection. An anti HBs titre less than 10 mIU/ml is regarded as nonresponse, more than 100 mIU/ml is considered as high level of immunity following vaccination.
Objectives: We conducted this study to know the Anti HBs titre in medical professionals and to correlate with the timing of vaccination.

Methods: Cross sectional observational study conducted in health care workers (HCW) of tertiary care hospital. A total of 300 HCWs were evaluated with Anti HBs titre using enzyme immunoassay. Detailed history regarding vaccination status was taken.
Results: Among 300 HCWs, 130 males (43%) and 170 females (57%) were there. Mean age of the HCWs were 35 years. Protective level of titre (>10 mIU/ml) was seen in 75%. High level immunity (>100 mIU/ml) was seen in 15%. Anti HBs titre was decreasing with increasing age (p value 0.008). As time elapses from last date of vaccination, level of immunity also declines (p value 0.01). Highest vaccination rate was associated with doctors (92%) and lowest with lower grade staff. Among 92 HCWS who had vaccination 10 years back, 23% had high level immunity, 39% had protective immunity, and 38% had waning immunity.
Conclusion: Significant number of HCWs has low Anti HBs titre, especially among low grade staff. Immunity was further decreasing with age and time since last vaccination. Hospitals should implement new policies to vaccinate all categories of HCWS initially followed by routine follow-up.

Abstract #1174

Prevalence of occult hepatitis in rheumatological patients on and before starting immunosuppressants

P. Arun[1], A. R. Venketeshwaran[1]

[1]Institute Of Medical Gastroenterology, Madras Medical College, Chennai, India

Introduction: Occult hepatitis B infection is presence of detectable HBV DNA in blood or liver with or without total anti-HBc in a HBsAg negative patient. HBV reactivation in individuals under immunosuppressive therapy is critical as they are prone for acute liver failure.
Objectives: The aim of this cross-sectional observational study is to assess the prevalence of occult hepatitis B infection in patients having rheumatologic disorders on immunosuppressant and also in immunosuppressant naïve patients.
Materials and methods: Patients admitted in Institute of Rheumatology during the time period of September 2018-January 2019 were evaluated. Patients on or yet to be started on immunosuppressant were evaluated with HBsAg, Total AntiHbc. If Total Anti Hbc came out as positive, HBV DNA was quantified.
Results: 72 patients were evaluated, of which 27(38%) males and 45 (62%) females were there. 25 (34.7%) patients had spondyloarthropathy, 10 (13.9%) had Takayasu arteritis, 37 (51.4%) had connective tissue disorders (SLE, SSC). High risk medications like Rituximab were given to 12 (16.7%), moderate risk (TNF alpha inhibitors) to 42 (58.3%), low risk (cyclophosphamide) to 18 (25%) patients. Blood transfusion and haemodialysis were present in 15 (20.8%) patients. Hepatitis B prior vaccination was present only in 16 (22.2%) patients. No significant association was there with Total anti Hbc(p value > 0.05). None of the patients had abnormal liver function test. 4 Rituximab patients were having Total Anti Hbc positivity, one had detectable HBV DNA.
Discussion: Prevalence of occult hepatitis in our study is 9.72%, which is higher compared with other studies. As the age advances, there was higher association with total anti Hbc positivity (p 0.005). The HBV DNA levels were higher.
Conclusion: Higher prevalence of occult hepatitis B was observed. Limitation of study was inability to do HBV DNA for patients without Total anti Hbc positivity. It should be made mandatory to screen patients before starting immunosuppressants.

Abstract #1177

Aggressive dose reduction of tenofovir (300 mg every 48 vs 72 h) can maintained HBV viral suppression in chronic hepatitis B patients with moderate renal impairment

Poosanasuwansri Karn[1], Chotiyaputta Watcharasak[1], Tanwandee Tawesak[1]

[1]Division of Gastroenterology, Department of Medicine, Siriraj Hospital, Mahidol University

Introduction: Tenofovir disoproxil fumarate (TDF) is one of the most potent nucleoside analogs (NA) for treatment of chronic hepatitis B (CHB) but long-term use of TDF can result in renal dysfunction requiring TDF dose modification but without renal improvement. Previous studies showed that TDF exposure in moderate renal impairment (eGFR 30–59 mL/min) was nearly 3 times of patients with normal eGFR.
Objectives: To evaluate efficacy of HBV viral control at 6 and 12 months and renal parameters compare between two TDF dose reduction regimens.
Methods: This is a non-inferiority, randomized controlled study including 46 virologically suppressed CHB patients who had moderate renal impairment. Patients were excluded if they had acute kidney injury, eGFR less than 30 mL/min. Patients were randomly assigned to receive TDF 300 mg either every 48 or 72 h for 12 months.
Results: Baseline HBV DNA before treatment initiation was 5.3 $\log_{10} \pm 1.4$ IU/mL. There was 23.9% with cirrhosis. All patients had no virological breakthrough at 6- and 12-months follow-up. There were trend of eGFR improvement in both groups and eGFR more than 60 mL/min in more aggressive dose reduction group. Other renal parameters did not significantly difference.
Conclusions: In TDF treated CHB patients who had moderate renal impairment, more aggressive dose reduction of TDF from every 48–72 h did not result in virological breakthrough at 6 and 12 months. Higher proportion of the patients in every 72 h group had improvement of renal function but did not reach statistically significance.

Abstract #1235

The correlation between APRI and FIB-4 scoring combination and liver stiffness in chronic hepatitis B Compared with transient elastrography

Pongbulaan A[1], Maimunah U[2], Dewi KF[1], Purbayu H[2], Sugiarto T[2], Miftahussurur M[1], Alimsardjono IP[2], Kholili U[2], Setiawan PB[2]

[1]Resident of Internal Medicine Department, Universitas Airlangga, Surabaya Indonesia, [2]Division of Gastroenterology and Hepatology, Internal Medicine Department, Universitas Airlangga, Dr. Soetomo General Academic, Surabaya Indonesia.

Introduction: Liver stiffness staging is important step during the management of chronic hepatitis B (CHB). However, Transient elastography (TE) is not widely available and there is a need for less expensive and simpler noninvasive approaches especially in terms of the hepatitis B elimination strategy worldwide. We evaluated the diagnostic performance of the APRI and FIB-4 scores compared to TE in detecting liver stiffness
Objective: To analyze the correlation between APRI and FIB-4 scoring combination and liver stiffness in CHB patients in the Gastroenterohepatology Outpatient Installation at Dr. RSUD. Soetomo Surabaya.

Methods: We perfomed a retrospective study of patient presenting with CHB who underwent TE between November 2018 and January 2019. APRI, FIB-4 and combined score APRI/FIB-4 scores were compared to TE.
Results: A total 70 patient presented with CHB were included. Multivariate analisis showed that the APRI score was the only independent factor for cirrhosis threshold (OR 16,66, P 0.000) and the FIB-4 score was the only independent factor for cirrhosis (OR 13,71, P 0.000). At threshold of cirrhosis APRI had the specitivity (80.6%), whereas FIB-4 had the specitivity (77.4%). Using combined APRI/FIB-4 score we improved the diagnosis performance at the cirrhosis threshold (OR 26,92, P 0.000) with had the greatest specitivity (93.5%).
Conclusion: The APRI/FIB-4 combination was more accurate at predicting liver cirrhosis threshold in CHB.

Abstract #1288

Preventative therapy of hepatitis B in grave's ophthalmopathy who required high dose methylprednisolone

Cahyani C[1], Kholili U[2]

[1]Resident of Internal Medicine Department, Universitas Airlangga, Surabaya, Indonesia, [2]Division of Gastroenterology and Hepatology, Internal Medicine Department, Universitas Airlangga, Dr.Soetomo General Academic, Surabaya, Indonesia

Introduction: Hepatitis B virus (HBV) reactivation associated with immunosuppressive is emerging to be an important cause of morbidity and mortality in patients with current or prior exposure to HBV infection. Prevention reactivation is better than treatment so screening HBV is very important, because adverse outcomes can be prevented by prophylactic or preemptive therapy using antiviral agents.
Case illustration: A man, 30 years old, a construction worker, consulted from the opthalmologist into internal medicine with active Grave's Opthalmopathy. Three months ago, he was diagnosed with grave's disease and antithyroid treatment had been suggested. The patient was planned injection of methylprednisolon 500 mg weekly for 6 weeks and continued 250 mg weekly for 6 weeks. Laboratory finding reactive HBsAg, HBV DNA 1.12×10^3 IU/ml, reactive HBeAg, fibroscan F 0-1, AST 27 U/L, ALT 29 U/L, FT4 6.4 ng/dl, and TSH 0.006 IU/ml. Preventative antiviral therapy should be given to avoid reactivation in patient. Lamivudin was given 100 mg once and scheduled periodically monitored signs of reactivation.
Discussion: Immunosuppression therapy is the most common cause of reactivation of HBV infection by inhibiting the production of interleukin, inhibiting NF-kB, and help HBV DNA replication through their interaction with glucocorticoid responsive element HBV (an element for the transcription process). Preemptive therapy is highly recommended because high risk of reactivation based on serologic status and immunosuppressive potency. Lamivudin can be first line in Indonesia and the main choice in several conditions such as preventative therapy in patients who will undergo immunosuppression or chemotherapy.

Abstract #1299

Correlation Between combined serum aminotransferase/platelet ratio index and serum hyaluronic acid levels with liver stiffness in chronic hepatitis B patients

Nabilah[1], Ummi Maimunah[2]

[1]Resident of Internal Medicine Department, Universitas Airlangga, Surabaya, Indonesia, [2]Division of Gastroenterology and Hepatology, Internal Medicine Department, Universitas Airlangga, Dr. Soetomo General Academic, Surabaya, Indonesia

Introduction: Serum hyaluronic acid (HA) is one of the most studied extracellular liver matrices, but its sensitivity and specificity are not very high. Aminotransferase/platelet ratio index (APRI) is easy to calculate, but it can only predict the severe hepatic fibrosis. There is a hypothesized that APRI in combination with different HA cut-off points would be a better predictor of fibrosis than individual parameters, and will be useful in both the diagnostic and therapeutic aspects.
Objective: To analyze the correlation between combined APRI and serum HA level with liver stiffness in chronic hepatitis B patients in the Gastroenterohepatology Outpatient Installation at RSUD. Dr. Soetomo Surabaya.
Methods: An observational cross sectional analytic study involving 70 samples of chronic hepatitis B patients. Serum HA was measured by the ELISA method. APRI was calculated using the formula AST (U/L)/(upper limit of the normal range) × 100/platelet count (10^9/L). Liver stiffness describes fibrosis being examined using Fibroscan. Data analysis and correlation using SPSS 25.0 with Spearman test, output p value and correlation coefficient (r) to find out the correlation.
Results: There were 70 samples with predominantly males (55.7%). The average age of the study subjects was 45.11 years old. The median serum hyaluronic acid level of the study subjects was 42.237 ng/mL, APRI median level was 0.349, and liver stiffness median level was 8.2 kPa. There was no significant correlation between combined APRI and serum hyaluronic acid levels with liver stiffness in the study subjects, but there is a significant positive correlation between serum hyaluronic acid levels only and liver stiffness with a moderate strength of $r = 0.518$ ($p = 0.003$).
Conclusion: Combined APRI and serum hyaluronic acid levels is still not strong enough to prove correlation with liver stiffness because there are several other factors that contribute determine the liver stiffness that requires further research.

Abstract #1342

Comparison of the efficacy of entecavir tablet and solution in patients with chronic hepatitis B: a preliminary result

Chuaypen N. [1], Chittmittraprap S. [1], Tangkijvanich P. [1]

[1]Center of Excellence in Hepatitis and Liver Cancer, Faculty of Medicine, Chulalongkorn University, Bangkok, 10330, Thailand

Background: Entecavir (ETV) is a first-line therapy for chronic hepatitis B (CHB) due to its potent antiviral effect and high genetic barrier. This study was aimed at comparing the efficacy of ETV tablet (Baraclude) and ETV solution (Encavir) in treatment-naïve patients with CHB.
Method: Patients with elevated serum ALT and HBV DNA were randomly selected to receive either ETV tablet (group A) or solution (group B) (0.5 mg/day) for 48 weeks. Serum ALT, HBeAg, anti-HBe, HBV-DNA and HBsAg levels were assessed at baseline and during therapy.
Results: In this prospective study, there were 24 and 25 patients in groups A and group B, respectively. At baseline, group A had higher mean ALT level compared with group B. However, the two groups were comparable in terms of age, gender, HBeAg status, HBV DNA and HBsAg levels, as well as liver stiffness measurement. The response rates during therapy was similar between the two groups. At weeks 24, there was no significant difference between groups in terms of ALT (36.2 ± 21.0 vs. 26.7 ± 14.7 IU/l, $P = 0.165$), HBV

DNA (1.6 ± 1.2 vs. 1.4 ± 1.2 IU/ml, $P = 0.705$) and HBsAg levels (3.5 ± 0.6 vs. 3.5 ± 1.2 IU/ml, $P = 0.942$). The rate of HBeAg seroconversion at week 24 was not significantly different between group A and B (9.1% vs. 12.5%, $P = 0.451$). There was no patient achieved HBsAg clearance. In addition, no adverse reactions were found in both groups.

Conclusion: ETV tablet and solution were comparable in their efficacy to suppress HBV-DNA and HBeAg seroconversion in treatment-naïve patients with CHB.

Table 1 Baseline characteristics of the participants in this study

	Group A (n=24)	Group B (n= 25)	*P*
Age (years)	42.5±12.7	40.5±13.2	0.564
Gender			
Male (%)	15(62.5)	12 (48.0)	0.308
Female (%)	9 (37.5)	13 (52.0)	
ALT (IU/L)	89.8±67.5	57.0±19.9	0.030*
HBeAg positive (%)	11 (45.8)	16 (64.0)	0.201
HBV DNA (log_{10} IU/ml)	6.3±1.3	6.2±1.8	0.874
HBsAg (log_{10} IU/ml)	3.5±0.7	3.9±0.7	0.084
Liver stiffness (kPa)	7.8±6.3	5.8±2.0	0.150

Abstract #1344

Coexistence of hepatitis B and hepatic sarcoidosis: case report

Poturoglu Sule[1], Cifcibasi Ormeci Asli[1], Calhan Turan[1], Dogruel Melike[2]

[1]University of Health Sciences Haseki Training and Research Hospital, Department of Gastroenterology, Istanbul, Turkey, [2]University of Health Sciences Haseki Training and Research Hospital, Department of Internal Medicine, Istanbul, Turkey

Introduction: The presence of hepatic granulomas is also rarely seen in liver biopsies of hepatitis B patients. Herein, we report a case of hepatic sarcoidosis who developed hepatic sarcoidosis during the follow-up with the diagnosis of compensated liver cirrhosis due to hepatitis B.

Case: Female patient was 66-year-old. Physical examination was normal. Liver enzymes were slightly elevated. Anti-Delta, anti-HCV, HBV-DNA were negative. The smooth muscle antibody was positive (1/3200). Autoimmune hepatitis score was 0. Tumor markers CA-15-3 and CA-19-9 were slightly elevated. In magnetic resonance imaging, the liver contours were lobulated and the parenchyma was heterogeneous. In the right lobe of the liver, contrast-enhanced examinations revealed mass lesions compatible with metastases. Intrahepatic bile ducts were wide in the left lobe. Common bile duct was 9 mm. Biopsy result of liver lesions was as follows: giant cells and lymphocytes with clusters of epithelioid histiocytes, including portal areas in the parenchyma, granulomatous inflammation. Brucellosis, syphilis, PPD Quantiferon tests were negative. ACE and IGG4 levels were normal. Gastroscopy showed grade 1–2 esophageal varices. Colonoscopy was normal. Positron emission tomography showed no evidence of malignancy. The patient received oral antiviral and 40 mg prednisolone was started. The lesions of the liver regressed within 3 weeks and the prednisolone dose was reduced and the patient was followed-up.

Conclusion: It is thought that immune mediated mechanism plays a role in the development of sarcoidosis. Hepatitis B infection also plays a role in triggering immunity. This association is presented because it is a rare condition.

Abstract #1351

Prognostic value of Gilbert's syndrome for liver fibrosis dynamics in chronic HBV infection

Kuhareva E. I.[1], Ogurtsov P. P.[1], Tarasova O.I .[1], Blinov D. E.[1]

[1]Peoples' Friendship University of Russia (RUDN University), Hospital Therapy Department of Medical Institute, Moscow, Russian Federation

Introduction: In chronic HBV infection patients, there is an increased level of lipid peroxidation products, which indicates a high oxidative stress in this population. Currently, the influence of antioxidant properties of unconjugated bilirubin in Gilbert's syndrome on the treatment of various diseases is widely discussed.

Objective: To Evaluate the prognostic value of Gilbert's syndrome (GS) for the dynamics of liver fibrosis (LF) in the natural course of chronic HBV infection.

Methods: 64 patients with chronic HBV infection were studied prospectively. The rs8175347 polymorphism in the UGT1A1 gene, (TA)5/6/7/8 was investigated. In 35 (54.7%) patients, changes in the UGT1A1 gene were detected, in 29 (45.3%)—the normal genotype (TA)6/(TA)6 was established. The duration of observation was 4.6 years. To assess the dynamics of LF, 53 patients underwent paired liver biopsy and 11 patients underwent paired transient elastography. Laboratory tests and their frequency were performed in accordance with clinical recommendations.

Results: The level of alaninaminotransferase ($p < 0.0001$), asparaginaminotransferase ($p = 0.001$), viral load ($p = 0.005$), the number of HBsAg ($p = 0.02$), GS ($p < 0.0001$) had statistical significance for the dynamics of LF. According to the results of logistic regression, GS had statistical significance ($p < 0.05$) in the forecast of probability of absence of negative dynamics of LF (OR = 10.075; 95% CI 3945–25.730; $p < 0.0001$). The area under the curve AUC model was 0.899 (95% CI 0.809–0.989; $p < 0.001$).

Conclusion: Gilbert's syndrome in the natural course of chronic HBV infection reduces the risk of progression of liver fibrosis by 10.1 times.

Abstract #1354

Circulating, dysfunctional Th2-biased follicular helper T cells dominate in patients with chronic hepatitis B infection

Xin Tong[1], Shengxia Yin[1], Yuxin Chen[2], Chao Wu[1]

[1]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China, [2]Department of Laboratory Medicine, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China;

Background: The generation of antibody against hepatitis B surface antigen (HBsAg) is lacking in patients with chronic hepatitis B infection (CHB). Since follicular helper T (Tfh) cells are essential for B cell differentiation into plasma cells, previous studies have suggested that dysregulated Tfh responses among CHB patients. However, the function of Tfh cells and B cell subsets among CHB patients have not been carefully dissected. Blood Tfh cells comprised three subsets: T helper 1 (Tfh1), Tfh2, and Tfh17 cells, with distinct capability to help B cells. Tfh2 and Tfh17 cells, but not Tfh1, were able to efficiently induce naïve B cells to produce immunoglobulins via IL-21. Here, we characterized the phenotype of Tfh cell and B cell subsets and explored the potential mechanisms responsible for the aberrant immune response to HBV.

Methods: Blood samples were collected from CHB patients and healthy individuals. The frequencies of peripheral Tfh cells ($CD4^+CXCR5^+$), Tfh1 cells ($CD4^+CXCR5^+CXCR3^+CCR6^-$), Tfh2 cells ($CD4^+CXCR5^+CXCR3^-CCR6^-$) and Tfh17 cells ($CD4^+CXCR5^+CXCR3^-CCR6^+$) and their activated status ($ICSO^+PD\text{-}1^+$) were characterized by flow cytometry. Further, the portion of B cells subsets was also determined, including total B cells ($CD19^+$), plasmablast B cells ($CD19^+CD27^{hi}IgD^-$), memory B cells ($CD19^+CD27^{low}IgD^-$) and double negative B cells ($CD19^+CD27^-IgD^-$). HBsAg-specific Tfh cells were identified by IL-21 secreting Tfh cells from PBMC co-cultured with HBsAg pooled peptides for 48 h.
Results: First, we identified a remarkably elevated level of both Tfh2 cells and activated Tfh2 cells, despite Tfh cells and Tfh17 cells were substantially decreased, and Tfh1 cells remained unchanged, compared to healthy individuals. Further, elevated B cells, but not HBsAg-specific B cells, were found in CHB patients. Nevertheless, in contrast to elevated activated Tfh2 cells, substantially diminished plasmablast B cells were observed in CHB patients. Consistently, activated Tfh2 cells were correlated with HBsAg+ double negative B cells ($p = 0.00$, $r = 0.47$), but not HBsAg+ plasmablast B cells, suggesting a poor capability of B cell helper for Tfh2 cells. Moreover, increased portion of Tfh cells was responsive to secrete IL-21 in CHB patients upon HBsAg peptide simulation, compared to healthy controls. Interestingly, as a co-inhibitory molecule that impairs Tfh differentiation and germinal center response, cytotoxic T lymphocyte-associated protein 4 (CTLA-4) were found to be significantly upregulated in these HBsAg-specific Tfh cells among CHB patients, but not healthy controls, suggesting an intrinsic defect of HBsAg-specific Tfh cells in CHB patients.
Conclusion: Circulating activated Tfh2 cells were identified to dominate in CHB patients, with poor capability of B cell helper function, which might contribute to the deficiency of viral specific humoral response during CHB course.

Abstract #1355

Serum gamma-glutamyl transpeptidase as a simple and useful indictor for predicting significant fibrosis in patients with chronic hepatitis B

Jian Wang[1], Rui Huang[1], Xiaomin Yan[1], Juan Xia[1], Bie Jia[1], Zhaoping Zhang[1], Weimao Ding[2], Chao Wu[1]

[1]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China, [2]Department of Hepatology, Huai'an No. 4 People's Hospital, Huai'an, Jiangsu, China

Introduction: Assessing the stages of liver fibrosis is critical in guiding the treatment of chronic hepatitis B (CHB). The gamma-glutamyl transpeptidase (GGT) was reported to be associated with the severity of liver diseases.
Objectives: We aimed to investigate the association between GGT and the severity of liver fibrosis in CHB.
Methods: Six hundred eighty-three treatment-naïve CHB patients who underwent liver biopsy were enrolled. Liver histology was evaluated using the Scheuer classification system. The diagnostic accuracy was evaluated by the area under the receiver operating characteristic curve (AUROC).
Results: The GGT level showed an increasing trend with fibrosis stages in CHB patients. The GGT level was positively correlated with the stages of liver fibrosis in entire CHB patients ($r = 0.346$, $p < 0.001$), HBeAg positive CHB patients ($r = 0.438$, $p < 0.001$) and HBeAg negative patients ($r = 0.307$, $p < 0.001$). GGT was an independent factor for predicting significant fibrosis ($S \geq 2$) in the entire CHB patients and HBeAg positive patients, but not in HBeAg negative patients. The AUROCs of GGT for predicting significant fibrosis were 0.658 (95% CI 0.6148–0.7016), 0.703 (95% CI 0.6453–0.7603) and 0.628 (95% CI 0.5616–0.6938) in entire CHB patients, HBeAg positive and HBeAg negative CHB patients, which was comparable with aspartate transaminase (AST) to PLT ratio index (APRI) ($p > 0.05$) and fibrosis-4 score (FIB-4) ($p > 0.05$).
Conclusion: The GGT level was positively correlated with the severity of liver fibrosis in CHB patients. The GGT level alone showed similar diagnostic accuracy for significant fibrosis in CHB patients as compared to APRI and FIB-4.

Abstract #1357

Gammaglutamyl transferase: a promising index for predicting antiviral treatment response in chronic hepatitis B patients

Jian Wang[1], Rui Huang[1], Jie Wei[1], Yue Yang[1], Yong Liu[2], Yuxin Chen[2], Xiaomin Yan[1], Zhaoping Zhang[1], Chao Wu[1]

[1]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China, [2]Department of Laboratory Medicine, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China.

Introduction: Baseline serum gammaglutamyl transferase (GGT) level was associated with sustained virologic response in chronic hepatitis C.
Objectives: We aimed to explore the association of GGT level with and hepatitis B e antigen (HBeAg) seroconversion of in CHB patients.
Methods: 431 treatment-naïve CHB patients between January 2010 and May 2019 were enrolled. 343 CHB patients in the immune clearance (IC) phase with available data who were treated by nucleos(t)ide analogues (NAs) and followed for 48 weeks. Complete response (CR) was defined as a serum HBV DNA < 500 IU/mL and HBeAg seroconversion by 48 weeks of NAs treatment.
Results: The GGT showed an increasing trend in patients with immune tolerant (IT) phase ($n = 351$) (15.0 U/L, IQR 11.7–19.4 U/L), low replicative (LR) phase ($n = 2200$) (17.5 U/L, IQR 13.4–24.6 U/L), IC phase ($n = 940$) (37.0 U/L, IQR 23.0–66.9 U/L) and HBeAg negative hepatitis (ENH) ($n = 540$) (43.2 U/L, IQR 26.7–76.0 U/L) ($p < 0.01$ between each two group). 42 (12.2%) of 343 CHB patients in IC phase achieved CR after NAs treatment for 48 weeks. Baseline GGT was significantly higher in CR patients (42.0 U/L, IQR 25.9–77.0 U/L) than non-CR patients (30.0 U/L, IQR 22.5–41.2 U/L) ($p = 0.004$). Multiple regression analysis showed baseline GGT level (OR 1.008, 95% CI 1.002–1.013, $p = 0.007$) was identified as an independent predictor of CR. The AUROC of GGT in predicting CR were 0.681, with a sensitivity of 57.14% and a specificity of 73.09%.
Conclusion: GGT level significantly elevated in IC and ENH phases of CHB patients and can independently predict the CR in CHB patients with IC phase.

Abstract #1375

The influence of metabolic syndrome on liver injury in patients with chronic hepatitis B

Jian Wang[1], Rui Huang[1], Xiaomin Yan[1], Zhaoping Zhang[1], Juan Xia[1], Weihua Wu[1],Weimao Ding[2], Chao Wu[1]

[1]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China, [2] Department of Hepatology, Huai'an No. 4 People's Hospital, Huai'an, Jiangsu, China.

Introduction: Concurrent with metabolic syndrome (MS) is not uncommon in chronic hepatitis B (CHB) patients. However, the impact of MS on the liver injury in CHB patients is controversial.
Objectives: We aimed to investigate the influence of MS on the liver injury in CHB patients.
Methods: Six hundred and forty-one consecutive CHB patients who had undergone liver biopsy were enrolled from two medical centers. Propensity score matching (PSM) method was used to adjust the imbalance of baseline confounders between CHB patients with and without MS.
Results: 92 (14.4%) CHB patients had MS in the cohort. The distribution of liver fibrosis stage in CHB patients without MS was: S0, 57 (10.4%), S1, 166 (30.2%); S2, 123 (22.4%); S3, 103 (18.8%) and 100 (18.2%) patients. For CHB patients concurrent with MS, the distribution of liver fibrosis stages was S0, 9 (9.8%), S1, 24 (26.1%) patients; S2, 19 (20.7%); S3, 14 (15.2%) and 26 (28.3%). The liver inflammation grades in patients without MS were: G0, 2 (0.4%), G1, 191 (34.8%); G2, 225 (41.0%); G3, 79 (14.4%), G4, 52 (9.5%) patients, while G0, 1 (1.1%), G1, 23 (25.0%); G2, 50 (54.3%); G3, 14 (15.2%), G4, 4 (4.3%) in patients with MS. The distribution of liver fibrosis ($P = 0.269$) and inflammation ($P = 0.066$) were not significant different between CHB patients with and without MS. The proportion of hepatic steatosis was higher in CHB patients with MS (35.9%) than patients without MS (18.6%, $P < 0.001$). PSM was used to adjust the imbalance of baseline confounders (Age, Sex, HBeAg status and HBV DNA). After PSM, 73 patients were included in each group. The proportion of hepatic steatosis was higher in CHB patients with MS (35.6%) than patients without MS (8.2%, $P < 0.001$). Liver fibrosis stages ($P = 0.029$) and inflammation grades ($P = 0.005$) were more severity in patients without MS than patients with MS.
Conclusion: CHB patients concurrent with MS had less severe liver fibrosis and inflammation than patients without MS. MS may had negative impacts on liver fibrosis and inflammation in CHB patients.

Abstract #1376

Impact of nonalcoholic fatty liver disease on liver fibrosis in patients with chronic hepatitis B: a propensity score matching analysis

Rui Huang[1], Jian Wang[1], Xiaomin Yan[1], Bei Jia[1], Weimao Ding[2], Juan Xia[1], Zhaoping Zhang[1], Chao Wu[1]

[1]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China, [2]Department of Hepatology, Huai'an No. 4 People's Hospital, Huai'an, Jiangsu, China.

Introduction: The impact of non-alcoholic fatty liver disease on liver fibrosis of chronic hepatitis B (CHB) remains controversial.
Objectives: We aimed to investigate the impact of NAFLD on liver fibrosis in CHB patients.
Methods: A total of 2109 treatment-naïve CHB patients were enrolled from two medical centers. The diagnosis of NAFLD was based on ultrasonography and the evaluation of liver fibrosis stages were based on aspartate transaminase (AST) to platelet ratio index(-APRI) and fibrosis-4 score (FIB-4). Another cohort which consisted of 544 CHB patients who received liver biopsy to determine the presence of NAFLD and the stages of liver fibrosis were enrolled. Propensity score matching (PSM) method was used to adjust the imbalance of baseline confounders between CHB patients with and without NAFLD.
Results: In the ultrasonography CHB cohort, 367 (17.4%) patients were diagnosed with NAFLD by ultrasonography. Patients with NAFLD ($n = 367$) exhibited a significant less severe liver fibrosis than patients without NAFLD ($n = 1742$) ($P < 0.001$). Using PSM to adjust the imbalance of baseline confounders (gender, age, ALT, platelet, HBeAg status and HBV DNA), 191 patients were included in each group. The fibrosis stage remains less severe in patients with NAFLD than patients without NAFLD ($P < 0.05$). In live biopsy cohort, NAFLD was presented in 93 (17.1%) patients. For patients concurrent with NAFLD, the stages of liver fibrosis were also less severe than patients without NAFLD before and after PSM ($P < 0.05$). By multivariate analysis, the present of NAFLD was an independently negative factor of significant liver fibrosis (OR 0.490, 95% CI 0.297–0.807, $P = 0.005$).
Conclusion: Concurrent with NAFLD was significantly associated with less severe liver fibrosis in CHB patients, suggesting its potential negative effects on the progression of liver fibrosis in CHB patients.

Abstract #1392

Association of EFTUD2 gene polymorphism with the risk to HBV infection and functional analysis

Zhu Chuanlong[1], Tian Anran[1], Hu Pingping[1], Xu Ruirui[1], Yuan Hui[1], Cai Jinyuan[1], Li Jun[1],

[1]Department of Infectious Disease, the First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu, China

Introduction: The splicing effect of *EFTUD2* on pre-mRNA can lead to differential expression of innate immune-related proteins, which plays an important role in the host's resistance to virus infection. Studies on the relationship between *EFTUD2* gene polymorphism and risk to HBV infection have not been reported.
Objectives: This study aimed to analyze the relationship betweenSNPs (single nucleotide polymorphisms) of EFTUD2 gene-and risk of HBV infection and illuminate the function of risk SNP.
Methods: We enrolled 448 cases of non-HBV infection and 379 cases of HBV infection in Zhangjiagang city, collectedthe results of blood routine examination, liver ultrasound and genotyped four SNPs (rs1071682, rs2277617, rs2289674 and rs3809756) of 827 subjects. The relationship between different genotypes of SNPs and risk of HBV infection were evaluated by SPSS 20.0. Wild-type A and mutant-type C allele of *EFTUD2* dual luciferase reporter vectors were constructed and transfected into HepG2 cells to investigate relative luciferase activity in different genotype vectors.
Results: In these four SNPs, only rs3809756 was significantly associated with the susceptibility to HBV($P < 0.05$). Rs3809756 CC genotype had a significantly increased risk of HBV infection than AA genotype (OR = 1.945, 95% CI 1.129–3.351, $P = 0.017$). Dual luciferase assay demonstrated that luciferase relative activity of rs3809756-C was significantly lower than rs3809756-A ($P < 0.05$).
Conclusion: Our data suggest that rs3809756 genotype of *EFTUD2* is associated with HBVsusceptibility and rs3809756 A > C may act as a cis-regulatory silencer element to reduce the expression level of *EFTUD2*.

Table 1. Demographic and clinical characteristics

Variables	Total (N=827)	Control (N=448)	Case (N=379)	*P*-value
Median age, year (IQR)	47.0 (41.5-55.0)	47.0 (41.3-55.0)	46.0 (38.0-56.0)	0.134[a]
Gender, n (%)				0.291[b]
Male	501 (60.6)	264 (58.9)	237 (62.5)	
Female	326 (39.4)	184 (41.1)	142 (37.5)	
Cirrhosis, n (%)				
No	532 (90.6)	372 (100.0)	160 (74.4)	<0.001[b]
Yes	55 (9.4)	0 (0)	55 (25.6)	
Fatty liver, n (%)				<0.001[b]
No	421 (71.7)	235 (63.2)	186 (86.5)	
Yes	166 (28.3)	137 (36.8)	29 (13.5)	
ALT (U/L)				
≤40	597 (85.3)	397 (89.0)	200 (78.7)	<0.001[b]
>40	103 (14.7)	49 (11.0)	54 (21.3)	
AST (U/L)				
≤40	631 (90.0)	426 (95.5)	205 (80.4)	<0.001[b]
>40	70 (10.0)	20 (4.5)	50 (19.6)	

Abbreviations: IQR, interquartile range; ALT, alanine transaminase; AST, aspartate transaminase.
[a]*P* value of Mann-Whitney U test among two groups. [b]*P* value of χ^2-test among two groups.

Table 2 Results of association analysis of selected SNPs with the risk of HBV-infected

SNPs (genotype)	Control, n (%) (N=448)	Case, n(%) (N=379)	OR(95%CI)[a]	*P*[a]
rs3809756				
TT	168 (39.4)	117 (31.8)	1.00	--
TC	185 (43.4)	177 (48.1)	1.516 (0.975-2.358)	0.065
CC	73 (17.2)	74 (20.1)	**1.945 (1.129-3.351)**	**0.017**
Dominant model			**1.634 (1.082-2.468)**	**0.020**
Additive model			**1.407 (1.077-1.838)**	**0.012**
rs1071682				
GG	356 (80.7)	316 (84.5)	1.00	--
GA	83 (18.8)	54 (14.4)	0.836 (0.491-1.422)	0.508
AA	2 (0.5)	4 (1.1)	1.414 (0.123-16.302)	0.781
Dominant model			0.850 (0.504-1.435)	0.544
Additive model			0.875 (0.531-1.443)	0.602
rs2277617				
TT	273 (63.0)	224 (60.7)	1.00	--
TG	140 (32.3)	129 (35.0)	1.082 (0.716-1.636)	0.707
GG	20 (4.7)	16 (4.3)	0.652 (0.232-1.834)	0.418
Dominant model			1.024 (0.687-1.525)	0.908
Additive model			0.963 (0.689-1.348)	0.827
rs2289674				
AA	338 (74.8)	312 (72.2)	1.00	--
AG	104 (23.0)	112 (25.9)	1.311 (0.857-2.006)	0.212
GG	10 (2.2)	8 (1.9)	0.506 (0.106-2.426)	0.395
Dominant model			1.232 (0.813-1.866)	0.326
Additive model			1.120 (0.773-1.623)	0.548

Logistic regression analysis, the adjustment factors were age, gender, liver cirrhosis and fatty liver. Abbreviations: OR, odds ratio; CI: confidence interval.

Abstract #1444

Tenofovir (TFV) or tenofovir alafenamide (TAF) concentration in breast milk and infants' cord blood, with tenofovir disoproxil fumarate (TDF) or TAF treatment in pregnancy

Li Bojun[1], Gu Ye[1], Wang Yan[1], Zhao Rui[1], Wei Yushi[1], Liu Qiong[1], Ma Qiang[1]

[1]Infectious Disease Department, The Sixth Hospital of Shenyang, Shenyang City, China PR

Background: There were no pharmacological data for TAF for prevention of mother-to-child transmission (pMTCT) in human during gestation or breastfeeding period for chronic hepatitis B women.
Objective: We aimed to determine the TAF or TFV concentration in breast milk and cord blood from mother-infant pairs, who received TDF or TAF Treatment from 28 weeks of pregnancy to delivery.
Method: Pregnant women with HBeAg positive and HBV DNA>10^6 IU/ml at 24 weeks of pregnancy was received either TDF or TAF treatment from 28 weeks of pregnancy to delivery to pMTCT. TAF or TFV concentration in breast milk (the median time obtained was 6.5 or 6 h after withdrawal, respectively) and cord blood samples were determined by liquid chromatography tandem mass spectrometry method in TDF or TAF groups, respectively.
Result: 26 mother-infant pairs had been enrolled in each group. TAF concentration was below the lower limit of quantitation (0.5 ng/ml) in all the cord blood and breast milk samples from TAF group, the median TFV concentration was 4.98 (IQR 0.73–7.24) ng/ml and 12.83 (IQR 7.46–29.46) ng/ml in cord blood and breast milk samples from TDF group. No infant had congenital malformation at birth.
Conclusion: This study demonstrated that TAF usage during gestation led to TAF undetectable in breastfeeding milk or cord blood. This result can further support TAF safe in infants during the 3th trimester of pregnancy for pMTCT and no impact on breastfeeding after TAF discontinuation at delivery of infants, but a lager sample size and long-term cohort study is still required.

Abstract #1452

Demographic dan clinical profile of HBV infection detected from pre-endoscopic screening in Makassar-Indonesia

Akiko Syawalidhany Tahir[1,2], Fardah Akil, Muhammad Luthfi Parewangi[1], Nu'man AS Daud[1], Rini Rachmawarni Bachtiar[1], Susanto H Kusuma[1], Amelia Rifai[1]

[1]Centre of Gastroenterology-Hepatology HAM Akil/DR.Wahidin Sudirohusodo General Hospital, [2]Division of Gastroenterology-Hepatology, Department of Internal Medicine, University of Hasanuddin, Makassar-Indonesia

Introduction: Indonesia has intermediate-prevalence of HBV infection range from 2 to 7%. Endoscopy devices are considered to be a potential risk for transmission of hepatitis among patients and pre-endoscopic screening is one of strategy in our population. Our previous study of prevalence HBV pre-endoscopic screening in Makassar found 8.2% above general data and clinical profile have not been describe.
Objectives: To describe the clinical profile of HBV infection from pre-endoscopic screening.
Methods: This retrospective study using pre-endoscopy screening data from 116 HBsAg+ patients between year 2017–2018. Demography, laboratory (liver biochemistry/serology/virology), radiology and fibroscan data were collected and determine new terminology of HBV infection according to European Association for the Study of the Liver (EASL).
Results: We found 83(71%) male, age ≥ 45 y.o in 74(63.8%) patients with median age 51.5 y.o. and 37(31.9%) works as self-employed. HBeAg negative 78(71.6%) with median of laboratory data: ALT 34U/L, APRI score 0.38, AFP 2.77 ng/ml; mean of HBV-DNA log and fibroscan : 4.38 ± 2.32IU/ml and 8.91 ± 5.35kPa. According to HBV terminology: HBeAg(+)/(−) chronic hepatitis 21(18.1%)/28(24.1%) and HBeAg(+)/(−) chronic infection 48(41.3%)/12(10.3%) respectively; 2(0.2%) chronic hepatitis from 7 patients without serology. Twenty-two (19%) patients have cirrhosis and no hepatocellular carcinoma are found.
Conclusion: Male and HBV chronic infection are majority of clinical profile in this study with 1/5 patients already in cirrhosis stage. This study shows the importance of pre-endoscopic screening to determine new patients hepatitis status earlier if screening in primary care unavailable.

Abstract #1464

Knowledge of hepatitis B virus infection and attitudes toward hepatitis B infected persons: a community-based cross-sectional study among general population in semarang, indonesia

Hery DP[1], Cecilia OP[1], Hesti TH[1], Didik I[1], Agung P[1], Hirlan[1]

[1]Division of Gastroentero Hepatology, Department of Internal Medicine, Diponegoro University, Dr. Kariadi Hospital, Semarang, Indonesia

Introduction: The prevalence of HBV infection in Indonesia categorized as moderate. However, study on knowledge of HBV are still limited. Such information is essential for designing effective HBV prevention and control program.
Objective: The aim of this study was to characterize knowledge and attitudes regarding HBV infection among general population in Semarang, Indonesia.
Methods: A community-based cross-sectional survey using pre tested questionnaire between February and August 2019 in Semarang, Indonesia. The questionnaire consisted of knowledge, attitudes toward HBV infected person, HBV screening and vaccination status. Knowledge status was compared using Chi square-test and logistic regression-test.
Results: In total 374 persons completed the survey. Only 46.3% participants had good knowledge of HBV. The factors associated with lack of knowledge were low education and income ($p = 0.001$ and $p = 0.006$ respectively). Participants with educational background lower than senior high school were 1,6 times likely to have lack of knowledge (PR 1610, 95% CI: 1354–1,914, $p < 0.001$). Low income group was 1.5 times likely to have lack of HBV knowledge (PR 1506, 95% CI 1173–1934, $p < 0.001$). These groups had probability nearly 50% of getting lack of knowledge about hepatitis B. 30.7% participants had negative attitudes toward hepatitis B infected people, 90,6% not knowing their hepatitis B viral status, and 81% didn't have complete vaccination.
Conclusion: This study showed low level of knowledge among general population in Semarang Indonesia associated with education and income level. Education among these groups may be a vital component in reducing the gaps in HBV knowledge.

Abstract #1470

Distribution of different hepatitis B phenotype in patients with chronic HBV infection

Youlin Shao[1], Tong Yan[1], Jiang Wang[2], Rui Huang[2], Xuebing Yan[3], Chuanwu Zhu[4], Biao Zhang[5], Chao Wu[2], Longgen Liu[1]

[1]Department of Hepatology, Changzhou Third People's Hospital, Changzhou, China, [2]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China, [3]Department of Infectious Disease, the Affiliated Hospital of Xuzhou Medical University, Xuzhou, Jiangsu, China, [4]Department of Hepatology, The Fifth People's Hospital of Suzhou, Suzhou, Jiangsu, China, [5]Department of Hepatology, Huai'an No. 4 People's Hospital, Huai'an, Jiangsu, China;

Introduction and objectives: We aimed to investigate the distribution of hepatitis B phenotype in a large cohort of patients with chronic HBV infection.
Methods: Totally, 4912 consecutive treatment-naïve chronic HBV infection patients were enrolled. Hepatitis B phenotype was defined based on 2016 AASLD and 2017 EASL guidelines.
Results: According to AASLD guidelines, the distribution of different immune state was: 126 (2.6%) patients in immune tolerant phase, 1269 (25.8%) patients in HBeAg-positive immune active phase, 1298 (26.4%) patients in inactive CHB phase and 692 (14.1%) patients in HBeAg-negative immune reactivation phase. However, 1527 (31.1%) patients did not fit into any of above phases and were considered as indeterminant: 1471 (29.9%) HBeAg negative patients (4.4% HBV-DNA$>2 \times 10^3$IU/ml and normal ALT, 25.5% HBV-DNA$\leq 2 \times 10^3$ IU/ml and elevated ALT) and 56 (0.11%) HBeAg positive patients (0.63% HBV-DNA $< 2\times10^4$IU/ml and elevated ALT; 0.5% HBV-DNA $< 1 \times 10^6$IU/ml and normal ALT). Based on EASL guidelines, 324(6.6%) patients were HBeAg-positive chronic infection, 1012 (20.6%) HBeAg-positive chronic hepatitis, 1991(40.5%) HBeAg-negative chronic infection and 463(9.4%) HBeAg-negative chronic hepatitis. Similarly, 1122(22.9%) patients belong to the indeterminant, including 1007(20.5%) HBeAg-negative patients (9.1% HBV-DNA $> 2\times10^3$IU/ml and normal ALT; 11.4% HBV-DNA $\leq 2 \times 10^3$IU/ml and elevated ALT), and 115 (2.4%) HBeAg-positive patients (2.1% HBV-DNA $< 1 \times 10^7$IU/ml and normal ALT; 0.2% HBV-DNA $< 1 \times 10^4$IU/ml and elevated ALT).
Conclusion: A substantial proportion of patients do not fit readily into one of the usual stages or phases. Future studies are needed to assess the liver disease severity and the need for antiviral therapy for patients with indeterminant category (NCT03097952).

Abstract #1471

Predictors of the stability of hepatitis B phenotype for HBeAg-negative patients in the grey zone

Li Zhu[1], Rui Huang[2], Jian Wang[2], Xuebing Yan[3], Biao Zhang[4], Longgen Liu[5], Chao Wu[2], Chuanwu Zhu[1]

[1]Department of Hepatology, The Fifth People's Hospital of Suzhou, Suzhou, Jiangsu, China, [2]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China, [3]Department of Infectious Disease, the Affiliated Hospital of Xuzhou Medical University, Xuzhou, Jiangsu, China, [4]Department of Hepatology, Huai'an No. 4 People's Hospital, Huai'an, Jiangsu, China, [5]Department of Hepatology, Changzhou Third People's Hospital, Changzhou, China

Introduction: The immune states of substantial chronic hepatitis B (CHB) patients cannot be determined into any stage by current guidelines.
Objectives: We aimed to investigate the predictors of stability of hepatitis B phenotype in HBeAg-negative patients who do not fit into any stage ("grey zone").
Methods: A total of 331 treatment-naïve HBeAg negative patients were enrolled, including group 1: 299 patients with HBV DNA $<$ 2000 IU/ml and elevated ALT (>30 U/L for men and >19 U/L for women), and group 2: 32 patients with HBV DNA $\geq$ 2000 IU/ml and normal ALT. Immune state was defined according to the 2016 AASLD guidelines.
Results: The median follow-up time was 14.7 months in group 1. 93 (31.1%) patients translated to inactive carrier state, 26 patients translated to reactivation state and 180 (60.2%) patients remained unchanged. Baseline HBV DNA $>$ 2000 IU/ml were significantly associated with reactivation (HR 3.178, 95% CI 1.415–7.140, $P = 0.005$). Baseline high HBV DNA levels (HR 1.963, 95% CI 1.146–3.363, $P = 0.014$) and low HBsAg levels (HR 0.735, 95% CI 0.619–0.872, $P < 0.001$) were significantly correlated with transition to inactive carrier state. The median follow-up time was 25.2 months in group 2. 17 (53.1%) patients translated to inactive carrier state, 6 (18.8%) patients translated to reactivation state and 9 (28.1%) patients were unchanged. There was no clinical index associated with transition to inactive carrier state or reactivation.
Conclusion: HBV DNA and HBsAg levels were predictors of immune state transition for HBeAg-negative patients in the grey zone. Monitoring the progress of states is needed for these patients (NCT03097952).

Abstract #1480

Distribution of vitamin D receptor gene *Fok*I polymorphism among HBsAg-reactive and HBsAg-nonreactive blood donors in Pekanbaru, Indonesia

Kemal Rahmat Azhari[1], Lestari Nita[2], Idola Otra[2], Arfianti[1], Oktora Reni[3], Gani Bebe[3]

[1]Department of Medical Biology, Faculty of Medicine, University of Riau, [2]Faculty of Medicine, University of Riau, [3]Blood Transfusion Unit, Indonesian Red Cross Pekanbaru

Introduction: Hepatitis B surface antigen (HBsAg) serves as biomarker for hepatitis B virus (HBV) infection. Indonesian Red Cross screens donor for HBsAg reactivity to minimise HBV transmission. *Fok*I polymorphism in vitamin D receptor (VDR) gene, rs2228570, has been studied regarding its association with hepatitis B susceptibility and progression.
Methods: We conducted preliminary study in Indonesian Red Cross Pekanbaru in October 2019–January 2020. We sampled 66 HIV-nonreactive blood donors, 33 donors were reactive for HBsAg and 33 donors were non-reactive for HBsAg. We conducted rs2228570 genotyping using Amplification Refractory Mutation System (ARMS) PCR.
Results: There were a total of 46 males (69.7%) and 20 females (30.3%) in our study samples. No significant gender difference was observed between HBsAg status groups, with 66.7% and 72.7% of males in HBsAg reactive and HBsAg nonreactive, respectively ($p = 0.789$). Mean age of the total sample population was 38.27 ± 10.88 years old, with no significant difference in mean age between HBsAg-reactive and nonreactive donors, 40.42 ± 11.31 years old and 36.12 ± 10.15 years old, respectively ($p = 0.109$). Distribution of *Fok*I genotypes in our sample population was 39.4% FF, 54.5% Ff, and 6.1% ff. No significant genotype difference was observed between HBsAg status groups ($p = 0.573$).
Conclusion: No significant difference was observed on *Fok*I genotype distribution between HBsAg status groups among blood donors in Pekanbaru. Characterisation of HBsAg-reactive blood donors, including the donor's and the viral genotypes, should be able to contribute to hepatitis B management in Indonesia.

Abstract #1494

Peginterferon and Entecavir combination therapy with Response-Guided-Therapy strategy improves outcome of non-early response Hepatitis B e antigen-positive patients

Lu Chen

Background: The efficacy of NAs and pegylated interferon (PegIFN) combination therapy is still controversial in hepatitis B e antigen positive ($HBeAg^+$) patients. Thus alternative approach(es) are explored to improve the efficacy of the management of $HBeAg^+$ patients. In this prospective study, it was determined the outcomes of $HBeAg^+$ patients who were initiated with PegIFN without early response, then followed either with extension of PegIFN monotherapy or PegIFN combined with entecavir (ETV).
Methods: $HBeAg^+$ patients with treatment naïve were initiated with PegIFN alfa-2a (PegIFNα-2a) for 24 weeks, only those patients without early response (HBsAg < 1500 IU/mL and HBV DNA $< 10^5$ copies/mL) were recruited in the current study. Among totally 91 $HBeAg^+$ patients at the end of treatment, 51 patients were treated with extension of PegIFNα-2a monotherapy, 40 patients were treated with extension of PegIFNα-2a and ETV combination. The efficacy was evaluated with hepatitis B surface antigen (HBsAg) decline and/or loss, together with hepatitis B virus (HBV) DNA decline and HBeAg clearance.
Results: It was demonstrated that better outcomes in response to PegIFNα-2a and ETV combination compared to PegIFNα-2a monotherapy, including more HBsAg decline and loss, HBV DNA decline and HBeAg clearance. Importantly, baseline HBsAg levels could predict the outcome of treatment, especially those patients with baselines HBsAg between 1500 and 20,000 IU/mL can benefit the most from combination therapy.
Conclusions: The combination therapy of PegIFNα-2a and ETV was more efficacy for $HBeAg^+$ patients without early response, and these with HBsAg between 1500 and 20000 IU/mL can achieve maximum benefit from this.

Abstract #1516

A comparative study of RDW, PLR, NLR to predict liver fibrosis and cirrhosis in chronic hepatitis B infection

Maimunah U[1], Windradi C[2], Nusi IA[1], Purbayu H[1], Sugihartono T[1], Setiawan PB[1]

[1]Division of Gastroenterology and Hepatology, Internal Medicine Department, Universitas Airlangga, Dr. Soetomo General Academic, Surabaya Indonesia, [2]Resident of Internal Medicine Department, Universitas Airlangga, Surabaya Indonesia.

Introduction: Chronic hepatitis infection usually related to liver fibrosis and cirrhosis. Early diagnosis and assessment of liver fibrosis plays a vital role for control of disease progression and therapeutic intervention. New insight for marker liver fibrosis and cirrhosis from hematological findings has been studied. Red-blood-cell distribution width (RDW), platelet to lymphocyte ratio (PLR), neutrophil to lymphocyte ratio (NLR) could be a potential marker. Aim of the present study was to compare RDW, PLR, NLR values and the level of fibrosis in chronic hepatitis B infection according to fibroscan.
Objective: To compare between red cell distribution width (RDW), PLR and NLR to liver fibrosis and cirrhosis related to hepatitis B virus infection in the Gastroenterohepatology Outpatient Installation at Dr. RSUD. Soetomo Surabaya.
Methods: We perfomed retrospective study of patient presenting with CHB who underwent laboratory and fibroscan test between January to June 2018. Hematological parameters and liver biochemistry were analyzed.
Results: 167 patients with an average age of 47.61 years, men and women ratio (4:1) with a mean RDW of 14.47 and fibroscan 20.59 kPA. RDW values showed significant results related to fibrosis in patients with chronic hepatitis B infection 3.23 CI 95% (1593–6573), p 0.002 with ROC 65.2%, sensitivity 82%. Those results were higher than PLR as a marker fibrosis and with sensitivity 59% OR 0.372 CI 95% (0.165–0.842) p 0.017 and cirrhosis 49% respectively OR 0.469 CI 95% (0.25–0.879) p 0.019.
Conclusion: RDW is potential to be non invasive marker of liver fibrosis in chronic hepatitis B infection

Abstract #1519

Antiviral compound screening against hepatitis B virus identify a candidate compound that inhibits HBsAg

Shingo Nakamoto[1], Nan Nwe Win[2], Kazufumi Kobayashi[1], Soichiro Kiyono[1], Masato Nakamura[1], Naoya Kanogawa[1], Takayuki Kondo[1], Tomoko Saito[1], Sadahisa Ogasawara[1], Eiichiro Suzuki[1], Yoshihiko Ooka[1], Ryosuke Muroyama[3], Akinobu

Tawada[1], Tetsuhiro Chiba[1], Makoto Arai[1], Tatsuo Kanda[4], Hiroshi Shirasawa[3], Naoya Kato[1]

[1]Gastroenterology, Chiba University hospital, Chiba, Japan, [2]Microbiology, University of Medicine, Yangon, Myanmar, [3]Molecular virology, Graduate School of Medicine, Chiba University, Chiba, Japan, [4]Internal Medicine, Nihon University School of Medicine

Introduction: The current antiviral treatments for hepatitis B virus (HBV) infection such as nucleoside/tide analogues are not curative. To identify new anti-HBV candidates having a new action mechanism, screening of a compound library was performed using HBV producing cells.
Methods: A library containing around 300 compounds were tested for anti-HBV activity using HepG2215 cells. After adding compounds for 3 days, the amount of HBsAg in the culture medium were assessed by CLEIA. MTS assay was performed for cytotoxicity. DMSO was used for control experiments. The assay was repeated from the hit compounds to evaluate reproducibility. Candidate compounds were tested for anti-HBV activity using HBV-infected human hepatocytes derived from chimeric mice with humanized liver (PXB cell).
Results: Eleven compounds were excluded from the analysis due to the cytotoxicity. Five compounds were found to consistently decrease the HBsAg level in the culture medium from HepG2215 cells without affecting cell viability. Among them, an oxadiazole derivative reduced the amount of HBsAg in the culture medium from HBV-infected PXB cells to 75% after 6 days of treatment. The compound also reduced HBV RNA in the cells quantified by real-time (RT)-PCR assay.
Conclusion: The present in vitro screening assay identified the anti-HBV drug candidate. The assay could be applied for further screening to identify antiviral compounds which decreases HBV antigen efficiently.

Abstract #1534

Add on pegylated interferon in the treatment of hepatitis B patient on nucleos(t)ide analogue therapy

Andri Sanityoso Sulaiman[1,2]

[1]Internal Medicine Department, Cipto Mangunkusumo Hospital Faculty of Medicine Universitas Indonesia, [2]Klinik Hati Prof. Ali Sulaiman Jakarta, Indonesia

Introduction: Nucleos(t)ide Analogue (NA) or using Peg-IFN (Pegasys) are two types of treatment used for chronic hepatitis B. NA is a regimen that is widely used due its ability to suppress the Hepatitis B virus and the lack of possible side effects. But, many chronic hepatitis B patients with an undetectable virus still have high HBsAg rates. Meanwhile, the use of Pegasys has been found to be more able to suppress HBsAg rates, but in some cases can cause significant side effects.
Objective: To describe the therapeutic effects of Peg-IFN and NA combination therapy in chronic hepatitis B (CHB) after completing 48 weeks combination therapy.
Methods: 10 patients receiving Pegasys + NA therapy for 48 weeks and had complete data were recruited for the study. The distribution of HBsAg, HBeAg, and HBV DNA before and after treatment were analyzed as mean or median.
Results: At the end of the therapy, 4/4 (100%) patients were able to achieve HBV DNA loss, 1/3 (33.3%) had HBeAg seroconversion, 3/10 (30%) patients had HBsAg loss, and 2/10 (20%) had HBsAg seroconversion. Beside that, patients had higher HBsAg decline (>1.5 log 10) on the 12th week of therapy were likely to achieve HBsAg loss at the end of treatment. Despite, there were 7 patients who didn't achieve HBsAg loss, all of them experienced HBsAg declined at end of treatment.
Conclusion: This study showed that combination therapy could be a good method to achieve HBsAg loss and HBsAg decline at 12th week could predict the ideal target therapy.

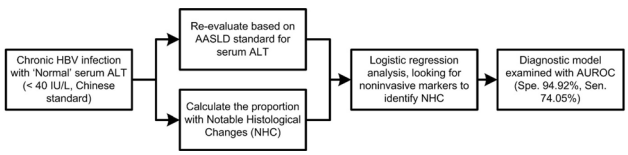
Abstract #1548

Noninvasive diagnostic model for hepatic inflammation and fibrosis in chronic hepatitis B with normal serum alanine aminotransferase

Li Xiaoke[1,2], Du Hongbo[1,2], Xing Yufeng[3], Xiao Huanming[4], Zhou Zhenhua[5], Chen Guang[1,2], Zhang Peng[6], Li Zhiguo[1], Liu Yan[1,2], Zhou Daqiao[3], Chi Xiaoling[4], Gao Yueqiu[5], Ye Yong'an[1,2]

[1]Department of Gastroenterology, Dongzhimen hospital Affiliated to Beijing University of Chinese Medicine (BUCM), Beijing, China, [2]Institute of Liver Diseases, BUCM, Beijing, China, [3]Department of Hepatology, Shenzhen TCM Hospital, Shenzhen, China, [4]Department of Hepatology, Guangdong Hospital of Traditional Chinese Medicine, Guangzhou, China, [5]Department of Hepatology, Shanghai Shuguang Hospital, Shanghai, China, [6]Department of Hepatology, Dongfang Hosptial Affiliated to BUCM, Beijing, China

Introduction: Upper limit of serum alanine aminotransferase (ALT) in chronic hepatitis B (CHB) patients are different between AASLD guideline (AG) and Chinese guideline (CG), where 35 IU/L for males and 25 IU/L for females in AG, 40 IU/L in CG.
Objective: To determine whether the AS is applicable in China, and to explore a noninvasive approach for assessing liver histology in patients with normal ALT.
Methods: We collected treatment naïve CHB patients with normal ALT (< 40 IU/L) in China, compared the histological changes between different ALT thresholds, and to discover markers for identifying progressive inflammation and fibrosis.
Results: We obtained 587 patients' data whose ALT < 40 IU/L, where 158 were judged abnormal ALT based on AS, 4.43% and 6.96% were classified as G0 and S0, notable histological change (NHC, total score ≥ 2) were confirmed in 79.11%. 3. NHC were found in 86.25% of 429 patients with normal ALT based on AS. 4. Age, HBsAg, HBeAg status, HBcAb and HBV DNA were highly associated with histological activity. Logistic regression model: risk score = 10.722–0.028*Age (years) -1.460*HBsAg (log10 IU/ml) + 0.194*HBV DNA (log10 IU/ml) − 2.759*HBeAg (positive = 1, negative = 0) – 0.003*HBcAb (S/CO). It could diagnose NHC with an AUROC of 0.87 (specificity 94.92%, sensitivity 74.05%) at a threshold of 0.85.
Conclusion: The incidence of histological changes might be underestimated in patients with normal ALT.



Abstract #1563

A retrospective study on HBsAg clearance rate after antiviral therapy in children with HBeAg-positive chronic hepatitis B infection aged 1–7 years old

Shishu Zhu[1], Yi Dong[1], Zhiqiang Xu[1], Limin Wang[1], Dawei Chen[1], Yu Gan[1], Fuchuan Wang[1], Jianguo Yan[1], Lili Cao[1], Pu Wang[1], George Lau[2], Hongfei Zhang[1]

[1]Pediatric Liver Disease Therapy and Research Center, The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China, [2]Humanity and Health Clinical Trial Center, Humanity and Health Medical Group, Hong Kong SAR, China

Objective: To investigate the HBsAg clearance rate after antiviral therapy in children with HBeAg-positive chronic hepatitis B (CHB) aged 1–7 years.
Methods: A retrospective analysis was performed for the HBsAg clearance rate in 293 children who were hospitalized in 302 Hospital of PLA from June 2006 to December 2013, met the inclusion criteria, received antiviral therapy, and were followed up for at least 6 months after the withdrawal of antiviral therapy. The t-test or the rank sum test was applied according to the distribution of continuous data, and the chi-square test was used for comparison of categorical data.
Results: The HBsAg positive rate of children's mothers was 91.1%. In the age groups of $>1-\leq 2$ years, $>2-\leq 3$ years, $>3-\leq 4$ years, $>4-\leq 5$ years, $>5-\leq 6$ years, and $>6-\leq 7$ years, the HBsAg clearance rates were 66.1%, 65.5%, 45.7%, 41.3%, 20.6%, and 27.6%, respectively. There were significant differences in HBsAg clearance rate between the age groups of $>1-\leq 3$ years and $>3-\leq 5$ years, $>1-\leq 3$ years and $>5-\leq 7$ years, and$>3-\leq 5$ years and $>5-\leq 7$ years (P = 0.001, 0.000, and 0.008). Of all children, 64.8% were boys, among whom 41.1% achieved HBsAg clearance, and 35.2% were girls, among whom 61.2% achieved HBsAg clearance. There was a significant difference in HBsAg clearance rate between boys and girls (P = 0.001). The children with pretreatment alanine aminotransferase (ALT levels of ≤80 IU/L, >80 IU/L, ≤200 IU/L, and >200 IU/L had HBsAg clearance rates of 40.7%, 5 1.2%, 47.6%, and 49.4%, respectively. There were no significant differences in HBsAg clearance rate between the ALT ≤ 80 IU/L and ALT > 80 IU/L groups and the ALT ≤ 200 IU/L and ALT > 200 IU/L groups (P = 0.101 and 0.778). There was no significant difference in HBsAg clearance rate between the pretreatment HBV DNA load $< 1 \times 10^7$ IU/ml and $\geq 1 \times 10^7$ IU/ml groups (54.9% vs 46.7%, P = 0.286). Of all children, 14.2% had genotype B and an HBsAg clearance rate of 57.1%, and 85% had genotype C and an HBsAg clearance rate of 39.5%. There was no significant difference in HBsAg clearance rate between the genotype B group and the genotype C group (P = 0.051). Of all children, 90.4% underwent liver biopsy, among whom 10.9% had severe liver fibrosis (F ≥ 3) and liver cirrhosis, as well as an HBsAg clearance rate of 31%. The non-severe liver fibrosis/liver cirrhosis group had an HBsAg clearance rate of 49.2%, and there was no significant difference in HBsAg clearance rate between these two groups (P = 0.065). There was no significant difference in HBsAg clearance rate between the liver inflammation grade (G) < 2 group and the G ≥ 2 group (39.5% vs 50.9%, P = 0.084). Of all children, 58.7% received interferon antiviral therapy alone and had an HBsAg clearance rate of 48.8% and 41.3% received interferon gone for 6 months followed by lamivudine antiviral therapy and had an HBsAg clearance rate of 47.1%. There was no significant difference between these two groups (P = 0.770).
Conclusion: In children with HBeAg-positive CHB aged 1–7 years who receive antiviral therapy, HBsAg clearance rate is correlated with age and sex, and the children aged < 5 years can achieve a higher HBsAg clearance rate.

Abstract #1564

Antiviral effect and clinical predictors of HBsAg seroconversion in children aged 1–6 years old with chronic hepatitis B Virus Infection

Shishu Zhu[1], Yi Dong[1], Zhiqiang Xu[1], Limin Wang[1], Dawei Chen[1], Yu Gan[1], Fuchuan Wang[1], Jianguo Yan[1], Lili Cao[1], Pu Wang[1], George Lau[2], Hongfei Zhang[1]

[1]Pediatric Liver Disease Therapy and Research Center, The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China, [2]Humanity and Health Clinical Trial Center, Humanity and Health Medical Group, Hong Kong SAR, China

Objective and aim: This study aimed to explore the outcome of long-term follow-up of chronic HBV infection and the factors affecting HBsAg seroconversion in children, to search for important immune factors related to HBsAg seroconversion and explore possible causal relationship.
Method: 236 children aged 1–6 years old with chronic hepatitis B who were admitted to 302 hospital from January 2012 to May 2018 were enrolled, a retrospective analysis was performed for their clinical data and follow-up data. Meanwhile, the clinical data of 116 patients aged 7–18 years were statistically analyzed.
Result: (1) A total of 352 patients with chronic HBV were enrolled. Among them, 236 patients were 1–6 years old and 116 patients were 7–18 years old. They were all treated with IFN. After follow-up observation for 144 weeks, we found that the HBsAg seroconversion rate of the two groups were 44.5% and 10.3% ($P < 0.05$). (2) In the baseline, the number of total lymphocytes, T cells, CD4 + T cells, B cells of HBsAg seroconversion patients at the age of 1–6 years old were higher than that of 7–18 years old patients ($P < 0.05$). (3) In the 1–6 years old group, the number of CD4 + T cells, B cells of HBsAg seroconversion patients were higher than that of HBsAg non-seroconversion patients ($P < 0.05$). (4) In group 1–6 years old, the age of treatment, sex, HBeAg, AST, the number of total lymphocytes, T cells, CD4+T cells, B cells were significantly associated with the achievement of HBsAg seroconversion by univariate analysis. (5) Among children aged 1–6 years, only the age of treatment was significantly associated with the achievement of HBsAg seroconversion by multivariate analysis.
Conclusion: The age of treatment was a predictor for HBsAg seroconversion, higher HBsAg seroconversion rate can be obtained before 6 years old.

Abstract #1565

A significant decrease in serum HBeAg levels at week 24: an early and effective index for identifying patients who would benefit from long-term entecavir therapy

Xi Zhang[1], Feng Ye[1], Xiaocui An[1], Xiaojing Liu[1], Lei Shi, Yunru Chen[1], Xueliang Yang[1], Jianzhou Li, Shumei Li[1]

[1]Department of Infectious Diseases, the First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, China

Background and aims: Seroconversion of HBeAg to anti-HBe either spontaneously or following antiviral therapy has been associated with significantly improved long-term clinical outcomes and survival in patients with chronic hepatitis B (CHB). Our previous study found that a significant decrease in serum HBeAg levels at week 24 was a useful on-treatment measurement for predicting HBeAg seroconversion after 96 weeks entecavir therapy. The aim of this study was to

determine its value in predicting clinical and virological outcomes after 12 years of entecavir therapy.
Methods: Thirty two HBeAg-positive naïve chronic hepatitis B patients treated with entecavir at a dose of 0.5mg daily for 12 years were evaluated. Serum HBsAg, HBeAg, ALT and HBV DNA levels were detected at baseline and in weeks 12, 24, 48, 96, years 4, 6, 8, 10, 12. APRI scores were assessed at baseline and then every 6 years.
Results: Incremental increases were noted in the rates of undetectable HBV-DNA, ALT normalization, HBeAg seroclearance, and HBsAg seroclearance, reaching 73.08%, 84.61%, 57.69% and 7.69%, respectively, by the 12th year. APRI scores decreased from 1.08 ± 0.75 to 0.41 ± 0.21 at years 12. The mean decline in HBeAg level from baseline was − 34.16 S/CO per year. Multivariate analysis identified a maintained reduction in HBeAg > 65% of pretreatment HBeAg values after 24 weeks of entecavir therapy is the strongest predictor for HBeAg seroconversion at years 12 (OR = 16.429, P = 0.03). There were no serious adverse events during therapy.
Conclusions: Entecavir was safe and effective for long-term therapy. A significant decrease in serum HBeAg levels at week 24 may be a good predictor for HBeAg seroconversion after 12 years entecavir therapy as well as 96 weeks. It could serve as an early and effective index for identifying patients who would benefit from long-term entecavir therapy.

Abstract #1592

The successfull profile theraphy of chronic hepatitis B patients in clinic gastroenterohepatology Saiful Anwar Hospital Malang Indonesia 2013–2017

Yeni Larasati[1], Syifa Mustika[2], Bogi Pratomo[2], Supriono[2]

[1]Resident of Internal Medicine, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia, [2]Gastroenterohepatology Division, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia

Introduction: Hepatitis B virus infection is a large and serious public health problem. At present there are an estimated 300 million people with persistent HBV worldwide, almost 74% (more than 220 million) living in Asian countries. The use of medication according to the guidelines can reduce the prevalence of HBV infection by 9.4% in 2007 to 7.1 in 2013 and in Indonesia there is an improvement from high endemicity to moderate HBV infection.
Objectives: The aim of this study was to describe distribution and determine successful antiviral drugs of chronic hepatitis B patients.
Methods: This research is a descriptive study with cross sectional approach. Data obtained through tracking medical records of patients. Univariate analysis was used to describe the frequency distribution of each variable, age, sex, anti-viral drugs, HBV DNA levels at month 0 and month 12, SGOT/SGPT level, complete blood count, and HBeAg. The results are described and presented in a table/percentage.
Results: The overall distribution of chronic hepatitis B patients in 2013-2017 was 251 patients and those who met the inclusion criteria were 151 patients, with details of 34 patients in 2013.44 patients in 2014, 62 patients in 2015, 55 patients in 2016 and 56 patients in 2017 Where are 178 male sufferers and 73 female sufferers. The successfull antiviral drugs of lamivudine, telbivudine, tenovofir and adenofir theraphy was significantly significant with p = 0.121; 0.008; 0.003 and 0.000. Where the use of tenovofir monotherapy has p0.003 and a combination of pegasys-tenovofir with p = 0.391.
Conclusion: Coverage rates antiviral drugs of chronic HBV infection patients in the Saiful Anwar Hospital Gastroenerohepatology clinic Malang conclude lamivudine, telbivudine, tenovofir, and adenovir have meaningful success rates according to treatment guidelines

Abstract #1612

Pilot program to assess national elimination of hepatitis B and C in Uzbekistan

Sadirova S[1], Shokhista B[1], Razavi H[2], Dunn R[2], Razavi-Shearer K[2], Musabaev E[1]

[1]Research Institute of Virology, Tashkent, Uzbekistan, [2]Center for Disease Analysis Foundation, Lafayette, Colorado, USA

Introduction: The Uzbekistan Hepatitis Elimination Pilot (UHEP) represents the first program that targets HBV/HCV elimination simultaneously. The learnings will be used to shape the national viral hepatitis elimination program.
Objective: Use operational research to optimize patient throughput and positive clinical outcomes for a national roll out.
Method: Free universal screening was provided in 3 polyclinics using rapid tests. HBV+ patients were tested for creatinine and HIV and were linked to care after consultation with a specialist. Blood was collected from HCV+ patients for core antigen, AST, platelet, and creatinine level tests before being linked to care. An electronic registry was used to track patients.
Results: In less than one month, 9200 people were screened resulting in a prevalence of 4.78% and 4.71% for HBV & HCV. 96% of HBV+ patients were tested, 57% were linked to care and 82% received a prescription for an antiviral. 94% of HCV+ patients had blood drawn, 96% had their APRI score assessed, 80% had their core antigen tested, 70% were linked to care and 49% received a prescription for an DAA. On average, the laboratory results were ready in 2.7 days, and patient consultation occurred in 3.3 days.
Conclusion: Initial results suggest HBV/HCV universal screening, lab tests and linkage to care is feasible using the existing healthcare infrastructure in Uzbekistan. The simplified testing and treatment have allowed us to test a large number of patients in only three polyclinics. The learnings from this program can be used to also shape other national hepatitis programs.

Abstract #1680

Unusual combined case of liver cirrhosis due to HBV-infection and Budd-Chiari syndrome

Sargsyants Narina[1]

[1]Elit-Med Medical Center, Yerevan, Armenia

Introduction: Budd–Chiari syndrome, are relatively rare and tend to be misdiagnosed. For diagnosis of BCS the AASLD Practice Guidelines and EASL Clinical Practice Guidelines for vascular disease of the liver, based on demonstrating obstruction of hepatic venous outflow tract by imaging examinations. Doppler ultrasonography was the initial technique of choice because of its noninvasiveness and high sensitivity and specificity.
Case report: Patient A.S., male, 66 years old, BMI = 30 kg/m^2, HBV-infection was diagnosed in January 2017 with ALT 350U/l, AST 205U/l, hyperglycemia 15.1mmol/l, PLT − 119 K/ml, HBeAg negative, anti-HBc-IgM positive. In dynamics we observed worsening of liver functions tests (Table 1) hyperbilirubinemia (total 148.7/direct 104.2 in 1 month), hypoalbuminemia (28 in 1 month), hypoprothrombinemia (up to 54% in 1 month), hyperfibrinogenemia (up to 710 in 1 month), high GGT (519 in 1 month). Abdomen US after 1 month—liver cirrhosis, portal vein 13 mm. Fibroscan in March 2017—all measurement with upper limit 75 kPa. In April 2017 quantitative HBsAg *(ARCHITECT, Abbott)* 27966 IU/ml and HBV DNA *(Abbott Real-Time^{TM})* 538 IU/ml, PCR on HDV RNA *(DNA-*

Technology with LLD 200 cps/mL) negative. Abdomen US and MRI in April 2017: liver cirrhosis, numerous hyperechoic focuses, caudate lobe enlargement, hepatic vein devoid of flow signal, Budd–Chiari syndrome. Tenofovir (TDF) started from 27.05.2017 with subsequent improvement of biochemical, US parameters and virological response.
Conclusion: This rare clinical case of advanced fibrosis due to combined chronic HBV-infection with liver cirrhosis and Budd–Chiari syndrome, clearly show improvement after tenofovir initiation.

Abstract #1692

Hepatitis B Infection Seroprevalence among population in Ngesrep, Semarang, Central Java: a cross-sectional study

Hery Djagat Purnomo[1], Hesti Triwahyu Hutami[1], Yohana Prima Ceria Anindita[2], Agung Prasetyo[1], Didik Indiarso[1], Hirlan[1], Cecilia Oktaria Permatadewi[1]

[1]Division of Gastroenterohepatology, Internal Medicine, Faculty of Medicine Diponegoro University/dr Kariadi General Hospital, Semarang, Indonesia, [2]Division of Endocrinology, Internal Medicine , Faculty of Medicine Diponegoro University/dr Kariadi General Hospital, Semarang, Indonesia

Introduction: Hepatitis B virus (HBV) infection is still a major public health problem. A nationwide study Riskesdas showed that seroprevalence of HBV infection in 2007 was 9.4%, and decreased to 7.1% in 2013. Although Indonesia is catagorized as intermediate prevalence of HBV infection, there was no relevant study in Semarang, Central Java. Information the seroprevalence of HBV in general population is lacking due to some factor, such as inadequate disease surveillance
Objective: This study conducted to determine the seroprevalence of HBV infection in Ngesrep, Semarang, Central Java
Methods: A cross sectional study was conducted in Ngesrep Semarang, on August 2016. Blood sample was collected and screened for Hepatitis B surface antigen (HBsAg) and Hepatitis B surface antibody (anti-HBs) using Enzyme Linked Immunosorbent Assay (ELISA). Additionally data about sex, age group were recorded.
Results: Overall 497 participants were included in this study, 65% was female, mean age was 48 $\pm$ 13 years. The prevalence of HBsAg Seropositive was 3.6% (n = 18). Among all participants, 35.6% (n = 177) were considered immune (anti-HBs positive), 60.76% (n = 302) participants had all markers negative (susceptible). No significant correlation was found between age group and seroprevalence of HBV ($p = 0.880$).
Conclusion: Seroprevalence of HBV infection among population in Ngesrep Semarang, Central Java was catagorized as intermediate. The immune protection might be from the response of natural infection or prior vaccination. This study recommends a national HBV screening and vaccination programme.

Abstract #1717

Use genechip and public database data to analyze the potential mechanism of MicroRNA in hepatitis B virus infection

Lin Shenglong[1], Wang Xiangmei[1], Ma Huaxi[1], Zhang Dongqing[1], Wu Wenjun[1], Lin Jiahuang[1], Liao Ziyuan[1], Lin Minghua[1], Gao Haibing[1]

[1]Department of Hepatology, Mengchao Hepatobiliary Hospital of Fujian Medical University, Fuzhou City of Fujian Province, PR China

Objective: Hepatitis B virus (HBV) is one of the leading causes of severe liver diseases and the mechanism of HBV infection with liver cells is still unclear. This study aims to investigate the potential mechanism of microRNA in HBV infection.
Methods: The peripheral blood samples were collected in the outpatient department of Mengchao Hepatobiliary Hospital of Fujian Medical University in 2017, including four chronic hepatitis B (CHB) patients and four healthy controls. Affymetrix GeneChip microRNA 4.0 was applied to detect the differential expressed microRNAs between CHB patients and healthy controls. The function of microRNAs was analyzed with bioinformatics tools and Gene Expression Omnibus (GEO) data, GSE58208.
Results: A total of six microRNA were differentially expressed in CHB patients, among them hsa-miR-122-5p (Fold Change = 219.49, P = 0.0073), hsa-miR-6794-5p (Fold Change = 2.21, P = 0.0322) , and hsa-miR-1226-5p (Fold Change = 1.61, P = 0.0343) were up-regulated; hsa-miR-619-5p (Fold Change = $-$ 3.55, P = 0.0026), hsa-miR-1273g-3p (Fold Change = $-$ 6.46, P = 0.0251) and hsa-miR-4440 (Fold Change = $-$ 15.79, P = 0.0478) were down-regulated. Further analysis showing that these microRNA could interact with HBV-DNA directly and impact the replication of the virus, in which hsa-miR-122-5p, hsa-miR-6794-5p and hsa-miR-1226-5p could influence the formation of ficolin-1 rich granule, ficolin-1 rich granule lumen, podosome and membrane ruffling, and regulate the cell membrane movement and cell-matrix adhesion.
Conclusion: MicroRNA could impact the molecular movement in the cell membrane and facilitate the invasion of the virus into liver cells and play an important role in HBV infection process.

Abstract #1723

Performance evaluation of a point-of-care (POC) molecular test (Xpert® HBV viral load (VL) assay) to strengthen and decentralize Hepatitis B virus management

Khodare Arvind[1], Gupta Ekta[1], Nitiksha[1], Singh Gaurav[1], Agarwal Kavita[1], Sharma Manoj[1], Sarin SK[1]

[1]Institute of liver and biliary sciences, New Delhi, India

Introduction: Estimation of HBV-VL is critical in hepatitis-B cascade-of-care and there is no POC molecular assay available for HBV-VL measurement.
Objectives: To evaluate the performance of recently launched a near point of care Xpert® HBV-VL assay against FDA approved platforms.
Methods: Total 172 archived plasma samples already tested for HBV DNA and HBsAg (119 positive and 53 negative for both HBV DNA and HBsAg) were retrieved from -80^{0}C. All the samples were parallelly tested on Xpert® HBV-VL assay (Cepheid, CA, USA), Abbott Real-Time assay (Abbott, Weisbaden, Germany), and COBAS® AmpliPrep/COBAS® TaqMan® HBV Test, v2.0 assay (Roche-Diagnostics, GmbH, Mannheim, Germany). Abbott and Roche assay were used as reference.
Results: The average HBV DNA detected by Xpert, Abbott and Roche assay was 4.81($\pm$ 2.24), 4.82($\pm$ 2.2) and 4.83($\pm$ 2.2) $\log_{10}$ IU/ml respectively. Xpert demonstrated excellent correlation with Abbott (R^2 = 0.947) and Roche (R^2 = 0.980). By Bland-Altman analysis the mean difference (95% Confidence Interval) in average viral load was 0.01 $\log_{10}$IU/ml and $-$ 0.05 $\log_{10}$IU/ml when compared with Abbott and Roche assay, respectively. The overall sensitivity, specificity, negative predictive value and positive predictive value of Xpert assay was found 97.5%, 100%, 94.65 and 100% respectively. Three false negative results were found by Xpert assay for samples with VL 1.3, 1.3 and 2.6 $\log_{10}$IU/ml.

Conclusion: The study has shown excellent performance of the Xpert® HBV-VL assay. It is a simplified, easy to use and has a potential to expand service delivery for better management of people living with Hepatitis-B Virus in centres with limited facilities and infrastructures.

Abstract #1735

Distribution of hepatitis B virus genotypes in georgia

Zarkua Jaba[1], Zakalashvili Mamuka[1], Orta Diana R.[2], Guevara-Garcia Rafael[2], Zhamutashvili Maia[1], Butsashvili Maia[3], Sartania Vakhtang[1], Metreveli David[1]

[1]Gastroenterology and Hepatology department, Medical center Mrcheveli, Tbilisi, Georgia, [2]BioCollections Worldwide Inc, Miami, FL, USA, [3]Department of clinical Immunology, Clinic Neolab, Tbilisi, Georgia

Introduction: Hepatitis B virus (HBV) infection is one of the major healthcare problems in the Republic of Georgia with a prevalence of 2.9% in the adult population. There is no published data on HBV genotype distribution in Georgia.
Objectives: The study aims to evaluate genotype distribution in Georgian HBV-infected patients and the association of genotypes with age, residence and gender.
Methods: Data was extracted from the clinical database of Mrcheveli medical center. Genotyping was performed using INNO-LiPA methodology. Statistical analysis was done using the statistical software SPSS 23.0.
Results: The total number of patients enrolled in the study was 84, of which 52 (62.1%) were males. Participants were mostly from Tbillisi (63.2%, N = 53). Even though HBV genotype D was more predominant, found in 57.1% (N = 48) of study participants, than genotype A, found in 42.9% (N = 36) of the study population, there was no significant difference in genotype associated with gender or place of residence. Age was significantly associated with genotype distribution. The majority of the participants (58.3%, N = 49) were 35 years old or younger. Genotype D was predominant in 71.4% of the study participants older than 35 years old, versus 46.9% of individuals 35 or younger with genotype D ($p < 0.001$). Genotype A, among those < 35 and > 35 was presented in 53.1% and 28.6% of cases, respectively.
Conclusion: Our data suggests that HBV genotype D is most prevalent among older Georgian patients chronically infected with hepatitis B. More than half of younger patients (35 years old or younger) have Genotype A.

Abstract #1739

Care cascade achieved by a program for micro-elimination of perinatal HBV transmission among pregnant women in peri-urban Yangon, Myanmar

Min MS[1], Htut HN[2], Richards A[3], Whelan R[1], Htoo E[1], Kyi KP[4], Shein HA[2], Win SY[2], Swe WW[5], Thura S[1]

[1]Community Partners International,Yangon, Myanmar, [2]B. K. Kee Foundation,Yangon, Myanmar, [3]University of California at Los Angeles, United State of Ameraica, [4]Myanmar Liver Foundation, Yangon, Myanmar, [5]North Okkalapa General Hospital, Yangon, Myanmar

Background: In Myanmar, access to prenatal screening for Hepatitis-B Virus (HBV) and interventions to prevent perinatal HBV transmission remain limited. This study explores the care cascade achieved by a collaborative pilot between government and non-government stakeholders to prevent perinatal HBV transmission in 6 wards (estimated 80,093 populations and 1379 pregnancies) near BKKee Clinic in peri-urban Yangon, Myanmar.
Methods: Descriptive analysis of the first year (10/2018-09/2019) of program data was conducted.
Results: 1269 (92.1%) pregnant women were screened at non-governmental BKKee Clinic and three government facilities using BKKee-provided HBsAg test kits. With an HBV prevalence of 2.9%, 37 women tested positive and 31 (83.8%) consented to the study. BKKee recruited 13 more HBsAg-positive women from clinic records to reach 44 participants. All 11/44 women with high viral load ($> 200{,}000$ IU/mL) at their first antenatal visit received tenofovir during pregnancy; all 8/11 who delivered to date achieved viral suppression at delivery and their newborns received HB-immunoglobulin within 24 h. All 32 newborns delivered to date received the HBV birth dose vaccine within 24 h from government providers for facility-based births (78%) and BKKee personnel for home-based births (22%). 24/27 (88.9%) infants who reached the age of routine childhood vaccination were linked by BKKee to government providers. 10/14 (71.4%) infants who reached the age of 6–7 months and completed 3 HBV vaccinations tested HBV-negative.
Conclusion: Preliminary results suggest that high coverage of prenatal HBV screening and prevention of perinatal HBV transmission is possible in a peri-urban population through government and non-government stakeholders' collaboration.

Abstract #1798

Efficacy and safety of switching to tenofovir alafenamide (TAF) in virally suppressed chronic hepatitis B patients (CHB) With hepatic impairment: week 24 results

Lim Young-Suk[1], Lampertico Pietro[2], Bae Ho[3], Chuang Wan-Long[4], Heo Jeong[5], Huang Yi-Hsiang[6], Lin Chun-Yen[7], Chen Chien-Hung[8], Flaherty John[9], Gaggar Anuj[10], Mo Shuyuan[11], Yee Leland J[12], Sethi Shalini[13], Jump Belinda[14], Huy Trinh[15], Tsang Tak Yin Owen[16], Hui Aric Josun[17], Janssen Harry LA[18]

[1]Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Songpa-gu, Seoul, South Korea, [2]CRC "A. M. and A. Migliavacca" Center for Liver Disease, Division of Gastroenterology and Hepatology , Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Università degli Studi di Milano , Milan, Italy, [3]Asian Pacific Liver Center, St. Vincent Medical Center, Los Angeles, USA; [4]Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan; [5]Department of Internal Medicine, College of Medicine, Pusan National University, Division of Gastroenterology and Hepatology, Pusan National University Hospital, [6]Division of Gastroenterology & Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, [7]Department of Gastroenterology and Hepatology, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan City, Taiwan, College of Medicine, Chang Gung University, Taoyuan City, Taiwan, [8]Division of General Medicine, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan, [9]Gilead Sciences, Foster City, CA, USA[10]Gilead Sciences, Foster City, CA, USA, [11]Gilead Sciences, Foster City, CA, USA, [12]Gilead Sciences, Foster City, CA, USA, [13]Gilead Sciences, Foster City, CA, USA, [14]Gilead Sciences, Foster City, CA, USA, [15]San Jose Gastroenterology, San Jose, USA, [16]Princess Margaret Hospital, Hong Kong, [17]Alice Ho Miu Ling Nethersole Hospital, Hong Kong;

[18]Toronto Centre for Liver Disease, Toronto General Hospital, University Health Network, Toronto, Canada, harry.janssen@uhn.ca.

Introduction: TAF, a tenofovir prodrug, has greater plasma stability and more targeted delivery of tenofovir to hepatocytes vs. TDF. Similar efficacy to TDF with improved renal/bone safety has been demonstrated for TAF in patients with compensated liver disease.
Objectives: To evaluate the efficacy and safety of switching to TAF in virally suppressed, hepatically-impaired, CHB patients.
Methods: This Phase 2 study included 31 CHB patients with a Child-Turcotte-Pugh (CTP) score of ≥ 7 and ≤ 12 at screening (or past history of CTP ≥ 7 and any score ≤ 12 at screening) who were taking TDF and/or other oral-antivirals for ≥ 48 weeks, with HBV DNA $<$ LLOQ for ≥ 24 weeks and < 20 IU/mL at screening. All patients were switched to TAF 25 mg QD and treated for 96 weeks. The co-primary endpoints were proportion with HBV DNA < 20 IU/mL and adverse events (AEs)/lab abnormalities at Week 24. Secondary endpoints included changes in hip/spine bone mineral density (BMD), and in estimated creatinine clearance by Cockcroft-Gault ($eGFR_{CG}$).
Results: At baseline, 61%, 29% and 10% patients were CTP Class A, B, or C, respectively. After 24 weeks of TAF treatment, all patients had HBV DNA < 20 IU/mL and 81% had normal ALT. Switching to TAF resulted in increases in hip/spine BMD, decreases in bone turnover markers, and an increase in $eGFR_{CG}$ with decreases in tubular markers. TAF was well-tolerated with few having Grade 3 or 4 AEs.
Conclusions: In hepatically-impaired CHB patients, switching to TAF from TDF/other oral-antivirals maintained viral suppression and improved bone and renal safety at Week 24.

Abstract #1800

HBV S gene immune epitopes characterization on indigenous populations in Indonesia

El-Khobar K[1], Turyadi[1], Wibowo DP[1], Rasyak MR[1], Witanto B[1], Ie SI[1], Thedja MD[1], Muljono DH[1,2,3]

[1]Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [2]Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [3]Faculty of Medicine and Health, University of Sydney, Sydney, Australia

Introduction: Hepatitis B virus (HBV) genetic diversity is affected by its host genetic background. The amino acid variation on Hepatitis B surface antigen (HBsAg) may influence HBV clinical progression and manifestation and needs to be characterized. HBsAg as the main target of the host's immune response contains the immune epitope for both B cells and human leukocyte antigen (HLA) specific T cells. The HBsAg immune epitopes on indigenous populations in Indonesia have yet to be characterized.
Objectives: To characterize HBsAg immune epitopes on indigenous populations in Indonesia.
Methods: HBV sequences from 61 HBsAg-positive samples (mean age 32.8, male: 30) from two indigenous population in Jambi (n = 22) and Papua (n = 39) were aligned with respective reference sequences to identify substitution on HLA-class-I-CTL (s20-s28 and s41-s49), HLA-class-II-CTL (s61-s31), and B-cells (s124-s148) epitopes. HBV genotype were determined by neighbor-joining phylogenetic tree construction.
Results: Samples were mostly HBV/C (98.4%) with one HBV/D. HBsAg substitutions found were: sG43R, sG44E, sA45V, sT47K/A/M (HLA-class-I-CTL−s41-s49) on 40 (65.6%) samples; sA17V, sG18V, sF20S, sR204K, sL26R (HLA-class-II-CTL), 36 (59.1%); sF134L/Y, sS143T, sG145A (B-cells), 4 (8.2%); and sF20S, sR24K, sL26R (HLA-class-I-CTL−s20-s28), 2 (3.3%). Most substitutions were found on Papuan samples, except for sT47K, sF134L, and sG145A.
Conclusion: HBsAg substitutions were mostly found in HLA-class-I-CTL epitope. Despite the same HBV/C genotype, isolates from Jambi and Papua have different HBsAg substitutions, which may reflect the effect of host genetic background on HBV genetic diversity. Functional studies are needed to understand the complex interaction between HBV and the host.

Abstract #1804

Bone and renal parameters following switch to tenofovir alafenamide after 96- or 144-weeks of tenofovir disoproxil fumarate treatment in East Asians with chronic HBV

Seto Wai-Kay[1], Kao Jia-Horng[2], Lim Seng-Gee[3], Peng Cheng-Yuan[4], Byun Kwan Soo[5], Inokuma Tetsuro[6], Lee June Sung[7], Flaherty John[8], Yee Leland J[9], Jump Belinda[10], Sethi Shalini[11], Mo Shuyuan[12], Gaggar Anuj[13], Fung Scott[14]

[1]Department of Medicine, The University of Hong Kong, Hong Kong, [2]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan; Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, [3]Division of Gastroenterology and Hepatology, National University Health System, Singapore; Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, [4]Division of Hepatogastroenterology, Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan, [5]Divisions of Gastroenterology and Hepatology Oncology and Hematology, Department of Internal Medicine, Korea University Medical Center, Seoul, Korea, [6]Department of Gastroenterology and Hepatology, Kobe City Medical Center General Hospital, Kobe, Japan; [7]Department of Internal Medicine, Inje University Ilsan Paik Hospital, Goyang, Korea, [8]Gilead Sciences, Foster City, CA, USA, [9]Gilead Sciences, Foster City, CA, USA, [10]Gilead Sciences, Foster City, CA, USA, [11]Gilead Sciences, Foster City, CA, USA, [12]Gilead Sciences, Foster City, CA, USA, [13]Gilead Sciences, Foster City, CA, USA, [14]Toronto Centre for Liver Disease, Toronto General Hospital, University Health Network, Toronto, Ontario, Canada.

Background: Tenofovir alafenamide (TAF) has shown similar efficacy to tenofovir disoproxil fumarate (TDF) with better bone and renal safety in 2 Phase 3 trials through 96 weeks. After a protocol amendment, some TDF patients received 96 weeks while others received 144 weeks of TDF treatment before rolling over to open-label (OL) TAF.
Objective: To examine whether duration of prior TDF treatment impacted changes in bone and renal parameters after 48 weeks of OL TAF treatment in the subset of East Asian (EA) patients with chronic HBV.
Methods: Among 190 EAs randomized to TDF, changes in bone mineral density (BMD) by DXA scans and renal parameters were assessed from OL baseline to Week 48 following switch to OL TAF.
Results: At Week 48, mean (SD) percent changes from OL baseline in hip-BMD were + 0.92 (2.32) and + 0.79 (2.47) and in spine-BMD were + 1.52 (2.68) and + 2.27 (3.51) for DB-TDF-144wks and DB-TDF-96wks, respectively. Similarly, median (Q1, Q3) changes from OL baseline in creatinine clearance ($eGFR_{CG}$) were + 2.4 (− 4.2, + 10.8) and +3.0 (− 3.0, + 8.4) mL/min for DB-TDF-144wks and DB-TDF-96wks, respectively. Similar trends in BMD and $eGFR_{CG}$ changes were seen in non-EAs. Following switching to OL TAF, improvements in bone and renal biomarkers were also observed.

Conclusions: In EA patients who switched to TAF from TDF, improvements were seen in bone and renal parameters.

Abstract #1808 **48-week safety and efficacy of switching to tenofovir alafenamide (TAF) from tenofovir disoproxil fumarate (TDF) in chronic HBV Asian patients with TDF risk factors (RF)**

Ahn Sang Hoon[1], Kao Jia-Horng[2], Hann Hie-Won[3], Fung Scott[4], Trinh Huy[5], Nguyen Tuan Trong[6], Paik Seung Woon[7], Gaggar Anuj[8], Flaherty John[9], Yee Leland J[10], Jump Belinda[11], Sethi Shalini[12], Wu George[13], Chuang Wan-Long[14]

[1]Severance Hospital, Seoul, South Korea; [2]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan; Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, [3]Thomas Jefferson University Hospital, Philadelphia, PA, USA, [4]Toronto Centre for Liver Disease, Toronto General Hospital, University Health Network, Toronto, Ontario, Canada, [5]San Jose Gastroenterology, San Jose, USA, [6]Research and Education, Inc.,San Diego, CA, USA, [7]Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, [8]Gilead Sciences, Foster City, CA, USA, [9]Gilead Sciences, Foster City, CA, USA, [10]Gilead Sciences, Foster City, CA, USA, [11]Gilead Sciences, Foster City, CA, USA, [12]Gilead Sciences, Foster City, CA, USA, [13]Gilead Sciences, Foster City, CA, USA[14]Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan,

Background: In a recent Phase 3 study (Study 4018) in HBV patients suppressed on TDF treatment, switching to TAF demonstrated non-inferior efficacy to continued TDF with superior bone and renal safety at Week 48.
Objective: To assess the safety and efficacy of switching to TAF from TDF in patients of Asian descent with risk factors for TDF toxicity as per current EASL and AASLD guidelines.
Methods: Virally suppressed patients (HBV DNA < 20 IU/mL at screening) on TDF were randomized (1:1) to switch to TAF or continue TDF for 48 weeks in a double-blind fashion. Viral suppression and changes in bone (BMD by DXA) and renal (creatinine clearance [$eGFR_{CG}$]) parameters were assessed over 48 weeks.
Results: Among the 400 Asian patients enrolled, 288 (72%) had at least 1 TDF RF. At Week 48, similar proportions with ≥1 RF had HBV-DNA < 20 IU/mL (TAF 97%; TDF 97%) and normal ALT by 2018 AASLD criteria (TAF 76%; TDF 73%). TAF subjects with ≥1 RF had increases in $eGFR_{CG}$ compared to decreases on TDF [median (Q1, Q3) change; TAF: + 2.6 (− 2.01, 7.34); TDF: − 2.7 (− 7.56, +15.79); $p < 0.0001$)]. Among patients with ≥ 1 RF, improvements were seen in BMD for TAF vs. continued declines in TDF patients at both spine ($p < 0.0001$) and hip ($p < 0.0001$).
Conclusion: Virally suppressed Asian patients with CHB and risk factors for TDF who switched to TAF showed improved bone and renal safety while efficacy was well-maintained.

Abstract #1809

Diagnostic validity of non-invasive tests for predicting liver fibrosis stage in chronic hepatitis B patients with high HBV DNA and ALT levels

Kose Sukran

Introduction: Determining the stage of liver fibrosis in chronic hepatitis B (CHB) patients is the main step of treatment decision. However, this method is invasive, difficult, expensive and have many complication risks.
Objectives: The aim of our study was to evaluate noninvasive markers of liver fibrosis; aspartate transaminase (AST)-platelet ratio index (APRI), 4 factors based fibrosis index (FIB-4), AST-Alanine transaminase ratio (AAR), age-platelet index(API), gamma-glutamyl transpeptidase-platelet ratio (GPR), RDW-platelet ratio (RPR), King's score, Fibro quotient (Fibro Q), MPV.
Methods: In this study, 143 treatment naiv CHB patients with HBV DNA > 2000 IU/mL and ALT > ULN were included. Data were obtained retrospectively from patients' follow-up files. Liver histopathology was calculated according to Ishak scoring system. The data was evaluated by using SPSS IBM 22.0 program.
Results: Of all patients 48.25 (n:69) were female and the mean age was 44.3/years. Distribution of each stage of fibrosis were F0; 18 (12.6%), F1; 26 (18.2%), F2; 54 (37.7%), F3; 23 (16.1%), F4; 12 (8.4%), F5; 8 (5.6%), F6; 2 (1.4%). Of the 10 noninvasive tests, 6 had the power to predict ≥F2 and 7 had ≥F3. The best diagnostic test in the ≥ F2 and ≥ F3 groups was Fibro Q. FIB-4 was the best diagnostic test in the ≥F4 and ≥F5 groups. The diagnostic performances of the tests are presented in Table 1.
Conclusions: Although liver biopsy is still the gold standard in the determination of fibrosis, the use of noninvasive tests before biopsy is particularly helpful in detecting or excluding significant fibrosis and cirrhosis. In our study 30.8% (n:44) patients' fibrosis stage were 0–1, which means they had undergone unnecessary biopsy. Fibro Q and FIB-4 evaluation before biopsy may reduce unnecessary biopsy.

Diagnostic significance of noninvasive markers according to fibrosis stage in hepatitis B patients with ALT> ULN and HBV DNA> 2000 IU/mL

HBV DNA >2000 IU/mL ALT >ULN (n=143)								
	AUC ≥F2 n=99	p value	AUC ≥F3 n=45	p value	AUC ≥F4 n=22	p value	AUC ≥F5 n=10	p value
APRI	0.577	0.144	0.561	0.239	0.701	**0.003**	0.699	**0.036**
FIB4	0.695	**0.000**	0.684	**0.000**	***0.823***	**0.000**	***0.836***	**0.000**
NLR	0.572	0.171	0.618	**0.024**	0.594	0.163	0.597	0.309
GPR	0.604	0.056	0.586	0.111	0.660	**0.022**	0.664	0.101
AAR	0.362	0.008	0.389	0.033	0.340	0.017	0.329	0.072
RPR	0.628	**0.014**	0.643	**0.006**	0.736	**0.000**	0.725	**0.018**
API	0.667	**0.001**	0.667	**0.001**	0.731	**0.001**	0.754	**0.007**
KING'S	0.653	**0.003**	0.631	**0.012**	0.789	**0.000**	0.787	**0.002**
FIBRO Q	0.697	**0.000**	0.689	**0.000**	0.758	**0.000**	0.783	**0.003**
MPV	0.647	**0.005**	0.609	**0.036**	0.605	0.119	0.555	0.561

Abstract #1811

Age-related features of the prevalence of viral hepatitis B and C among acute trauma patients in Uzbekistan

Mirzaev U[1,2], Matyakubov J[1], Rakhimov A[1], Akita T[1], Ohisa M[1], Musabaev E[2], Tanaka J[1]

[1]Department of Epidemiology Infectious Disease Control and Prevention, Hiroshima University, Japan, [2] Scientific-Research Institute of Virology, Tashkent, Uzbekistan

Introduction: Uzbekistan, being an endemic country for viral hepatitis B and C, cannot yet afford to find out the real prevalence of hepatitis.
Objectives: We aimed to find out the prevalence of hepatitis B and C by age decades among acute trauma patients in Uzbekistan.
Methods: We collected medical data for all 9,656 (male 4966 and female 4690, mean age: 36.7 ± 21.1) acute trauma patients for the period 01.01.2018–01.06.2019 of the Republican Scientific and Practical Center of Traumatology and Orthopedics. The study complies with the principles of the Helsinki Declaration and approved by Hiroshima University Ethics Committee (E-1732).

Results: The prevalence of HBV and HCV among acute trauma patients is 3.0%, 3.6%, respectively. The HBV, HCV prevalence among 2582 acute trauma patients who were till 20 years old was 0.62%, 0.54%, while that among 7074 people who were over 20 years was 3.85%, and 4.68%, respectively. The age-specific HBV prevalence reached a peak of 8.96% in men at the age of 30–39 years, at the same time HCV's peak − 7.4% registered in women at the group over 60.
Discussion: The low prevalence of both hepatitis at the group 0–20 probably related to the improvement of the healthcare system in the last 20 years and implementation of vaccination against hepatitis B in Uzbekistan.

Abstract #1833

Patient Reported Outcome (PRO) of Chronic Hepatitis B Patients: case study in Dr. Kariadi General Hospital Medical Center

Delia Fransiska[1], Hesti Triwahyu Hutami[2], Hery Djagat Purnomo[2]

[1]Undergraduate Student, Faculty of Medicine, Diponegoro University, Semarang, Indonesia, [2]Lecturer, Faculty of Medicine, Diponegoro University, Semarang, Indonesia

Background/Aims: Indonesia is a country with high endemicity hepatitis B. Patients with chronic liver disease have experienced a long disease with a variety of symptoms and long-term treatment that can reduce the quality of life. This study aimed to investigate the health-related quality of life (HRQL) of chronic hepatitis B patients at RSUP Dr Kariadi Semarang.
Method: This research is a cross-sectional study that involved 100 patients consisting of 80 Chronic Hepatitis B (CHB) patients and 20 cirrhosis patients. Quality of life was measured using the Chronic Liver Disease Questionnaire (CLDQ) and the Short Form-36 (SF-36) questionnaire.
Results: The average age of the respondents is 44 years old and the highest sex was male (62%). There are 28% of research subjects have comorbid diseases and 64% of research subjects received antiviral treatment. There was an insignificant difference in the quality of life between CHB and cirrhosis, the HRQOL in the HBV group (6.19 ± 0.69) higher than cirrhosis group (6.00 ± 0.83). Antiviral gives effect on the quality of life of patients, quality life after administration of therapy was better than before the administration of therapy (5.47 ± 0.88 vs 6.15 ± 0.72) p = 0.000. The severity of the disease (Fibroscan) and the presence of comorbidities was an insignificant difference in the quality of life.
Conclusion: Antiviral therapy can contribute to improving the patient's HRQL, quality life after administration of therapy was better than before the administration of therapy.

Abstract #1848

Distribution and correlation of steatosis and fibrosis degree in chronic hepatitis b patients using transient elastography

Danes J[1], Waleleng B J[2], Tendean N[2], Gosal F[2], Rotty L[2], Winarta J[2], Waleleng A[2]

[1]Department of Internal Medicine, Faculty of Medicine Sam Ratulangi University, Manado, Indonesia, [2]Division of Gastroentero-Hepatology, Department of Internal Medicine, Faculty of Medicine Sam Ratulangi University / Prof. Dr. R. D. Kandou Hospital, Manado, Indonesia

Introduction: Studies for hepatic steatosis (HS) and chronic hepatitis B (CHB) are limited, also relationship between HS and CHB remains unclear. Coexisting HS and CHB may affecting the patient's prognosis.
Objectives: To determine the frequency of HS in CHB patients measured by controlled attenuation parameter (CAP) and to describe the distribution and correlation of fibrosis and inflammation in different steatosis grading.
Methods: The population in this study were CHB patients that visited hepatology-outpatient-clinic of Prof. dr. R. D. Kandou during November–December 2019. All patients were examined for transient elastography (Fibroscan) and CAP was calculated. Fibrosis was staged on a 0–4 scale: F0, no fibrosis; F1, portal fibrosis without septa; F2, portal fibrosis and few septa extending into lobules; F3, numerous septa extending to adjacent portal tracts or terminal hepatic venules and F4, cirrhosis. Steatosis grading was assessed as S0 (no steatosis, CAP 0–247 dB/m), S1 (mild steatosis, CAP 248–267 dB/m), S2 (moderate steatosis, CAP 268–279 dB/m) and S3 (severe steatosis, CAP ≥ 280 dB/m).
Results: A total of 44 CHB patients were included, the mean age was 43.36 ± 12.63 years old and most patients were male (27 patients, 61.3%). Total of 10 patients (22.7%) were diagnosed as severe fibrosis (F3–F4). HS was found in 12 patients (27%) of which 5 patients (11.36%) were diagnosed as severe steatosis (S3). There are no significant correlation between HS and fibrosis grading (p = 0.892, r = 0.21).
Conclusions: HS and fibrosis were common in CHB patients. Assessment using Fibroscan yielding discrepancy between HS and fibrosis grading.

Abstract #1853

Comparison of FIB-4 and APRI scoring systems for liver fibrosis staging in HBeAg-negative chronic hepatitis B

Fehmi Tabak

Introduction: A liver biopsy is a gold standard for staging liver fibrosis in chronic hepatitis B (CHB). However, some serum fibrosis markers may be useful as non-invasive alternative methods.
Objectives: To compare the utility of fibrosis-4 score (FIB-4) and AST-to-platelet-ratio-index (APRI) in liver fibrosis and the effects of antiviral therapy on these markers in patients with HBeAg negative CHB.
Methods: In this retrospective study, HBeAg negative CHB patients who were treated with anti-viral drugs for at least three years between 2005 and 2019 were included.
Results: A total of 200 patients with a mean age of 44 ± 12 and 64% male were evaluated. Twenty-seven patients (13.5%) had liver cirrhosis. Mean duration of treatment was 74.2 ± 26.9 month (range 36–168). The area under receiver-operating characteristic curves (AUROC) for detecting cirrhosis were: FIB-4 = 0.86 (0.77–0.95) and APRI = 0.75 (0.66–0.85). The use of APRI and FIB-4 in combination considerably predicted cirrhosis (sensitivity 67%, specificity 90%). The AUROC for detecting modified Histologic Activity Index F2, F3 and F4 were: FIB-4 = 0.34 (0.26–0.42) and APRI = 0.36 (0.28–0.44), FIB-4 = 0.53 (0.42–0.63) and APRI = 0.50 (0.40–0.61), FIB-4 = 0.50 (0.37–0.63) and APRI = 0.50 (0.37–0.63) respectively. APRI and FIB-4 scores after at least 3 years of treatment decreased 0.676 ± 1.113 ($p < 0.001$) and 0.51 ± 0.75 points ($p < 0.001$) compared on baseline. APRI and FIB-4 sensitivity for the diagnosis of cirrhosis after antiviral treatment were 7.5% and 48% respectively.

Conclusion: This study shows that FIB-4 score is more reliable than APRI score for the diagnosis of cirrhosis. However, these markers especially APRI should not be used for the diagnosis of cirrhosis in patients under antiviral treatment.

Abstract #1876

The regression of liver fibrosis during antiviral treatment, assed by transient elastography in chronic hepatitis B patients with and without liver cirrhosis

Cokorde Istri Yuliandari Krisnawardani K.[1], I Dewa Nyoman Wibawa[2], I Ketut Mariadi[2], I Gde Somayana[2], I Gusti Agung Suryadarma[2]

[1]Division of Gastroenterohepatology, Department of Internal Medicine, Faculty of Medicine, Udayana University/ Udayana University Hospital, Badung, Bali, Indonesia, [2]Division of Gastroenterohepatology, Department of Internal Medicine, Faculty of Medicine, Udayana University/Sanglah Hospital, Denpasar, Bali Indonesia

Introduction: Antiviral treatment in chronic hepatitis B (CHB) patients lead to suppression of viral replication, reduce inflammation, and regression of liver fibrosis.
Objective: This study aimed to assess the liver fibrosis regression during antiviral treatment in CHB patient with and without liver cirrhosis.
Methods: CHB patients who underwent two repeated transient elastography (TE) from January 2018 until December 2019 were included in this study. The average interval measurement is about 6 month from first TE, and the result were classified according to Metavir (F0-F4) score. Quantitative differences between two measurement were analyze. All subject were treated with antiviral (nucleos(t)ide analog). The fibrosis regression were compared between 2 groups (cirrhosis and non-cirrhosis). The factors that influence the regression of liver fibrosis were identified.
Result: Ninety five subjects with CHB were included in this study, 35 subjects were in cirrhosis group, and 60 subjects were in non-cirrhosis group. Thirty eight (40%) from all subjects had reduced liver stiffness, 50 (52.6%) had neither reduced liver stiffness nor increased liver stiffness (stagnant), but 7 (7.5%) subjects had liver stiffness progression ($p \leq 0.001$). Liver fibrosis regression were greater non cirrhosis group (43.8%), compared with cirrhosis group (27.5%) ($p = 0.03$). In univariate analysis showed age, gender, and duration of antiviral were related with regression of liver fibrosis, however these parameter did not reach a statistical significance in multivariate analysis.
Conclusion: Liver stiffness changes occurred in CHB patients receiving antiviral treatment. Although liver fibrosis regression was found greater in non-cirrhosis group, the regression also occurs in cirrhosis group.

Abstract #1890

Value of liver function test in predicting liver stiffness in patients with chronic hepatitis b infection: a preliminary study

Dwijo Anargha Sindhughosa[1], I Dewa Nyoman Wibawa[2], I Gusti Agung Suryadarma[2], I Ketut Mariadi[2], Gde Somayana[2], Cok Istri Yuliandari[2]

[1]Internal Medicine Resident, Faculty of Medicine of Udayana University/Sanglah Hospital, Denpasar, Bali, Indonesia, [2]Gastroenterohepatology Division, Faculty of Medicine of Udayana University/Sanglah Hospital, Denpasar, Bali, Indonesia

Introduction: Liver stiffness is an excellent noninvasive approach to determine liver fibrosis and cirrhosis. It closely related with other complication, e.g. portal pressure or esophageal varices. However, the availability of the device remains limited, particularly in rural area.
Objective: This study aimed to determine the value of liver function tests (ALT, AST, INR, albumin, total bilirubin and thrombocyte) in predicting liver stiffness in patients with chronic hepatitis B infection.
Methods: This was a cross-sectional study involving a total of 30 patients with chronic hepatitis B infection, aged more than 18 years. Patients with body mass index (BMI) < 25 kg/m^2, diabetes mellitus, malignancy, chronic kidney disease (CKD) and human immunodeficiency virus (HIV) infection were excluded. Liver stiffness measured using transient elastography. Linear regression analysis was employed to obtain the formula to predict liver stiffness.
Results: This study involving 30 patients with mean age of 47.63 $\pm$ 9.68 years. All variables were transformed to normalize the data, except for thrombocyte. Bivariate correlation analysis obtained that AST, INR, albumin, bilirubin and thrombocyte were correlated with liver stiffness ($p < 0.05$), except for ALT ($p = 0.052$). All variables were included in multivariate analysis using linear regression. Analysis with linear regression obtained the following formula to predict liver stiffness: log liver stiffness = $0.923 + 0.288 \times \log$ ALT $- 0.004$ x exp albumin ($R^2 = 50.2\%$). All criteria for linear regression were fulfilled.
Conclusion: From several liver function test available, albumin and ALT level may benefit in predicting the measurement of liver stiffness.

Abstract #1908

Correlation between Fibroscan, Fibrosis-4 (FIB-4), De Ritis Ratio, and AST Platelet Ratio Index (APRI) to Predict Liver Fibrosis in Hepatitis B Patients, Sanglah Hospital 2019

WE Radityo[1], IDN Wibawa[2], IGA Suryadarma[2], IK Mariadi[2], G Somayana[2]

[1]Residency of Internal Medicine, Faculty of Medicine Udayana University / Sanglah Hospital, Denpasar, Bali, Indonesia, [2]Gastroentero Hepatology Department / Internal Medicine Faculty of Medicine Udayana University, Sanglah Hospital, Denpasar, Bali, Indonesia

Introduction: Chronic Hepatitis B (CHB) is recognized as a cause of chronic liver disease. The assessment of liver fibrosis is essential for predicting the prognosis and outcomes of chronic liver disease such as liver cirrhosis and hepatocellular carcinoma. Alternative methods of non-invasive laboratory and radiological testing for the assessment of liver fibrosis have advantages such as user-friendly technique, with immediate results, and high patient acceptance.
Objectives: This study is aimed to find correlation between Fibroscan, FIB-4, APRI, and De Ritis ratio in assessing liver fibrotic of CHB patients in Sanglah Hospital.
Method: This is an observational (analytic cross-sectional) study involving CHB patients who underwent Fibroscan in outpatient setting in Sanglah Hospital Bali Indonesia. Laboratory result of patients from hospital database included in this study. The correlation test between Fibroscan, FIB-4, APRI, and De Ritis ratio were analyzed by statistical program; and $p \leq 0.05$ was considered as statistically significant.
Results: In this study, 80 patients were analyzed including 54 (67.5%) males and 26 (32.5%) females. The mean age was 43.1 years (SD: 12.0, range: 19–73). The mean stiffness score was 6.37 kPa. There

was weak significant correlation between Fibroscan and FIB-4, and Fibroscan and APRI score. The strong significant correlation was found between FIB-4 and APRI score. Meanwhile there was no significant correlation from De Ritis ratio and fibroscan result.
Conclusion: In this study, Fibroscan, FIB-4, and APRI score has a correlation in predicting liver fibrosis of CHB patients.

Abstract #1922

Anti-HBs level and its correlation with HBV infection profile in Indonesian population

El Khobar K[1], Turyadi[1], Wibowo DP[1], Rasyak MR[1], Witanto B[1], Ie SI[1], Thedja MD[1], Muljono DH[1,2,3]

[1]Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [2]Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [3]Faculty of Medicine and Health, University of Sydney, Sydney, Australia

Introduction: Antibody to hepatitis B virus (HBV) surface antigen (anti-HBs) may appear as the result of Hepatitis B vaccination and/or resolved infection. However, anti-HBs-positive alone does not guarantee for safe blood, since antibody to HBV core antigen (anti-HBc) and HBV DNA can still be detected in these samples. Since anti-HBs level may decline overtime, but increase by repeated infection, its level could be correlated with HBV infection profile, especially in endemic areas.
Objective: To evaluate anti-HBs level correlation with HBV infection profile in Indonesian population.
Methods: We screened 1417 apparently healthy subjects from several populations in Indonesia (mean age 28.89 ± 13.77, 41.92% male) for HBsAg, anti-HBs, and anti-HBc. The samples were classified into anti-HBs-positive/anti-HBc-positive and anti-HBs-positive/anti-HBc-negative groups. The correlations between anti-HBs titre, serological profile, gender, and age were analyzed.
Results: HBsAg, anti-HBs, and anti-HBc prevalence was 16.44%, 29.64%, and 49.68%, respectively. Anti-HBs-positive samples were mostly female (59.62%), mean age 27.35 ± 13.37, 5.23% HBsAg-positive, 70.31% anti-HBc-positive, and 23.28% HBV DNA-positive. Anti-HBs-positive/anti-HBc-positive group were slightly older 28.88 ± 13.74 vs 23.80 ± 11.82 ($p = 0.0002$), had overall higher anti-HBs titres ($p = 0.1998$), with significant correlation in the 500–1000 mIU/mL anti-HBs-titre group ($p = 0.0012$), and correlated with HBV DNA ($p < 0.0001$).
Conclusion: High anti-HBs titre (500–1000 mIU/mL) was correlated with anti-HBc and HBV DNA positivity in asymptomatic subjects. Increasing trends of anti-HBs and anti-HBc prevalence with age could reflect horizontal transmission. Additional HBV testing would be required for blood products originating from older subjects (> 28 years old) with high anti-HBs titres and anti-HBc-positive to ensure blood transfusion safety in HBV endemic areas.

Abstract #1935

Correlation of TGF- β1 and Non-invasive fibrosis test

IK Mariadi[1], PDW Wiguna[1], IDN Wibawa[1]

[1]Gastroenterohepatology Division, Department of Internal Medicine, Faculty of Medicine, Udayana University, Sanglah General Hospital, Bali, Indonesia

Introduction: TGF-β as a profibrotic mediators was produced by Macrophages. TGF-β is responsible for activation -transdifferentiation of quiescent hepatic stellate cells to a myofibroblast (MFB) phenotype. MFBs are the principal source of extracellular matrix protein accumulation and prominent mediators of fibrogenesis. TGF-β1 has essential roles in liver physiology and pathology and contribute to all stages of disease progression: from liver injury through inflammation, fibrosis, cirrhosis and HCC. In this study aim to know the correlation of TGF-β1 with the non-invasive fibrosis test.
Methods: We performed a cross sectional analytic study in chronic hepatitis B patients in Sanglah General Hospital. The sample was patients with mild, moderate and severe fibrosis base on Transient Elastography. We correlated TGF-β1 with Transient Elastography (TE), aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio (AAR), AST-to-platelet ratio index (APRI), and fibrosis-4 (FIB-4) score.
This study was approved by the Ethics Commission of the Medical Faculty of Udayana University.
Results: In this study we involved 80 chronic hepatitis B patients, 54 (67.5%) was male and the rest 26 (32.5%) was female. The metavir score base on TE were F1 (41 patients), F2 (28 patients), and F3 (11 patients). The mean of AAR was 1.17 ± 0.96, APRI was 0.3 ± 0.14, FIB4 was 0.13 ± 0.12.
Results of spearmen correlation test, there was significant negative correlation between TGF-β1 with APRI score and FIB4 score, with $r = -0.4$; $p < 0.001$, $r = -0.42$; $p < 0.001$, consecutively. But no significant correlation between TGF-β1with TE and AAR.
Conclusions: There is a negative correlation between TGF-β1 with APRI and FIB4 score.

Abstract #1936

Negative relationship between hepatic steatosis and high hepatitis B viral load:A case-control study

Huang Yan[1], Cao Zhujun[1], Gan Qinyi[1], Xie Qing[1]

[1]Department of Infectious Diseases, Rui-Jin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Introduction: The potential interaction between chronic hepatitis B (CHB) and nonalcoholic fatty liver disease (NAFLD), two prevalent liver diseases worldwide, is still controversial. We investigated the influencing factor of histologically proven hepatic steatosis in treatment-naive CHB patients without excessive alcohol intake.
Objectives: Consecutive CHB patients who underwent liver biopsy from January 2009 to December 2018 were included and available clinical and biopsy data were recorded.
Methods: Percutaneous liver biopsy was performed using a 16G Temno needle. Liver histology was assessed by two pathologists who specialized in hepatopathology (XJC and WHF) without knowledge of the clinical data. The histopathology results were reported in Scheuer's scoring system for inflammation grades (G0–G4) and fibrosis stages (S0–S4).
Results: Fatty liver(hepatic steatosis ≥ 5%) was histologically proven in 392 patients (29.1%) among a total of 1349 patients.Of these, 392 steatotic patients were matched with non-steatotic controls in a 1:1 ratio by age and gender. The mean age of the 784 patients (73.21% male) was 40.4 years.Median serum HBV DNA was lower in steatotic individuals than in controls (5.0 vs 5.3 log IU mL-1 , $P < 0.05$). The inverse relationship between viral load and steatosis remaining significant in multivariate analysis (odds ratio 0.891, 95% CI 0.816–0.972, $P < 0.05$).With increased steatosis severity,median HBV DNA levels decreased (5.20 and 3.9 log IU mL-1 in mild steatosis (5% ≤ hepatic steatosis < 33%) and severe steatosis(hepatic steatosis ≥ 33%), respectively, $P < 0.05$).There is no relationship between steatosis and advanced fibrosis (S > 3) (P = 0.16), as well as

the association between steatosis and obvious inflammation(G ≥ 2) (P = 0.16).
Conclusion: Increasing steatosis was independently associated with lower serum HBV DNA levels, suggesting its negative relationship between hepatic steatosis and high viral replication.

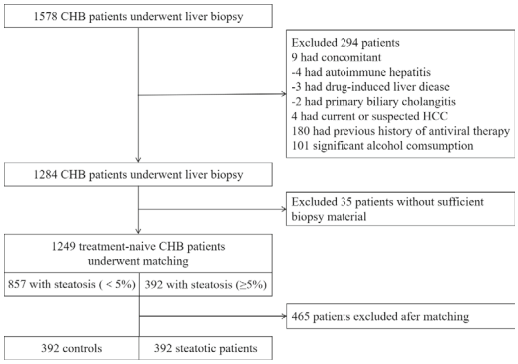


Figure 1. Patients recuitment and matching. HCC,hepatocellular carcinoma;significant alcohol consumption: defined as alcohol intake of ≥ 20 g per day in men and ≥ 10 g per day in women.

Abstract #1940

Pregnant woman with HbSAg positive: how should we manage? A systematic review

Pratama, A.A[1], Christiandari, Y[2]

[1]Medical Doctor in Prima Husada Hospital, Sukorejo, East Java, Indonesia, [2]Internist in Prima Husada Hospital, Sukorejo, East Java, Indonesia

Introduction: Around 2 billion people are suffered from chronic hepatitis and 240 millions among them are pregnant. Data from RISKESDAS in 2014 showed that the highest number of pregnant women with hepatitis in Indonesia was found in West Papua, South Sulawesi and East Java. HBV DNA was detected in maternal serum with the percentage of 29.68% while in placenta is 21.67% and 10.93% in umbilical cord. The success rate of prophylaxis reached 95% and the remaining 5% failed, especially in Asia.
Objective: This systematic review aimed to determine the best time for providing prophylactic and breastfeeding.
Method: This systematic review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyzes (PRISMA) protocol guideline. Each author conducted studies prospecting during November–December 2019 through several databases. Data extraction from studies that fulfilled inclusion and exclusion criteria was carried out using standard tables developed by the authors.
Result: HBV DNA which exceeds 200,000 especially in third trimester should receive medication although it is more influential among Mongoloid compared to American and Caucasian. Prophylaxis is recommended, principally to those who want to breastfeed but the use of Tenovofir or Lamivudine must be noted while Telbivudine is safe. The best time for medication is between 28 and32 weeks and can be continued until 6 months, particularly in patients with HBeAg positive.
Conclusion: Mother to child transmission can be prevented by providing category B medication between 28 and 32 weeks of pregnancy and breastfeeding can still be given, especially by those who have received prophylaxis.

Abstract #1945

HBV core promoter and precore regions study in Indonesian chronic hepatitis B patients' natural history revealed mutational hotspots

Turyadi[1,2], Witanto B[1], Rasyak MR[1], Wibowo DP[1], Daud NAS[2], Ie SI[1], Parewangi AML[2], El-Khobar K[1], Thedja MD[1], Massi MN[2], Muljono DH[1,2,3]

[1]Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [2]Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [3]Faculty of Medicine and Health, University of Sydney, Sydney, Australia

Introduction: Based on the host-virus complex interaction, the natural history of chronic hepatitis B (CHB) can be divided into 4 phases: immune tolerant (IT), immune clearance (IC), low/non-replicative (LR) and e-negative hepatitis (ENH). Mutation in core promoter (CP) region may affect CHB progression since it plays important role in hepatitis B virus (HBV) replication. CP mutation may also affect both precore (PC) and pregenome RNAs production, vital for HBeAg production and viral replication, respectively.
Objectives: To identify mutational hotspots in HBV CP and PC regions in CHB patients.
Methods: 549 CHB patients (69.4% male, median age 43.68 ± 13.27) were recruited and sorted into CHB phases based on HBeAg serostatus, viral load, and ALT level. HBV region (nt1600–1900) were directly sequenced and analyzed. Predominant nucleotide was used as reference, with 10% cut-off for each hotspot.
Results: Twenty-five hotspots were identified; two mutations (A1686C, G1721A) associated with increased viral load, three (G1626M, A1686C, C1799G) with increased ALT, two (G1626M and G1899A) with increased AST, and five (C1631T, A1686C, T1753V, A1846Y, G1896A) with HBeAg status difference. Specifically, A1762T/G1764A double mutations had significant impact on the entrance from IT to IC (odds ratio [OR] 2.78 (95% confidence interval [CI] 1.58–4.91), $p = 0.0002$), and A1686C, A1752B, and G1896A on HBeAg seroconversion from IC to LR (OR 10.89 (2.06–111.40), $p = 0.001$; 3.01 (1.06–10.57), $p = 0.036$; and 2.596 (1.39–4.91), $p = 0.0006$, respectively). We found mutation A1686C that has never been associated with CHB progression.
Conclusions: This study discovered 25 CP/PC hotspots with several mutations that may influence the natural history of CHB.

Abstract #1946

Association of tumor necrosis factor-α and interleukin-10 promoter gene polymorphisms with chronic hepatitis B natural history progression in indonesian population

Turyadi[1,2], Witanto B[2], Rasyak MR[2], Wibowo DP[2], El-Khobar K[2], Parewangi AML[3], Thedja MD[2], Yusuf I[3], Massi MN[3], Patellongi I[3], Syafruddin[2,3], Muljono DH[1,2,3]

[1]Postgraduate School, Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [2]Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [3]Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [4]Faculty of Medicine and Health, University of Sydney, Sydney, Australia

Introduction: Based on the host-agent interaction, the natural history of chronic hepatitis B (CHB) is categorized into four phases: immune tolerant (IT), immune clearance (IC), low replicative (LR), and

HBeAg-negative immune reactivation (ENH). CHB progression is a complex process with often unpredictable outcomes. Single nucleotide polymorphisms (SNPs) at promoters' region of tumor necrosis factor-alpha (TNF-α) and interleukin-10 (IL-10) had been associated with HBV susceptibility and worsen prognosis.
Objectives: To assess the association between TNF-α and IL-10 SNPs with CHB progression in Indonesian patients.
Methods: TNF-α-308G/A and IL-10-592A/C SNPs from 249 CHB patients (mean age: 42 ± 13.267; male/female: 182/67) (IT:67, IC:27, LR:88, ENH:67) were detected using polymerase chain reaction with restriction fragment length polymorphism (PCR-RFLP). The associations of SNP with CHB progression were presented in odds ratio (OR) value with 95% confidence interval (CI) using ordinal logistic regression analysis with age as covariates.
Results: The GA and AA genotypes of TNF-α-308 were infrequently found and were not further analyzed. For IL10-592A/C, there was no significant difference between genotype AA (reference), AC, and CC with CHB progression ($p > 0.05$). However, the odds of genotype AC to develop advanced CHB phase was 2.385 (95% CI 1.02–5.66, Wald $x^2 = 3.991$, $p = 0.046$) times higher compared to genotype CC.
Conclusion: Overall, TNF-α-308G/A and IL-10-592A/C SNPs are not good predictors towards the CHB natural history progression in Indonesian patients. However, caution needs to be taken for genotype AC with the highest probability to develop advanced CHB. Further study with larger sample size is warranted.

Abstract #1980

Evaluation of prothrombin index in chronic hepatitis B patients

Kose Sukran

Introduction: Prothrombin index (PI) is one of the early indicators of liver damage and reflects lung synthesis capacity. There are studies in the literatüre indicating that it can be used to predict advanced liver failure.
Objectives: The aim of this study was to investigate the association of PI with other liver function tests and to determine whether it can be used to predict significant liver fibrosis or not.
Methods: A total of 547 treatment naive patients aged 18 years or older with chronic hepatitis B were included. Patients with comorbidities were excluded from the study. Laboratory results were retrospectively reviewed. Liver biopsy results was calculated according to Ishak scoring system. SPSS 22.0 software was used for statistical analysis.
Results: Of the patients included in the study, 284 (51.9%) were female and the median age was 41/year. The number of patients according to the stages of fibrosis were F0, 94 (17.2%); F1, 144 (26.3%); F2, 218 (39.9%); F3, 55 (10.1%); F4, 21 (3.8%); F5, 13 (2.4%); F6 was 2 (0.4%). Correlation test showed significant correlation with PI and age, AST, ALT, INR, Platelet, HBV DNA, HBsAg quantitative levels ($p < 0.05$) (Table 1). In ROC analysis, PI could predict significant fibrosis (≥ F3) (AUC: 0.600, p: 0.034).
Discussion: PI is included in the calculations of noninvasive indirect tests such as PGA index and Fibrometer which are used to predict liver fibrosis. In our study, ROC analysis showed that PI alone is sufficient to predict significant fibrosis (≥F3).
Conclusion: Prothrombin index is easily applicable, inexpensive method that can be used to predict liver fibrosis stage.

Table: Correlation Analysis of Prothrombin Index with Age, AST, ALT, GGT, HBV DNA, HbsAg Quantitative, Fibrosis and Histological Activity Index

	P value	Correlation coefficient
Age	**0.000**	0.232
AST	**0.002**	-0.129
ALT	**0.000**	-0.162
ALP	0.065	-0.082
GGT	0.527	-0.041
INR	**0.000**	-0.896
Platelet	**0.039**	0.089
HBV DNA	**0.010**	-0.161
HbsAg Quantitative	**0.004**	-0.310
Fibrosis	0.786	-0.012
Histological activity index	0.169	0.59

Abstract #1981

Effectiveness of community-based health education for improving knowledge of viral hepatitis b infection among reproductive aged adults in Peri-urban Yangon, Myanmar

Htoo, Eindra[1], Min, Myat Sandi[1] Htut, Hnin Nandar[2], Whelan, Rachel[1], Richards, Adam[3], Shein, Htun Aung[2], Win, Su Yee[2], Kyi, Khin Pyone[4], Swe, Win Win[5], Thura, Si[1]

[1]Community Partners International, Yangon, Myanmar, [2]B.K.Kee Foundation, Yangon, Myanmar, [3]University of California at Los Angeles, United States of America, [4]Myanmar Liver Foundation, Yangon, Myanmar, [5]Liver Unit, North Okkalapa General Hospital, Yangon Myanmar

Introduction: Although Myanmar has the highest rate of perinatal hepatitis B virus (HBV) infection in Southeast Asia, HBV knowledge remains low. This study assesses the impact of health education (HE) sessions delivered by community health workers (CHWs) on knowledge of maternal-to-child transmission of HBV among reproductive aged adults in a peri-urban area of Yangon.
Methods: Adults attending a 2-h HE session completed a 15-item questionnaire before and after the HE session. Factors associated with improved HBV knowledge, (at least 80% correct answers) were assessed using simple and multiple linear and logistic regression.
Result: Among total 544 participants, 413 completed the questionnaires. Most respondents were female (91.5%), married (77.5%), and had not graduated beyond middle school (61.1%). Before the HE session the mean knowledge score was 71.5%, and was associated with educational attainment and ward of residence. Knowledge improved among all participant subgroups ($p < 0.001$), and the proportion of respondents who answered at least 12 questions (80%) correctly doubled, from 40.4 to 81.8%. In crude and adjusted models, knowledge improved most among those with a primary education or less, attenuating though not eliminating the educational gradient in knowledge of HBV transmission.
Conclusion: Community education sessions can improve HBV knowledge among peri-urban residents of Yangon. Although individuals with the least education may benefit most, additional effort may be required to eliminate education-related inequities of health knowledge.

Abstract #1989

Correlation between platelet-lymphocyte ratio and degree of liver fibrosis in chronic hepatitis B patients

Ni Made Anggreni Yudhawati[1], I Dewa Nyoman Wibawa[2], I Gusti Agung Suryadarma[2], I Ketut Mariadi[2], Gde Somayana[2], Cok Istri Yuliandari[2]

[1]Internal Medicine Resident, Faculty of Medicine of Udayana University/Sanglah Hospital, Denpasar, Bali, Indonesia,

[2]Gastroenterohepatology Division, Faculty of Medicine of Udayana University/Sanglah Hospital, Denpasar, Bali, Indonesia

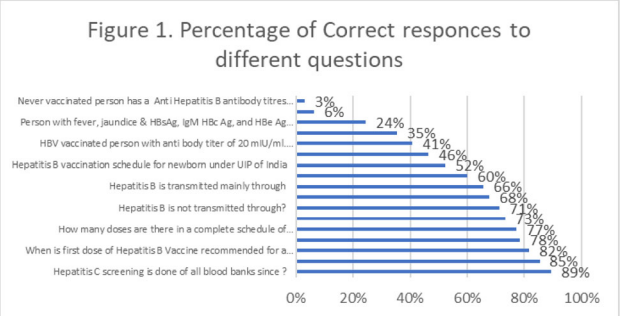
Introduction: Chronic hepatitis B is a disease that involves interactions between the hepatitis B virus, hepatocytes, and host immune conditions. Inflammation plays a role in the severity of chronic hepatitis B. Several studies have shown the platelet-lymphocyte ratio as a marker of inflammation that can be used as a predictor of severity in several diseases, including liver cancer and chronic hepatitis C. The role of the platelet-lymphocyte ratio in chronic hepatitis B is currently unclear and the data are still limited.
Objective: This study aimed to evaluate the correlation of platelet-lymphocyte ratio with severity of liver fibrosis in patients with chronic hepatitis B.
Methods: In this analytic cross-sectional study we included chronic hepatitis B patients who underwent outpatient care at the Gastroenterohepatology clinic at Sanglah Hospital. All subjects underwent investigations of a complete blood and fibroscan examination to determine degree of liver fibrosis. The Spearman correlation test was used to determine the relationship of the platelet-lymphocyte ratio with the degree of liver fibrosis.
Results: This study consisted of 73.6% men and 26.4% women. The Spearman correlation test obtained a significant negative correlation between the platelet-lymphocyte ratio and the degree of liver fibrosis ($r = -0.342$, $p < 0.01$).
Conclusion: This study obtained a negative correlation between the platelet-lymphocyte ratio and the degree of liver fibrosis. This result indicates the platelet-lymphocyte ratio may be used as a predictor of the severity of liver fibrosis in patients with chronic hepatitis B.

Abstract #2053

Piloting practical innovations to increase the efficacy of traditional awareness modalities for general population for spreading awareness about hepatitis B and C infections

Neeraj Raizada, Ashwini Kedar, Anil Agarwal, Sami Farooqui, Jyoti Agarwal, Dipti Katyal, Deepti Dubey, Ekta Gupta, Shiv K. Sarin

Introduction: Despite significant prevalence of hepatitis B and C in India, awareness about it is very low amongst the general population. Impact of traditional methods for creating awareness is low since as they are largely unappealing to masses. Innovations in engaging people to improve awareness are crucial to curtail this silent epidemic.
Objectives: Piloting innovative strategies for increasing awareness amongst general population
Methodology: A massive awareness drive was undertaken at Delhi Metro Stations from 1st to 10th Dec, 2019, using traditional modalities of awareness - display of banners, brochure distribution & interpersonal-communication. For better engagement of commuters an 'online quiz' on hepatitis B&C was organized, with incentives for participation and for achieving high scores. We assessed cost-effectiveness and acceptability of this intervention over and above traditional interventions.
Results: 5110 commuters were engaged out of which 800 (15.6%) took online quiz. The acceptability was assessed in terms of uptake rate of quiz, which was quite high-one respondent every 2.25 min. While respondents could answer most basic questions on the subject correctly, incorrect responses largely included more complex aspects of HBV/HCV care. Overall, 63% answered > 50% questions correctly and 38% scored > 80%. Average cost of reaching one person by traditional methods was found to be $0.5 and incremental cost of $0.8 per person for implementing quiz.
Conclusions: The quiz provided useful insights into outcome of interventions in increasing the awareness on the subject at a nominal additional cost, an aspect which could not be assessed for traditional interventions. Adopting cost-effective innovations for effective engagement may garner better results in generating awareness.



Abstract #2058

Curtailing the silent epidemic of Hepatitis B & C: experiences in implementation of an innovative 'Call to action' initiative

Neeraj Raizada, Ashwini Kedar, Anil Agarwal, Dipti Katyal, Jyoti Agarwal, Sami Farooqui, Deepti Dubey, Reshu Agarwal, Ekta Gupta, Shiv K. Sarin

Introduction: HBV and HCV infections are silent epidemics as infected people remain asymptomatic for a long time. Thus, > 80% of infected remain unaware about their infection and often seek care when they become symptomatic at advanced stage of liver disease. Strategies to end this silent epidemic include, 'increased'—awareness, voluntary screening for HBV & HCV and vaccination, through community action. To address these aspects a call to action initiative was initiated.
Objective: Implementation of a 'call to action' initiative to promote voluntary screening for HBV & HCV and HBV vaccination
Methodology: Series of awareness camps on HBV & HCV were conducted, which included awareness talk and free voluntary HBV vaccination and HCV & HBV screening for participants. Participants were also encouraged to take a "Pledge" to get their family screened and vaccinated on their own initiative and also generate community dialogue. Outcome of the initiative was assessed by self-administered questionnaire which was randomly administered to approx. 20% participants at time of second/third dose of HBV vaccination.
Results and Conclusion: This initiative enrolled 4671 participants from Nov, 2018 to 19, of which > 80% availed free screening and vaccination. The initiative was able to generate a community action with > 55% participants getting their family members screened and vaccinated; > 80% engaged in community dialogue on HBV and HCV.
This innovative 'Call to action' wherein awareness activity was complemented by free voluntary screening and vaccination was able to "catalyse" significant community action. Concerted efforts at a larger scale may lead to community movement for voluntary screening and vaccination.

Table: Outcome indicators for the initiative (Data collected from randomly selected 769 participants)

	N= 769	Percentage (%)
Participants who voluntarily got their family members screened for hepatitis B and C infection	425	55.3
Participants who voluntarily initiated HBV vaccination for their family members	437	56.8
Participants who initiated a dialogue about HBV and HCV in Community with family and friends	650	84.5
Participants who felt that they have a better understanding of HBV & HCV after the intervention	724	94.1

Abstract #2085

Correlation between Aminotransferase to Platelet Ratio Index (APRI) Score, FIB-4, and Red Distribution Width to Platelet Ratio (RPR) with Degree of Liver Fibrosis in Patients with Chronic Hepatitis B Infection.

A. A. Ketut Yunita Paramita[1], I Dewa Nyoman Wibawa[2], I Gusti Agung Suryadarma[2], I Ketut Mariadi[2], Gde Somayana[2], Cok Istri Yuliandari[2]

[1]Internal Medicine Resident, Faculty of Medicine of Udayana University/Sanglah Hospital, Denpasar, Bali, Indonesia, [2]Gastroenterohepatology Division, Faculty of Medicine of Udayana University/Sanglah Hospital, Denpasar, Bali, Indonesia

Introduction: Although liver biopsy is a golden standard to determine degree of liver fibrosis, this method is invasif. We need non invasif diagnostic tests to predict degree of liver fibrosis to optimize the management of chronic hepatitis B infection.
Objective: This study aimed to evaluate the correlation between APRI score, FIB-4, and RPR to degree of liver fibrosis according to transient elastography liver stiffness measured by FibroScan.
Methods: A total of 48 patients with chronic hepatitis B infection were included in this study. Patient with chronic kidney disease, malignancy and coincide with hepatitis C and HIV infection were excluded. For each patient, the scores was calculated using the following formula: APRI = [(AST level/ULN)/platelet count (10^9/L)] × 100, FIB-4 = [age × AST/platelet count (10^9/L) × $\sqrt{}$ALT] and RPR = [RDW: platelet count (10^9/L)].
Result: Of the 48 patients, 23 patients with mild-moderate fibrosis (metavir F0–2) and 25 patients with severe fibrosis (metavir F3-4) were found. There are significant relationships between APRI score ($p < 0.001$, $r = 0.55$), FIB-4 ($p < 0.001$, $r = 0.56$), and RPR ($p = 0.006$, $r = 0.39$) with severe fibrosis. Either APRI score, FIB-4, and RPR may predict severe fibrosis in patients with chronic hepatitis B infection (cut off for APRI score: 1.15, sensitivity 68%, specificity 69.6%. Cut off for FIB-4: 2.46, sensitivity 68%, specificity 69.6%. Cut off for RPR: 0.07, sensitivity 72%, specificity 73.9%).

Abstract #2093

Thrombocytopenia associated with non cirrhotic hepatitis B

Darmayani A.[1], Pramana T.Y[2], Kusnanto P[2]

[1]Student of Internal Medicine Subpecialist Education Program, Dr. Moewardi Hospital / Medical Faculty of UNS, Surakarta-Indonesia,[2]Staff of Internal Medicine Subpecialist Education Program, Dr. Moewardi Hospital / Medical Faculty of UNS, Surakarta-Indonesia

Introduction: Trombocytopenia is a well recognized complication of infections, including those from hepatotropic viruses. The pathogenesis of thrombocytopenia in non-cirrhotic hepatitis B patients is not fully understood.
Case illustration: A 58-year-old woman reported history of hepatitis B and demonstrated no stigmata of liver cirrhosis in physical examination. Blood count showed low platelet (22.000 cells/ml) with normal haemoglobin and total leucocyte. Liver function tests such as hemostasis and protein electrophoresis were normal. Transaminase enzymes were normal. Bone marrow aspiration revealed elevated of thrombopoetic system as a perifer response with adequate number of megakaryocytes. Viral marker showed positive HbsAg with negative HbeAg, negative of anti-HCV and HIV. HBV DNA was 2.840 IU/ml. Platelet antibody was negative. Liver and spleen in abdominal ultrasound were still normal. Fibroscan was 4.9 kPa. Esophago-gastro-duodenoscopy showed antral gastritis without *Helicobacter pylori* infection.
Discussion: Chronic infections, such as HCV, HIV and *Helicobacter pylori* have been linked to secondary immune thrombocytopenia, in which antibodies targeting the microorganisms cross-react with platelet glycoproteins (GP), resulting in accelerated platelet clearance. In HBV infected cirrhotic patients, antibody response to GPIIb-IIIa has been also suggested as one of the mechanism of thrombocytopenia. Furthermore, abnormal platelet kinetics and platelet-specific GP have been detected in early stages of hepatitis B related liver disease. However, how HBV induces thrombocytopenia in this non-cirrhotic patient can not to be determined yet, especially after platelet antibody was negative.
Conclusion: Based on the above data, our patient was diagnosed as thrombocytopenia associated with non-cirrhotic hepatitis B.

Abstract #2104

A comparison of risks for hepatocellular carcinoma in chronic hepatitis B initially treated with entecavir or tenofovir

Lee Hyo Young[1], Oh Hyunwoo[2], Yoon Eileen L.[3†], Jun Dae Won[4†], Ahn Sang Bong[1], Jeong Jae Yoon[5], Kim Hyoung Su[6], Jeong Soung Won[7], Kim Sung Eun[8], Shim Jae-Jun[9], Cho Yong Kyun[10], Sohn Joo Hyun[11]

[1]Department of Internal Medicine, Nowon Eulji Medical Center, Eulji University College of Medicine, Seoul, Republic of Korea, [2]Department of Internal Medicine and Liver Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea, [3]Department of Internal Medicine, Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Republic of Korea, [4]Department of Internal Medicine, Hanyang University Hospital, Hanyang University College of Medicine, Seoul, Republic of Korea, [5]Department of Gastroenterology and Hepatology, National Medical Center, Seoul, Korea, [6]Department of Internal Medicine, Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Republic of Korea, [7]Department of Internal Medicine, Soonchunhyang University College of Medicine, Soonchunhyang University Seoul Hospital, Seoul, Republic of Korea, [8]Department of Internal Medicine, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang-si, Republic of Korea, [9]Department of Internal Medicine, Kyung Hee University School of Medicine, Seoul, Korea, [10]Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [11]Department of Internal Medicine, Hanyang University Guri Hospital, Hanyang University College of Medicine, Guri-si, Republic of Korea

Introduction: Risk evaluations of hepatocellular carcinoma (HCC) in entecavir (ETV) and tenofovir (TDF) treated chronic hepatitis B

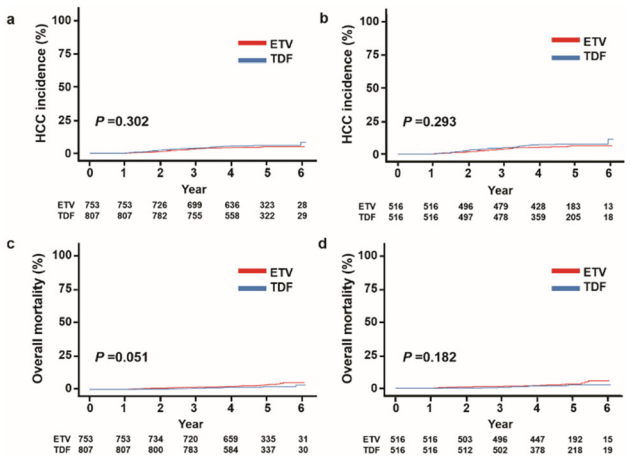
(CHB) patients have shown contradicting results in several retrospective cohort studies. Considerable "censored" data, insufficient "observation period", and different "observation periods" between the drugs are unsolved issues in previous studies.

Objectives: We aimed to compare the incidence of HCC development between two oral nucelos(t)ide analogues over the same "observation period".

Method: We examined retrospective data from treatment naïve CHB patients who were first treated with either ETV or TDF between 2011 and 2015 at nine academic hospitals in Korea. Clinical outcomes were observed for 4.7 ± 1.0 years and minimum observation duration was guaranteed for 3 years in both the groups.

Results: A total of 1,560 treatment naïve patients (753 in the ETV group and 807 in the TDF group) were included. In the entire cohort, mean and median "observation periods" were 4.6 ± 1.0 and 4.8 (Interquartile rage (IQR), 4.2-5.4) years, respectively. 92.4% of TDF and 92.7% of ETV treated patients were followed up during the observational period. In this cohort, 34 out of 753 patients (4.5%) in the ETV group and 45 out of 807 patients (5.6%) in the TDF group developed HCC under antiviral treatment during the follow up period; the incidences were not different between the groups. Moreover, these rates were not different between the drugs based on the 516-pair propensity score-matched population.

Conclusion: Incidence of HCC was similar between ETV and TDF treated patients over the same observation period (clinical trial No. KCT0003487).



Abstract #2127

The effect of Entecavir and Tenofovir on renal function in chronic hepatitis B patients

Guclu Ertugrul[1], Okan Huseyin Dogus[1], Baran Ali İrfan[2], Ince Nevin[3], Ogutlu Aziz[1], Karabay Oguz[1]

[1]Department of Infectious Diseases and Clinical Microbiology, Sakarya University Faculty of Medicine, Sakarya, Turkey, [2]Department of Infectious Diseases and Clinical Microbiology, Van Yuzuncu Yıl University Faculty of Medicine, Van, Turkey, [3]Department of Infectious Diseases and Clinical Microbiology, Duzce University Faculty of Medicine, Duzce, Turkey

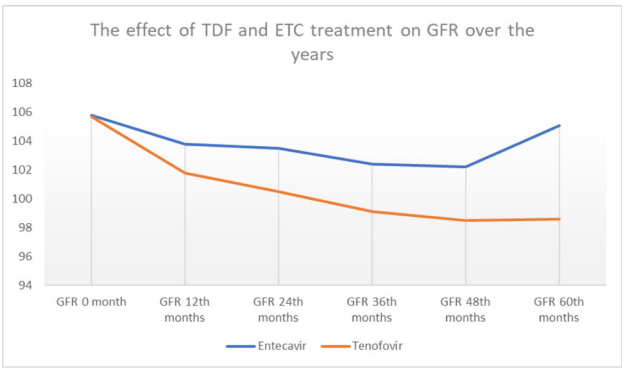
Introduction: Potent antivirals such as tenofovir disoproxil fumarate (TDF) and entecavir (ETC) are recommended in the treatment of chronic hepatitis B (CHB).

Objectives: The aim of this multicenter study was to investigate the effect of long-term use of TDF and ETC on glomerular filtration rate (GFR) in CHB treatment.

Methods: Demographic information such as age and sex, and serum creatine values were retrospectively taken from the files of patients who had been treated for at least 60 months with TDF or ETC. The GFR value was calculated using the 4-variable Modification of Diet in Renal Disease (MDRD) formula.

Results: In total, 178 patients (59.6% male, 40.4% female) were included in the study. The mean age of the patients was 44.9 years and while, 130 of them were treated with TDF, 48 of them were treated with ETC. The mean age of patients treated with TDF was 44.03 years, while those treated with ETC were 47.4 years. The change in GFR rates of patients treated with TDF and ETC was statistically similar up to 48 months ($p > 0.05$). However, GFR rates at the 60th month of treatment were found to be statistically lower in the TDF arm compared to ETC ($p = 0.02$) (Fig. 1).

Conclusion: The change in GFR was similar in the first years of CHB patients receiving TDF and ETC treatment, but it changed against TDF in the following years. Renal function should be monitored very closely especially in patients who have been using TDF for a long time.



GFR: Glomerular filtration rate; TDF: tenofovir disoproxil fumarate; ETC:Entecavir

Figure 1: The effect of Tenofovir and Entecavir treatment on glomerular filtration rate over the years.

Abstract #2128

Fib 4 in pregnant mother with hepatitis B and neonatal jaundice

Desi Maghfirah[1], Fauzi Yusuf[1], Azzaki Abubakar[1], Dewi Karlina Rusly[2], Darnifayanti[3]

[1]Gastroenterohepatology division of Internal Medicine Department, [2]Department of Obstetrics and Gynecology, [3]Department of Child Health Sciences, Medical Faculty, Universitas Syiah Kuala, Banda Aceh, Indonesia

Introduction: Hepatitis B infection is endemic throughout the world, mother-to-child transmission is an important mode of viral propagation. The infection can transmit to their children or may suffer adverse pregnancy outcomes.

Objective: This study aims to investigate the relationship of Fibrosis 4 (Fib 4) with neonatal jaundice.

Method: This study is a retrospective cohort study conducted on pregnant mother with hepatitis B virus infection who underwent labor at the General Hospital dr. Zainoel Abidin Banda Aceh from 2017 to July 2019. Data was taken from the patient's medical record.

Result: In this study, there were 70 patients with 50 cesarean (71.4%), vaginal delivery 14 (20%), curettage 1 (1.4%) and abortion 4 (5.7%). There were 3 (4.3%) babies born with neonatal jaundice. Fib 4 values 0.74 (0.3–1.9). If using a low cut-off Fib 4 (1.45) for significant fibrosis with a specificity of 42% and a sensitivity of 89%, it was found that there were 5.7% of patients experiencing fibrosis but there is no relationship between fibrosis with neonatal jaundice with p 0.265.

Conclusion: Studies have also shown that by giving hepatitis B immunoglobulin and hepatitis B vaccine to the neonates shortly after birth, vertical transmission can be prevented in most of the children born to hepatitis antigen B positive mothers. In this study we found there is no relationship between fibrosis with neonatal jaundice, but hepatitis antigen B neonates need to be checked.

Abstract #2134

HBV Functional Cure of Antiviral Therapy in Chronic Hepatitis B: One Year Study

Iswina Reniarti[1,2], Muhammad Luthfi Parewangi,[1] Fardah Akil,[1] Nu'man AS Daud,[1] Rini Rachmawati Bachtiar,[1] Susanto H Kusuma,[1] Amelia Rifai[1]

[1]Centre of Gastroenterology-Hepatology HAM Akil/DR.Wahidin Sudirohusodo General Hospital, [2]Division of Gastroenterology-Hepatology, Department of Internal Medicine, University of Hasanuddin, Makassar-Indonesia

Introduction: Currently, there are two main treatment options for chronic hepatitis B (CHB) patients with a nucleos(t)ide analogue (NA) or with IFNa, currently pegylated (PegIFNa). Surrogate endpoints of HBV functional cure measure biochemical, virological, and histological outcomes. Each of these agents, given as monotherapy, has been shown to produce virological, biochemical, and histological benefit. The biochemical and histological responses usually parallel HBV-DNA suppression.
Objective: To evaluate the HBV functional cure of antiviral therapy in CHB patients.
Methods: This restrospective cohort study using 165 patients CHB whose received antiviral. Demography, laboratory (liver biochemistry/serology/virology), and transient elastography (TE) data were collected and determine into virological, serological, biochemical, and histological respons according to terminology of Hepatitis B guidelines with follow-up at month 3, 6, 9 and 12 therapy compared to pre-treatment.
Results: Of them, 160(97%) patients received NA and 5(3%) received PegIFNa. Ninety-two (55.8%) with ALT $\geq$60IU/ml, 55 (33.3%) HBeAg(+), 101(61.2%) grad e$\geq$ F2 with median of HBV-DNA 6.2log$_{10}$IU/ml, ALT 72.5 IU/ml and TE 9.05kPa. Undetectable HBV-DNA at month-3/6/9/12 were 5(9.8%)/12(23.5%)/ 3(5.9%)/ 8(15.7%) respectively; primary non-respons 3 (5.9%) and partial respons 13 (25.5%) patients. Loss of HBeAg, normalization of ALT and improvement of fibrosis (F0F1) at month-3/6/9/12 were 5 (12.2%)/6(14.6%)/5 (12.2%)/ 5 (12.2%); 58 (69%)/12 (14.3%)/1 (1.2%)/2 (2.4%) and 29 (29.3%)/11 (11.1%)/9 (9.1%)/6 (6.1%) respectively. Of all subjects, 28(54.9%) had complete virological response, 21 (51.2%) serological response, 73 (86.9%) biochemical response and 55(55.5%) achieved histological improvement. One patients with telbivudine had biochemical/virological/ histological response at 3-month therapy.
Conclusion: Our study demonstrated that antiviral therapy can achieved virological/serological/histological responses >50% and >85% in biochemical improvement at 1 year study of CHB patients.

Abstract #2135

Association between vitamin D serum levels with the length of undetected Viral load of Hepatitis B Virus

Neneng Ratnasari

Background: High prevalence of vit D (25-(OH)D3) deficiency was seen in patients with HBV and HCV infection in worldwide. Vit D is significantly associated with virus replication in chronic HBV infection. But the efficacy of vit D treatment in HBV patient was still inconsistent. The aim of study is to know the association between vit D serum levels with the length of undetected viral load of HBV
Methods: The cross sectional with retrospective study was performed to HBV patients at Dr. Sardjito Hospital Yogyakarta, Indonesia. All subject who were treated using antiviral orally, age $\geq$ 18 year old, male/female were included as subjects. Patients who have comorbidity such as: HIV, liver malignancy and non-liver malignancy were excluded. Vit D, HBeAg qualitative, HBV DNA quantitative was assessed by Hospital clinical pathology laboratory. Data were analyzed using STATA.
Results: The 35 subjects (23 male; 12 female) were meet the inclusion criteria, mean of age 39.74 $\pm$ 12.02 yo. Significant difference of vit D level was showed in genders (male 27.96 $\pm$ 14.38 vs female 18.04 $\pm$ 11.42; p = 0.047; ng/ml). No significant difference in DNA category 20.000 IU/ml (26.29 $\pm$ 13.29 vs. 21.95 $\pm$ 15.37; p > 0.05); and HBeAg category (25.77 $\pm$ 12.06 vs. 23.11 $\pm$ 16.49; p > 0.05). No correlation with the length of HBV DNA (r = 0.04) and HBeAg undetected (r = 0.54)
Conclusion: No association between vit D serum level with the length of undetected viral-load HBV DNA, and the level of vit D in male is higher the female significantly.

Abstract #2145

Activation of innate immunity by CRISPRa as an antiviral strategy to tackle HBV infection

Brezgin S.[1], Kostyushev D.[1], Kostyusheva A.[1], Babin Y.[1], Goptar I.[2], Nikiforova A.[2], Bayurova E.[3,4], Gordeychuk I.[3,4,5], Isaguliants M.[3,4,6,7], Chulanov V.[1,5]

[1]National Medical Research Center of Tuberculosis and Infectious Diseases, Ministry of Health, Moscow 127994, Russia, [2]Izmerov Research Institute of Occupational Health, Gene Engineering and Biotechnology, Moscow 105275, Russia, [3]NF Gamaleya Research Center of Epidemiology and Microbiology, Moscow 123098, Russia, [4]Chumakov Federal Scientific Center for Research and Development of Immune-and-Biological Products of Russian Academy of Sciences, Moscow 108819, Russia, [5]Sechenov First Moscow State Medical University, Moscow 119146, Russia, [6]Department of Pathology, Riga Stradins University, LV-1007 Riga, Latvia, [7]Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, SE-171 76 Stockholm, Sweden

CRISPRa (CRISPR activation) targeting APOBEC/AID genes is a technology proved to activate target gene transcription in a very precise and robust manner. Previously, we demonstrated activation of APOBEC/AID genes and potent anti-HBV activity of CRISPRa transfected into HBV-permissive cell lines. CRISPRa induced 5-100,000-fold increase in APOBEC/AID mRNAs levels, dramatic decline in HBV intermediates (> 99% reduction in HBV RNAs, DNA and cccDNA levels), reduced HBsAg production and disappearance of HBcAg from transfected cells. Noteworthy, HBV cccDNA was heavily mutated by APOBEC/AID factors with typical patterns of C->T and G->A mutations. Additionally, we demonstrated that APOBEC3A and APOBEC3B do not exhibit genotoxic and cytotoxic activity using immunocytochemistry, western blotting, comet assay and NGS, whereas APOBEC3G inflicts DNA damage and AID induces expression of pro-apoptotic factors. Activation of target APOBEC/AID genes was highly specific, as co-transfection of shRNAs to mRNAs of CRISPRa-activated genes abolished anti-HBV

activity of the CRISPRa approach. Additionally, we utilized CRISPRa not only as an antiviral approach but as a tool to screen for human RNases, factors of cGAS/STING pathway and DNA damage response factors to identify novel antiviral factors and factors involved in HBV life cycle. Surprisingly, several human RNases (RNase 10 and MCPIP1) activated by CRISPR induced > 90% decline in all HBV markers. To conclude, CRISPRa is a promising technology to develop anti-HBV curative therapies and a potent tool to investigate HBV life cycle.

Abstract #2167

Efficacy of pegylated interferon-alpha-2a in hepatitis D infected patients. Experience from the Tertiary Care Hospital in Karachi

Nazish Butt[1], Riaz Hussain[1], Lajpat[1], Sabir[1], Hanisha Khemani[1], Ali Khan[1]

[1]Jinnah Postgraduate Medical Centre, Karachi.

Background and Aims: Hepatitis Delta Virus (HDV) is a unique virus because it needs Hepatitis B Virus (HBV) for its replication hence, survival. Pegylated Interferon-Alpha-2a (PEG-alfa-2a) is the only option available for the treatment of HDV. In the present study, we aimed to assess the efficacy of PEG-alfa-2a in patients with HDV infection.
Method: We enrolled all 165 patients with chronic HDV at Gastroenterology section of medical unit IV, Jinnah Postgraduate Medical Centre On presentation, all patients were positive for both Anti-HDV and HBsAg, who were treated for 48 weeks with PEG-alfa-2a. Evaluation of HBV and HDV infection through Polymerase chain reaction (PCR) was done at 6-month, and 12-month intervals. All laboratory values were repeated on regular intervals to assess the efficacy and side effects of therapy.
Results: From total 165 patients, Eighteen patients lost to follow up, 20 patients stopped treatment due to side effects of Interferon and 20 patients were excluded from the study due to liver cirrhosis, rest of 107 patients, 76 (71%) were male while 31 (29%) were female with a mean age of 27.84 $\pm$ 10.52 years. Baseline investigations showed: Hemoglobin, 13.12 + 2.04 g/dL; platelets, 200.73 $\pm$ 91.31 $\times$ 10^9/L; and On PCR, HDV DNA was confirmed in every collected sample, with a mean value of 10786066.28 $\pm$ 31826055.19, while HBV DNA was detected in 44 (41%) patients. Duration of treatment was 12 months, 25 (23%) patients achieved the 48-weeks End Treatment Response (ETR), 27 (25%) patients showed partial response to Peg-INF, while 51% had treatment failure (Null response or Non-responders).
Conclusion: Interferon therapy in patients with CHD shows a sub-optimal outcome. Only 23% achieved ETR. Patients with treatment failure or null response should urgently be given an effective alternative option.

Abstract #2188

Chronic hepatitis B management in clinical practice in Fuzhou Province, China: retrospective cross-sectional analysis of electronic medical record data

Meng Xing[1], Liu Sen[1], Dong Jane[1] and Gillespie Iain Andrew[2*]

[1]GSK Institute for Infectious Diseases and Public Health, Beijing, China; [2]GSK Value Evidence & Outcomes, London, UK

Introduction: There have been few published reports on the treatment rate of chronic hepatitis b virus (HBV) infection in real-world practice in China. This study is the first to review a large regional Chinese electronic medical record (EMR) database in the HBV area (GSK-sponsored study 208571).
Objectives: To describe the characteristics of HBV patients overall and by the treatment status in a cross-sectional review of an EMR database.
Methods: A cohort of chronic HBV infection patients in the National Health Medical Big Data Platform (Fuzhou) Regional Database (covering 37 hospitals) was identified in 2017 through diagnostic and laboratory codes/values. An algorithm, developed to reflect international treatment guidelines, was applied to stratify patients into treatment-status groups (treated, indicated-but-not-treated or not-indicated-not-treated), utilizing demographic, clinical (cirrhosis, fibrosis) and biochemical (HBsAg, HBeAg, DNA, ALT) characteristics.
Results: In total, 21,614 chronic HBV infection patients were identified. The peak age distribution was between 25-50 years (65.71%); 68.6% were male. Co-infection was rare (0.04% with HIV/HCV; 1.77% with HDV). Liver fibrosis, cirrhosis and hepatocellular carcinoma was observed in 13.40%, 11.96% and 0.81% respectively. Half (49.56%) were treated (nucleos(t)ide analogues (NUCs) 99.91%; interferon-based 0.07%, NUC/IFN combinations 0.02%). Among 21,050 patients evaluable by our algorithm, 50.06%, 14.61% and 35.33% were treated, indicated-but-not-treated and not-indicated-not-treated, respectively.
Conclusion: Data from this large Chinese EMR database demonstrated a substantial number of patients (15%) did not receive therapy despite meeting treatment criteria, signifying the need to better understand the barriers to treatment. Complete analyses of the dataset will be subject to future reports.

Abstract #2189

Profile of hepatitis B in pregnant women of central Aceh District

Adlin Herry[1]

[1]Datu Beru Public Hospital, Takengon

Introduction: Pregnant women who suffer from Hepatitis B can cause problems for her and her babies, than can transmit it to other people. In Indonesia there are 5.3 million mothers get pregnant every year with positive HBsAG with an average rate of 2% every year, will give birth to 120.000 babies with Hepatitis B and 95% of them are potensial to suffer from Hepatitis B in 30 years later
Objectives: The Purpose of this prospective study was to describe the profile of pregnant women who suffer from Hepatitis B in central aceh district, it can also be used to national data study and to increase knowledge of pregnant women who suffer from Hepatitis B.
Methods: The study was conducted at Datu Beru Public hospital, from June 2017 to June 2019. The data of the study are taken for Pregnant women with HBsAg Positive who refered from several public health centers in central aceh district.
Results: Amount 48 cases, The Average patients was 24.26 years old with high school and undergraduated education, all patients know they had Hepatitis B for the first time while they had taken screening test in public health centers. 29 (61%) transmission of these cases were generally unknown, 5 (10%) cases were from their husband who had suffered from Hepatitis B, 4 (8%) cases were from their family who had suffered from Hepatitis B. The use of intravenous vitamins which are not its indication and intravenous drugs such as antipiretik were 9 (19%) cases. And a case (2%) with history of previous blood tranfusion. From All of the cases, 13 patients had given birth already, 8 patients gave birth via pervaginam and 5 patients via Sectio caesaria without previous HBsAg data. From 48 patients with Hepatitis B, 10

patient with increase SGOT and SGPT value 3 times higher than upper limit value with the average HBV DNA value was 3×10^8 unit/ml. All patients who had been treated with Tenovofir 300 mg/day in the Third Trimester, and after 6 months of observation, cases with HBV DNA were negative. The babies born are given complete vaccinations and immunoglobulins.

Abstract #2196

The Association between health-related quality of life and demographic characteristics in patients with chronic hepatitis B

Alay Handan[1], Yılmaz Sinan[2], Parlak Mehmet[1], Kesmez Can Fatma[1], Pür Nurdan[1]; Ataturk

[1]Ataturk University Faculty of medicine, Department of Infectious Diseases and Clinical Microbiology, Erzurum, Turkey, [2]Ataturk University Faculty of medicine, Department of Public Health, Erzurum, Turkey

Objectives: The purpose of this study was to measure health-related quality of life (HRQoL) in patients with chronic hepatitis B (CHB) and to assess its association with demographic characteristics.
Material-method: One hundred twenty-four patients presenting to the infectious diseases polyclinic between 01 December, 2019, and 15 January, 2020, were included in the study. Patients' sociodemographic characteristics were recorded, and Short Form 36 consisting of 36 questions evaluating HRQoL was completed using the face-to-face interview technique.
Results: Seventy-eight patients (62.9%) were women and 46 (37.1%) were men. Patients' mean age was 39.9±12.9 years, and mean duration of disease was 86.5 ± 70.4 months. The physical component score (PCS) and general health score were significantly lower in women than in men ($p < 0.05$). When HRQoL was evaluated in terms of marital status, PCS was better in single patients than in married individuals ($p < 0.05$). PCS and mental component scores were lower in patients living in rural villages than in those living in urban districts and the provincial center ($p < 0.05$). PCS values differed significantly between illiterate patients and university graduates ($p < 0.05$). Analysis of quality of life in terms of smoking status and occupation revealed similar score distributions for all domains (Table 1). A weak negative correlation was observed between age and PCS, with PCS decreasing as age increased.
Conclusion: Various sociodemographic characteristics can adversely impact on HRQoL in patients with CHB. It is of considerable importance for patients to be started on appropriate antiviral therapies and to be assessed in terms of demographic characteristics, and for suitable clinical support to be provided when required.

Abstract #2207

Correlation of depression and APRI index in management of chronic hepatitis B patient

Wardani Kristia[1], Budiono Rahmad[1], Pratomo Bogi[2], Supriono[2], Mustika Syifa[2]

[1]Resident of Internal Medicine, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia, [2]Gastroenterohepatology Division, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia

Introduction: The global depression population in 2015 is estimated to be 4.4%, which increased by 18.4% between 2005 and 2015, nearly half of these people live in the South-East Asia Region and Western Pacific Region. Depression is not only a major global public health concern, but also a common comorbidity among patients who experience chronic diseases, such as Hepatitis. Phsychiatric problem in chronic hepatitis estimated 38.1–51.1% which mostly mild-moderate depression and anxiety.
Objective: The aim of this study is to analyse correlation between depression, and APRI score index in chronic Hepatitis B management.
Methods: A total of 83 outpatient consume antiviral drug was selected, and those who have no history of psychiatrical problem before, nor other chronic disease (Diabetes Mellitus, Hypertension). Hamilton Depression Rating Scale (HDRS) was used to measure depression severity. Statistical analysis using Spearman test was significant if $p < 0.05$.
Result: The average duration of Hepatitis B therapy was 16 ± 14,24 months, tenofovir and telbivudin was the most drug of choice (48.19%) which related with depression ($p = 0.04$; $r = 0.22$). The duration of Hepatitis B therapy have no correlations with the HDRS score ($p > 0.05$). Occurance of depression was high in patient with high APRI index despite correlation to HDRS score $p > 0.05$.
Conclusion: Depression has no corellation with duration of therapy, but choice of drug tenofovir and telbivudin might correlated with mild depression. APRI index might be correlate with depression, despite unsignificant result.

Abstract #2234

Evaluation of sequential therapy peg-interferon and nucleos(t)ide analogue compared to monotherapy in patients with chronic hepatitis B: evidence-based case report

Andri Sanityoso Sulaiman[1,2]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Klinik Hati Prof. Ali Sulaiman. Jakarta, Indonesia

Introduction: Chronic Hepatitis (CHB) remains as one of global health problems that may lead to the development of liver cirrhosis and hepatocellular carcinoma (HCC). Patients with chronic hepatitis B infection should be followed up to identify possible changes in disease status, such as HBsAg seroconversion.. Nucleos(t)ide Analogue (NA) is known to be effective in suppressing the viral load but it's associated with the high risk of resistance in long term use, so that adding an immunomodulator can be an alternative treatment
Study objective: This study aimed to evaluate the response at the end of sequential therapy (NA and Peg-IFN) compare with monotherapy in suppressing HBsAg.
Method: Online search was done on PubMed nd researchgate The keywords, inclusion, and exclusion criteria were also applied. The articles were appraised to discuss validity, importance, and applicability
Result: Zhang, et al. (2019) study shown the proportion of patients in whom HBsAg was reduced by >1500 IU/mL from baseline level was significantly higher ($P < 0.05$) in the early combination group (61/108, 56.5%) than in the NA monotherapy (63/151, 41.7%). Heng Chi (2017) study From week 0 to 48, a greater decrease in the HBsAg level was achieved in patients who received peginterferon add-on therapy as compared to patients who continued NA monotherapy (− 0.40 vs. − 0.15 log IU/mL; $P = 0.005$)
Conclusion: Based on these two studies, it can be concluded that sequential therapy (NA and Peg-IFN) can be effectively made HBsAg loss and seroconversion.

Abstract #2239

Therapeutic vaccination in chronic hepatitis B

Andri Sanityoso Sulaiman[1,2]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Klinik Hati Prof. Ali Sulaiman. Jakarta, Indonesia

Background: There are two types of hepatitis B therapy that have been approved, namely interferon (IFN) and nucleoside analogues. However, nucleoside analogues have low efficacy for sustaining viral suppression after therapy is stopped, while IFN has many side effects during and after therapy. Polyclonal immunomodulators and specific antigen-based immune therapy for HBV (therapeutic vaccination) have been tried in chronic hepatitis B.

Objectives: This study aimed to review the effectiveness of therapeutic vaccination by comparing to current standard therapies such as IFN.

Methods: Literature searching was conducted by using database Pubmed, Science Direct, dan Cochrane. The keywords, inclusion criteria were also applied. The selected article was appraised to discuss the validity, importance, and applicability.
Results. Seng Gee Li, et al. study concluded Therapeutic vaccination has little or no effect on patients with positive HBeAg on loss of HBsAg, HBeAg seroconversion, and reduction of HBV DNA with a Risk of Difference (RD) of 0.02 (95% CI, 95% − 0.04 to 0.06, respectively). Mahtab, et al. (2018) study showed sustained control of HBV DNA was significantly more common in NASVAC group ($p < 0.05$) at 24 weeks of follow up. Zaman, et al. (2019) showed reduction in hepatitis B surface antigen (HBsAg) levels from baseline to week 24, was not greater with addition of GS-4774.
Conclusion: This study indicates that the impact of therapeutic vaccination in the treatment of chronic infectious diseases will depend on the capacity of designing the adequate antigens and adjuvant strategies as well as the selection of the most suitable immunization route(s) and candidate recipients.

Hepatitis C

Oral presentations

Abstract #53

Real-life efficacy of daclatasvir/asunaprevir combination therapy for genotype 1b chronic hepatitis C patients in Hong Kong

Hui Yee Tak[1], Tong KN Ronald[2], Wong LH Grace[3], Liu D Sienna[3], Liu Ken[3], Ma Yiu Keung[4], But YK David[5], Mak Wing Yan[3], Chan MC Jacky[6], Lai Kin Bon[7], Loo Ching Kong[8], Ng C Y Annie[2], Lai Moon Sing[9], Chan Chun Wing[10], Lau YL Joulen[11], Fan TT Tina[12], Hui J Aric[13], Lam CY Belsy[14], Cheung Wing I[15], Tsang TY Owen[6], Lam S Karen[6], Lai SW Lawrence[14], Luk Wai Fun[6], Li KK Michael[4], Lao Wai Cheung[11], Lam TW Jodis[1], Tsang WC Steven[12], Kung Kam Ngai[7], Chow Wai Hung[10], Chan Angel[10], Chan SY Rosita[13], Yau SN Wendy[4], Lui KL Thomas[5], Shan HS Edwin[2], Fung YY James[5], Chan LY Henry[3], Yuen Man Fung[5], Wong WS Vincent[3]

[1]Department of Medicine, Queen Elizabeth Hospital, Hong Kong, China, [2]Department of Medicine and Geriatrics, Caritas Medical Centre, Hong Kong, China, [3]Department of Medicine and Therapeutics, State Key Laboratory of Digestive Disease, Institute of Digestive Disease, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, China, [4]Department of Medicine and Geriatrics, Tuen Mun Hospital, Hong Kong, China, [5]Department of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong, China, [6]Department of Medicine and Geriatrics, Princess Margaret Hospital, Hong Kong, China, [7]Department of Medicine and Geriatrics, United Christian Hospital, Hong Kong, China, [8]Department of Medicine and Geriatrics, Kwong Wah Hospital, Hong Kong, China, [9]Department of Medicine North District Hospital, Hong Kong, China, [10]Department of Medicine, Yan Chai Hospital, Hong Kong, China, [11]Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong, China, [12]Department of Medicine, Tseung Kwan O Hospital, Hong Kong, China, [13]Department of Medicine, Alice Ho Miu Ling Nethersole Hospital, Hong Kong, China, [14]Department of Medicine and Geriatrics, Pok Oi Hospital, Hong Kong, China, [15]Department of Medicine, Our Lady of Maryknoll Hospital, Hong Kong, China, Corresponding author: Dr. Yee Tak Hui, Department of Medicine, Queen Elizabeth Hospital, 30 Gascoigne Road, Yau Ma Tei, Kowloon, Hong Kong (email: huiyeetak@gmail.com)

Introduction: The effectiveness and safety of daclatasvir (DCV) and asunaprevir (ASV) combination therapy for patients chronically infected with hepatitis C virus (HCV) genotype 1b have not been previously evaluated in Hong Kong.
Objectives: To study the efficacy of DCV/ASV combination therapy for chronic HCV patients in Hong Kong.
Methods: HCV-infected patients who were treated with DAV/ASV combination therapy from 2015 to 2019 were retrieved from the database of the Hong Kong HCV Registry.
Results: Eighty-seven patients with chronic HCV infection (genotype 1b) had completed DCV/ASV therapy with sustained virological response (SVR) results. Their median age was 62 (IQR 53–69) and 51.7% were male. 58.6% of them had liver cirrhosis, 5.7% had HBV co-infection and 25.3% had prior treatment with pegylated interferon. Before treatment, 96.6% of them were tested negative for resistance-associated variants (RAV). Only three patients remained viremic after treatment and the overall SVR12 rate was 96% (modified ITT analysis). 10.2% of them experienced minor self-limiting side effects (fatigue, nausea, diarrhea, skin rash and dizziness). 8.0% patients have grade 3 or 4 elevation of ALT. But only 2 patients (2.3%) required premature termination of therapy at week 15 and 18 due to significant ALT elevation. Prior pegylated interferon treatment ($P = 1.00$) and liver cirrhosis ($P = 0.920$) are not associated with lower SVR rate.
Conclusion: DCV/ASV is a highly effective direct acting antiviral but 8% of patients will have significant elevation of ALT during therapy.

Abstract #106

Downregulation of TNF-α predicts HCC development in chronic hepatitis C patients with advanced fibrosis after viral eradication

Lu, Ming-Ying[1], Huang, Chung-Feng[1,2], Yeh, Ming-Lun[1,2], Wang, Shu-Chi [3], Huang, Jee-Fu[1,2], Dai, Chia-Yen[1,2], Chuang, Wan-Long[1,2], Yu, Ming-Lung [1,2]

[1]Faculty of Internal Medicine and Graduate Institute of Medicine, School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan. [2]Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital,

Kaohsiung Medical University, Kaohsiung, Taiwan. [3]Department of Medical Laboratory Science and Biotechnology, Kaohsiung Medical University, Kaohsiung, Taiwan

Introduction: Successful HCV eradication did not eliminate HCC development among patients with advanced fibrosis. Clearance of HCV by DAA or IFN results in reconstitution of immune surveillance. We aimed to investigate the impact of differential cytokine expression on the development of HCC following antiviral therapy.
Methods: 50 HCV patients with advanced fibrosis receiving pegIFN/RBV and 50 age-, sex- and fibrosis-matched HCV patients receiving DAA who achieved sustained virologic response (SVR) were enrolled in this study. The primary endpoint is the development of HCC. Cytokines profile were measured at baseline and SVR12 or SVR24 follow-up. A total of 64 cytokines was detected by the multiplex immunoassay.
Results: HCC developed in 12 (IFN group n = 11, DAA group n = 1) of the 97 patients over 459 person-years of follow-up after HCV eradication. In univariate analysis, the variation of tumor necrosis factors (TNF)-α and TWEAK (TNF-like weak inducer of apoptosis) after antiviral therapy were significantly associated with the development of HCC. The multivariate Cox regression model showed the reduction of TNF-α ($\Delta = -5.7$ pg/ml) was the independent risk factor of HCC (HR = 11.54, 95% CI = 2.27–58.72, p = 0.003). We established an HCC predictive model as follows: Score = 5 × Gender (male = 1, female = 0) + 8 × △TNF ($\leqq$-5.7, yes = 1, no = 0) + 11 × ΔTWEAK ($\leqq -70$, yes = 1, no = 0). Time-dependent ROC analysis revealed the 3-year, 5-year, 10-year, and 13-year AUC were 0.815, 0.836, 0.870, and 0.916, respectively.
Conclusion: Reduction of TNF-α after antivirals predicts HCC development in chronic hepatitis C patients with advanced fibrosis after successful viral eradication.

Abstract #176

Clinical validation of Genedrive point of need device in the Asian population to address decentralized Hepatitis C confirmation

Amy Yuh Ling Tay[1], Htet Htet Toe Wai Khine[2], Swee Jin Tan[2], Chee Hoe Low[2], Wah Wah Phyo[1], Juling Wang[1], Seng Gee Lim[1]

[1]Yong Loo Lin School of Medicine, National University of Singapore, [2] Sysmex Asia Pacific Pte Ltd

Introduction: To support viral hepatitis testing needs in decentralized settings, this study evaluates the Genedrive and HCV RNA assay. Designed for straightforward operations and minimal sample handling, this point of need IVD device and assay can deliver an RNA test result in 90 minutes to confirm HCV infection.
Objectives: We report the first Genedrive HCV RNA evaluation using Asian samples, consisting of HCV genotypes 3 and 6. Clinical sensitivity and specificity for samples before, during and post treatment were compared.
Methods: A total of 256 HCV pre-characterised plasma and serum samples from the National University Hospital archive were tested in a blinded fashion. Corresponding serology and real-time PCR viral load (VL) data were used to evaluate accuracy of Genedrive results.
Results: The study results demonstrated 100% sensitivity and specificity for treatment naïve HCV patient samples. For post-treated cohort, 100% specificity was observed for samples with undetectable VL and one negative result below assay LOD (104 IU/mL). This sample was drawn during treatment, and the patient subsequently achieved sustained viral load (SVR), evidenced by EOT undetectable VL. No significant differences were observed between plasma or serum samples, or different HCV genotypes. Genedrive HCV RNA positively identified samples as low as 4540 IU/mL (plasma) and 3330 IU/mL (serum) in this limited dataset. Rerun rates were at 2.3% of the 256 samples.
Conclusion: The Genedrive offers HCV RNA confirmatory testing in a compact, portable and straightforward platform. Results from the current evaluation demonstrates good sensitivity and specificity for Asian samples of genotypes 3 and 6, in comparison with VL derived from real-time PCR.

Abstract #185

Georgian National Hepatitis C Elimination Program: Does genotyping for RF1_2k/1b recombinant strain still matter?

Marine Karchava[1,2,3] ,Nikoloz Chkhartishvili [1], ,Lali Sharvadze[1,2,4], ,Akaki Abutidze[1,2,4], ,Natia Dvali1, ,Lana Gatserelia[1,2], Mrs. Lela Dzigua[1], ,Natalia Bolokadze[1,4], Tengiz Tsertsvadze[1,2,4]

[1]Infectious Diseases, AIDS and Clinical Immunology Research Center, [2]Hepatology Clinic- Hepa, [3]Petre Shotadze Tbilisi Medical Academy, [4]Ivane Javakhishvili Tbilisi State University,

Introduction: Since 2015, Georgia has been working towards the country-wide elimination HCV infection, defined as a 90% reduction in prevalence by 2025. Since the initiation, more than 60000 patients were treated and cured. Treatment response rates largely depended on DAA regimen used and HCV genotype.
Methods: We report treatment response rates among HCV genotype 2 patients including RF1_2k/1b strain treated either by Interferon based regimens, Sofosbuvir/Ribavirin(SOF/RBV), Ledipasvir/ Sofosbuvir/ Ribavirin (LDV/SOF/RBV) and Sofosbuvir/Velpatasvir (SOF/VEL) repectively.
Results: Overall, 685 HCV genotype 2 patients were enrolled. Of those, 502 (73.2%) had RF1_2k/1b strain and 183 (26.7%) HCV 2a, 2k, or 2c subtypes. RF1_2k/1b distribution by gender was statistically significant (p = 0.003) attesting higher prevalence of these strain between male population (77.9% versus 61.9%). As of October, 2019 sustained virologic response (SVR) was available for 395 individuals. SVR was 96.6% (89/92) among genotype 2 and 91.7% (278/303) among RF_2k/1b patients (p = 0.16), with an overall rate of 92.5% (367/395). Highest SVR rate was observed in SOF/VEL and LDV/SOF/RBV group for both genotypes (100% and 99.2%) and lowest among SOF/RBV group (73.6%). Among RF1_2k/1b patients treatment with SOF/VEL and LDV/SOF/RBV was superior (SVR-100.0% (15/15 and 197/197) to SOF/RBV for 12 weeks (SVR 68.5% (50/73).
Conclusion: Since, SOF/RBV is no longer available for Georgian national hepatitis C elimination program and all HCV genotypes are treated by either SOF/VEL and LDV/SOF/RBV regimens, The testing for recombinant strain have lost it SVR power, therefore modification of current laboratory guidelines toward testing simplification is suggested.

Abstract #238

The effectiveness and safety of glecaprevir/pibrentasvir in chronic hepatitis C with refractory factors in real world; KTK 49 Liver Study Group

Koichi Takaguchi

Background: We aimed to evaluate the effectiveness and safety of glecaprevir and pibrentasvir (G/P) especially among patients with

these refractory factors, and the influence of these factors on treatment.
Methods: In a prospective, multicenter study involving 33 medical institutions, 1439 patients were treated with G/P, and their efficacy and safety were analyzed.
Results: Overall SVR12 rates were 99.1% (1397/1410) in the per-protocol-analysis, and genotype sustained virologic response (SVR)12 rates were: genotype 1, 99.4% (707/711); genotype 2, 99.4% (670/674); genotype 3, 80.0% (16/20). DAA-naïve patients (P = 0.008) with HCV genotype except 3 (genotype 1 vs. 3, p = 2.68×10^{-5}; genotype 2 vs. 3, p = 3.28×10^{-5}) had significantly higher SVR 12 rates. No significant deference was observed between CKD stage 1–3 (99.1% [1209/1220]) and chronic kidney disease (CKD) stage 4–5 (98.9% [188/190]) patients, or between cirrhotic (99.0% [398/402]) and non- cirrhotic (99.1% [999/1008]) patients. Multiple logistic regression analysis revealed genotype 3 (p = 4.06 × 10-5) and past experience of IFN-free DAAs (p = 0.029) were both significantly independent predictors of non-SVR.
Conclusions: G/P regimen is highly effective and safe to treat CHC patients even with refractory factors such as CKD and advanced liver fibrosis. However, patients with past experience of IFN-free DAA treatment and genotype 3, CKD stage 4 or 5, and advanced liver fibrosis should be more closely observed.

Abstract #290

Antiviral therapy against chronic hepatitis C is associated with a reduced risk of oral cancer

Su Tung-Hung[1,2], Tseng Tai-Chung[1,2,3], Liu Chun-Jen[1,2,34], Chou Shih-Wan[1], Liu Chen-Hua[1,2,3], Yang Hung-Chih[1], Chen Pei-Jer[1,2,3,45], Chen Ding-Shinn[1,2,3,4,6], Chen Chi-Ling[4], Kao Jia-Horng[1,2,3,4,5]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, [2]Department of Internal Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan, [3]Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan; [4]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, [5]Department of Medical Research, National Taiwan University Hospital, Taipei, Taiwan, [6]Genomics Research Center, Academia Sinica, Taipei, Taiwan

Introduction: Chronic hepatitis C (CHC) has been linked to oral cancer with inconsistent results.
Objectives: To investigate the association between CHC and oral cancer, and the development of oral cancer after anti-hepatitis C virus (HCV) therapy.
Methods: We conducted a population-based cohort study during 2004–2012 from the Taiwan National Health Insurance Research Database. CHC patients without anti-HCV therapy were matched with those non-HCV patients by age, sex, and comorbidities. Moreover, CHC patients who underwent pegylated interferon and ribavirin (PegIFN/RBV) therapy were matched with CHC patients without anti-HCV therapy.
Results: A total of 100,058 patients were included in the HCV and non-HCV cohorts, respectively. Their mean age were 59 years, and 50% were male. CHC infection significantly increased the cumulative incidence of lichen planus and oral cancer. After adjustment for confounders and competing mortality, CHC infection significantly increased the risk of oral cancer (hazard ratio [HR]: 1.677, 95% confidence interval [CI] 1.392–2.020, P < 0.001). Another 23,735 CHC patients without anti-HCV therapy were matched with 23,735 CHC patients in the treatment cohort. After adjustment for confounders and competing mortality, the risk of oral cancer was significantly reduced in CHC patients receiving anti-HCV therapy (HR: 0.652, 95% CI 0.479–0.887, P = 0.007). To minimize the inclusion of pre-existing unidentified oral cancer, we excluded oral cancer developed within the first year of CHC or anti-HCV therapy, and found these association remained statistically significant.
Conclusion: CHC significantly increases the risk of oral cancer. Moreover, PegIFN/RBV antiviral therapy significantly reduces the risk of HCV-related oral cancer.

Abstract #385

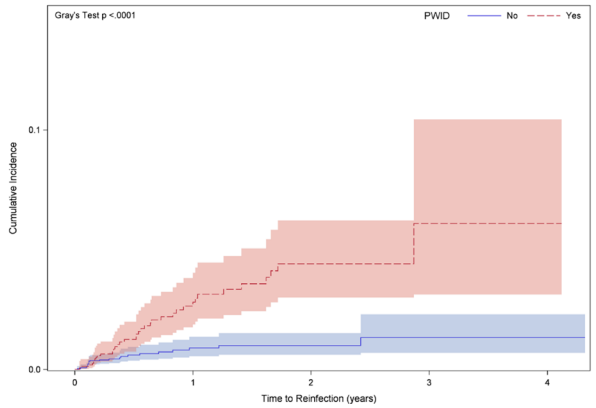
Hepatitis C virus reinfection after successful treatment with direct acting antiviral therapy in Canada

Janjua NZ[1,2], Wong S[1], Bartlett S[1,3], Butt ZA[1, 2], Wong J,[1,2] Adu P, [1,2] Samji H,[1] Yu A[1], Pearce M,[1,2] Alvarez M[1], Binka M[1], Mel Krajden[1,3], The BC Hepatitis Testers Cohort Team

[1]British Columbia Centre for Disease Control, Vancouver, BC, Canada, [2]School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada, [3]Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada

Introduction: People who inject drugs (PWID) can be effectively treated with direct-acting antiviral therapies (DAA), however, HCV reinfection remains a concern.
Objectives: We estimated HCV reinfection rates among DAA-treated individuals in a population-based cohort study in British Columbia (BC), Canada.
Methods: HCV-infected individuals the BC Hepatitis Testers Cohort treated with DAAs who achieved sustained virologic response(SVR) and had ≥1 subsequent HCV RNA measurement from SVR until April 9, 2019 were followed. Reinfection was defined as a positive RNA measurement after SVR. PWIDs were identified using a validated algorithm. Crude reinfection rates per 100 person-years (PYs) were calculated and Cox proportional hazards modelling was performed to identify factors associated with reinfection.
Results: Among 5,702 individuals who received DAA treatment, the majority were male (n = 3704, 65%), born < 1965(n = 5298, 93%), and about a quarter were PWID (1613, 28.3%). Among PWID, 42% received opioid-agonist therapy (OAT) after HCV treatment. We identified 62 reinfections during 4,834.70 PYs of follow-up post SVR, yielding a reinfection rate of 1.28/100 PYs. Reinfection rates were higher among PWID (n = 36, 2.36/100 PYs) than non-PWIDs (n = 26, 0.79/100 PYs). In a multivariable model for PWID, birth after 1975(adjusted hazards ratio (AHR): 4.69, 95% CI 2.07–10.62) and male sex (AHR: 4.1, 95% CI 1.6–10.5) were associated with re-infection. Antipsychotic treatment was associated with lower re-infection risk (AHR: 0.55, 95% CI 0.27–1.12). No reinfections were detected among PWID who received uninterrupted OAT, while the re-infection rate was 3.42/100 PY among those with interruptions.
Conclusions: Population-level reinfection rates after DAA therapy are higher among PWID—especially younger males. Uninterrupted OAT and antipsychotic treatment was protective against reinfection.

Figure: Cumulative incidence of HCV reinfection following SVR by injection drug use



Abstract #480

Genotype misclassification and its impact on treatment choices, outcomes, and drug resistance

Howe, AYM British Columbia Centre for Disease Control, British Columbia, Canada. De Salazar, A. Hospital Universitario San Cecilio, Granada, Spain.Di Maio, VC. University of Rome Tor Vergata, Rome, Italy. Poppin, S. Erasmus University Medical Center, Rotterdam, Netherlands. Fourati, S. Centre National de Réference des Hépatites B, C et delta, Créteil, France. Tay, ESE. Westmead Institute for Medical Research, NSW, Australia Rodrigo, C. University of New South Wales, Sydney, Australia. Cunningham, E. Kirby Institute, New South Wales, Australia. Kjellin, M. Uppsala University, Uppsala, Sweden. Fay F. Laboratorio CIBIC, Rosario, Argentina. Sfalcin, J. Laboratorio CIBIC, Rosario, Argentina. Gomes, P. Laboratorio de Biologia Molecular, LMCBM, Serviço de Patologia Clínica, Centro Hospitalar Lisboa Ocidental, Hospital Egas Moniz, Lisbon and CiiEM, Almada, Portugal. Boucher, C. Erasmus University Medical Center, Rotterdam, Netherlands. De Knegt RJ. Erasmus University Medical Center, Rotterdam, Netherlands. Poljak, M. University of Ljubljana, Slovenia. Lunar M. University of Ljubljana, Slovenia. Salmon, D. Paris Descartes University, Paris, France. Usubillaga, R. Paris Descartes University, Paris, France. Sayan, M. Kocaeli University Faculty of Medicine, Kocaeli, Turkey. Mor, O. Sheba Medical Center, Ramat-Gan, Israel. Seguin-Devaux, C. Luxembourg Institute of Health, Luxembourg, Luxembourg. Lloyd, A. University of New South Wales, Sydney, Australia. Pawlotsky, JM. Centre National de Réference des Hépatites B, C et delta, Créteil, France. Grebely, J. Kirby Institute, New South Wales, Australia. Lennerstrand, J. Uppsala University, Uppsala, Sweden. Knops, E. University Hospital Cologne, Cologne, Germany. Kaiser, R. University Hospital Cologne, Cologne, Germany. Chulanov, V. Reference Center for Viral Hepatitis; Central Research Institute of Epidemiology, Moscow, Russia. Jimenez, M. Hospital Universitario de Valme, Seville; Spain. Perez AB. Hospital Miguel Servet, Zaragoza; Spain. Cabezas, J. Hospital Reina Sofia, Murcia, Spain. Douglas, M. Westmead Institute for Medical Research, NSW, Australia. Ceccherini-Silberstein, F. University of Rome Tor Vergata, Rome, Italy. Harrigan, R. University of British Columbia, British Columbia, Canada. F Garcia, F. Instituto Investigación Biosanitaria Ibs., Granada, Spain

Introduction: Genotype (GT) determination remains useful for Hepatitis C virus (HCV) management. Discordant GT/subtype determined by commercial genotyping assays have been reported.

Objectives: To retrospectively examine the impact of GT misclassification on HCV treatment and outcomes.

Methods: 1765 HCV sequences and treatment data were collected from 16 countries through SHARED. The sequence-based GT/subtypes were compared with those reported by the clinics. Patients with discordant GT/subtypes were examined for the regimens administered, treatment response, and drug resistance.

Results: Sequence-based genotyping using ICTV reference mapping accurately determines GT/subtype in HCV. Discordances between clinically- and sequence-based GT/subtypes were observed in 304/1765 (17%) patients: 7% at the GT level, and 10% at the subtype level. GT1b and GT3 isolates represented most of the GT discordant cases with a discordant rate at 13% (57/430) and 9% (50/568), respectively. For the discordant GT1bs, 91% were classified as GT3 by sequence-based genotyping, and 79% of the misdiagnosed patients were treated with inappropriate regimens. Drug resistance mutations, Y93H, A30K/S, and L62S within NS5A, were detected in 58%, 27%, and 17%, respectively, following treatment failure.For the 50 discordant GT3, 38 (76%) turned out to be GT1b, and 11 (22%) GT1a. There was no significant impact on regimen choice.Genotyping is significantly associated with treatment response: 111/121 (92%) of the GT discordant patients failed therapy, whereas 891/1245 (72%) of the GT concordant patients failed ($P < 0.0001$).

Conclusions: GT misclassification may lead to inappropriate regimen choices and treatment failure. Sequencing can be used to study GT/subtypes, drug resistance, and transmission.

Abstract #481

Genotype misclassification and its impact on treatment choices, outcomes, and drug resistance

Howe, AYM[1], De Salazar, A[2], Di Maio, VC[3], Poppin, S[4], Fourati, S[5], Tay, ESE[6], Rodrigo, C[7], Cunningham, E[8], Kjellin, M[9], Fay F[10], Sfalcin, J[11], Gomes, P[12], Boucher, C[13], De Knegt RJ[14], Poljak, M[15], Lunar M[16], Salmon, D[17], Usubillaga, R[18], Sayan, M. Kocaeli[19], Mor, O[20], Seguin-Devaux, C[21], Lloyd, A[22], Pawlotsky, JM[23], Grebely, J[24], Lennerstrand, J[25], Knops, E[26], Kaiser, R[27], Chulanov, V[28], Jimenez, M[29], Perez AB[30], Cabezas, J[31], Douglas, M[32], Ceccherini-Silberstein, F[33], Harrigan, R[34], F Garcia, F[35]

[1]British Columbia Centre for Disease Control, British Columbia, Canada, [2]Hospital Universitario San Cecilio, Granada, Spain, [3]University of Rome Tor Vergata, Rome, Italy, [4]Erasmus University Medical Center, Rotterdam, Netherlands, [5]Centre National de Réference des Hépatites B, C et delta, Créteil, France, [6]Westmead Institute for Medical Research, NSW, Australia, [7]University of New South Wales, Sydney, Australia, [8]Kirby Institute, New South Wales, Australia, [9]Uppsala University, Uppsala, Sweden, [10]Laboratorio CIBIC, Rosario, Argentina, [11]Laboratorio CIBIC, Rosario, Argentina, [12]Laboratorio de Biologia Molecular, LMCBM, Serviço de Patologia Clínica, Centro Hospitalar Lisboa, [13]Ocidental, Hospital Egas Moniz, Lisbon and CiiEM, Almada, Portugal, [14]Erasmus University Medical Center, Rotterdam, Netherlands, [15]Erasmus University Medical Center, Rotterdam, Netherlands, [16]University of Ljubljana, Slovenia, [17]University of Ljubljana, Slovenia, [18]Paris Descartes University, Paris, France, [19]Paris Descartes University, Paris, France, [20]University Faculty of Medicine, Kocaeli, Turkey, [21]Sheba Medical Center, Ramat-Gan, Israel, [22]Luxembourg Institute of Health, Luxembourg, Luxembourg, Carole, [23]University of New South Wales, Sydney, Australia, [24]Centre National de Réference des Hépatites B, C et delta, Créteil, France, [25]Kirby Institute, New South Wales, Australia, [26]Uppsala University, Uppsala, Sweden, [27]University Hospital Cologne, Cologne, Germany, [28]University Hospital Cologne, Cologne, Germany, [29]Reference Center for Viral

Hepatitis; Central Research Institute of Epidemiology, Moscow, Russia, [30]Hospital Universitario de Valme, Seville; Spain, [31]Hospital Miguel Servet, Zaragoza; Spain, [32]Hospital Reina Sofia, Murcia, Spain, [33]Westmead Institute for Medical Research, NSW, Australia, [34]University of Rome Tor Vergata, Rome, Italy, [35]University of British Columbia, British Columbia, Canada, [36]Instituto Investigación Biosanitaria Ibs., Granada, Spain

Introduction: Genotype (GT) determination remains useful for Hepatitis C virus (HCV) management. Discordant GT/subtype determined by commercial genotyping assays have been reported.
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Conclusions: GT misclassification may lead to inappropriate regimen choices and treatment failure. Sequencing can be used to study GT/subtypes, drug resistance, and transmission.

Abstract #483

Characteristics of resistance-associated substitutions in "Unusual" hepatitis C (HCV) Subtypes

Popping, S. Erasmus University Medical Center, Rotterdam, Netherlands. Fourati, S. Centre National de Réference des Hépatites B, C et delta, Créteil, France. Howe, AYM. British Columbia Centre for Disease Control, British Columbia, Canada. De Salazar, A. Hospital Universitario San Cecilio, Granada, Spain. Di Maio, VC. University of Rome Tor Vergata, Rome, Italy. Tay, ESE. Westmead Institute for Medical Research, NSW, Australia Rodrigo, C. University of New South Wales, Sydney, Australia. Cunningham, E. Kirby Institute, New South Wales, Australia. Kjellin, M. Uppsala University, Uppsala, Sweden. Sfalcin, J. Laboratorio CIBIC, Rosario, Argentina. Gomes, P. Laboratorio de Biologia Molecular, LMCBM, Serviço de Patologia Clínica, Centro Hospitalar Lisboa Ocidental, Hospital Egas Moniz, Lisbon and CiiEM, Almada, Portugal. Poljak, M. University of Ljubljana, Slovenia. Lunar M. University of Ljubljana, Slovenia. Sayan, M. Kocaeli University Faculty of Medicine, Kocaeli, Turkey. Mor, O. Sheba Medical Center, Ramat-Gan, Israel. Salmon, D. Paris Descartes University, Paris, France. Usubillaga, R. Paris Descartes University, Paris, France. Seguin-Devaux, C. Luxembourg Institute of Health, Luxembourg, Luxembourg. Carole. Soulier, A. Centre National de Réference des Hépatites B, C et delta, Créteil, France. Lloyd, A. University of New South Wales, Sydney, Australia. Grebely, J. Kirby Institute, New South Wales, Australia. Lennerstrand, J. Uppsala University, Uppsala, Sweden. Kaiser, R. University Hospital Cologne, Cologne, Germany. Zhigalkina, P. Reference Center for Viral Hepatitis; Central Research Institute of Epidemiology, Moscow, Russia. Chulanov, V. Reference Center for Viral Hepatitis; Central Research Institute of Epidemiology, Moscow, Russia. De Knegt RJ. Erasmus University Medical Center, Rotterdam, Netherlands. Douglas, M. Westmead Institute for Medical Research, NSW, Australia. Ceccherini-Silberstein, F. University of Rome Tor Vergata, Rome, Italy. Harrigan, R. University of British Columbia, British Columbia, Canada. F Garcia, F. Instituto Investigación Biosanitaria Ibs., Granada, Spain. Boucher, C. Erasmus University Medical Center, Rotterdam, Netherlands. Pawlotsky, JM. Centre National de Réference des Hépatites B, C et delta, Créteil, France. ***on behalf of the contributing members of the SHARED database***

Introduction: HCV is highly variable with 8 genotypes and >84 subtypes. Recently, "unusual" subtypes in patients from African and Asian origin have been associated with lower response rates to Direct-Acting Antivirals (DAAs).
Objectives: To characterize the post-treatment failure RAS among unusual HCV subtypes, defined as GT1-non1a/b, GT2-non2a/b, GT3-non3a, GT4-non4a/d, GT5, and GT6.
Methods: Data from patients who failed DAAs as per the EASL guidelines were extracted from the SHARED database. Genotype and subtypes were sequence-derived, and RASs were analyzed at positions according to the 2018 EASL guidelines.
Results: We identified a 6% prevalence (74/1176) of unusual subtypes among patients who failed NS5A inhibitor-containing regimens, including GT1g (n = 2), 1l (n = 5), GT2c (n = 8), 2q (n = 2), 2i/j (n = 1 each), GT3h (n = 7), 3b (n = 6), 3k (n = 2), GT4r (n = 13), 4v/4ns (n = 3 each), 4g/4o (n = 2 each), 4b/4f/4k/4n/4q/4t (n = 1 each), GT6q (n = 3), 6e/6h/6p/6r/6xe (n = 1 each). Patients were treated with SOF+LDV+/−RBV (n = 18), SOF+DCV+/−RBA (n = 15), SOF+-VEL+/−RBV (n = 13), GZR+EBR (n = 11), 2D/3D+/−RBV (n = 11, GLP+PIB (n = 5), or other regimens (n = 1). At failure, all patients harbored NS5A RAS regardless of their subtype with a mean of 3 NS5A RAS/sample. Failures with GT6h/p/r/xe carried 5 to 6 NS5A polymorphisms possibly associated with reduced susceptibility to NS5A inhibitors. All GT3b failing patients harbored the NS5A A30K+L31M+S62D/E combination. In patients failing NS3 protease inhibitor-based therapy, combinations of NS3 RASs were detected: R155Q/A156T/D168N/E in GT4g, Y56H+D168V in GT6q, and A156F/D168V in GT6a. Two GT4r patients had NS5B S282T RAS.
Conclusions: Unusual subtypes may be overrepresented among DAA failures. In-vitro characterization of RAS in these subtypes is needed.

Abstract #534

Hepatocellular carcinoma post direct-acting antivirals in Australian hepatitis C-related advanced fibrosis/cirrhosis patients

Emilia Prakoso

Background: Direct-acting antiviral (DAA) is effective in HCV eradication. However, controversies emerged around their impact on hepatocellular carcinoma (HCC) incidence. We report the first Australian data on HCC incidence in DAA-treated patients with advanced fibrosis/cirrhosis and contributing factors.
Methods: A retrospective single-centre study was performed in patients with HCV-related advanced fibrosis/cirrhosis treated with DAAs between April 2015 and December 2017. Patients with prior

HCC were included if they had complete response to HCC treatment, and were excluded if they had incomplete radiological response, indeterminate nodules, or received palliative therapy.
Results: 138 patients completed DAA and 133/138 achieved sustained virologic response (SVR12). The median follow-up was 23.8 months (246.2 patient-years). 10/138 patients had prior HCC and 5/10 developed recurrence. 7/128 patients without prior HCC developed *de novo* HCC (5.5%).
Median time from DAA commencement to HCC diagnosis was 34 weeks in recurrent HCC and 52 weeks in *de novo* occurrence ($p = 0.159$). In patients with prior HCC, those with recurrence (vs those without) had shorter median time between their last HCC treatment and DAA commencement (12 vs 164 weeks, $p < 0.001$).

On bivariate analysis, failed SVR ($p = 0.011$), platelets ($p = 0.005$), MELD ($p = 0.029$), AFP ($p = 0.013$), and prior HCC ($p < 0.001$) were associated with HCC development post-DAA. On multivariate analysis, significant factors were prior HCC (OR 4.8, $p = 0.010$), failed SVR (OR 2.83, $p = 0.016$) and platelet count (OR 0.97, $p = 0.009$).
Conclusion: Our study suggests more advanced liver disease, failed SVR and prior HCC were associated with HCC development post-DAA. There were high rates of recurrence in those who started DAA earlier.

Abstract #536

Real-life efficacy of glecaprevir and pibrentasvir for genotype 2 chronic hepatitis C

Hyung Joon Yim*, Sang Jun Suh, Young Kul Jung, Jung Tae Kim, Han Ah Lee, Tae Hyung Kim, Sun Young Yim, Young-Sun Lee, Jong Jin Hyun, Yeon Suk Seo, Ji Hoon Kim, Jong Eun Yeon, Kwan Soo Byun, Sun Ho Um

Department of Internal Medicine, Korea University Medical College, Seoul, Korea (the republic of)

Aims: Glecaprevir and Pibrentasvir (GP) are available for management of chronic hepatitis C (CHC) in Korea. The aim of the study is to evaluate the real-life efficacy of GP for genotype 2 CHC.
Methods: Since 2018, the patients who received GP at Korea University Medical Center were investigated retrospectively. We analyzed CHC patients with genotype 2 only. Sustained virologic response at week 12 post-treatment (SVR12) was assessed.
Results: 147 patients were treated by GP regimen. 110 patients were excluded from analysis; 34 patients were non-genotype 2, and 76 patients' SVR12 data were not available since current initiation of treatment. At the present time, 37 patients were included for analysis.The median age was 55 (26-77) years (male, 45.9%). The median HCV RNA level was 602,000 (49-14,400,000) IU/mL. Two patients (5.4%) experienced previous directly acting antiviral failures (sofosbuvir). Patients with liver cirrhosis (21.6%) were treated for mean 11.8 ± 0.2 weeks while non-cirrhotic patients (78.4%) were treated for mean 8.0 ± 0.2 weeks. The SVR12 was 100%. No patient showed treatment failure or relapse. Additionally, we compared the data with those of 122 genotype 2 CHC patients treated by SR at Korea University Medical Center until 2017 which showed 96.3% of SVR12 rate by PP analysis. There was no significant difference between 100% (GP) and 96.3% (SR) in SVR12 rate (p = 0.591).
Conclusions: Efficacy of GP regimen was excellent in real-life setting. Although the SVR12 rate of GP were not significantly different from that of SR, it was efficacious even in previous SR failures.

Abstract #549

Can near point of care HCV RNA tests serve as holy grail in the HCV care continuum: an evaluation study of Genedrive HCV RNA test

Padhi Abhishek[1], Gupta Ekta[2], Singh Gaurav[3], Sharma M[4], Sarin S K[5]

[1]Department of clinical virology, Institute of liver and biliary sciences, New Delhi, India, [2]Department of clinical virology, Institute of liver and biliary sciences, New Delhi, India, [3]Department of clinical virology, Institute of liver and biliary sciences, New Delhi, India, [4]Department of Hepatology, Institute of liver and biliary sciences, New Delhi, India, [5]Department of Hepatology, Institute of liver and biliary sciences, New Delhi, India

Introduction: In the HCV cascade of care, maximum lost to follow up occur between HCV serological testing and HCV RNA confirmatory test. HCV RNA tests done as point of care in a decentralized manner can bridge this gap. Genedrive, a near point of care HCV RNA test is one such assay and can help in finding the missing millions.
Objectives: Performance evaluation of Genedrive HCV RNA test was done comparing it with Abbott HCV RNA in an Indian demographic setting and across a range of different genotypes commonly found in India.
Methods: Once thawed clinical samples from 320 patients: 150 HCV RNA positive and 170 HCV RNA negative and negative for antibody to HCV were included in the study and tested on Genedrive system.
Results: No discordance was seen between Genedrive and Abbott HCV assay with a sensitivity of 100% (95% CI 97.9–100) and a specificity of 100% (95% CI 97.9–100). Overall diagnostic accuracy of Genedrive was found to be 100% (95% CI 98.9 to 100). An excellent correlation was seen between the two assays (concordance correlation coefficient, r = 1). Genotype 3 was the commonest, seen in 86(61.8%) cases. Median HCV RNA load was 5.65 $\log_{10}$ (range 5.04–6.09 $\log_{10}$) IU/ml. The limit of detection for detection of HCV RNA in the present study for Genedrive was 102 IU/ml.
Conclusion: Genedrive HCV assay offers a great potential to be used as a point of care Nucleic acid amplification test (NAAT) for a real time confirmation of chronic HCV infection in any clinical setting.

Abstract #664

Need to generate awareness regarding diagnosis and treatment services for Hepatitis-C: filling the gaps to achieve Hepatitis-C elimination

Aggarwal Kavita[1], Gupta Ekta[1], Agarwal Reshu[1], Singh Nikky[1], Rani Nitiksha[1], Sarin SK[2]

[1]Department of Clinical Virology, Institute of Liver & Biliary Sciences, New Delhi, India, [2]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Globally, more than 50% of all Hepatitis-C virus (HCV) infections occur in six countries including India. Unfortunately, only around 20% HCV infected people were diagnosed and 13% were treated in 2016. Lack of awareness regarding diagnosis and treatment services is one of the major barriers in achieving WHO goal of Hepatitis-C elimination.
Objective: To assess knowledge, attitude and practices regarding Hepatitis-C in patients attending health facility.
Methods: This cross-sectional study was undertaken in a super specialty hospital of Delhi among the patients visiting Out-Patient

Department for minor ailments. Already known cases of Hepatitis-C were excluded. Pre-tested questionnaire focusing on knowledge, attitude and practice domains was administered to the participants. Each item was allocated score of 1 for best response and cumulative score was calculated for every participant.

Results: Four-twenty patients participated in the study with mean age and male to female sex ratio of 41.73 ± 17.46 years and 4:3 respectively. One-hundred (23.81%) participants had ever heard of Hepatitis-C. The maximum scores in knowledge, attitude and practice domain were 15, 6 and 8 with median scores of 6.50 (IQR: 3.25–8.00), 3 (IQR: 2–3) and 2 (IQR: 0–5) respectively. Only 57% patients knew that Hepatitis-C was treatable. Eighty-four (84%) patients would approach allopathic health facility if infected with Hepatitis-C. Only 8% patients got screened for Hepatitis-C in past. Fifty-one (51%) patients would undergo further investigations and treatment if diagnosed with Hepatitis-C.

Conclusion: The study demonstrated need to create awareness to achieve Hepatitis-C elimination in view of poor knowledge, attitude and practices.

Abstract #724

The alteration of gut microbiota composition in patients with hepatitis C virus (HCV) monoinfection and human immunodeficiency virus (HIV) coinfection

Jinato T.[1], Chuaypen N.[1], Chittmittraprap S.[1], Avihingsanon A.[2], Tangkijvanich P.[1]

[1]Center of Excellence in Hepatitis and Liver Cancer, Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, Bangkok, 10330, Thailand, [2]The HIV Netherlands Australia Thailand Research Collaboration (HIV NAT), Bangkok, Thailand

Background: Gut microbiota composition changed has been described in hepatitis C virus (HCV) infection. Beside HCV monoinfection, co-infection with HCV and human immunodeficiency virus (HIV) is also common. However, the effect of HCV/HIV co-infection and gut dysbiosis are not well characterized in patients.

Objectives: The purpose of this study was to examine the alteration of gut microbiome compare in chronic HCV mono- and HCV/HIV co-infection.

Method: Fecal specimens from Thai patients with HCV mono- and co-infection were collected and extracted for DNA. Gut microbial compositions were analyzed using 16S ribosomal RNA sequencing by Illumina MiSeq sequencing platform.

Results: This study included 58 patients with mono-infection and 28 patients with co-infection, who were age and gender-matched. Compared with the mono-infected group, patients with co-infection exhibited lower alpha and Shannon diversity of gut microbiota. Co-infected individuals also showed significantly lower in the relative abundance of genus *Faecalibacteria* (6.34 ± 5.96 vs. 8.57 ± 6.24, $P = 0.043$) and *Blautia* (1.66 ± 1.19 vs. 2.71 ± 2.29, $P = 0.044$), but higher in *Agathobacteria* (4.31 ± 8.23 vs. 1.87 ± 1.72, $P = 0.032$). Among patients with cirrhosis, *Prevotella* was significantly higher in co-infection compared with mono-infection (7.5 ± 8.5 vs. 1.08 ± 2.66, $P = 0.007$). Of note, *Faecalibacteria* and *Agathobacteria* were weakly correlated with patients' body mass index ($r = 0.214$, $P = 0.049$ and $r = 0.241$, $P = 0.026$, respectively), but did not correlate with severity of liver disease.

Conclusions: This is the first study that reported the comparison of gut microbiome profiles in patients with HCV mono- and HCV/HIV co-infection. The difference of microbe community in HIV occurrence might be related to increase of disease progression in co-infected patients.

Abstract #787

Second-generation DAAs for HCV: real-life efficacy in the RESIST-HCV(Rete Sicilia Selezione Terapia – HCV) cohort

Distefano M.[1], Cacciola I.[2], Petta S.[3],, Calvaruso V.[4], Scifo G.[5], Di Lorenzo F.[6], Sanfilippo A.[7], Di Rosolini M.A.[8], Davì A.[9], Benanti F.[10], Cacopardo B.[11,] Licata A.[12], Giannitrapani L.[13], Cannavò M.R.[14], Russello M. [15], Madonia S.[16], Bavetta M.G.[17], Digiacomo A.[18], Averna A. [19], Larocca L.[20], Bertino G.[21], Bronte F.[22], Guarneri L.[23], Scalisi I.[24], Iacobello C.[25], Colletti P. [26], Cartabellotta F. [27], Alaimo G. [28], Portelli V. [29], Pollicino T. [30], Ceccherini-Silberstein F. [31], Squadrito G.[32], Raimondo G. [33], Craxì A. [34], Di Marco V.[35] on behalf of RESIST-HCV (Rete Sicilia Selezione Terapia - HCV)

[1–5]UOC Malattie Infettive, Ospedale Umberto I° Siracusa, ASP Siracusa, Siracusa, Italy, [2–30–32–33]UOC Epatologia Clinica e Biomolecolare and AOUP G Martino, Dipartimento di Medicina Interna e Sperimentale, University of Messina, Messina, Italy [3–4–17–22–34–35]Sezione di Gastroenterologia e Epatologia, Dipartimento Biomedico di Medicina Interna e Specialistica (Di.Bi.M.I.S.), University of Palermo, Palermo, Italy, [6–7] UOC Malattie Infettive, ARNAS Civico–Di Cristina–Benefratelli, Palermo, Italy [8 –9]UOC Malattie Infettive, Ospedale di Modica, ASP Ragusa, Ragusa, Italy, [10–11]UOC Malattie Infettive, ARNAS Garibaldi–Nesima, Catania, Italy [12–13]UOC Medicina Interna, AOUP Paolo Giaccone, Palermo, Italy [14–15]UOSD Epatologia, ARNAS Garibaldi–Nesima, Catania, Italy [16]UOC Medicina Interna, AO Villa Sofia–Cervello, Palermo, Italy [18]UOC Medicina Interna, Ospedale di Comiso, ASP Ragusa, Ragusa, Italy [19]UOC Malattie Infettive, Ospedale di Caltanissetta, ASP Caltanissetta, Caltanissetta, Italy [20]UOC Malattie infettive, AOUP G Rodolico, Catania, Italy.[21]UOC Medicina Interna, AOUP G Rodolico, Catania, Italy [23]UOC Malattie Infettive, Ospedale di Enna, ASP Enna, Enna, Italy [24.]UOC Medicina Interna, Ospedale di Mazzara del Vallo, ASP, Trapani, Italy, [25]UOC Malattie Infettive, AO Cannizzaro, Catania, Italy, [26]UOC Malattie Infettive, Azienda Ospedaliera Universitaria Paolo Giaccone, Palermo, Italy, [27]UOC Medicina Interna, Ospedale Buccheri La Ferla, Palermo, Italy [28]UOC Medicina Interna, Ospedale di Agrigento, ASP Agrigento, Agrigento, Italy [29]UOC Malattie Infettive, Ospedale di Trapani, ASP Trapani, Trapani, Italy, [31] Department of Experimental Medicine, University of Rome Tor Vergata

Introduction: RESIST-HCV registers in Sicily all HCV patients treated with DAAs, allowing efficacy evaluation.

Objective: Evaluate second-generation regimens (SOF/VEL; GLE/PIB; EBV/GRZ) SVR rates.

Methods: We analyzed 4,087 naïve treated between March 2017 and December 2018.

Cirrhosis was diagnosed by liver stiffness ≥ 12 KPa (Fibroscan) and/or by presence of esophageal varices and/or biopsy METAVIR stage 4 fibrosis.

Results: By ITT analysis 95.1% (3,878/4,078) achieved SVR. 125 (3.1%) did not complete therapy. 11 (0.3%) died for liver-related (5) or unrelated (6) causes while on treatment. 20 (0.5%) discontinued treatment due to adverse events and 94 (2.2%) did not have virology available for SVR evaluation. 75 (1.8%) did not achieve SVR: of them, 14 were still HCV-RNA positive at ETR and 61 showed a virological relapse after ETR.By PP analysis 98.1% (3878/3953) obtained an SVR. Chronic hepatitis (CE) and Gt 1a, 1b, 2 or 4 obtained SVR rates higher than 99% when treated with pangenotypic regimes (SOF/VEL or GLE/PIB). SVR rates above 96% were obtained in cirrhosis and Gt 1a,1b, 2 or 4 treated with SOF/VEL or GLE/PIB. Adding ribavirin to SOF / VEL in Gt 3 CE or cirrhosis did not enhance SVR rates. Genotype 1b with CE or cirrhosis, when

treated with EBV/GRZ had an SVR in 95.9% and 94.7% of cases, respectively, mostly due to post-ETR relapses.
Conclusions: Current DAA regimens, especially if pangenotypic, obtain response rates of at least 95% in a real-life situation. Adding ribavirin to SOF/VEL seems unnecessary in Gt3 patients, regardless of fibrosis.

Abstract #937

Seroconversion of hepatitis C during dialysis in Major cities of Pakistan

Talal khurshid[1], Mashood Ali,[1] Muhammad Umar[2], Tayyab Saeed Akhtar[2], Madeha Irfan[2]

[1]Department of Gastroenterology, Pims Islamabad. [2]Department of Medicine, Holy Family Hospital / Rawalpindi Medical College, Rawalpindi

Background: Hepatitis C is highly prevalent in Pakistan. Several studies worldwide have shown that patients undergoing hemodialysis are at a risk for developing Hepatitis C. So this study was carried out to determine the proportion of patients undergoing hemodialysis who seroconverted from HCV negative to HCV positive status in our hospitals.
Methods: This descriptive cross-sectional study was conducted at four tertiary care hospitals of Punjab from January 2016 to March 2016 on patients undergoing hemodialysis currently. With the help of WHO Sample Size Calculator, at confidence level 95%, absolute precision 5% and anticipated population proportion 14%, the minimally required sample size was calculated to be 186 patients but we included 190 patients in our study. Sampling technique was stratified random sampling based on hospital and gender. Our inclusion criterion was all those patients who were Hepatitis C negative (determined by HCV serology, based on the principle of immunochromatography) at the initiation of dialysis and remained negative for the subsequent 6 months after the initiation of hemodialysis. Our exclusion criteria was all those patients who seroconverted to HCV positive with 6 months of initiation of hemodialysis (the period corresponding to the incubation period of hepatitis C virus.) and those who were dialyzed on emergency basis. The patients' records were thoroughly checked and information regarding their HCV status at initiation of dialysis and HCV status in later serology tests was recorded. Patients who were HCV negative at baseline but later confirmed to be HCV positive, based on HCV serology were considered seroconverted. All the data was entered and analyzed in Statistical Package of Social Sciences, SPSS (version 22). For All the categorical variables like gender of patient, renal diagnosis, HCV status positive or negative, etc. frequencies along with percentages were calculated. For continuous variables like age of patient, duration since initiation of dialysis (in months) and duration since seroconverted (in months), mode, mean along with standard deviation were calculated.
Results: Out of 190 patients who were HCV negative at the initiation of dialysis, 93 (i.e. 48.9%) patients converted to HCV positive status whereas 97 (i.e. 51.05%) patients remained HCV negative throughout the study. The mean time taken for seroconversion was 18.04 months (SD $\pm$ 15.43) months). The median was 12 months, with an inter quartile range of 14 months.
Conclusion: The proportion of HCV seroconversion in our hemodialysis units is very high.
Keywords: HCV, seroconversion, hemodialysis, ESRD, chronic kidney failure, immunochromatography, serology.

Abstract #961

Abbott RealTi*m*e HCV dried blood spot assay

Mak, Wai Bing[1], Webb, Erika[1], Wiesneth, Russell[1] ,Lucic, Danijela[1] ,Ho, Shiaolan[1] ,Abravaya, Klara[1]

[1]Abbott Molecular, Inc., 1300 East Touhy Avenue, Des Plaines, IL 60018-3315, USA

Introduction/objectives: HCV viral load in peripheral blood is an important marker for disease prognosis and therapeutic effectiveness. Conventional viral load tests require large volume of plasma/serum and impose stringent conditions on sample collection/processing/storage/shipment. Majority of global HCV burden lies in low/middle-income countries that lack sufficient resources. Identification of HCV infected patient is scarcely available in these areas. Dried Blood Spot (DBS) usage could eliminate many logistical and technical limitations.
Methods: This study evaluates a viral load method from DBS under-development using Abbott RealTi*m*e HCV. 70 uL blood was dispensed onto 1 spot of Ahlstrom/Munktell or Whatman903 card and air-dried before storage in sealable bag containing desiccants. When tested, 1 DBS was excised and placed into a sample tube containing 1.3mL Abbott *m*DBS buffer. After 30min incubation at ambient temperature with manual mixing before and after, the tube was loaded onto the instrument. HCV RNA was extracted and assembled into PCR reactions by Abbott *m*2000*sp* and amplified/detected by *m*2000*rt*.
Results: This method exhibited good linearity for HCV DBS samples, from $<$ 1000 IU/mL through 100,000,000 IU/mL. Viral quantification for DBS samples correlated well with liquid plasma results. HCV DBS samples exhibited good stability at 30 ± 2 °C, 2-8°C and -20 ± 5 °C, in addition to condition of 85% high humidity. The diagnostic specificity was 100%, and the sensitivity was $<$ 1000 IU/mL by Probit analysis, processing 1 DBS.
Conclusion: Excellent viral load performance was achieved when testing DBS samples with Abbott RealTi*m*e HCV and *m*2000 instruments. Small sample volume, ease of collection/processing, and excellent stability make DBS suitable for resource-limited regions.

Abstract #1051

Kinetics of plasma mac-2 binding protein glycosylation isomer level in hepatitis c patients with cirrhosis

Saut Horas H Nababan, Kemal F Kalista, Chyntia OM Jasirwan, Juferdy Kurniawan, C. Rinaldi Lesmana, Andri Sanityoso Sulaiman, Irsan Hasan, Rino A Gani.

Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Background: Previous study has shown that Mac-2 binding protein glycosylation isomer (M2BPGi) has good accuracy in diagnosing liver fibrosis in patients with chronic hepatitis C. Here, we studied the kinetics of plasma M2BPGi levels in hepatitis C patients with cirrhosis before, during and after direct-acting antivirals (DAA) treatment.
Methods: We measured and compared plasma M2BPGi levels of hepatitis C patients with cirrhosis before (n = 13) and during sofosbuvir/daclatasvir treatment (n = 8) as well as after sustained virological response (SVR) (n = 11). Liver stiffness was measured using transient elastography (TE). The AST to Platelet Ratio Index (APRI) and Fibrosis-4 (FIB-4) index were also calculated.

Results: The median and interquartile range (IQR) of plasma M2BPGi in pre-DAA was 11.74 cutoff index (COI) (IQR 11.71), during DAA 4.15 COI (IQR 7.29) and after SVR 2.68 COI (IQR 2.64). Compared with TE-based liver stiffness measurement, APRI and FIB-4 index, there was a significant decreasing trend for plasma M2BPGi levels toward the SVR group (p-value trend = 0.009).
Conclusion: Plasma M2BPGi levels were decreasing after DAA in hepatitis C patients with cirrhosis. This rapid decreasing trends may be associated with the improvement of inflammation after DAA treatment.

Abstract #1099

Factor associated with treatment failure of DAA for chronic hepatitis C—a nationwide real-world HCV Registry Program (TACR) in Taiwan

Chi-Yi Chen[2], Kuo-Chih Tseng[3], Ching-Chu Lo[4], Pin-Nan Cheng[5], Cheng-Yuan Peng[6], Ming-Jong Bair[7], Chih-Lang Lin[8], Chi-Ming Tai[9], Chi-Chieh Yang[10], Chih-Wen Lin[11], Chun-Yen Lin[12], Chia-Chi Wang[13], Wei-Wen Su[14], Lee-Won Chong[15], Pei-Lun Lee[16], Tsai-yuan Hsieh[17], Chih-Lin Lin[18], Chun-Chao Chang[19], Chun-Ting Chen[20], Chao-Hung Hung[21], Wei-Lun Tsai[22], Guei-Ying Chen[23], Szu-Jen Wang[24], Chia-Sheng Huang[25], Kwok-Hsiung Chou[26], Cheng-Hsin Chu[27], Chien-Hung Chen[28], Tzong-Hsi Lee[29], Lein-Ray Mo[30], Yi-Hsiang Huang[31], Yung-Fa Chen[32], Chen-Hua Liu[33], Sheng-Shun Yang[34], Jui-Ting Hu[35], Chi-Tan Hu[36], Hsing-Tao Kuo[37], Chun-Che Lin[38], Jian-Neng Gao[39], Shih-Jer Hsu [40], Jain-Yu Cheng[41], Pei-Chien Tsai[1], Mei-Hsuan Lee[31], Chung-Feng Huang[1], Chun-Jen Liu[33], Chia-Yen Dai[1], Rong-Nan Chien[12], Jia-Horng Kao[33], Ming-Lung Yu[1].

[1]Kaoshiung Medical University Hospital, Kaohsiung Medical University, [2]Ditmanson Medical Foundation Chia - Yi Christian Hospital, [3]Dalin Tzu Chi Hospital, [4]St. Martin De Porres Hospital, [5]National Cheng Kung University Hospital, [6]China Medical University Hospital, [7]Mackay Memorial Hospital,Taitung Branch, [8]Keelung Chang Gung Memorial Hospital, [9]E-Da Hospital, [10]Show Chwan Memorial Hospital, [11]E-Da Dachang Hospital, [12]Linkou Chang Gung Memorial Hospital, [13]Taipei Tzu Chi Hospital, [14]ChangHua Christian Hospital, [15]Shin Kong Wo Ho-SU Memorial Hospital, [16]Chi Mei Hospital, Liouying Branch, [17]Tri-Service General Hospital, [18] Taipei City Hospital, Renai Branch, [19]Taipei Medical University Hospital, [20]Tri-Service General Hospital, Penghu Branch, [21]Chiayi Chang Gung Memorial Hospital, [22]Kaohsiung Veterans General Hospital, [23]Penghu Hospital, [24]Yuan's General Hospital, [25]Yang Ming Hospital, [26]Chou Kwok-Hsiung Clinic, [27] Taipei Mackay Memorial Hospital, [28]Kaohsiung Chang Gung Memorial Hospital, [29]Far Eastern Memorial Hospital, [30]Tainan Municipal Hospital, [31]Taipei Veterans General Hospital, [32]Taipei Municipal Wanfang Hospital, [33]National Taiwan University Hospital, [34]Taichung Veterans General Hospital, [35]Cathay General Hospital, [36]Hualien Tzu Chi Hospital, [37]Yongkang Chi Mei Hospital, [38]Chung Shan Medical University Hospital, [39]National Taiwan University Hospital, Hsinchu Branch, [40]National Taiwan University Hospital, Yunlin Branch, [41]Tao Yuan General Hospital

Background/aims: TASL HCV Registry (TACR) is a nationwide registry program organized and supervised by Taiwan Association for the Study of the Liver. The present study aimed to evaluate the factors associated with treatment efficacy for CHC patients in Taiwan.
Methods: By Oct 2019, 16 tertiary hospital, 23 community hospital and one primary care clinics across the country join the TACR program. The primary objective was sustained virological response, defined as undetectable HCV RNA 3 months after end-of-treatment (SVR12).
Results: A total of 10,068 CHC patients were enrolled in the current analysis (mean age, 63.6 years, female 57.1%, HCV genotypes, GT1b 65.7%/GT2 33.7%, cirrhosis 44.6%, liver decompensation 8.7%, preexisting HCC 12.0% and HBV co-infection 6.9%). The overall SVR12 rate was 98.3%, with 98.7%, 98.1%, 98.4% and 97.4% in treatment-naïve non-cirrhotics, treatment-naïve cirrhotics, treatment-experienced non-cirrhotics and treatment-experienced cirrhotics patients, respectively. The most important factors independent associated with treatment failure was DAA adherence < 60% (odds ratio [OR]/95% confidence intervals [CI] 122.5/49.9–300.9, P < 0.0001, followed by HIV co-infection (OR/CI 4.39/1.57–12.32, P = 0.005), the use of daclatasvir/asunaprevir (OR/CI 3.41/2.01–5.79, P < 0.0001) and sofosbuvir/ribavirin (OR/CI 4.57/3.15–6.62, P < 0.0001) compared with others, and preexisting HCC (OR/CI : 2.27/1.53–3.38, P < 0.0001). There existed a dose response relationship between DAAs adherent rate and SVR12 rate (trend P < 0.0001, figure 1 D).
Conclusions: DAAs are highly effective in treating CHC patients in real-world setting of Taiwan. Ensuring DAA adherence and selection of optimal DAA regimens are key determinants in HCV elimination in real world clinical practice.

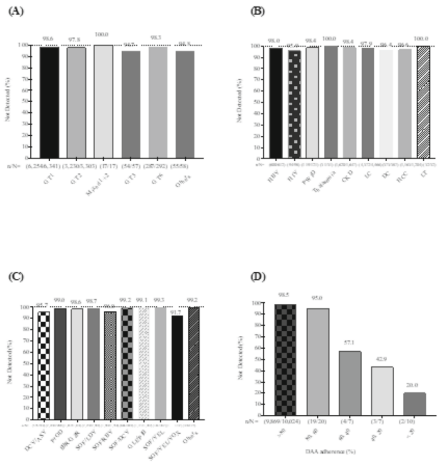


Figure 1. SVR by HCV genotype (A), by special population (B), by DAA regimen (C), and by DAA adherence (D)

Abstract #1100

Treatment efficacy and safety of sofosbuvir with velpatasvir for chronic hepatitis C among uremic patients under maintenance hemodialysis-an interim report of ERASE-C

Ming-Lung Yu[1], Chung-Feng Huang[1], Yu-Ju Wei[1], Ming-Lun Yeh[1], Ching-I Huang[1], Wen-Yi Lin[2], Yi-Hung Lin[1], Po-Cheng Liang[1], Ta-Wei Liu[3], Chia-Yen Dai[1], Jee-Fu Huang[1], Wan-Long Chuang[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [2]Department of Occupational Medicine, Kaohsiung Municipal Hsiao-Kang Hospital, Taiwan, [3]Department of Internal Medicine, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan

Introduction: The real world evidence of sofosbuvir (SOF)/velpatasvir (VEL) in the treatment of uremic patients with HCV infection is limited.
Objectives: The current study aimed to address the efficacy and tolerability of SOF/VEL in treating chronic hepatitis C (CHC) patients on maintained hemodialysis.

Methods: An outreach treatment strategy using 12-week SOF/VEL was adopted in 18 hemodialysis units.
Results: A total of 105 patients were included (mean age 66.2 years, female 48.6%, hepatitis B virus dual infection 7.6%, pre-existing hepatocellular carcinoma 6.7%, liver decompensation 0.9%). By the end of October 2019, the rate of undetectable HCV RNA at treatment week 1, week 2, week 4, end-of-treatment (EOT) and post-treatment 4 weeks (SVR4) was 46.7% (49/105), 72.4% (76/105), 90.5% (95/105), 93.3% (98/105) and 91.0% (91/100), respectively, in full-analysis-set population, and was 48.4% (44/91), 74.7% (68/91), 95.6% (87/91), 100% (90/90) and 100% (88/88), respectively, in modified full-analysis-set population. There was no relapse between EOT and SVR4 assessment. Ten patients discontinued therapy before the end-of-treatment. Of them, 5 were considered treatment related (dizziness [n = 1], nausea/vomiting [n = 2], epigastric pain [n = 2]), whereas the other 5 serious adverse events were unrelated to treatment regimen (sepsis [n = 3], acute myocardial infarction [n = 1] and pneumonia [n = 1]). The most common adverse event was fatigue (9.3%), followed by pruritus (8.4%).
Conclusions: Twelve weeks of SOF/VEL was highly effective in uremic CHC patients in the interim analysis. A satisfactory final treatment outcome may be anticipated in the full patient set.

Abstract #1171

Evaluation of the role of peripheral blood monocytes in prediction of response to direct acting antiviral drugs in chronic HCV patients

El-Sayed Ibrahim[1], Eman Abdelsameea[1], Ayman Alsebaey[1], Sabry Moawad Abdelmageed[2] and Maha Elsabaawy[1]

[1]Department of Hepatology and Gastroenterology, National Liver Institute, Menoufia University, Shebeen El-Kom, Egypt, [2]Department of Clinical Biochemistry, National Liver Institute, Menoufia University, Shebeen El-Kom, Egypt

Background: HCV infection eradication had not become a dream in the era of direct acting antiviral therapies (DAAs). However, prediction of relapse post-treatment had to be more speculated.
Aim: To evaluate the role of peripheral blood monocytes (PBMCs) HCV as a predictor of post-treatment relapse.
Methods: This case control study was conducted on 118 chronic HCV patients treated with DAAs with achievement of end of treatment response (ETR). HCV PCR at PBMNs was evaluated in relation to ETR and SVR.
Results: One hundred and twelve cases had SVR 24 (57 males/55 females; mean age 46.9 $\pm$ 10.2 years old), with only six relapsers (5.1%). Triple HCV RNA negativity was significantly lower in relapsers than in patients who achieved SVR (16.7% versus 92.9%, p = 0.001). Cases with two positive strands were associated with 2 relapsers (33.3%) and complete failure to achieve SVR. The highest relapse rate (50%) was detected in those single positive stranded with 8 (7.1%) responders. Factors affecting treatment response were; Absence of esophageal varices (p = 0.019), triple HCV RNA negativity (p = 0.001), albumin (p = 0.018), platelets (p = 0.049), INR (p = 0.003), creatinine (p = 0.030) and MELD score (p = 0.007). However, multivariate analysis had declared negativity of triple HCV RNA to be the only significant predictor of achieving SVR after treatment with different regimens of DAAs with 208.38 Odds Ratio and 95% CI (4.93–8809.97) and p value = 0.005.
Conclusion: Relying on presence of HCV on PBMCs at the end of treatment with DAAs might be a trustworthy independent predictor of relapse.

Abstract #1194

The role of hepatitis C virus core antigen in the determination of treatment response after direct acting anti-viral agents

Chayanupatkul, Maneerat[1]; Chuaypen, Natthaya[2]; Chittmittraprap Salyavit[2]; Tangkijvanich, Pisit[2]

[1]Department of Physiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [2]Center of Excellence in Hepatitis and Liver Cancer, Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Introduction: Hepatitis C virus core antigen (HCVcAg) has been proven to be a reliable and cost-saving method in the diagnosis of HCV. The evidence, however, is not clear whether HCVcAg can be reliably used to monitor treatment response with direct acting antiviral agents (DAAs).
Objectives: To determine the correlation between HCV RNA and HCVcAg at each time point during DAA treatment including the determination of sustain virological response at 12 and 24 weeks post-treatment (SVR12 and SVR24)
Methods: Patients with HCV genotype 1 were enrolled. Treatment-naïve patients were treated with grazoprevir and elbasvir for 12 weeks. Treatment-experienced patients were treated with the combination plus weight-based ribavirin for 16 weeks. HCV RNA and HCVcAg were measured at baseline, week4, end-of-treatment, week 12 post-treatment and week24 post-treatment. HCV RNA level < 12 IU/mL and HCVcAg < 3 pg/mL were considered undetectable.
Results: Eight-nine patients had complete data for the analyses. The rate of SVR12 was 97.8%. Three patients who achieved SVR12 (3.4%) relapsed at week24 post-treatment. The correlation coefficient between HCV RNA and HCVcAg at baseline, week 4, end-of-treatment, week12 post-treatment and week24 post-treatment were 0.81 ($p < 0.001$), 0.23 ($p = 0.03$), 0.46 ($p < 0.001$), 0.82 ($p < 0.001$) and 0.92 ($p < 0.001$), respectively. Undetectable HCVcAg at 12 weeks post-treatment correctly predicted SVR12 in all patients. However, undetectable HCVcAg at 12 weeks post-treatment did not predict relapse at week24 post-treatment.
Conclusion: HCVcAg correctly predicted SVR12 with good correlation between HCVcAg and HCV RNA. HCVcAg is a potentially lower-cost alternative to HCV RNA in the determination of treatment response with DAAs.

Abstract #1230

The side effects of direct acting antivirals in hepatitis c patients are associated with oatp 334 T > G variant

Zuhal Mert Altintas[1], Engin Altintas[2].

Mersin University Faculty of Medicine, Medical Genetics[1], Gastroenterology[2], Mersin, Turkey.

Introduction: The aim of this study was to investigate whether there is a relationship between the side effects of hepatitis C treated with direct-acting antivirals (DAA) and the variants of organic anion-transporting polypeptide (OATP) used by these drugs as transporters.
Methods: 199 hepatitis C patients using DAA (ledipasvir / sofosbuvir or ombitasvir / paritaprevir / ritonavir $\pm$ dasabuvir) and 162 controls were included in the study. Side effects of the patients were recorded during the treatment. 388 A > G, 521 T > C, 334 T > G and 699 G > A variations of OATP genes were studied by PCR-RFLP method.

Results: 53 of 199 patients (26.6%) had side effects. Skin lesions were detected in 19 (9.5%), weakness in 18 (9%), pruritus in 11 (5.5%) and nausea in 5 (2.5%). There was a significant relationship between be having the 334 T > G of among the variants which are evaluated, and side effects (for all of them, $p < 0.001$). The frequency of 334 T > G variant was 130/199, 65.3% in the patient group and 102/161, 63% in the control group and indicated a balanced distribution (Hardy Weinberg balance $p = 0.05$).
Conclusion: We found an association between DAA-related side effects and 334 T> G variant in OATP gene in hepatitis C patients.

Abstract #1240

Ledipasvir/sofosbuvir for patients coinfected with chronic hepatitis C and hepatitis B in Taiwan: follow-up 108 weeks posttreatment

Liu CJ[1], Chuang WL[2], Sheen IS[3], Wang HY[4], Chen CY[5], Tseng KC[6], Chang TT[7], Massetto B[8], Suri V[8], Camus G[8], Jiang D[8], Zhang F[8], Gaggar A[8], Hu TH[9], Hsu YC[10], Lo GH[11], Chu CJ[12], Chen JJ[13], Peng CY[14], Chien RN[15], Chen PJ[16]

[1]Graduate Institute of Clinical Medicine, Department of Internal Medicine and Hepatitis Research Center, National Taiwan University College of Medicine and Hospital, Taipei City, Taiwan, [2]Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung City, Taiwan, [3]Linkou Chang Gung Memorial Hospital, Taoyuan City, Taiwan, [4]MacKay Memorial Hospital, Taipei City, Taiwan, [5]Chia-Yi Christian Hospital, Chia-Yi City, Taiwan, [6]Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Chia-Yi City, Taiwan, [7]National Cheng Kung University Hospital, Tainan City, Taiwan, [8]Gilead Sciences, Inc., Foster City, California, USA, [9]Kaohsiung Chang Gung Memorial Hospital, Kaohsiung City, Taiwan, [10]Changhua Christian Hospital, Changhua City, Taiwan, [11]E-Da Hospital, Kaohsiung City, Taiwan, [12]Taipei Veterans General Hospital, Taipei City, Taiwan, [13]Chi Mei Hospital, Tainan City, Taiwan, [14]China Medical University Hospital, Taichung City, Taiwan, [15]Keelung Chang Gung Memorial Hospital, Keelung City, Taiwan, [16]National Taiwan University College of Medicine and Hospital, Taipei City, Taiwan

In persons chronically coinfected with hepatitis C virus (HCV) and hepatitis B virus (HBV), HCV treatment with direct-acting antivirals can lead to reactivation of HBV. We evaluated the frequency and characteristics of HBV virologic and clinical reactivation during ledipasvir/sofosbuvir (LDV/SOF) treatment and 108-week follow-up.

In Taiwan, 111 patients with HCV/HBV coinfection received 12-weeks of LDV/SOF. HBV virologic reactivation was defined as postbaseline increase in HBV DNA from either < lower limit of quantification (LLOQ, 20 IU/mL) to ≥ LLOQ or ≥ LLOQ to > 1 $\log_{10}$ IU/mL. HBV clinical reactivation was defined as HBV virologic reactivation with alanine aminotransferase (ALT) > 2 × upper limit of normal (ULN). Logistic regression analysis was used to evaluate factors associated with HBV virologic or clinical reactivation.

All 108 patients maintained HCV suppression through 108 weeks posttreatment. HBV virologic reactivation occurred in 73% of patients (81/111). Clinical reactivation occurred in 9% of participants (10/111). Majority of HBV virologic reactivation (86%, 70/81) occurred by follow-up week 12. Clinical reactivation was generally more delayed, happening between week 12 and 48 of follow-up in 4 patients. Eight patients (7%, 8/111) initiated HBV therapy. In univariate and multivariate analyses, no factors were associated with HBV virologic or clinical reactivation.

Among HCV/HBV coinfected patients treated with direct-acting antivirals for HCV, HBV virologic reactivation occurred in majority of patients during treatment and follow-up. HBV virologic reactivation was asymptomatic; only a minority initiated HBV treatment. Notably, clinical reactivation is transient and may still occur >3 months after end of therapy.

Abstract #1244

Real world efficacy of direct antiviral drugs in the treatment of chronic hepatitis C and influence on liver stiffness and APRI

Liang Jing, Han Tao, Liu Fang, Zhang Yaping, Xiang Huiling, LV Hongmin, YE Qing

Department of Gastroenterology, Tianjin Third Central Hospital, Tianjin 300170, China

Objective: The aim of this study was to investigate the real-world viral response of chronic hepatitis C (CHC) patients and the influence on liver stiffness measurement (LSM) and AST/platelets ratio index (APRI) under the current direct acting antivirals (DAA) treatment.
Patients and methods: The study included 212 consecutive patients of CHC, and was conducted at Tianjin Third Central Hospital from April 1, 2018 till November 31, 2018. All patients were treated with DAA for 12–24 weeks. The sustained virological response (SVR) and the changes of LSM and APRI from baseline were evaluated at the 12th week after treatment.
Results: 212 patients with chronic hepatitis C were included in our study, 174 of whom had completed the whole course of DAA treatment and 12 weeks follow-up. Among the patients included, cirrhosis accounted for 35.4%, gene 1b, 2a, 3a and 6a accounted for 75%, 18.3%, 4.2% and 2.4% respectively. Following DAA treatment, 98.3% and 95.4% of CHC patients acquired sustained virus response at the end of treatment and 12 weeks after treatment respectively. Overall SVR12 were 96.3%, 93.1%, 80% and 100% in patients with genotype 1b, 2a, 3a and 6a, respectively. At 12 weeks after treatment ,the level of LSM and the value of APRI were significantly decreased from baseline (9.8 kpa vs 11.4 kpa, $P = 0.01$ and 0.34 vs 0.76, $P < 0.01$),LSM decreased significantly in the non-cirrhotic patients (7.6 kpa vs 8.8 kpa, $P < 0.01$) than in cirrhotic patients(17.4Kpa vs 19.8Kpa,$P = 0.15$).
Conclusion: In this real-world study, the overall SVR12 rate of CHC patients treated with DAA reached 95.4%, the LSM and APRI significantly decreased at 12weeks after DAA treatment.
Keywords: Chronic hepatitis C, Direct acting antivirals, Sustained virus response, Liver stiffness measurement.
AST/platelets ratio index

Table 1 Baseline characteristics of patients treated with DAA

Characteristics	Patients （N=212）
Sex, male, n (%)	96 (45.3)
Age, years, median (range)	58 (24-85)
Cirrhosis, n, (%)	75 (35.4)
HCV RNA,log10IU/mL, median (range)	6.1(2.3-7.6)
ALT,U/L,mean (SD)	63.0 (64.1)
AST,U/L,mean(SD)	56.4 (47.3)
ALP, U/L,mean(SD)	92.6 (38.6)
GGT, U/L,mean(SD)	58.8(63.4)
TBIL,μmol/L, mean(SD)	17.1(10.3)
HGB,g/l, mean (SD)	141.1(17.8)
PLT*10⁹/l, median (range)	151(20-429)
Creatinine (μmol/L), median (range)	63.5(40-1478)
FibroScan, kPa, median,(range)	11.4 (4.2-57.4)
APRI, median,(range)	0.8(0.1-6.8)
Treatment-naïve, n, (%)	181 (85.4)
Genotype	
1b n (%)	159(75.0)
2a n (%)	39(18.3)
3a n (%)	9(4.2)
6a n (%)	5(2.4)

Table 2 Changes of liver stiffness and APRI after DAA treatment

	Baseline		PTW12		T value	P value
	n	Media（Q25，Q75）	n	Media（Q25，Q75）		
LSM	185	11.4(7.7,19.1)	139	9.8(6.9,16.3)	-2.5	0.01
Cirrhosis	63	19.8(12.8,24.9)	47	17.4(12.7,22.1)	-1.4	0.15
Non-Cirrhosis	122	8.8(7.2,13.0)	92	7.6(6.6,10.7)	-2.9	<0.01
APRI	192	0.76(0.56,2.25)	149	0.34（0.25,0.64）	-2034.5	<0.001
Cirrhosis	72	1.37(0.80,2.11)	53	0.73（0.52,1.34）	-312.5	<0.001
Non-Cirrhosis	120	0.54(0.31,0.95)	96	0.29(0.21,0.36)	-843	<0.001

PTW12, 12 weeks after treatment

Abstract #1323

Global and regional burden of hepatitis C virus (HCV) mortality and disability-adjust life years (DALYs), 2015–2019: an analysis of the Global Burden of Disease Study 2019

Lindsey Hiebert[1], Brittney Sheena[2], Angelique Harris[1], Mae Dirac[2], Theo Vos[2], John Ward[1]

[1]Coalition for Global Hepatitis Elimination, Task Force for Global Health, Atlanta, GA, USA, [2]Institute for Health Metrics and Evaluation, University of Washington, Seattle, Washington, USA

Introduction: In 2016, WHO set an HCV elimination goal defined as a 65% reduction in HCV related mortality by 2030. Hepatitis burden of disease data are needed to monitor progress towards this elimination goal.
Objective: To estimate trends in HCV-related mortality and DALYs for 2015-2019
Methods: From GBD 2015–2019, the HCV-related all-age mortality rate from acute HCV, cirrhosis and other chronic liver diseases and primary liver cancer was aggregated globally and for IHME super-regions. DALYs were calculated as previously described [1]. Estimates were adjusted for numbers treated for HCV in Egypt (3.2M), Australia (83,100), and Japan (535,000).
Results: From 2015 to 2019, the global HCV-related mortality rate for all ages increased by 5% from 6.7 to 7.0 (6.1–8.0) per 100,000. HCV mortality increased more in Southeast Asia, East Asia and Oceania (8%) and South Asia (10%). Globally, DALYs were estimated at 14.8M (12.8–16.9 M) in 2019. South Asia had the greatest HCV DALY burden (2.9M [2.2–3.5 M]). In all, 21 low- and middle-income (LMIC) countries represent 66% of the global DALY burden. Ten LMIC Asian countries represent 45% of the global burden. In contrast to global and regional increases, mortality in Egypt, Australia and Japan declined from 2015 to 2019 after adjustment for treatment, as much as 23% in Egypt.
Conclusions: HCV mortality is increasing globally. Egypt, Japan, and Australia demonstrate how HCV testing and treatment scale-up leads to substantial mortality declines. Similar scale up is needed in high burden Asian countries. With the inclusion of treatment data, the GBD study can monitor progress towards elimination.

Table 1. Mortality-rate per 100,000 related to hepatitis C, 2015, 2019, and percent change 2015-2019 and DALYS due to hepatitis C, 2019, by IHME super-regions

	Mortality rate related to hepatitis C (per 100,000), 2015	Mortality rate related to hepatitis C (per 100,000), 2019	Percent change in mortality rate, 2015-2019 (%)	DALYs due to hepatitis C, 2019
Global	6.7 (5.9 – 7.4)	7.0 (6.1 – 8.0)	5%	14.8M (12.8 – 16.9M)
Southeast Asia, East Asia, and Oceania	6.2 (5.5 – 7.0)	6.7 (5.8 – 7.7)	8%	4.0M (3.4 – 4.6M)
Central Europe, Eastern Europe, and Central Asia	7.7 (6.5 – 9.2)	7.4 (6.1 – 8.9)	-4%	0.9M (0.8 – 1.1M)
High-Income	11.0 (10.0 – 12.1)	11.5 (10.1 – 12.9)	5%	2.5M (2.2 – 2.8M)
Latin America and Caribbean	5.5 (5.2 – 6.8)	6.5 (5.5 – 7.7)	19%	1.1M (0.9 – 1.3M)
North Africa and Middle East	10.8 (8.8 – 12.6)	11.1 (8.3 – 13.9)	3%	1.7M (1.2 – 2.1M)
South Asia	4.3 (3.8 – 5.0)	4.8 (4.0 – 5.7)	10%	2.9M (2.3 – 3.5M)
Sub-Saharan Africa	4.4 (3.6 – 5.3)	4.5 (3.6 – 5.5)	2%	1.6M (1.3 – 2.0M)

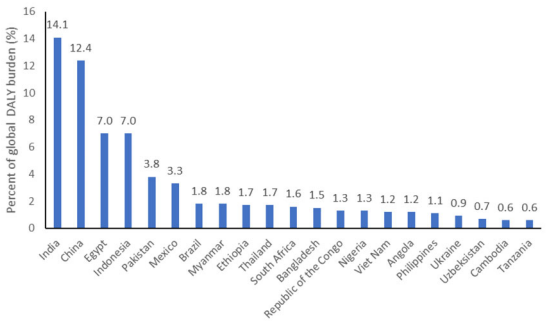


Figure 2. Top 21 low- and middle-income countries for HCV DALY burden

Abstract #1365

Real-world effectiveness and safety of approved interferon (IFN)-free direct acting antivirals (DAA) in chronic hepatitis C (CHC) patients: a multicenter REAL-C study of mainland China

Fanpu Ji[1], Jie Li[2], Li Liu [3], Jing Liang[4], Junping Liu[5], Qi Wang[6], Xiaozhong Wang[7], Dachuan Cai[8], Rui Huang[9], Yuemin Nan[10], Mingyuan Zhang[11], Shuangsuo Dang[1], Qiang Zhu[12], Lingdi Liu[10],Junyi Li[3], Qiang Xu[7], Zongfang Li[13,14], Wanhua Ren[2], Hongying Pan[15], Leslie Y. Kam[16], Changqing Zhao[17], Sally Tran[16], Ramsey Cheung[16,18], Junqi Niu[11], Wu Chao[9], Hong Ren[8], Xie Wen[6], Jia Shang[5], Fengmei Wang[4], Mindie H. Nguyen[16]

[1]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an, Xi'an Jiaotong University, Xi'an, PRC, [2]Department of Infectious Disease, Shandong Provincial Hospital Affiliated to Shandong University, Ji'nan, Shandong, PRC, [3]Department of Hepatology, The Third People's Hospital of Kunming, Kunming,

PRC, [4]Department of Gastroenterology and Hepatology, Tianjin Third Central Hospital, Tianjin, China, [5]Department of Infectious Diseases, Henan Provincial People's Hospital, Zhengzhou, PRC, [6]Center of Liver Diseases, Beijing Ditan Hospital, Capital Medical University, Beijing, PRC, [7]Hospital of Traditional Chinese Medicine Affiliated to Xinjiang Medical University, Urumqi, PRC, [8]Department of Infectious Diseases, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, PRC, [9]Department of Infectious Diseases, Nanjing Drum Tower Hospital, Nanjing University Medical School, Nanjing, PRC, [10]Department of Hepatology, The Third Hospital of Hebei Medical University, Shijiazhuang, PRC, [11]Department of Hepatology, First Hospital of Jilin University, Changchun, PRC, [12]Department of Gastroenterology, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, Shandong, PRC, [13]Shaanxi Provincial Clinical Research Center for Hepatic & Splenic Diseases, the Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, PRC, [14]National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, the Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, PRC, [15]Department of Infectious Diseases, Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College, Hangzhou, PRC, [16]Division of Gastroenterology and Hepatology, Stanford University Medical Center, Palo Alto, CA, USA, [17]Department of Cirrhosis, Institute of Liver Disease, Shuguang Hospital, Shanghai University of T. C. M., Shanghai, PRC, [18]Division of Gastroenterology and Hepatology, Veteran Affairs Palo Alto Health Care System, Palo Alto, CA, USA

Background/aims: Globally, China has the highest HCV burden, but its real-world DAA data are limited. We aimed to study the real-world outcome of China FDA-approved DAA therapies across mainland China.

Methods: The REAL-C study is a multinational real-world IFN-free DAA-treated CHC registry of 15 mainland China and 16 other Asian centers. The primary outcome was SVR 12 weeks or more following end of treatment.

Results: A total of 1224 CHC patients from 12 mainland China centers were registered: Mean age 51.2, 49% male, 33% cirrhotic, 5% treatment-experienced, 2% HCC, 62.2% GT1, 20% GT2, 16% GT3/6. The most commonly used regimens were ProD (n = 281, 23%), followed by SOF+RBV (n = 254, 21%), SOF/VEL±RBV (n = 229, 21%) and EBR/GZR (n = 201, 17%). To date, SVR data were available for 756 patients. Overall, SVR was 98.7% (Table 1), lower with cirrhosis ($P = 0.01$) but not prior HCC or prior treatment. SVR were 98.9% for GT1, 97.8% for GT2, 98.2% for GT3 and 100% for GT6. All GT1 patients treated with SOF+DCV (n = 64), EBR/GZR (n = 144), and SOF/VEL (n = 42) achieved SVR but less with 24-week SOF+RBV (97.0%) and 12-week PrOD (98.0%). SVR with SOF/VEL ± RBV for all GTs was 99.3% (140/141). Anemia was the most common (12.5%, mostly with RBV) but there was no early treatment discontinuation. Two patients with baseline hepatic decompensation died.

Conclusions: In real-world Chinese patients with diverse GTs, Chinese FDA-approved INF-free DAAs were well-tolerated and provided high cure rates (98.7% overall). All Chinese CHC patients should be considered for DAA therapies.

Table 1 SVR in ongoing registry of real-world Chinese patients treated with DAA

	n / N	95% CI	P-value
Overall	746/756	98.7% (0.94-0.99)	
Baseline cirrhosis	237/244	97.1% (0.94-0.99)	0.01
None	497/500	99.4% (0.98-0.99)	
Prior HCC	10/10	100%	0.71
No prior HCC	731/741	98.7% (0.98-0.99)	
Prior Treatment			0.33
IFN Treatment naïve*	714/723	98.8% (0.98-0.99)	
IFN Treatment experienced	29/30	96.7% (0.83-0.99)	
Genotype (GT)			0.99
1 total	449/454	98.9% (0.97-0.99)	
1 untyped	2/2	100%	
1 a	2/2	100%	
1 b	443/448	98.9% (0.97-0.99)	
1 m	2/2	100%	
2	133/136	97.8% (0.98-0.99)	
3	111/113	98.2% (0.94-0.99)	
6	36/36	100%	
GT 1			0.18
SOF+RBV	32/33	97.0% (0.84-0.99)	
3D	150/153	98.0% (0.94-0.99)	
ASV+DCV	15/16	93.8% (0.70-0.99)	
SOF+DCV	64/64	100%	
EBR/GZR	144/144	100%	
SOF/VEL	42/42	100%	
Others	2/2	100%	
GT 2			
SOF+RBV	70/73	95.9% (0.88-0.99)	0.10
SOF/VEL	42/42	100%	
Other regimens	21/21	100%	
GT 3			
SOF+RBV	32/33	97.0% (0.84-0.99)	0.63
SOF+DCV	33/33	100%	
SOF/VEL	46/47	97.9% (0.89-0.99)	
GT 6			
SOF+RBV	16/16	100%	
SOF+DCV	9/9	100%	
SOF/VEL	10/10	100%	
ELB/GZR	1/1	100%	

*IFN treatment naïve includes those with no prior treatment and those with prior non-IFN treatment (ie, DCV+ASV, SOF, or unknown).

Abstract #1367

Real-world effectiveness and safety of elbasvir plus grazoprevir for hepatitis C virus genotype 1b infection: a multicenter, prospective, registered study in Northwest China

Wei Zhang[1], Xiaozhong Wang[2], Manling Bai[3], Caini He[4], Hong Du[5], Wenling Jia[6], Hong Wan[7], Nan Wang[8], Yongping Zhang[9], Yu Li[10], Zhangqian Chen[1], Qiang Xu[2], Yunyu Zhao[4], Shen Li[11], Xiaolan Fu[4], Xinyu Liu[4], Xiaoqing Yang[7], Xiaoyun Ma[3], Fulin Zhang[6], Feng Guo[2], Xinggang Bai[3], Hailing Liu[12], Jianjun Fu[8], Jianqi Lian[5], Jiuping Wang[1], Fanpu Ji[4,13,14]

[1]Department of Infectious Diseases, Xijing Hospital of Air Force Medical University, Xi'an, China, [2]Department of Hepatology, Hospital of Traditional Chinese Medicine Affiliated to Xinjiang Medical University, Urumqi, China, [3]Department of Infectious Diseases, People's Hospital of Wuwei City, Wuwei, China, [4]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an, Xi'an Jiaotong University, Xi'an, China, [5]Department of Infectious Disease, Tangdu Hospital of Air Force Medical University, Xi'an, China, [6]Department of Hepatology, Tumor Hospital of Wuwei City, Wuwei, China, [7]Department of Infectious Diseases, Lanzhou Second People's Hospital, Lanzhou, China, [8]Department of Infectious Diseases, the Affiliated Xi'an Central Hospital of Xi'an Jiaotong University, Xi'an, China, [9]Department of Infectious Diseases, People's Hospital of Xinjiang Autonomous Region, Urumqi, China, [10]Department of Infectious Diseases, Shaanxi Provincial People's

Hospital, Xi'an, China, [11]Shaanxi Provincial Centre for Disease Control and Prevention, Xi'an, China, [12]Department of Infectious Diseases, Central Hospital of Xianyang City, Xianyang, China, [13]National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, the Second Affiliated Hospital, Xi'an Jiaotong University, Xi'an, China, [14]Key Laboratory of Environment and Genes Related to Diseases, Xi'an Jiaotong University, Ministry of Education of China, Xi'an, China,

Background/aims: China has the highest HCV burden in the world, with HCV genotype 1/1b being the most prevalent genotype. This study assesses elbasvir (EBR)/grazoprevir (GZR) for patients with HCV GT1b infection in the clinical setting.
Methods: This multicenter, real-world cohort study consisted of 103 Chinese patients who were treated with EBR (50mg)/GZR (100mg) for a fixed 12-week duration. We evaluated the sustained viral response rate 12 weeks after the end-of-treatment (SVR12), longitudinal liver and renal parameters, and adverse events (AEs).
Results A total of 103 CHC patients were registered as of 07/01/2019: Mean age 50.2 years, 26.2% older than 65, 39.8% male, 38.8% cirrhotic, 68.9% HCVRNA ≥1,000,000IU/ml, 4.85% HBsAg+, 2.91% renal dysfunction (one hemodialysis-dependent), 1.94% with HCC and 0.97% treatment-experienced. End-of-treatment response (EOTR) data were available in 102 patients, SVR12 in 73 and one lost follow-up. The overall EOTR in ITT and per-protocol populations were 98.1% and 99%; and SVR12 rates were 97.3% (72/74) and 98.6% (72/73), respectively. There was no significant change during treatment or follow-up period in serum creatinine, but mild improved eGFR in all 3 patients with baseline renal dysfunction was observed. In contrast, the serum AFP (14.6 ± 6.3 vs. 4.1 ± 2.5 vs.3.2 ± 2.1ng/ml, $P < 0.01$) and ALT (58.3 ± 25.2 *vs* .22.3 ± 16.4 *vs.* 23.2 ± 15.1IU/ml, $P < 0.01$) levels decreased in comparison with the baseline. There was no serious AEs and early treatment discontinuation.
Conclusions: EBR plus GZR for patients with HCV GT1b infection was highly effectiveness and safety in Northwest China. In addition, liver parameters and AFP levels improved longitudinally.

Abstract #1369 **100% SVR rate of 12-weeks sofosbuvir (SOF)/velpatasvir (VEL) with or without ribavirin for treatment of chronic HCV infection including GT3 and cirrhosis in Northwest China**

Qiang Xu[1],Wei Zhang[2], Yuxiu Ma[3], Caini He[4], Liting Zhang[5], Yilihamu Abulitifu[6], Yu Li[7], Nan Wang[8], Hongli Wang[9], Yunyu Zhao[4], Peigen Gao[4], Xingyang Su[4], Shen Li[10], Feng Guo[1], Zhangqian Chen[2], Hailing Liu[11],Xiaoqin Gao[5], Jianjun Fu[8], Guoying Yu[3], Xiaozhong Wang[1], Jiuping Wang[2], Yongping Zhang[6], Fanpu Ji[4,12,13]

[1]Department of Hepatology, Hospital of Traditional Chinese Medicine Affiliated to Xinjiang Medical University, Urumqi, China, [2]Department of Infectious Diseases, Xijing Hospital of Air Force Medical University, Xi'an, China, [3]The second Department of Hepatology, the Fourth People's Hospital of Qinghai Province, Xining, China, [4]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an, Xi'an Jiaotong University, Xi'an, China, [5]Department of Infectious Disease, First Hospital of Lanzhou University, Lanzhou, China, [6]Department of Infectious Diseases, People's Hospital of Xinjiang Autonomous Region, Urumqi, China, [7]Department of Infectious Diseases, Shaanxi Provincial People's Hospital, Xi'an, China, [8]Department of Infectious Diseases, the Affiliated Xi'an Central Hospital of Xi'an Jiaotong University, Xi'an, China, [9]The Sixth Department of Hepatology, The Eighth hospital of Xi'an City, Xi'an, China, [10]Shaanxi Provincial Centre for Disease Control and Prevention, Xi'an, China, [11]Department of Infectious Diseases, Central Hospital of Xianyang City, Xianyang, China, [12]National and Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, the Second Affiliated Hospital, Xi'an Jiaotong University, Xi'an, China, [13]Key Laboratory of Environment and Genes Related to Diseases, Xi'an Jiaotong University, Ministry of Education of China, Xi'an, China,

Background/aims: Treatment with SOF/VEL has resulted in high sustained virological response (SVR) rates in patients with hepatitis C virus (HCV) genotypes 1–6 infection in clinical trials and real-world settings, but its real-world data in China is lack. We aimed to study the real-world outcome of China FDA-approved SOF/VEL in Northwest China.
Methods: In this multicenter, prospective, real-world cohort study, we recruited patients from 10 sites from Northwest China, who were chronically infected with HCV genotypes 1–6. Patients received SOF (400mg)/VEL (100mg) for 12 weeks, and with ribavirin for GT3 cirrhosis and any decompensated cirrhosis. The primary endpoint was SVR at 12-weeks post-treatment (SVR12) and adverse events (AEs).
Results: Between 06/01/2018 and 03/30/2019, 113 patients were enrolled in the study, all of them completed the treatment course and follow-up ≥ 12 weeks. Mean age 52.4 years, 34.5% older than 60, 49.6% male, 54% cirrhotic (11 with decompensated cirrhosis), 55.8% HCVRNA ≥1,000,000IU/ml, 10.6% HBsAg+, 7.1% renal dysfunction, 4.4% treatment-experienced, 36.3% GT1 (n = 41), 43.4% GT2 (n = 49), 15% with GT3 (9/7/1 with 3a/3b/3) , or un-typed (n = 6). Overall, nineteen patients received ribavirin treatment, 94.5% (86/91) patients have undetectable HCVRNA after 4-weeks treatment. All 113 patients achieved SVR12. Among 12 patients with HBsAg+, 4 with detectable HBVDNA, none of them occurred HBV reactive. Compared with baseline, the serum AFP (20.3 ± 9.3 vs .4.2 ± 2.3ng/ml, $P < 0.01$) and ALT (75.5 ± 45.1vs.30.0 ± 17.4IU/ml, $P < 0.01$) levels decreased, as well as increased ALB (40.4 ± 10.1vs.43.5 ± 8.3g/L, $P < 0.01$), at post-treatment 12-weeks. Overall AEs rate is 20.3%, and the most common AEs is fatigue (9.7%), one patient need short interruption of treatment due to edema.
Conclusions: In this real-world cohort study, treatment with SOF/VEL with or without ribavirin achieved high SVR12 rates with excellent safety profile among patients with HCV GT1/2/3 infection including patients with GT3 and cirrhosis.

Abstract #1378

Virologic causes for DAA treatment failure of chronic hepatitis C

Chun-Ming Hong

Background and aims: Chronic hepatitis C (CHC) is common in Taiwan, as about 4% of population are positive for anti-HCV Ab. Among them, around 70% carry HCV RNA, therefore about 500,000 cases are CHC patients. The Bureau of National Health Insurance has started to reimburse DAAs (direct-acting antiviral agents) since 2017. Preliminary data from Hepatitis C Flagship Project Office showed an HCV cure rate of 97%, meaning that there are still 2–3% of patients who fail to clear HCV despite completing the treatment. In order to understand the causes of treatment failure in Taiwan, it is essential to conduct a clinical and virologic study of these DAA failure patients.
Method: Through collaboration with several hospitals and clinics nationwide, we recruited 40 DAA failure patients. These patients received at least four-week treatment of DAA therapy. Clinical information as well as serum samples were obtained after informed consent. We established polymerase chain reaction (PCR) platform for NS3/4A, NS5A and NS5B, and then identified mutated RAS (resistance-associated substitution) by population sequencing.

Results: In these 40 patients, only one patient did not complete treatment due to hyperbilirubinemia. Sixteen patients had genotype 1b infection, twelve had genotype 2, and two had genotype 3.
Till now, we completed RAS (resistance associated substitution) analysis for 21 patients among these 40 patients. Eight cases were found to have no known RAS according to its genotype and DAA regimen, and the rest 13 cases were found to have at least one mutated RAS. Y93 in NS5A was the most RAS, and its frequency of mutation (91%) was significantly higher than that in HCV database (14%). The frequency of mutation of Y56 in NS3 and L31 in NS5A were also higher than those in HCV database. On the other hand, the frequency of mutation of D168 in NS3 and L159 as well as C316 in NS5B were not higher than those in HCV database. Furthermore, two cases were noted with post-DAA HCV genotypes that were different from the baseline genotypes, suggesting initial mixed infections or a reinfection.
Conclusion: Our study suggests that known RASs are the major virologic cause for treatment failure. Those without known RASs warrant further investigation in order to propose appropriate rescue therapies.

Abstract #1398

Variceal Recurrence 4 years beyond endoscopic band ligation in hepatitis C patients who achieved sustained virological response post direct acting antiviral therapies

El-Sayed Ibrahim[1], Eman Abdelsameea[1], Mohamed I. Youssef[2], Helmy El-Shazly[1], Abd-El Aleem A.El-Gendy[3], Doaa Elwazzan[4], Ayman Ahmed Sakr[5], Mervat Ragab Nassar[5], Amr Aly Elshormilisy[6], Sahar Badr El-Din[7], Ahmad Madkour[8], Mostafa Kamal[9], Yasmine M. Amrousy[9], Shimaa Abdelsattar[10], Nora M. Aborehab[11], Nada Osama[12] and Mohamed Abdel-Samiee[1]*

[1]Department of Hepatology and Gastroenterology, National Liver Institute, Menoufia University, Menoufia, Egypt, [2]Department of Internal Medicine, Al-Azhar University, Cairo, Egypt, [3]Department of Clinical Pathology, Al-Azhar University, Cairo, Egypt, [4]Department of Tropical Medicine, Faculty of Medicine, Alexandria University, Alexandria, Egypt, [5]Department of Tropical Medicine, Faculty of Medicine, Menoufia University, Menoufia, Egypt, [6]Department of Internal Medicine, Helwan University, Cairo, Egypt, [7]Department of Pharmacology, Al-Azhar University, Cairo, Egypt, [8]Department of Endemic Medicine, Faculty of Medicine, Helwan University, Cairo, Egypt, [9]Department of Clinical and Chemical Pathology, Faculty of Medicine, Helwan University, Cairo, Egypt, [10]Department of Clinical Biochemistry, National Liver Institute, Menoufia University, Menoufia, Egypt, [11]Department of Biochemistry, Faculty of Pharmacy, October University for Modern Sciences and Arts (MSA), Cairo, Egypt, [12]Department of Biochemistry, Faculty of Pharmacy, Menoufia University, Menoufia, Egypt

Introduction: Direct antiviral therapies (DAAs) are highly effective, safe and are changing the prognosis and burden of the disease. Sustained virologic response (SVR) is now achieved in > 90% of the patients and is associated with improvements in liver function, fibrosis and overall survival. Portal hypertension is also expected to improve with virological response, paralleling the improvements in liver inflammation and liver fibrosis.
Objectives: to evaluate the rate of recurrence of esophageal varices by long duration follow up inpatients treated with different regimens of DAAs and achieved SVR.
Methods: 176 patients were infected with chronic HCV, achieved 24 weeks SVR post DAAs treatment, and had history of endoscopic obliteration of their esophageal varices and continuing on maximum tolerable dose of propranolol. They were subjected to follow up upper gastrointestinal endoscopy repeated every 6 months until 4 years.
Results: 52 patients (29.5%) had recurrence of esophageal varices during the 4-year follow up upper GIT endoscopy. By multivariate analysis, the platelet count was the only variable with significant association, P-Value = 0.007*. By ROC we identified baseline platelet count of 96,000/ microliter as having 100% sensitivity (95% confidence interval- CI [91–100%]) and 74% specificity (95% CI [65–81%]).The positive predictive value was 62% (CI [51–72%] and the negative predictive value was 100% (CI [95–100%].The area under the curve (AUC) = 0.84.
Conclusion: Patients who achieved SVR post DAAs shows significant decrease in the recurrence of esophageal varices post endoscopic obliteration. Baseline platelet count is strongly predictor for the recurrence.

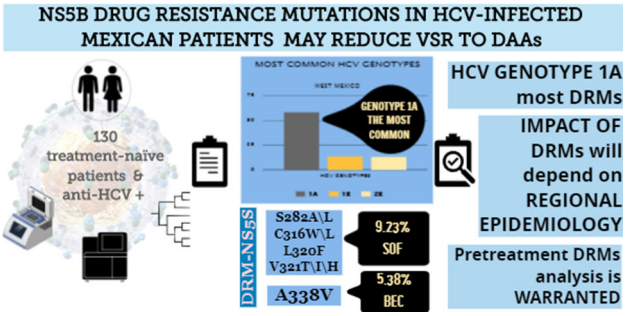
Abstract #1439

NS5B drug resistance mutations in naïve hepatitis C virus-infected mexican patients may reduce virological-sustained response to direct-acting antivirals

[1]Panduro A., [1]Laguna-Meraz S., [1]Jose-Abrego A., [1]Roman S.

[1]Department of Molecular Biology in Medicine, Civil Hospital of Guadalajara-Fray Antonio Alcalde and Health Sciences University Center, University of Guadalajara, Guadalajara, Jalisco, Mexico

Introduction: Currently, the new direct-acting antivirals (DAAs) are highly effective to achieve virological sustained response in 90–95% among hepatitis C virus (HCV)-infected patients. However, there are few studies regarding the prevalence of drug resistance mutations (DRMs) among naïve HCV-infected patients in Mexico, ignoring if the available treatments with DDAs are suitable to suppress the main genotypes circulating among the Mexican population.
Objective: To identify DRMs in the HCV NS5B region in naïve HCV-infected Mexicans patients.
Methods: In an analytical, cross-sectional study, 130 naïve HCV-infected patients were included. HCV viral load was measured by an RT-PCR assay, anti-HCV antibodies by a 3rd-generation ELISA, and the NS5B region was directly sequenced using standard procedures. DRMs were identified using the MEGA 7 and geno2pheno (http://geno2pheno.org) software programs. Statistical analysis was performed using the SPSS program.
Results: The average age was 49.1 years, 42.3% (n = 55) were male and 57.7% (n = 75) were female. HCV genotypes were 1a (58.5%), 1b (13.8%), 2b (13.1%), 3a (12.3%) and 2a (2.3%). DRMs present in 14.62% (n = 19/130) were Genotypes 1a and 2b had the highest amount of DRMs and they were mainly against sofosbuvir in 9.23% (n = 12/130) and beclabuvir in 5.38% (n = 7/130).
Conclusion: Herein, a high number of DRMs against sofosbuvir was found. Since it is currently one of the main DDAs indicated in HCV-infected patients in Mexico, it is warranted that pretreatment DRM tests be performed to achieve a higher virological sustained response among these patients.



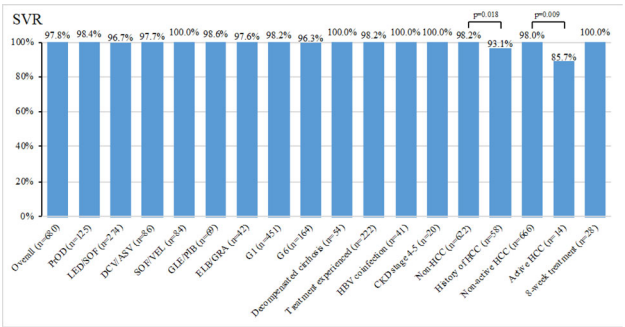
Abstract #1445

A territory-wide real-world study of the efficacy and safety of direct-acting antivirals for chronic hepatitis C patients in Hong Kong

Tong KN Ronald[1], Hui Yee Tak[2], Wong LH Grace[3], Liu D Sienna[3], Liu Ken[3], Ma Yiu Keung[4], But YK David[5], Mak Wing Yan[3], Chan MC Jacky[6], Lai Kin Bon[7], Loo Ching Kong[8], Ng C Y Annie[1], Lai Moon Sing[9], Chan Chun Wing[10], Lau YL Joulen[11], Fan TT Tina[12], Hui J Aric[13], Lam CY Belsy[14], Cheung Wing I [15], Tsang TY Owen[6], Lam S Karen[6], Lai SW Lawrence[14], Luk Wai Fun[6], Li KK Michael[4], Lao Wai Cheung[11], Lam TW Jodis[2], Tsang WC Steven[12], Kung Kam Ngai[7], Chow Wai Hung[10], Chan Angel[10], Chan SY Rosita[13], Yau SN Wendy[4], Lui KL Thomas[5], Shan HS Edwin[1], Fung YY James[5], Chan LY Henry[3], Yuen Man Fung[5], Wong WS Vincent[3] [Hong Kong HCV Registry]

[1]Department of Medicine and Geriatrics, Caritas Medical Centre, Hong Kong, China, [2]Department of Medicine, Queen Elizabeth Hospital, Hong Kong, China, [3]Department of Medicine and Therapeutics, State Key Laboratory of Digestive Disease, Institute of Digestive Disease, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, China, [4]Department of Medicine and Geriatrics, Tuen Mun Hospital, Hong Kong, China, [5]Department of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong, China, [6]Department of Medicine and Geriatrics, Princess Margaret Hospital, Hong Kong, China, [7]Department of Medicine and Geriatrics, United Christian Hospital, Hong Kong, China, [8]Department of Medicine and Geriatrics, Kwong Wah Hospital, Hong Kong, China, [9]Department of Medicine North District Hospital, Hong Kong, China, [10]Department of Medicine, Yan Chai Hospital, Hong Kong, China, [11]Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong, China, [12]Department of Medicine, Tseung Kwan O Hospital, Hong Kong, China, [13]Department of Medicine, Alice Ho Miu Ling Nethersole Hospital, Hong Kong, China, [14]Department of Medicine and Geriatrics, Pok Oi Hospital, Hong Kong, China, [15]Department of Medicine, Our Lady of Maryknoll Hospital, Hong Kong, China

Introduction: Limited real-world data exists for direct-acting antivirals (DAAs) in Hong Kong (HK).
Objectives: To study the overall treatment efficacy and safety of the 6 DAAs for patients with chronic HCV infection in HK.
Methods: Data from patients treated with DAAs from February 2014 to April 2019 was retrieved from the database of the HK HCV Registry. Baseline characteristics and safety were performed with intention to treat analyses (n = 715). Efficacy analysis was performed with modified intention to treat methodology (n = 680).
Results: Baseline characteristics were median age 62 (54-69), male (52.3%), cirrhosis (63.2%), decompensated cirrhosis (9.1%), history of HCC (8.8%) and active HCC (2.2%). The genotype distribution was G1 (66.4%), G2 (2.9%), G3 (5.7%), G4 (0.1%) and G6 (23.9%). The overall SVR rate was 97.8% (95% CI 96.7–98.9%). Subgroup SVR rates according to different DAAs, genotypes and other parameters were as follows: PrOD (98.4%), LED/SOF (96.7%), DCV/ASV (97.7%), SOF/VEL (100%), GLE/PIB (98.6%), ELB/GRA (97.6%), G1(98.2%), G6(96.3%), decompensated cirrhosis (100%), treatment-experienced (98.2%), HBV coinfection (100.0%), CKD stage 4–5 (100%) and 8-week treatment (100%). Non-HCC was significantly associated with higher SVR rate (non-HCC vs history of HCC; 98.2% vs 93.1%, p = 0.032; OR 4.176 (95%CI 1.283-13.591), p = 0.018). 26 patients (3.7%) had premature discontinuation of treatment. The common causes included liver failure (n = 4, 0.6%) of which 2 cases resulted in death, grade 3 or above ALT or bilirubin elevation (n = 3, 0.4%; n = 3, 0.4%) and UGIB (n = 2, 0.3%).
Conclusion: The 6 DAAs were highly effective and safe. Non-HCC was significantly associated with higher SVR rate.



Abstract #1456

Significant fibrosis in TE and APRI score associated with severity of liver dysfunction in HCV infection

Andika Sulaiman Tunasly*, Nu'man AS Daud, Fardah Akil, Andi Muhammad Luthfi Parewangi, Rini Rachmawarni Bachtiar, Susanto H Kusuma, Amelia Rifai

Centre of Gastroenterology-Hepatology HAM Akil, DR.Wahidin Sudirohusodo General Hospital, Division of Gastroenterology-Hepatology, *Department of Internal Medicine Hasanuddin, University of Hasanuddin, Makassar-Indonesia

Introduction: Liver fibrosis is a key predictive factor for advanced disease including endpoints such as cirrhosis and progressively varies markedly in hepatitis C virus (HCV) infected. The Child-Turcotte-Pugh score (CP) is currently used to determine the survival of patients with chronic liver disease and cirrhosis. Numerous studies have shown noninvasive measure of liver fibrosis such as transient elastography (TE) and the aspartate aminotransferase (AST) to platelet ratio index (APRI) as validated tool in chronic HCV with clinical usefulness in the diagnosis of liver fibrosis and cirrhosis. However, few study has explored the clinical significance these 2 noninvasive tool with the severity of liver dysfunction in HCV patients.
Objectives: To evaluate the correlations of TE and APRI score with CP as a marker of liver dysfunction in HCV patients.
Methods: Between 2017 and 2018, a total of 137 HCV patients underwent TE (Fibroscan) and calculated for APRI and Child-Turcotte-Pugh score (CP). Fibroscan >6.25kPa and APRI score >0.7 are significant fibrosis. This retrospective cross-sectional study using correlation analysis of spearman's correlation coefficient test.
Results: Of them 69.3%, 29.2%, and 1.5% had CP class A, B, and C, respectively. Mean of TE 14.73 ± 13.61kPa and median APRI score 0.6. Ninety-three (80.9%) in TE and 60 (43.8%) in APRI score have significant fibrosis/cirrhosis. TE (coefficient r: 0.314, p = 0.001) and

APRI score (coefficient r: 0.214, p = 0.012) significantly correlated with Child-Pugh score B/C.
Conclusion: Significant fibrosis in TE and APRI score are positively associated with the severity of liver dysfunction in HCV patients.

Abstract #1522

Demographic and clinical profile of hepatitis C virus infection patients in Makassar-Indonesia

Ulfa Ansfolorita M.*, Nu'man AS Daud, Fardah Akil, Muhammad Luthfi Parewangi, Rini Rachmawarni Bachtiar, Susanto H Kusuma, Amelia Rifai

Centre of Gastroenterology-Hepatology HAM Akil/DR.Wahidin Sudirohusodo General Hospital, Division of Gastroenterology-Hepatology *Department of Internal Medicine, University of Hasanuddin, Makassar-Indonesia

Introduction: Globally, an estimated 71 million people have chronic hepatitis C virus (HCV) infection with prevalence 1.0%. In Indonesia, prevalance of HCV is increase from 2.1 to 2.5% based on Riskesdas 2007–2013. Data of the epidemiology and demographic distribution of HCV infection in Indonesia, specifically in Makassar is limited.
Objectives: To describe demography and clinical profile of HCV infection patients
Methods: This retrospective-descriptive study using data from our outpatients center between year 2017 and 2018. Demography, risk factors, laboratory (liver biochemistry/serology/virology), radiology and fibroscan data were collected.
Results: From 24.444 patients, we found 215 (0.9%) AntiHCV(+) and 207 patients were included in this study. Male 138 (66.7%) and 69 (33%) female, mean age 49 $\pm$ 15year with 67(33.5%) works as civil servant. Risk factors such as unknown 11 2(54.1%), hemodialysis 59 (28.5%), injecting drug users 20 (9.7%), blood transfusion 10(4.8%), and history of surgery 6(2.9%). Co-infection with HIV in 17(21%) and HBV in 20 (9.7%); 7 (4%) had fatty liver. Median of laboratory data: ALT 46U/L and APRI score 0.57, range of AFP < 0.5 to $>$ 400ng/ml; mean of HCV-RNA log 5.59 $\pm$ 1.28IU/ml and fibroscan 8.91 $\pm$ 5.35kPa. Hepatocellular carcinoma (HCC) was found in 6 (3.5%) patients and 74 (35.7%) have cirrhosis with Child-Pugh A/B/C 95 (69.3%)/40(29.2%)/2 (1.5%) respectively. Eighty-four (40.6%) without treatment and 123(59.4%) were treat with regimen peg-interferon in 5(4%) and direct-acting antiviral (DAA: sofosbuvir/simeprevir/daclastavir/elbasvir/grazoprevir) in 118(96%) of cases.
Conclusion: Prevalance of HCV is 0.9%. Male and HCV chronic infection without unknown risk factor with relatively have HCC and cirrhosis as complication are clinical profile in this study. Early treatment in our population are appropriate.

Abstract #1535

Evaluation of the effect of hepatitis C infection on quality of life

Onur Gültekin, Elif Şahin, Özlem Kandemir, Ali Kaya

Objectives: The aim of this study is to evaluate the effect of hepatitis C (HCV) infection on the quality of life and the factors that might play a role in this effect.

Materials/methods: The study included 200 anti-HCV positive, CHC patients older than 18 years. A questionnaire containing the socio-demographic and treatment status of the patients, SF-36 and Turkish version of CLDQ-HCV (KKHA-HCV) questionnaires were conducted to the patients at March 2017. After the questionnaires were conducted, the patients' files were scanned and the clinical and laboratory findings were obtained and used to determine the factors that could have an effect on health-related quality of life (HRQOL) scores calculated by the questionnaire.
Results: HCV infection was shown to reduce the HRQOL ($p < 0.05$). This was shown to be associated with female gender ($p < 0.05$), absence of a regular work or income ($p < 0.05$), poor economic status ($p < 0.05$), living in a district ($p < 0.05$), co-morbid disease ($p < 0.05$), intravenous drug use ($p < 0.05$), smoking ($p < 0.05$), being HCV-RNA positive and treatment-naive ($p < 0.05$). In patients with HCV infection, the factor that significantly lowers all aspects of HRQOL is the absence of a regular work or income ($p < 0.05$). It was shown that the elderly ($\geq$65 years) patients are affected mostly physically, young (18–44 years) patients are affected mostly emotionally by HCV infection ($p < 0.05$). In our study, it was found that being married is associated with higher HRQOL ($p < 0.05$).
Conclusions: HCV infection reduces health-related quality of life. However, with new antiviral therapies, we think that HRQOL will increase in HCV patients.

Abstract #1551

The role of non-neutral mutation in the NS5A region of HCV and virological response in HCV-HIV coinfected patients with Peg-IFN/RBV therapy

Juferdy Kurniawan[1], Rino Alvani Gani[1], Samsuridjal Djauzi[1]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Nonstructural protein 5A (NS5A)-interferon sensitivity determining region (ISDR)/protein kinase R-binding domain (PKR-BD) has a role in determining successfulness of pegylated interferon/ribavirin (Peg-IFN/RBV) therapy. Single nucleotide polymorphism (SNP)-interleukin 28B (IL-28B) is predicted to affect hepatitis C virus (HCV) quasi-species evolution. The effects of HCV NS5A non-neutral mutation and SNP IL-28B to response treatment is still unclear.
Objectives: This study is done to determine the presence and role of NS5A-ISDR/PKR-BD region mutations and host SNP IL-28B on the success of Peg-IFN/RBV therapy in HCV-human immunodeficiency virus (HIV) coinfected patients.
Methods: A prospective cohort study was performed. Plasma samples were collected from 134 subjects with HCV-HIV coinfection prior to therapy. All of them were treated with Peg-IFN/RBV for 48 weeks. Examination of HCV ribonucleic acid (RNA) was performed 24 weeks after the end of therapy to assess sustained virological response (SVR).
Results: Non-neutral mutation $\geq$ 1 was found in 23 coinfected patients and higher in SVR group (14 patients) compared to non-SVR group (9 patients). This study showed that HCV NS5A non-neutral mutation was associated higher SVR achievement. No association was found between non-neutral mutation and SVR in coinfected patients. Interaction of CC-gene with non-neutral mutation was not associated with SVR.
Conclusion: Interaction of CC-gene and non-neutral mutation was not associated with SVR. The incidence of non-neutral mutation is more numerous in HCV-HIV coinfected patients who achieve SVR. There was no significant association between SNP IL-28B and non-neutral NS5A mutation.

Abstract #1560

DAAs associated with a higher incidence of hepatocellular carcinoma in treatment naïve CHC Chinese after sustained virologic response-as compared to pegylated interferon-based therapy

Dong Ji[1,2], Guo-feng Chen[1,2,†], Ping Han[1], Cheng Wang[2,3], Qing Shao[1,2], Vanessa Wu[2,3], Yudong Wang[2,3], Xiao-xia Niu[1,2], Gregory Cheng[3], Selwyn J. Hurwitz[4], Raymond F. Schinazi[4], George Lau[2,3]

[1]The Fifth Medical Center of Chinese PLA General Hospital (302 Hospital), Beijing, China, [2]The Fifth Medical Center of Chinese PLA General Hospital (302 Hospital)-Hong Kong Humanity and Health Hepatitis C Diagnosis and Treatment Centre, Beijing, China, [3]Humanity and Health Clinical Trial Center, Humanity and Health Medical Group, Hong Kong SAR, China, [4]Center for AIDS Research, Laboratory of Biochemical Pharmacology, Department of Pediatrics, Emory University School of Medicine, Atlanta, GA 30322, USA

Background: The incidence of hepatocellular carcinoma (HCC) decreased significantly in chronic hepatitis C (CHC) patients with sustained virologic response (SVR) after pegylated-interferon plus ribavirin (PR) therapy. It remains controversial whether there is any difference in HCC incidence after SVR using direct-acting antiviral agents (DAAs), as compared to PR therapy.
Methods: We compared the rate of SVR and the incidence of HCC after SVR in treatment-naïve CHC Chinese who had completed either DAAs or PR therapy in a prospective observational study (NCT02578693). Those with SVR were followed up at 12–24 weekly intervals with surveillance for HCC performed by ultrasonography and alpha-fetoprotein (AFP) at each visit. Propensity score matching [PSM] and inverse probability of treatment weighting [IPTW]) were adapted to remove the confounding effects. Multivariate Cox proportional hazards regression analysis was used to explore factors associated with post-SVR occurrence of HCC.
Results: Between October 2015 and May 2017, SVR was observed in 519 of 533 (97.4%) and 817 of 1202 (68.0%) CHC patients with completion of DAAs and PR therapy, respectively ($p = 0.0001$). With a median follow-up of 3 years after SVR, occurrence of HCC was significantly lower in patients treated with PR (3.3%) versus DAAs therapy (6.5%, log rank test, $p = 0.016$). By adjusted Cox analysis, use of DAAs [HR 2.0, 95% CI (1.3–3.0)], older age (> 55 years) [HR 2.5, 95% CI (1.6–3.8)], higher AFP level (>20 ng/ml) [HR 3.9, 95% CI (2.7–5.8)], diabetes mellitus[HR 5.0, 95% CI (3.3–7.7)] and higher LSM (>17.5 kPa) [HR 5.8, 95% CI (3.9–8.6)] at SVR were associated with increased risk of HCC.
Conclusions: HCC surveillance in CHC patients with SVR should be performed more stringently in those with high risk factors and treated with DAAs.

Abstract #1573

Clinical outcome in patients with hepatitis C infection after direct-acting antiviral treatment in Myanmar

Win Win Swe[1], Aye Thida[1], Kay Khine Thwe[1], Aye Aye Lwin[2], Khin Sanda Aung[3]

[1]Department of Hepatology, North-Okkalapa General and Teaching Hospital, University of Medicine, [2]Department of Medical Research, [3]Department of Public Health, Myanmar

Introduction: Currently, a number of countries including Myanmar have obtained an access to direct acting antiviral therapy (DAA) for Hepatitis C Viral infection (HCV), which has been treating with Myanmar simplified treatment guideline aiming for HCV elimination. The Myanmar National Hepatitis Control Program is using sofosbuvir and daclatasvir combination for large scale treatment.
Objective: The study aimed to assess the efficacy and safety of sofosbuvir-daclatasvir combined treatment in Myanmar patients with HCV infection at North-Okkalapa General and Teaching Hospital.
Methods: A total of 868 HCV RNA positive, treatment naïve adults were treated with combined sofosbuvir-daclatasvir for 12weeks and 24weeks to non-cirrhotic and cirrhotic patients respectively excluding those with HIV coinfection, hepatocellular carcinoma, eGFR < 30ml/min, on anti-tuberculous treatment, pregnancy and lactation. Sustained virological response (SVR), safety of DAA, and risk factors were explored.
Results: About 65.9% were treatment completed and SVR resulted. 22.9% were waiting for SVR check and 2.1% were loss of follow-up by 11 treatment defaulters and 7 deaths in the study analysis. Age range was 18-90 years and gender ratio was 342:526. Hepatitis B coinfection was 3.6%. Baseline (mean) HCV RNA was 5.83 ± 0.98 and 5.57 ± 1.08 $\log_{10}$IU/ml in 12weeks and 24weeks treatment duration respectively. Overall SVR achievement rate was 90%, 91.2% in 12weeks duration and 88% in 24weeks duration. Side effect was only found in two patients.
Conclusion: Experience of generic sofosbuvir-daclatasvir in Myanmar patients with HCV infection proved to be safe and associated with a high SVR rate in both 12weeks and 24weeks treatment duration.

Abstract #1703

Treatment of hepatitis C virus infection in patients with cancer in the era of direct acting antivirals—an Indonesian national cancer center experience

Siregar L[1], Waspodo AS[1], Loho IM[1], Elaine S[1], Swadari R[1], Budi E[1]

[1]Department of Gastroenterology and Hepatology, "Dharmais" Cancer Hospital, Indonesian National Cancer Center Hospital, Jakarta, Indonesia

Background: The decision to start direct-acting antivirals (DAA) treatment in HCV infected patients with cancer has been largely influenced by the cancer treatment plan and clinical judgment. The aim of this current study was to explore the practice of HCV treatment with DAA in "Dharmais" hospital, the Indonesian National Cancer Center.
Methods: Medical records of HCV infected patients with cancer who received DAA treatment between January 2016 and November 2019, were retrospectively analyzed.
Results: A total of 10 HCV infected patients with cancer that were treated with DAA, were included in this study. Of 10 patients, 9 had solid cancer and 1 had hematological cancer. Screening of HCV infection before cancer treatment was done in 9 patients. Two patients had metastatic cancer at diagnosis and seven patients received chemotherapy. Liver cirrhosis was diagnosed in five patients. Two patients received ledipasvir and sofosbuvir, while eight patients received daclatasvir and sofosbuvir. Undetectable viral load at 12-week follow-up (SVR12) was achieved in six patients. Two patients died due to progression of primary cancer before the end of DAA treatment, one patient died due to deterioration of liver function, and one patient died due to primary cancer after finishing DAA treatment. One patient, who achieved SVR 12, died one year after DAA treatment due to primary cancer.

Conclusion: Prognosis of primary cancer and patients' life expectancy should be determined before starting DAA treatment. Further study should be done to explore the benefits of DAA in HCV patients with cancer.

Abstract #1878

Noninvasive indices for monitoring disease course as an alternative to vibration controlled transient elastography in liver fibrosis staging in chronic hepatitis C: comparison of data in pre and post-treatment period

Shubham Jain

Introduction: Recent advent of non-invasive measures of hepatic fibrosis level in chronic hepatitis C patients has reduced the need for liver biopsy significantly.
Aim: To evaluate the diagnostic performance of scores using serum markers compared to Vibration Controlled Transient Elastography (VCTE) in detecting significant fibrosis (F3) or cirrhosis (F4).
Methodology: We retrospectively analysed 155 patients with CHC who underwent VCTE at baseline and after SVR 12. AST/Platelet Ratio Index (APRI), Lok Index, Bonacini Cirrhosis Discriminant Score (CDS), Göteborg University Cirrhosis Index (GUCI) score and FIB-4 scores were compared to VCTE were calculated in pre-treatment as well as post SVR 12.
Results: FIB-4 was found to predict significant fibrosis (F3) compared to other 4 parameters in pre-treatment as well as post-treatment period. The optimal cut-off value was 2.13 and 1.64 in pre-treatment and post-treatment period respectively. The sensitivity of FIB-4, CDS, Lok Index, GUCI and APRI were 76%, 60%, 80%, 88% and 84% in pre-treatment and 85% for all in post-treatment period; specificity 96%, 100%, 80%, 80% and 80% in pre-treatment and 93.3%, 90%, 73.3%, 96.6% and 96.6% respectively in post-treatment period and accuracy 86%, 80%, 80%, 84% and 82% in pre-treatment and 90%, 88%, 78%, 92% and 92% respectively in post-treatment period. Similarly, on ROC analysis, AUC value was 92.9%, 89.1%, 83.2%, 87.2% and 87.3% in pre-treatment and 96.3%, 90.5%, 84.7%, 96.9% and 97% respectively in post-treatment period.
Conclusion: As VCTE is not available at every corner of the country, these non-invasive markers can be used for follow up of patients post-treatment.

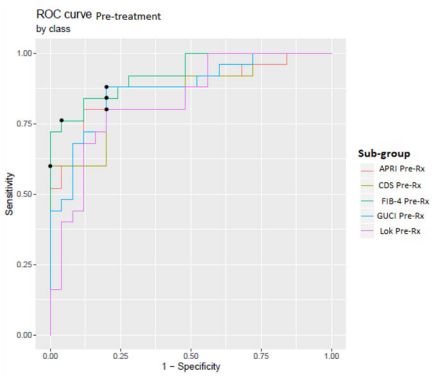


Fig 1: Overall performance comparison of various serum markers for predicting significant fibrosis (F3) by ROC curve in pre-treatment period.

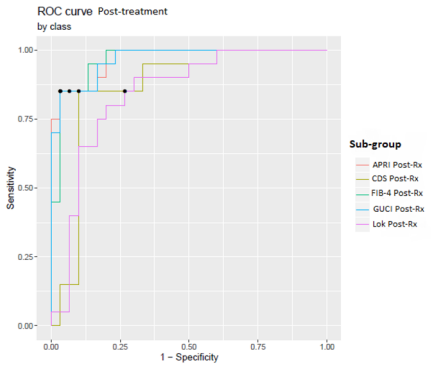


Fig 2: Overall performance comparison of various serum markers for predicting significant fibrosis (F3) by ROC curve in post-treatment period.

Abstract #1893

Sofosbuvir plus Velpatasvir combination is safe and effective in treating chronic hepatitis C in patients with end stage renal disease (ESRD).

Duseja Ajay, Taneja Sunil, De Arka, Mehta Manu, Premkumar Madhumita, Dhiman Radha Krishan

Department of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh, India, 160012

Background and objective: There is sparse data on use of Sofosbuvir based directly acting antivirals (DAAs) in patients with chronic hepatitis C (CHC) with end stage renal disease (ESRD). Data on use of sofosbuvir plus velpatasvir (Sof/Vel) combination in these patients is not available from the Asia-Pacific. Objective of the study was to evaluate the safety and efficacy of full dose Sof/Vel in CHC patients with ESRD.
Methods: Thirty six CHC patients with ESRD receiving maintenance hemodialysis were included in a real life prospective study. The study had the approval of Institute's Ethics Committee. All patients irrespective of genotype; presence of cirrhosis; treatment naïve or experienced were treated with fixed full dose Sof/Vel (400 mg/100 mg) given daily for 12 weeks. Efficacy was assessed by sustained virological response (SVR12) with negative HCV RNA 12 weeks after the end of treatment (ETR). Side effects if any were recorded in all patients.
Results: The median HCV RNA level in 36 CHC patients [Males 29(80.5%), mean age 41.1 ± 14.8 years] was 6.8×10^5 IU/ml. HCV genotype was available in 19 patients with predominant genotype 1 in 15 (79%). Four (11.1%) patients had evidence of cirrhosis (LSM ≥13 kPa on Fibroscan) and 8 (22.2%) patients were treatment experienced. ETR and SVR12 data was available in 26 patients; 10 patients are still on treatment. All 26 patients (100%) achieved ETR and all but one patient (96%) achieved SVR12. All 36 patients tolerated the Sof/Vel combination with no patient reporting any serious adverse event.
Conclusion: Sofosbuvir plus Velpatasvir combination is safe and effective in CHC patients with ESRD.

Abstract #2013

Obesity is associated with low sustained viral response among patients treated with direct acting antivirals

Butsashvili Maia[1], Abzianidze Tinatin[1], Gamezardashvili Ana[1], Gulbiani Lasha[1], Samadashvili Zaza[2], Kamkamidze George[1]

[1]Health Research Union, Tbilisi, Georgia. [2]State University of New York, Albany, NY, USA.

Introduction: Georgia has a high burden of hepatitis C virus (HCV) infection. In April 2015, in collaboration with CDC and other partners, Georgia launched National HCV elimination program that included free of charge treatment for all HCV infected persons.
Objective: To evaluate factors associated with sustained viral response (SVR), with the special focus on obesity, among patients treated with direct acting antivirals (DAA).
Methods: Data were extracted from the HCV Elimination program database at the clinic Neolab. Treatment were provided by sofosbuvir/ribavirin (SOF/RBV) with or without interferon (IFN) and sofosbuvir/ledipasvir (LDV) with or without RBV. Treatment outcomes were analyzed by demographic and clinical data, including body mass index (BMI), the degree of liver fibrosis and treatment regimen.
Results: SVR result was available for 4578 patients, treated during 2015-2019, by the time of data analysis. Overall, SVR was achieved in 96% of patients. By bivariate analysis, variables significantly associated with SVR were treatment regimen (lower cure rate for SOF/RBV than for SOF/LDV with or without Ribavirin), genotype (with genotype 3 having highest cure rate compared to genotypes 2 and 1), liver fibrosis stage, BMI (98.7% for BMI < 30 kg/sqm vs 92.6% for BMI ≥ 30 kg/sqm), age (lower on older patients), gender (higher among females), platelet count, ALT and AST. After adjustment, significant association of SVR was observed with genotype, fibrosis stage, treatment regimen and obesity (obese vs. non-obese patients aOR = 6.16, 95% CI 3.55–10.68).
Conclusion: Obesity is the strong independent risk-factor associated with lower SVR rate.

Abstract #2164

Serum mac-2-binding protein glycosylation isomer M2BPGi compared to transient elastography to predict liver stiffness in hepatitis C patients on hemodialysis

Andri Sanityoso Sulaiman[1], Ni Made Hustrini[2], Rachmadianti Sukma Hanifa[1]

[1]Hepatology Division, Department of Internal Medicine Faculty of Medicine Universitas Indonesia, [2]Department of Internal Medicine Faculty of Medicine Universitas Indonesia

Introduction: Patients undergo hemodialysis have higher risk to get infected by Hepatitis C Virus that can lead to the progression of liver fibrosis. The measurement of liver fibrosis is crucial for evaluating the eligibility of patients toward certain kind of treatment. Transient Elastography (TE) is a commonly used method for predicting liver fibrosis non-invasively but can't be used in ascites condition in which most of hemodialysis patients have risk of it.
Objective: This study aimed to evaluate M2BPGi's role for assessing liver fibrosis in hemodialysis patients in Cipto Mangunkusumo National Central General Hospital.
Method: 38 treatment naïve hepatitis C patients on HD were measured for liver stiffness by two methods: FibroScan® and M2BPGi. Spearman correlation and one-way anova were used to evaluate the study data. Cut off value of M2BPGi level and its diagnostic ability to classify liver stiffness were evaluated by ROC curve.
Result: The mean of M2BPGi values progressively increased according to LSM: 1.877 ± 0.877 COI For F0-F1, 2.456 ± 1.404 COI for F2-F3, and 3.109 ± 1.239 COI for $\geq$ F4 ($p < 0.05$). Moderate correlation between M2BPGi level and liver stiffness was found ($\rho = 0.406$, $p < 0.05$). The cutoff value of M2BPGi for significant fibrosis ($\geq$ F2) was 1.325 COI (AUROC: 0.706, Sn: 0.867, Sp: 0.349, PPV: 0.46, NPV: 0.8) and for cirrhosis ($\geq$ F4) was 2.570 COI (AUROC: 0.754, Sn: 0.625, Sp: 0.67; NPV: 0,87, PPV: 0,33)
Conclusion: Serum M2BPGi had a moderate correlation with liver stiffness measurement by FibroScan® and was good for predicting significant fibrosis

Abstract #2248

Preliminary results of Phase II study: 100% SVR rates following twelve-week treatment with narlaprevir ritonavir and sofosbuvir combination in patients with HCV Genotype 1 infection

Vladimir P. Chulanov[1,2], Denis A. Gusev,[3] Vasily A. Isakov[4], Elena A. Klimova[5], Olga O. Znoyko[5], Konstantin V. Zhdanov[6], Sergey N. Batskikh[7], Svetlana N. Kizlo[3], Nina A. Mamonova[7], Konstantin V. Kozlov[6], Vitaliy S. Sukachev[6], Elena P. Tarkhova[8], Emiliya N. Krasavina[8], Mikhail Y. Samsonov[8]

[1]National Medical Research Center for Tuberculosis and Infectious Diseases, Moscow, Russian Federation, [2]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation, [3]Centre for the Prevention and Control of AIDS and Infectious Diseases, Saint Petersburg, Russian Federation, [4] Department of Gastroenterology and Hepatology, Federal Research Center of Nutrition, Biotechnology and Food Safety, Moscow, Russian Federation, [5]A.I. Evdokimov Moscow State University of Medicine and Dentistry, Moscow, Russian Federation, [6]Federal State Budgetary Military Educational Institution of High Education "Kirov Medical Military Academy" of the Ministry of Defense of Russian Federation, Saint Petersburg, [7]Central Research Institute of Epidemiology, Moscow, Russian Federation, [8]JSC R-Pharm, Moscow, Russia

Introduction: Narlaprevir (NVR) is a potent NS3 protease inhibitor of hepatitis C virus (HCV) used with ritonavir (RTV). This is the first study evaluating combination of NVR/RTV and NS5B inhibitor sofosbuvir (SOF) in patients with chronic HCV GT1 infection.
Objectives: Multicenter, open-label, the phase II study investigating the efficacy, safety, and tolerability of both a 12-week and a shorter 8-week treatment regimen of NVR/RTV+SOF combination in treatment-naive non-cirrhotic patients with chronic HCV GT1 infection.
Methods: Patients received NVR 200 mg QD co-administered with RTV100 mg QD + SOF 400 mg QD for 12 or 8 weeks. The primary efficacy endpoint was sustained virologic response rate at post-treatment week 12 (SVR12). Safety and rates of SVR12 (HCV RNA\15 IU/mL) for 12-week arm are reported.
Results: In total, 70 patients were screened in 12-week arm and 60 patients were enrolled. At the time of the primary analysis (15 Jan 2020) all 60 patients (100%;95% CI 94–100%) in the 12-week arm achieved SVR12.
No serious adverse events (AEs) were registered. During treatment period any AEs experienced 28 (46.7%) patients. All of these were Grade 1 or 2, were transient, not related to study treatment and did not lead to treatment discontinuation. The most frequently reported AEs were diarrhea (8.3%) and headache (8.3%).
In conclusion, the combination of NVR/RTV and SOF for 12 weeks resulted in 100% SVR and well tolerated by treatment-naive non-cirrhotic patients with chronic HCV GT1 infection. Data on SVR and safety of 8-week arm will be available in June 2020.

Poster Presentations

Abstract #39

Changes in iron profile, lipids and glucose levels after eradication of chronic hepatitis C virus by direct acting anti-viral agents (DAAs)

El-Sherif Assem[1], Abd El-Razek Fathy Ghamry[1], Eldahshan Magdy[1], Hussein Mohammed Salah[1], Mahmoud Abdel Haleem Assem[2], El Shorbagy Mohammed[3], Eliwa Ahmed[1]*, El Kassas Mohamed [4]

[1]Department of internal medicine, Faculty of Medicine, Al-Azhar University, Cairo, Egypt. [2]Hepatogastroenterology and infectious diseases Department, Faculty of Medicine, Al-Azhar University, Cairo, [3]Clinical Pathology Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt. [4]Endemic Medicine Department, Faculty of Medicine, Helwan University, Cairo, Egypt. m_elkassas@yahoo.com

Background: Like other viruses, hepatitis C virus (HCV) needs constituents of host cells to proliferate and iron is considered as one of the most important constituents. So, Chronic HCV often appears to be associated with disturbances in iron homeostasis.
Objective: The aim of this study was to evaluate the changes in iron profile, lipids and glucose levels after eradication of chronic hepatitis C virus by DAAs among Egyptian HCV patients.
Patients and methods: This prospective cohort study was conducted on 180 subjects, 150 patients with chronic HCV whom received different DAAs regimens at one of the specialized HCV treatment facilities (Group A), and a group of 30 healthy volunteers (Group B), in the period from January 2017 to September 2018.
Result: Before treatment, serum iron, ferritin, transferrin saturation and triglycerides were significantly higher among HCV patients when compared to controls ($p < 0.001$), while serum TIBC, transferrin, hepcidin, hepcidin/ferritin ratio, cholesterol were significantly lower in HCV patients in comparison with controls ($p < 0.001$). Following HCV eradication with DAAs, serum iron, ferritin, transferrin saturation, triglycerides and HBA1c were significantly decreased. On the other hand, serum TIBC, transferrin, hepcidin, hepcidin/ferritin ratio and serum cholesterol were significantly increased.
Conclusion: The improvement in the iron parameters associated with improvement in triglyceride and glucose levels may also suggest an improvement of metabolic functions of the liver following HCV eradication. Rapid decrease in serum ferritin after DAAs treatment may reflect a quick regression of inflammation after inhibition of viral replication.

Abstract #50

Risk of end stage renal diseases among chronic hepatitis C patients after Interferon based therapy: a real world nation wide cohort study in Taiwan (T-COACH)

Yu Ming Lung

Introduction: Treating HCV was suggested to improve renal outcome, and achieving SVR has a beneficial effect on the kidney disease in most, but not all, patients.
Objectives: The aim of this study is to explore the risk factors of ESRD among CHC patients treated with interferon-based regimen, and the percentage of developing ESRD of these patients who achieving SVR or not.
Methods: This study finally enrolled 12,697 hospital-based HCV patients with interferon-based therapy from our database, which is linked to database of National Health Insurance Bureau (NHIB). Basic characters, risk factors, annual incidence of ESRD and eGFR (TMDRD) were analyzed.
Results: Among CHC patients who achieved SVR or not, the percentage of developing ESRD were 0.217% and 0.265%, respectively. Diabetes, hypertension and whose eGFR was less than 60 ml/min/m2 at the time point of baseline were the risks for developing ESRD of this study. SVR was not the risk of ESRD. CHC patients whose HCV genotype 1 and HCV RNA $\leq$400 KIU/ml at the time point of baseline had lower risk to develop ESRD, but no significant differences were noted.
Conclusion: Even no significant difference was noted, the annual incidence of ESRD was lower among CHC patients who achieved SVR, and antiviral therapy for CHC patients was benefit, and controlling diabetes and hypertension might be reduce the incidence of progression to ESRD.

Abstract #66

Combination treatment of sofosbuvir plus daclatasvir for 12 weeks in HCV genotype 3-infected bangladeshi patients: achievment of a sustained virological response

Shahera Umme[1], Jahan Munira[2], Mahtab Mamun[3], Tabassum Shahina[4]

[1]Medical Officer, Department of Virology, Bangabandhu Sheikh Mujib Medical University. Shahbag, Dhaka-1000, [2]Professor, Department of Virology, Bangabandhu Sheikh Mujib Meical University, [3]Professor and Chairman, Department of Hepatology Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka-1000, [4]Professor and Chairman-Department of Virology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, 1000

Introduction: Hepatitis C virus (HCV) is a major cause of chronic liver disease affecting close to 170 million people worldwide. All-oral combination therapy is desirable for patients with chronic hepatitis C virus (HCV) infection. The combination of sofosbuvir (a nucleotide polymerase inhibitor) and daclatasvir, a NS5A replication complex inhibitor, demonstrate that it is one of the most promising antiviral therapies.
Objectives: To evaluate the efficacy and treatment response of Sofosbuvir plus Daclatasvir in patients infected with HCV genotype 3.
Methods: A total 24 HCV infected patients with genotype 3 were included in this study. Patients received tab sofosbuvir 400 mg plus tab daclatasvir 60mg daily for 12 weeks. Outcome was assessed at the end of 4 weeks, 12 weeks and 24 weeks to see the rapid viral response (RVR), early viral response (EVR) and sustained viral response (SVR) respectively.
Results: The study population comprised 50% male and 50% female. Among them 29.2% were between 41-50 ages and 25% were between 31 and 40 ages. 37.5% patient's complaints for loss of appetite. 79.2% were genotype 3b and 20.8% were genotype 3a. All patients received sofosbuvir (400 mg) and daclatasvir (60 mg) for 12 weeks. RVR, EVR and SVR were achieved in 79.16%, 100% and 100% patients respectively.
Conclusion: All patients (100%) with genotype 3 achieved SVR after the completion of therapy with sofosbuvir and daclatasvir. The combination of sofosbuvir and daclatasvir for 12 weeks appears to be a very good treatment option in HCV infected patients in Bangladeshi population.

Abstract #119

Extrahepatic malignancy among chronic hepatitis C patients after antiviral therapy: a real-world nationwide study on Taiwanese chronic hepatitis C cohort (T-COACH)

Chung-Feng Huang[1], Hsueh-Chou Lai[2], Chi-Yi Chen[3], Kuo-Chih Tseng[4], Hsing-Tao Kuo[5], Chao-Hung Hung[6], Jing-Houng Wang[7], Jyh-Jou Chen[8], Pei-Lun Lee[8], Rong-Nan Chien[9], Chi-Chieh Yang[10], Gin-Ho Lo[11], Chi-Ming Tai[11], Chih-Wen Lin[11], Jia-Horng Kao[12,13], Chun-Jen Liu[12,13], Chen-Hua Liu[12,13], Sheng-Lei Yan[14], Ming-Jong Bair[15], Chun-Yen Lin[9], Wei-Wen Su[16], Cheng-Hsin Chu[17], Chih-Jen Chen[17], Shui-Yi Tung[6], Ching-Chu Lo[18], Pin-Nan Cheng[19], Yen-Cheng Chiu[19], Chia-Chi Wang[20], Jin-Shiung Cheng[21], Wei-Lun Tsai[21], Han-Chieh Lin[22], Yi-Hsiang Huang[22,23], Ming-Lun Yeh[1], Jee-Fu Huang[1], Chia-Yen Dai[1], Wan-Long Chuang[1], Pei-Chien Tsai[1], Cheng-Yuan Peng[2], Ming-Lung Yu[1]

[1]Hepatobiliary Division, Department of Internal Medicine and Hepatitis Center Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [2] School of Medicine, China Medical University, Division of Hepatogastroenterology, Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan, [3]Department of Internal Medicine, Chiayi Christian Hospital, Chiayi, Taiwan, [4]Department of Gastroenterology, Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Chia-Yi, Taiwan, [5]Division of Hepato-gastroenterology, Department of Internal Medicine, Chi Mei Medical Center, Tainan, Taiwan, [6]Division of Hepatogastroenterology, Department of Internal Medicine, ChiaYi Chang Gung MemorialHospital, Chiayi, Taiwan, [7]Division of Hepatogastroenterology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan, [8]Division of Gastroenterology and Hepatology, Chi-Mei Medical Center, Liouying, Tainan, [9]Division of Hepatology, Department of Gastroenterology and Hepatology, Linkou Medical Center, Chang Gung Memorial Hospital, Taiwan, [10]Division of Gastroenterology, Department of Internal Medicine, Show Chwan Memorial Hospital, Changhua, Taiwan, [11]Division of Gastroenterology and Hepatology, Department of Medicine, E-Da Hospital, I-Shou University, Kaohsiung, Taiwan, School of Medicine, College of Medicine, I-Shou University, Kaohsiung, Taiwan, [12]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, [13] Division of Gastroenterology and Hepatology, the National Taiwan University Hospital, Taipei, Taiwan, [14]Division of Gastroenterology, Department of Internal Medicine, Chang Bing Show-Chwan Memorial Hospital, Changhua City, Taiwan, [15]Division of Gastroenterology, Department of Internal Medicine, Taitung Mackay Memorial Hospital, Taitung City, Taiwan, [16]Division of Gastroenterology, Department of Internal Medicine, Changhua Christian Hospital, Changhua, Taiwan, [17]Division of Gastroenterology, Department of Internal Medicine, MacKay Memorial Hospital, Taipei, Taiwan, [18]Department of Internal Medicine, St. Martin De Porres Hospital - Daya, Chiayi, Taiwan, [19]Division of Gastroenterology and Hepatology, Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan, [20]Division of Gastroenterology, Department of Internal Medicine, Taipei Tzuchi Hospital, The Buddhist Tzuchi Medical Foundation, New Taipei City, Taiwan, [21]Division of Gastroenterology and Hepatology, Department of Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, [22]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, [23] Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan

Introduction: Chronic hepatitis C virus (HCV) infection is associated with many extrahepatic manifestations, of which non-hepatocellular carcinoma (HCC) malignancies are one of the important presentations.
Objective: We aimed to evaluate whether achieving a sustained virological response (SVR, defined as HCV RNA seronegativity throughout posttreatment 24-week follow-up) could reduce the risk of non-HCC malignancy in a real-world nationwide Taiwanese Chronic Hepatitis C Cohort (T-COACH).
Methods: A total of 10,174 chronic hepatitis C patients who had received interferon-based therapy (8,186 SVR and 2,528 non-SVR) enrolled in T-COACH and were linked to the National Cancer Registry database for the development of twelve extrahepatic malignancies, including those with potential associations with HCV and with the top-ranking incidence in Taiwan, over a median follow-up period was 3.79 years (range 0–16.44 years).
Results: During the 44,354 person-years of follow-up, 324 (3.02%) patients developed extrahepatic malignancies, without a difference between SVR and non-SVR patients (annual incidence: 0.69% vs. 0.87%, respectively). Compared to SVR patients, non-SVR patients had a significantly higher risk of gastric cancer (0.10% vs. 0.03% per person-year, P = 0.004) and non-Hodgkin's lymphoma (NHL) (0.08% vs. 0.03% per person-year, respectively, P = 0.03). When considering death as a competing risk, non-SVR was the only independent factor associated with gastric cancer (hazard ratio [HR]/95% confidence intervals [CI] 3.29/1.37–7.93, P = 0.008). While patients were stratified by age, the effect of SVR in reducing gastric cancer (HR/CI 0.30/0.11–0.83) and NHL (HR/CI 0.28/0.09–0.85) was noted only in patients aged < 65 years but not those aged > 65 years.
Conclusions: HCV eradication reduced the risk of gastric cancer and NHL in particular among younger patients, indicating that chronic hepatitis C patients should be treated as early as possible.

Abstract #140

Comorbidities and concomitant medications in Romanian HCV patients

George Sebastian Gherlan[1,2,3], Madalina Mihaela Neata[2], Augustina Culinescu[3], Nicoleta Mazilu[3], Raluca Dirtu[1,3], Simin Aysel Florescu[1,3], Emanoil Ceausu[1,3], Petre Iacob Calistru[1,2,3]

[1]"Carol Davila" University of Medicine and Pharmacy, Bucharest, [2]"Dr. Victor Babes" Center of Diagnostics and Treatment, Bucharest, [3]"Dr. Victor Babes" Clinical Hospital of Infectious and Tropical Diseases, Bucharest

Introduction: New direct acting antivirals (DAA) treatments in HCV infection are well tolerated and achieve cure in over 95% of the patients with the first cure. The main issue remains the possibility of drug-drug interaction. In Romania, National Insurance provides access to ombitasvir/paritaprevir/dasabuvir+ritonavir, sofosbuvir/ledipasvir and elbasvir/grazoprevir.
Objectives: We aimed to evaluate the comorbidities of the patients that entered DAA treatment and their concomitant medications.
Methods: Data regarding comorbidities and concomitant medications of all patients that were evaluated for DAA therapy in two centers were collected retrospectively. Data regarding demographics,

previous interferon treatment, liver fibrosis and coinfections have also been collected.

Results: A total number of 204 patients entered the analysis, 155 were females. Their age was between 23 and 82 years, mean age 61.2. 4 patients had HBsAg positive, while other 59 were only HBcAb positive of which 24 had HBsAB positive. 20 patients were only HBsAb positive (vaccinated). 74 patients had previous interferon treatment. 166 patients (81.37%) had at least one comorbidity. They had between 1 and 9 concomitant comorbidities. Most frequent comorbidities were arterial hypertension (109), ischemic heart disease (50), type II diabetes mellitus (38), dyslipidemia (37), thyroid function alterations (30). 157 patients (76.96%) had at least one concomitant medicine (between 1 and 10). Most frequently prescribed were diuretics (85 patients), beta blockers (77) angiotensin-convertase inhibitors (60).

Conclusions: More than 3/4 of our patients had one or more concomitant medication in their treatment at the beginning of DAA treatment for HCV infection, making sometimes the choice of DAA regimens difficult.

Abstract #143

Efficacy and safety of glecaprevir/pibrentasvir for pangenotypic chronic hepatitis C patients - A real-world experience of single medical center in Taiwan

Chi-Yu Lee [1], Zong-Sian Cai [2,3], Ching-Wei Chang [2,3], Ming-Jen Chen [2,3], Tsang-En Wang [2,3]

[1]Department of Internal Medicine, MacKay Memorial Hospital, Taipei City, Taiwan. [2]Division of Gastroenterology and Hepatology, Department of Internal Medicine, MacKay Memorial Hospital, Taipei City, Taiwan. [3]Department of Medicine, MacKay Medical College, New Taipei City, Taiwan. Department of Internal Medicine, MacKay Memorial Hospital, Taipei City, Taiwan

Introduction: Globally, an estimated 71 million people have chronic hepatitis C (CHC) and Taiwan is a hyperendemic area of CHC. Glecaprevir/pibrentasvir (GLE/PIB), the direct-acting antiviral agent for the treatment of CHC, is the first pangenotypic regimen licensed in Taiwan. We present the real-world experience from a single medical center in north Taiwan.

Objectives: We aimed to investigate the efficacy and safety of GLE/PIB in Taiwanese patients with CHC.

Methodology: From September 2018 to July 2019, we retrospectively reviewed 90 patients with CHC who were undergone direct-acting antiviral agents with GLE/PIB at MacKay Memorial Hospital. The primary endpoint was the rate of sustained virologic response at week 12 off therapy (SVR-12). The secondary endpoint was incidence of adverse events (AEs).

Results: Among 90 patients, 6 patients lost follow-up for personal issues. A total of 84 CHC patients were per-protocol analysed. The baseline characteristics of patients are listed as table 1. The median age was 62 years and 44 (52%) patients were males. The overall per-protocol SVR-12 rate was 98%. Two patients failed to achieve SVR-12. One discontinued GLE/PIB due to intolerable AEs, and the other was transferred to other medical center due to high HCV RNA viral load at 4th week after taking GLE/PIB. The common AEs were insomnia (17%), abdominal discomfort (17%) and fatigue (12%), which are listed as table 2. None had hepatic decompensation or death.

Conclusion: GLE/PIB regimen is highly effective and safe for pangenotypic CHC patients even with compensated cirrhosis or chronic kidney disease stage 4-5.

Table 1 Baseline characteristics of 84 chronic hepatitis C patients

Genotype	1a (N=8)	1b (N=12)	2 (N=50)	3 (N=6)	6 (N=6)	Mixed (N=2)	All (N=84)
Age, years (Mean, SD)	53.75 (5.73)	61.67 (13.41)	65.7 (13.03)	53 (12.07)	49.0 (12.08)	57.5 (9.19)	61.49 (13.31)
Male (N, %)	2 (25)	6 (50)	24 (48)	5 (83)	5 (83)	2 (100)	44 (52)
Fatty liver (N, %)	3 (38)	5 (42)	19 (38)	2 (33)	3 (50)	1 (50)	33 (39)
Cirrhosis (N, %)	2 (25)	2 (17)	10 (20)	2 (33)	2 (33)	1 (50)	19 (23)
CKD stage 4-5 (N, %)	1 (13)	1 (8)	13 (26)	0 (0)	0 (0)	0 (0)	15 (11)
HIV infection (N, %)	1 (13)	0 (0)	0 (0)	2 (33)	2 (33)	0 (0)	5 (6)
HTN (N, %)	2 (25)	6 (50)	32 (64)	1 (17)	0 (0)	0 (0)	41 (49)
DM (N, %)	1 (13)	1 (8)	16 (32)	1 (17)	1 (17)	0 (0)	20 (24)
HCC (N, %)	0 (0)	2 (17)	3 (6)	0 (0)	0 (0)	0 (0)	5 (6)
INF-experienced (N, %)	1 (13)	2 (17)	6 (12)	0 (0)	2 (33)	0 (0)	11 (13)
Statin (N, %)	2 (25)	0 (0)	7 (14)	0 (0)	1 (17)	0 (0)	10 (12)
Prokinetics (N, %)	1 (13)	2 (17)	4 (8)	0 (0)	0 (0)	0 (0)	7 (10)
Antacid (N, %)	0 (0)	0 (0)	4 (8)	1 (17)	1 (17)	0 (0)	6 (7)
H2RA (N, %)	1 (13)	2 (17)	10 (20)	1 (17)	2 (33)	0 (0)	16 (19)
PPI (N, %)	0 (0)	2 (17)	1 (2)	0 (0)	1 (17)	1 (50)	5 (6)
Alcohol (N, %)	4 (50)	3 (25)	7 (14)	1 (17)	2 (33)	1 (50)	18 (21)

CKD, chronic kidney disease; HIV, human immunodeficiency virus; HTN, hypertension; DM, diabetes mellitus; HCC, hepatocellular carcinoma; INF, interferon; H2RA, histamine-2-receptor antagonist; PPI, proton pump inhibitor

Table 2 Adverse events with Glecaprevir/pibrentasvir

Genotype	1a (N=8)	1b (N=12)	2 (N=50)	3 (N=6)	6 (N=6)	Mixed (N=2)	All (N=84)
Nausea (N, %)	0 (0)	2 (17)	1 (2)	0 (0)	1 (17)	0 (0)	4 (5)
Vomiting (N, %)	0 (0)	1 (8)	1 (2)	0 (0)	0 (0)	0 (0)	2 (2)
Acid regurgitation (N, %)	0 (0)	2 (17)	2 (4)	0 (0)	0 (0)	0 (0)	4 (5)
Abdominal discomfort (N, %)	1 (13)	3 (25)	7 (14)	1 (17)	2 (33)	0 (0)	14 (17)
Loose stool (N, %)	0 (0)	0 (0)	1 (2)	0 (0)	1 (17)	0 (0)	2 (2)
Constipation (N, %)	0 (0)	1 (8)	2 (4)	1 (17)	0 (0)	0 (0)	4 (5)
Headache (N, %)	0 (0)	1 (8)	5 (10)	0 (0)	0 (0)	0 (0)	6 (7)
Dizziness (N, %)	0 (0)	1 (8)	0 (0)	1 (17)	1 (17)	0 (0)	3 (4)
Fever (N, %)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Cough (N, %)	0 (0)	1 (8)	4 (8)	1 (17)	1 (17)	0 (0)	7 (8)
Insomnia (N, %)	1 (13)	1 (8)	12 (24)	0 (0)	1 (17)	0 (0)	14 (17)
Limb numbness (N, %)	0 (0)	1 (8)	1 (2)	0 (0)	0 (0)	0 (0)	2 (2)
Leg edema (N, %)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Fatigue (N, %)	3 (38)	2 (17)	4 (8)	1 (17)	0 (0)	0 (0)	10 (12)
Decreased appetite (N, %)	0 (0)	0 (0)	4 (8)	1 (17)	0 (0)	0 (0)	5 (6)
Pruritus (N, %)	2 (25)	3 (25)	4 (8)	0 (0)	0 (0)	0 (0)	9 (11)
Dyspnea (N, %)	0 (0)	0 (0)	1 (2)	0 (0)	1 (17)	0 (0)	2 (2)
Palpitation (N, %)	0 (0)	0 (0)	1 (2)	1 (17)	0 (0)	0 (0)	2 (2)

Abstract #144

Real world data from Turkey: is sofosbuvir/ledipasvir with or without ribavirin treatment for chronic hepatitis C really safe ?

[1]Demirturk N, [2]Aygen B, [3]Celik I, [4]Mistik R, [5]Akhan S, [6]Barut S, [7]Ural O, [8]Batirel A, [9]Simsek F, [10]Ersoz G

[1]Afyon Saglik, Bilimleri University Medical Faculty Department of Infectious Disease and Clinical Microbiology, Afyonkarahisar, TURKEY, [2.]Bilgehan Aygen, Erciyes University Medical Faculty Department of Infectious Disease and Clinical Microbiology, Kayseri, TURKEY, [3.]İlhami Çelik, Saglik Bilimleri University Kayseri Education and Research Hospital Department of Infectious Diseases and Clinical Microbiology, Kayseri,TURKEY, [4.] Reşit Mıstık, Medicana Hospital, Infectious Disease Clinic, Bursa, TURKEY, [5.] Sıla Akhan , Kocaeli University Medical Faculty Department of Infectious Disease and Clinical Microbiology, Kocaeli, TURKEY.[6.] Şener Barut Gaziosmanpasa University Medical Faculty Department of Infectious Disease and Clinical Microbiology, Tokat, TURKEY. [7]Onur Ural, Selcuk University Medical Faculty Department of Infectious Disease and Clinical Microbiology, Konya, TURKEY, [8.] Ayşe Batırel, Saglik Bilimleri University Kartal Lütfi Kırdar Education and ResearchHospital, Department of InfectiousDiseasesandClinicalMicrobiology, [9.]Funda Şimşek, Saglik Bilimleri University Ok Meydanı Education and Research Hospital Department of Infectious Diseases and Clinical Microbiology, [10]Gülden Ersöz, Mersin University Medical Faculty Department of Infectious Disease and Clinical Microbiology, Mersin, TURKEY

Objectives: In this study, we aimed to investigate the safety of Sofosbuvir (SOF) based therapies in chronic hepatitis C (CHC) in real-world clinical practice.

Methods: Data from patients with CHC treated with SOF/Ledipasvir (LDV) ± Ribavirin (RBV) or SOF/RBV in 31 centers across Turkey between April , 2017 and August, 2018 were recorded in a nationwide database among infectious disease specialists. Advers events of treatment were analyzed.

Results: The mean age of the patients was 51.28 ± 14.2 and 293 (55.8%) were female. The majority had HCV genotype 1b infection (65%), 75.04% were treatment-experienced, and 381 patients (72.6%) were non-cirrhotics. SOF/LDV ± RBV treatment was given to 477 patients and 48 patients were received SOF/RBV according to HCV genotype. The total SVR12 rate was 99% in all patients.

The side effects observed were evaluated in 528 patients. The number of patients with any advers events was 148 (28.03%). The adverse events are shown in Table 1. Inthe group that was planned to be treated with SOF/LDV for 12 weeks, for one patient, the treatment was terminated early due to the purplish discoloration of the tongue in the fourth week of treatment and in one patient, treatment was terminated early due to severe fatigue in the eighth week of treatment. In 10 out of 192 patients (5.2%) who received RBV, RBV dose was decreased due to anemia, and in 5 (2.6%) patients RBV treatment was stopped (Table 2) .

Discussions: SOF based therapies were found to have a very good safety profile in clinical trials.

Table 1: All advers events and laboratory abnormalities

	SOF/LDV 12 weeks, n=120 (%)	SOF/LDV+RBV 12 weeks, n=126 (%)	SOF/LDV 24 weeks, n= 213 (%)	SOF/LDV+RBV 24 weeks, n= 18 (%)	SOF/RBV 12 weeks, n= 24(%)	SOF/RBV 24 weeks, n= 24(%)	Total n=525 (%)
Weakness	21 (17.5)	23 (18.3)	18 (8.5)	5 (27.8)	2 (8.3)	3 (12.5)	72 (13.7)
Headache	18 (15)	7 (5.6)	17 (8)	5 (27.8)	-	-	47 (9)
İnsomnia	14 (11.7)	2 (1.6)	5 (2.3)	4 (22.2)	-	-	25 (4.8)
Nausea / vomiting	9 (7.5)	5 (4)	6 (2.8)	3 (16.7)	1 (4.2)	-	24 (4.6)
Fatigue	13 (10.8)	1 (0.8)	4 (1.9)	3 (16.7)	-	-	21 (4)
Pruritus	4 (3.3)	10 (8)	1 (0.5)	2 (11.1)	2 (8.3)	2 (8.3)	21 (4)
Abdominal pain	3 (2.5)	4 (3.2)	5 (2.3)	-	-	-	12 (2.3)
Anorexia	3 (2.5)	4 (3.2)	2 (0.9)	-	-	1 (4.2)	10 (1.9)
Increased appetite and weight gain	5 (4.2)	3 (2.4)	1 (0.5)	-	-	-	9 (1.7)
Dizziness	2 (1.7)	3 (2.4)	3 (1.4)	-	-	-	8 (1.5)
Arthralgia	2 (1.7)	1 (0.8)	2 (0.9)	1 (5.6)	-	1 (4.2)	7 (1.3)
Rash	1 (0.8)	4 (3.2)	-	-	-	-	5 (1)
***Other**	11 (9.2)	6 (4.8)	9 (4.2)	3 (16.7)	2 (8.3)	2 (8.3)	33 (6.3)
Increased total bilirubin (1.5-3xULN)**	-	2 (1.6)	2 (0.9)	-	-	-	4 (0.8)
Elevated transaminase(2-6xULN)**	2 (1.7)	-	6 (2.8)	-	-	-	8 (1.5)
Anemia (Hb<10gr/dl)	-	11 (8.7)	2 (0.9)	-	2 (8.3)	3 (12.5)	18 (3.4)

Table 2: Adverse events

	SOF/LDV 12 weeks, n=123 (%)	SOF/LDV+RBV 12 weeks, n=126 (%)	SOF/LDV 24 weeks, n= 213 (%)	SOF/LDV+RBV 24 weeks, n= 18 (%)	SOF/RBV 12 weeks, n= 24(%)	SOF/RBV 24 weeks, n= 24(%)	Total n=528 (%)
Any adverse events	44 (35.8)	43 (34.1)	40 (18.8)	10 (55.6)	4 (16.7)	7 (29.2)	148 (28.03)
Serious AEs	-	-	-	-	-	-	-
Discontinuation treatment	2 (1.6)	-	-	-	-	-	2 (0.4)
							***n=192**
RBV dose reduction	-	7 (5.6)	-	-	-	3 (12.5)	10 (5.2)
Discontinuation of RBV	-	5 (3.9)	-	-	-	-	5 (2.6)

Abstract #148

Direct-acting antivirals for treatment of chronic hepatitis C after living donor liver transplantation had no impact on hepatocellular carcinoma recurrence

Osama Elbahr, Lamiaa Hamed, Talaat Zakareya, Mohamad Eltabakh, Amany A Saleh, and Mohamad Abbasy

National liver Institute, Egypt

Introduction: Chronic Hepatitis C (HCV) related liver cirrhosis and hepatocellular carcinoma (HCC) are leading indications for liver transplantation (LT). Recently used direct-acting antiviral agents (DAA) for treatment of HCV have led to high rates of HCV eradication in liver graft recipients. However, their impact on HCC recurrence after liver transplantation (LT) was not fully investigated.

Aim: To evaluate the impact of HCV clearance using DAA agents in liver transplant recipients on HCC recurrence post living donor liver transplantation (LDLT).

Methods: In the period between 2012 and 2018, at the liver transplant unite in the National Liver Institute, we retrospectively evaluated 39 liver transplant recipient who underwent LDLT for HCV related liver cirrhosis and within Milan criteria HCC. All patients received post transplantation anti HCV treatment. Patients had a minimum of 1 years of follow-up after completion of treatment.

Results: The mean age of the studied patients was 51 ± 7.5 years (range 35–61), mostly males (97.4%). 14 patients (36%) had diabetes mellitus and 12 patients (31%) were hypertensive. As regard HCV treatment after transplant, 12 patients (31%) received Interferon based regimen (interferon plus weight-based ribavirin) treatment for 48 weeks. The other 27 patients (69%) received DAAs based regimen. sofosbuvir in combination with: ribavirin (SOF/RBV) for 24 weeks (n = 11), Simeprevir (SOF/SIM) for 12 weeks (n = 4), and daclatasvir with or without ribavirin (SOF/DCV ± RBV) for 12/24 weeks according to the stage of liver fibrosis and eligibility for ribavirin (n = 12). All patients who received (SOF/SIM) were on Tacrolimus or Rapamune based immunosuppression. Overall, 28 (72%) recipients had Sustained virological response at 12 weeks after completion of treatment (SVR12), seven patients (18%) relapsed after achieving end of treatment response. while 4 patients (10%) were non responders. Five patients (13%) have HCC recurrence, 3 (7%) in patents who had received interferon based regimen and 2 (5%) in patents who had received DAAs based regimen, with no statistical significant difference between the two groups p = 0.16.

Conclusion: HCV clearance after liver transplantation using DAAs did not increase the rate of HCC recurrence.

Abstract #162

A Real-World Study: efficacy of SOF combined with RBV in the treatment of chronic hepatitis C in Guangzhou population

Zhang Chunlan, Feng Qianchang, Xu Min, Li Jianping

Department of Liver Disease, Guangzhou the Eighth People's Hospital, Guangzhou Medical University, Guangzhou City, Guangdong Province, China 510060

Introduction: China is a high-incidence area for chronic infection of HCV, there is a total people of about 10 million. HCV infection is highly chronic and the onset is concealed. It is one of the important causes of active hepatitis, cirrhosis and hepatocellular carcinoma. If not treated in time, 15% to 30% of patients will progress to cirrhosis within 20 years.

Objectives: Since the introduction of the first generation of direct-acting antiviral agents (DAAs) in 2011,anti-HCV treatment has shifted from IFN-based regimens to full oral drug regimens.This study investigated the efficacy and safety of Sofosbuvir (SOF) combined with Ribavirin (RBV) in the treatment of chronic hepatitis C in 30 patients from the real world of Guangzhou (multiple chronic disease and predominantly genotype 6a).

Method: 30 chronic hepatitis C (CHC) patients combined chronic diseases were analyzed retrospectively, who took treatment of SOF combined with RBVfor 12–24 weeks and followed-up for 12–24 weeks from outpatient between December 2017 and July 2019.

Virological response at end of treatment(ETVR)and sustained virologicalresponse (SVR) were observed at the 12-week follow-up after drug withdrawal.

Result The genotype, ETVR, SVR12, combined diseases and drugs in 30 patients with CHC are shown in Table 1.20 cases were received complicated 1 to 3 kinds of drugs, no drug-drug interaction (DDI) occurred.

Conclusion SOF combined with RBV treatment is effective (100%) in the real-world multiple combined diseases and predominantly 6a genotype in Guangzhou, and it is safe.

Table. 1 The genotype, ETVR, SVR12, combined diseases and drugs in 30 patients with CHC

Genotype	N	ETVR (%)	SVR12 (%)	Combined disease (n)	drugs(n)
6a	11	100 (11/11)	100(11/11)	5 kinds	5kinds
1b	9	100 (9/9)	88.89 (8/9)	5 kinds	5 kinds
2a	8	100 (8/8)	100(8/8)	3 kinds	3kand
3a	1	100 (1/1)	100 (1/1)	1 kind	1 kind
3b	1	100 (1/1)	100 (1/1)	1 kind	1 kind
Total	30	100(30/30)	96.67(29/30)	1 kind(16) 2kinds(3) 3kinds(1)	1 kind(16) 2kinds(3) 3kinds(1)

Abstract #180

Resistance-associated substitution and ledipasvir/sofosbuvir therapy with patients chronic hepatitis C in Mongolia

Oidov Baatarkhuu[1,7,8], Nyamsuren Naranzul[1], Shih-Jer Hsu[2], Sukhee Enkhzaya[3], Tai-Chung Tseng[4], Tulgaa Khosbayar[5], Damba Enkhtuya[6], Dogsom Ivshinkhorol[6], Jazag Amarsanaa[7], Jia-Horng Kao[4]

[1]Department of Infectious Disease, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [2]Department of Internal Medicine, National Taiwan University Hospital Yunlin Branch, Yunlin, Taiwan, [3]Department of Comprehensive Laboratories, National Center for Communicable Diseases, Ulaanbaatar, Mongolia, [4]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, [5]Department of Molecular Biology and Genetics, School of Bio-Medicine, Mongolian National University, Of Medical Sciences, Ulaanbaatar, Mongolia, [6]Department of Hepatology, Happy Veritas Liver Diagnostic Center, Ulaanbaatar, Mongolia, [7]Mongolian Association for the Study of Liver Diseases, Ulaanbaatar, Mongolia, [8]Mongolian Academy of Medical Sciences, Ulaanbaatar, Mongolia

Introduction: Mongolia has the highest prevalence of hepatitis C virus (HCV) infection worldwide. Ledipasvir/sofosbuvir (LDV/SOF) was introduced to Mongolia since 2016 for HCV eradication. It has been reported that HCV resistance-associated substitutions (RASs) would affect theeffectiveness of LDV/SOF in western chronic hepatitis C (CHC) patients.

Objectives: To investigate the effectiveness of LDV/SOF and the impact of RAS on the treatment outcome in Mongolian CHC patients.

Methods: Patients with genotype (GT) 1b HCV infection were prospectively enrolled inMongolia and treated with LDV/SOF for 12 weeks. The proportion of pre-treatment NS5AY93H RAS in viral quasispecies was measured with next-generation sequencing. The endpointof LDV/SOF effectiveness was sustained virological response at post-treatment week 12 (SVR12).

Results: A total of 94 CHC patients were evaluated. The baseline Y93H proportion was < 1% in74 patients, 1e15% in 7, 15e50% in 2, and 50% in 11. All patients completed 12-week LDV/SOFtreatment and the SVR rate was 90.4%. The rate of failure to achieve SVR12 for patients withY93H < 1%, 1e15%, and _15% were 0%, 14.3%, and 61.5%, respectively (p for trend Z0.001). Inunivariable analysis, older age, baseline alanine transaminase level < 40 U/mL, and a higher-proportion of Y93H were associated with treatment failure. In multivariable analysis, only a higher proportion of Y93H was associated with treatment failure (p Z 0.022).

Conclusion: LDV/SOF therapy achieves a high SVR rate in Mongolian CHC GT1b patients withoutbaseline Y93H RAS. A higher proportion of Y93H may severely undermine the effectiveness ofLDV/SOF.

Abstract #229

A comprehensive people-centered outreach health-care system targeting HCV micro-elimination in hyperendemic areas of Taiwan (COMPACT)—establishment of a model toward HCV elimination

Ming-Lung Yu[1,2], Ching-I Huang[1,2], Po-Cheng Liang[1], Yu-Ju Wei[1], Po-Yao Hsu[1], Chang-Ting Hsu[1], Ming-Lun Yeh[1,2], Chung-Feng Huang[1,2], Jee-Fu Huang[1,2], Chia-Yen Dai[1,2], and Wan-Long Chuang[1,2]

[1]Hepatobiliary Division, Department of Internal Medicine and Hepatitis Center, Kaohsiung Medical University Hospital, [2]School of Medicine and Hepatitis Research Center, College of Medicine, and Center for Cancer Research and Center for Liquid Biopsy, Kaohsiung Medical University, Kaohsiung, Taiwan

Background: Taiwan National Health Insurance started reimbursement of direct-antiviral-agents (DAA) for hepatitis C virus (HCV) in 2017.

Objectives: We hypothesize that implementation of an outreach program is effective in increasing rates of HCV linkage-to-care rates in HCV hyperendemic (> 25%) villages in Taiwan.

Methods: The program by an "outreach HCV-checkpoint team" and an "outreach HCV-eliminating team" is implemented in Chidong/Chikan from January 2019. The screen was based on "door-by-door" strategy. HCV viremic subjects are linked to outreach HCV-eliminating team subsequently.

Results: By October 2019, 1965 residents were enrolled in the study and successfully completed the screen program. The mean age was 53 years old with 1173 (59.7%) male subjects. The mean AST and ALT levels were 29.4 and 31.3 IU/L, respectively. 208 (10.6%) subjects were seropositive for HBsAg positive with four subjects seropositive for anti-HDV. 558 (28.4%) subjects we seropositive for anti-HCV. 234 (41.9%) were seropositive for HCV RNA. HCV GT1b was the most prevalent genotype (54.0%), followed by HCV GT2 (37.4%). Of 447 subjects with fibroscan assessment, 67 (15.0%) had fibroscan > 12.5 kPa (24.1%, 47/195 in HCV viremics vs. 7.9%, 20/252 in HCV non-viremics, P < 0.001). At enrollment, only 327 (58.6%) anti-HCV-positive subjects had HCV awareness; 267 of 327 (81.7%) had accessed HCV disease; 145 (54.3%) of accessed subjects had received antivirals.

Conclusion: There remain huge gaps in each HCV care cascade step among HCV patients in a HCV hyperendemic area. Comprehensive outreach screening and treatment programs are highly effective and necessary to overcome the hurdle toward HCV micro-elimination.

Abstract #235

Effective treatment of chronic hepatitis C in prisons

E. Vashakidze, T. Imnadze, I. Mikadze, N. Kipiani, T. Gegeshidze, L. Sharvadze, M. Zhamutashvili

State Medical University, Department of Infectious Diseases, Tbilisi, Georgia Ministry of Corrections of Georgia, Medical Department

Background: Hepatitis C is one of the most actual problems of healthcare in Georgia. The incidence of HCV infection is highest in population compared with other eastern European countries. This problem is particularly severe in imprisoned patients. In general, the frequency of HCV in imprisoned subjects is 3–4 times higher compared with general population.
Material/methods: The aim of the study was to identify the effect of antiviral therapy with latest direct antiviral drugs in HCV infected imprisoned patients and management of treatment's side effects in this cohort. 300 patients with chronic hepatitis C were taken under observation. The patients were divided into 3 groups according to HCV genotype: 1a/1b genotype – 150, 2a/2c genotype – 20, 3a genotype – 130 patients. 2 subgroups were identified in each group (based on Fib4): low fibrosis degree (Fib4 < 1.45) and high fibrosis degree (Fib4 > 3.25). The patients were treated with Harvon—1a/1b genotype, with Harvon+Ribavirin 2a/2c and 3a genotypes. The treatment course took 12 or 24 weeks.
Results: Successful completion of treatment was achieved in 149 patients from type I genotype [99.3%], 20 patients from type 2 genotype [100%] and 126 patients from type 3 genotype [97.0%] subgroups. The side effects and their management were not significantly different from the results of antiviral treatment conducted in other population.
Conclusions: Thus, this program will improve not only the life quality of the imprisoned patients, but also will significantly decrease the overall medical expenses due to prevention of the disease progression and further infection transmission respectively.

Abstract #247

Efficacy of a new treatment regime including narlaprevir/ritonavir and daclatasvir in treatment-naïve patients with chronic HCV genotype 1b infection under decentralized medical care

Rymarenko Natalia[1], Achkasova Tatiana[2], Usova Svetlana[3]

[1]Medical Academy named after SI Georgievskiy, Crimea Federal University named after Vernadskiy, Simferopol, Russia; [2] Medical Academy named after SI Georgievskiy, Crimea Federal University named after Vernadskiy, Simferopol, Russia; [3] Republican Clinical Hospital for Infections in Children, Simferopol, Russia

Introduction: To treat the patients with the HCV genotype 1b infection, in 2019 a new combination has been used: narlaprevir (NVR)/ritonavir (RTV) and daclatasvir (DCV).
Objectives: The efficacy assessment has been performed for this combination.
Methods: the combination of NVR/RTV+DCV was prescribed to treatment-naïve patients with the chronic HCV genotype 1b infection, without hepatic cirrhosis. The patients received narlaprevir 200 mg with ritonavir 100 mg and daclatasvir 60 mg once a day for 12 weeks. The assessment of virologic response was performed after the end of the treatment.
Results: in total, 165 patients from 23 to 82 years old (mean, SD 56.1 $\pm$ 13.3) started the treatment, including 113 (68.5%) females; time from diagnosis varied from 0.5 to 20 years, the METAVIR score was F0 to F3 (94 (57.0%) had F0–1, 56 (34.0%) had F2, 15 (9%) had F3). In total, 149 (90.3%) patients completed the treatment, 16 (9.7%) patients have the treatment ongoing. After 3 months of the treatment, the HCV RNA was undetectable in 144 patients (96.6%) who had completed the treatment. None had significant adverse effects requiring the treatment discontinuation.
Conclusions: the efficacy of narlaprevir/ritonavir + daclatasvir therapeutic regimen was demonstrated at the end of treatment in treatment-naïve patients with the chronic HCV genotype 1 infection, without hepatic cirrhosis, in the conditions of decentralized medical care. Final conclusion will be made when SVR12 results are accessible.

Abstract #248

Viral interference between dengue virus and hepatitis C virus infections

Po-Cheng Liang[1]; Kuan-Yu Chen[1]; Chung-Hao Huang[4]; Ko Chang[4]; Po-Liang Lu[4]; Ming-Lun Yeh[1–3]; Chung-Feng Huang[1–3]; Ching-I Huang[2,3]; Meng-Hsuan Hsieh[1,3,5]; Chia-Yen Dai[1–3,5]; Zu-Yau Lin[1]; Shinn-Chern Chen[1,3]; Wan-Long Chuang[1–3]; Yen-Hsu Chen[4*]; Jee-Fu Huang[1–3,6*]; Ming-Lung Yu[1–3,7,8*]

[1]Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [2]Graduate Institute of Clinical Medicine and [3]Faculty of Internal Medicine and Hepatitis Research Center, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, [4]Infectious Diseases Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [5]Department of Preventive Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [6]Centre for Liquid Biopsy, Kaohsiung Medical University, Kaohsiung, Taiwan, [7]Institute of Biomedical Sciences, National Sun Yat-Sen University, Kaohsiung, Taiwan [8]Center For Intelligent Drug Systems and Smart Bio-devices (IDS^{2}B) and Department of Biological Science and Technology, College of Biological Science and Technology, National Chiao Tung University, Hsin-Chu, Taiwan

Background: Both Dengue virus (DENV) and HCV cause global health impact, belong to the same Flaviviridae family and could induce hepatitis. Whether there exists viral interference between them deserve exploring. We aimed to investigate the interaction between the two viruses and their impact on clinical outcome.
Methods and results: Totally, 515 Patients confirmed with dengue fever (DF) were enrolled during 2014–2015. 32 patients (6.21%) were seropositive for HCV antibodies (anti-HCV); 12 of 32 anti-HCV-positive patients had detectable HCV-RNA at the presentation of DF. The proportion of dengue hemorrhagic fever and severe dengue was comparable between patients with or without anti-HCV, and between those with or without HCV-RNA. 11 of 32 patients received HCV-RNA testing in a median interval of 23 months after DF, which revealed a significant increase of HCV-RNA levels (5.43 ± 0.77 vs 3.09 ± 1.24 log IU/mL, follow-up vs acute-DF phase, $p = 0.003$). Four of 11 patients with baseline HCV-RNA values before DF demonstrated a nadir virological response during acute DF. We also included age- and sex- and follow-up duration-matched HCV mono-infected patients as a control, which showed significantly bigger delta HCV-RNA changes in patients with DF than in the control group during the same follow-up period (2.34 ± 1.15 vs $- 0.27 \pm 0.76$ logs IU/ml, $P < 0.001$). Finally, our in-vitro experiments disclosed HCV nonstructural protein 5A was downregulated in Con1 HCV replicon cells infected by DENV1.
Conclusion: HCV was suppressed by DENV both clinically and experimentally, implying the possible viral interference. Nevertheless, no impact was observed in either disease outcome.

Abstract #252

Real-world effectiveness of sofosbuvir /velpatasvir/voxilaprevir as a hepatitis C virus infection salvage treatment

Naveed Z. Janjua[1], James Wilton[1], Darrel Cook[1], Stanley Wong[1], Zahid A. Butt[1,2], Sofia Bartlett, Margo Pearce, Alnoor Ramji[4], Eric Yoshida[4], Amanda Yu[1], Maria Alvarez[1], Mawuena Binka[1], Mel Krajden[1,3], The BC Hepatitis Testers Cohort Team

[1]British Columbia Centre for Disease Control, Vancouver, BC, Canada [2]School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada [3]Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada [4]Department of Medicine, Division of Gastroenterology, University of British Columbia, Vancouver, BC, Canada

Background: We assessed the effectiveness of sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX) in treating treatment experienced patients with HCV genotype 1 (GT1) to genotype 6 (GT6) infection in a large population-based Canadian cohort.
Methods: This analysis included individuals who had virological failure after prior DAA therapy and then initiated SOF/VEL/VOX for retreatment, had at least one HCV RNA test since treatment initiation to June 30, 2019, and were followed for SVR to Oct 9, 2019 in the BC Hepatitis Testers Cohort. The primary outcome was SVR at 12 weeks following end of HCV treatment.
Results: Overall, 166 people treated with SOF/VEL/VOX (n = 136) or SOF/VEL/VOX+Ribavirin (n = 30) were included in the analysis. The majority were GT1 (n = 90, 54.2%) and GT3 (n = 52, 31.3%) followed by GT2 (n = 16, 9.6%), male (83.1%) and aged $\geq$ 50 years (92.2%). The largest proportion of patients had received sofosbuvir/ledpisavir (39.2%), followed by sofosbuvir+ ribavirin (15.6%) and sofosbuvir/velpatasvir (12.0%) as their last treatment. The overall SVR with SOF/VEL/VOX salvage treatment was 94.6% (157/166). SVR for GT1, GT2 and GT3 was 95.6%, 100%, and 90.4%, respectively. SVR for those with cirrhosis was lower compared to those without cirrhosis (87.5% vs 95.8%, P = 0.1). SVR rates were lower among those with cirrhosis than those without cirrhosis in those previously treated with SOF/VEL (66.7% vs 88.2%), SOF/LDV (85.7% vs 96.1%), any SOF-containing regimen (86.4% vs. 95.7%) and a NS5A+SOF regimen (83.3% vs. 94.2%).
Conclusion: In this real-world cohort of patients with virological failure, retreatment with SOF/VEL/VOX results in SVR rates of more than 90% across all genotypes; however, SVR was lower for those with underlying cirrhosis.

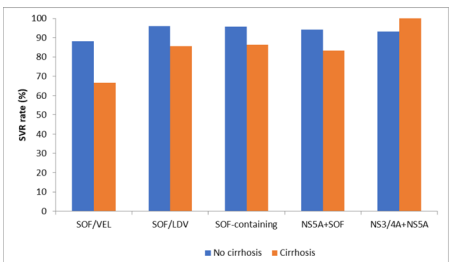


Figure. SVR among patients treated with SOF/VEL/VOX by cirrhosis status and previous treatment experience

Abstract #259

Safety of sofosbuvir-based regimens for the treatment of chronic HCV infection in patients with mild or moderate renal impairment

M. Sulkowski[1], F. Durand[2], K.R. Reddy[3], E. Lawitz[4], M. Bourlière[5], N. Cheinquer[6], S. Scherbakovsky[6], A. Chokkalingam[6], L. Ni[6], A. Gaggar[6], W.Y. Lu[6], M. Colombo[7]

[1]Professor of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, [2]Hôpital Beaujon, University Paris Diderot, Clichy, France, [3]Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA, [4]Texas Liver Institute, University of Texas Health Science Center, San Antonio, Texas, USA, [5]Hépato-Gastro-Entérologie, Hôpital Saint Joseph, Marseille, France, [6]Gilead Sciences, Inc., 7Fondazione IRCCS Ca' Granda Osepdale Maggiore Policlinico, Milan, Italy

Introduction: The major metabolite of sofosbuvir (SOF), GS-331007, is cleared renally and tends to accumulate in patients with chronic kidney disease (CKD). However, there are a substantial amount of data showing that this accumulation is not clinically significant, even in patients with end stage renal disease. This retrospective analysis of 37 Phase 2 and 38 Phase 3 studies presents the safety profile of SOF-based therapies (LDV/SOF, SOF/VEL and SOF/VEL/VOX) in patients with mild to moderate CKD as well as in patients with normal renal function.
Results: 8181 patients were included in this analysis. Mean baseline eGFR was 118.2, 69.3, and 43.6 mL/min/1.73 m^2 for patients with normal renal function (n = 6575), mild (n = 1499), or moderate (n = 107) renal impairment, respectively. The mean eGFR at post-treatment follow-up week 4 was 114.4, 69.9, and 46.3 mL/min/1.73 m^2 for patients with normal renal function (n = 5519), mild (n = 1285), or moderate (n = 90) renal impairment, respectively. When comparing baseline levels with those of post-treatment follow-up week 4, there was no clinical difference observed. Baseline characteristics were generally similar across groups, except patients with impaired renal function were older. Table 1 provides a summary of adverse events (AEs). Rates of Grade 3–4 AEs and discontinuations due to AEs were similar across groups. Patients with moderate renal impairment had higher rates of SAEs but most were not treatment-related.
Conclusion: Sofosbuvir-based regimens were safe and well-tolerated in patients with mild or moderate renal impairment. Renal function remained stable throughout treatment, and similar rates of AEs were observed across all treatment groups.

Overall Summary of Safety in Patients Treated with a SOF-containing Regimen According to Renal Function

Subjects Experiencing Adverse Events N (%)	Normal Renal Function N=6575	Mild Renal Impairment N=1499	Moderate Renal Impairment N=107
Grade 3-4 AE n (%)	193 (2.9)	58 (3.9)	6 (5.0)
SAE	191 (2.9)	52 (3.5)	9 (7.6)
Treatment-Related SAE	9 (0.1)	2 (0.1)	1 (0.8)
Treatment Discontinuation due to AE	25 (0.4)	7 (0.5)	1 (0.8)
Death	20 (0.3)	7 (0.5)	0

Abstract #299

Strategies towards the HCV microelimination: Search of viremic patients in the databases of the Valencia General Hospital Area

Moises Diago

Patients RNA-HCV or Positive Core Antigen N=2291	2007-2010 N (%)	2011-2014 N (%)	2015-2018 N (%)
Belonging to other areas	140 (17.5%)	39 (5.3%)	108 (14.2%)
Coming from the penitentiary centre	220 (27.6%)	244 (33.2%)	146 (19.2%)
Sent to other centres	23 (2.9%)	32 (4.4%)	30 (4.0%)
Under treatment	2 (0.3%)	10 (1.4%)	42 (5.5%)
Waiting for treatment	1 (0.1%)	6 (0.8%)	91 (12.0%)
Previous to one-step diagnosis	0	39 (5.3%)	40 (5.3%)
Exitus	14 (1.8%)	30 (4.1%)	45 (5.9%)
No treatment indication	24 (3.0%)	75 (10.2%)	140 (18.4%)
Alcohol or drugs addiction	6	28	27
Elderly patients	1	7	31
Serious or terminal disease	5	18	37
Mental disease	6	13	18
Bad HIV control	3	5	3
Reticent to treatment	3	3	15
Others	0	1	9
Lost	362 (45.4%)	240 (32.7%)	95 (12.5%)
Treatment neglect	4	5	6
Not send to the specialist	244	111	51
Social issue	1	6	6
Unknown	113	118	32
Treatment failure/ Re-infection	4 (0.5%)	4 (0.5%)	4 (0.5%)
No classification	8 (1.0%)	15 (2.0%)	18 (2.4%)
TOTAL	798	734	759

Abstract #301

Barriers HCV elimination for screening and treatment in people who inject drugs after prison in Japan

Morizono Shusuke

Introduction: Many HCV patient infected by drug injection. The spread of hepatitis C virus has become a social problem due to the spread of drugs.
Objective: We manage to improve screening and linkage to care after prison.
Method: In japan there is a rehabilitation facility for prisoner after they get out prison. They become social independent at the facility. We go to 3 facility three times in a year. 20 people live in the facility. We interview clinical history and examine blood test from 2010. If prisoner have HCV infection, we treat them with economical support.
Results: We investigate 5 years data (2015 ~ 2019) about screening and treatment in people who inject drugs after prison. 398people were interviewed and had blood test in 5 years. 62 people (male38 female24) were suspected to infect hepatitis C in 5 years. The average age was 47.1 years old (from 27 to 69 years old). 35 people (8.8%) were HCV RNA positive. HCV genotype was 1type 13people, 2type 21peple, type unknown 1person. 12 patients had a previous infection. 21patients (5.2%) were treated HCV with DAA. Treatment regimen was Glecaprevir +Pibrentasvir 4, Sofosbuvir+Ribavirin9, Sofosbuvir+Ledipasvir 6, the other regimen 2. SVR was 100%. Serious side effect was 0%.
Conclusion: Prisoner are highly infected with hepatitis C. They can't receive treatment by economical problem. Our plan continue to eradicate Hepatitis C. This HCV elimination activity is PWID provide a unique opportunity to upscale HCV Screening, treatment and linkage to the community would support effectiveness for HCV Elimination.

Abstract #356

Revisiting epidemiology of viral hepatitis C in rural areas of Egypt (results from a screening campaign)

Allam Mahmoud,[1] Morad Wesam[2]

[1]Hepatology and gastroenterology department, National Liver Institute, Menoufia University, Egypt, [2]Epidemiology and Preventive Medicine department, National Liver Institute, Menoufia University, Egypt

Objectives: Egypt has the highest known prevalence of hepatitis C (HCV) in the world, a problem which represents a major challenge to healthcare policymakers in the country. In this study, we aimed to highlight on the prevalence of HCV infection in rural areas of this country and to clarify the association between different risk factors and the prevalence of HCV infection.
Methods: A screening campaign was conducted in five villages present in rural Menoufia Governorate. Blood samples from consented participants were tested for HCV antibodies. For assessment of the contribution of different risk factors with HCV infection, we interviewed participants to complete the study questionnaire. Results were tabulated and analyzed by suitable statistical tests to assess the prevalence of HCV infection in these areas and possible risk factors that are significantly associated with infection.
Results: Out of 14,000 participants, 14.8% (n = 2071) of the screened sample tested positive for HCV antibodies. Various risk factors were significantly associated with higher risk for acquiring HCV including parenteral anti-schistosomaiasis therapy, invasive medical procedures and other important risk factors.
Conclusion: One of each six in the population of rural Menoufia is seropositive for HCV. Our results thus confirm the severity of the current disease burden in the Nile Delta of Egypt. There are significant risk factors associated with HCV infection, suggesting the need for more strict infection control measures specially upon using invasive medical procedures.

Abstract #360

Assessment of liver fibrosis using APRI score after treatment with elbasvir/grazoprevir in patients with hepatitis C infection and chronic kidney disease on hemodialysis

Laksono Bayu[1], Agustanti Nenny[2], Supriyadi Rudi[3]

[1]Department of Internal Medicine, Faculty of Medicine, Dr Hasan Sadikin Hospital, Bandung, Indonesia, [2] Division of gastroenterology and Hepatology, Department of Internal Medicine, Faculty of Medicine, Dr Hasan Sadikin Hospital, Bandung, Indonesia, [3] Division of Nephrology and Hypertension, Department of Internal Medicine, Faculty of Medicine, Dr Hasan Sadikin Hospital, Bandung, Indonesia

Introduction: Approximately 5–60% of hemodialysis patients are infected with Hepatitis C virus (HCV). The survival rate of hemodialysis patients with hepatitis C is lower than patients without hepatitis C due to the risk of liver fibrosis and cardiovascular disease. The combination of Elbasvir and Grazoprevir is the drug of choice for these patients. Eradication of HCV can reduce liver fibrosis. APRI score can evaluates liver fibrosis. The aim of this study is to assess liver fibrosis using APRI score after Elbasvir/Grazoprevir therapy.
Methods: This is quasi-experimental study without a control group during April-November 2019 in Dr. Hasan Sadikin Hospital, Bandung. Patients with Anti HCV reactive and HCV RNA detected were included. APRI score and HCV RNA tests were performed before and after 12 weeks of therapy (sustained virological response-SVR12). The data were analyzed using paired T-test at a 95% confidence level.
Results: Out of 30% of hemodialysis patients are known to be infected with HCV. A number of 38 HCV patients in the hemodialysis unit were given Elbasvir/Grazoprevir for 12 weeks. The APRI score before therapy was 0.337 and 12 weeks after therapy was 0.277 (p-value = 0.007). The HCV RNA SVR 12 undetectable in 97% of subjects after the therapy.
Conclusion: In conclusion, the combination of Elbasvir/Grazoprevir is expected to reduce the degree of fibrosis and to achieve 97% SVR12 after 12 weeks of therapy in hemodialysis patients with HCV.

Abstract #362

The safety and efficacy of sofosbuvir/velpatasvir in pediatric patients 6 to < 18 years old with chronic hepatitis C infection

M.M. Jonas[1], R. Romero[2], E.M. Sokal[3], P. Rosenthal[4], G. Verucchi[5], C.H. Lin[6], J. Wen[7], M.R. Narkewicz[8], S. Bansal[9], J. Shao[10], S. Hsueh[10], A. Gaggar[10], K. Kersey[10], W.Y. Lu[10], R.P. Gonzalez-Peralta[11], D.H. Leung[12], W.F. Balistreri[13], K.F. Murray[14], K.B. Schwarz[15]

[1]Boston Children's Hospital, Boston, MA, USA, [2]Emory University School of Medicine and Children's Healthcare of Atlanta, Atlanta, GA, USA, [3]Cliniques Universitaires Saint-Luc, UC Louvain, Brussels, Belgium, [4]University of California San Francisco, San Francisco, CA, USA, [5]University of Bologna, Bologna, Italy [6]Children's Hospital Los Angeles, Los Angeles, CA, USA, [7]University of Pennsylvania and The Children's Hospital of Philadelphia, Pennsylvania, USA, [8]University of Colorado School of Medicine and Children's Hospital of Colorado, Aurora, USA, [9]Kings College Hospital, London, United Kingdom, [10]Gilead Sciences, Inc, Foster City, CA, USA, [11]Pediatric Gastroenterology, Hepatology and Liver Transplant, AdventHealth for Children, Orlando, FL, USA, [12]Baylor College of Medicine and Texas Children's Hospital, Houston, TX, USA, [13]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA, [14]University of Washington School of Medicine and Seattle Children's Hospital, Seattle, WA, USA, [15]Johns Hopkins University School of Medicine, Baltimore, United States, Boston, MA, USA

Introduction: Direct-acting antiviral regimens have been approved for the treatment of HCV in adolescents aged 12 to < 18 years, but for younger children, the standard of care is still interferon-based therapy. The current study evaluated the safety and efficacy of sofosbuvir (SOF)/velpatasvir (VEL) in children 6 to < 18 years old.
Methods: In this open-label study, patients 6 to < 12 years old received SOF/VEL 200/50 mg and 12 to < 18 years old received SOF/VEL 400/100 mg once daily for 12 weeks. The efficacy endpoint was SVR12. Safety was assessed by adverse events (AEs) and clinical/laboratory data. Intensive pharmacokinetic (PK) was done to confirm the appropriateness of the chosen dose in a subgroup of patients of each age group.
Results: A total of 102 adolescents (12 to < 18 years old) and 73 patients 6 to < 12 years were enrolled and treated. Majority of subjects were GT1 (75%), female (51%), white (80%), treatment-naïve (85%), and vertically infected (91%). Intensive PK confirmed that the doses selected were appropriate. The SVR12 rate among adolescents was 95% (97/102) and among the 6 to < 12 years old was 92% (67/73); one patient in each age group had virologic failure and the remaining 9 patients did not achieve SVR for non-virologic reasons. Most AEs were mild or moderate. Five subjects had a serious AE and 2 discontinued due to AEs, none of which was attributed to treatment. The most common AEs were headache, fatigue, and nausea in adolescents and vomiting, cough and headache in younger children.

Abstract #373

Successful antiviral therapy reduced risk of schizophrenia among chronic hepatitis C patients: a nation-wide real-world study of Taiwanese cohort (T-COACH)

Chi-Yi Chen[1,*], Pei-Chien Tsai[2,3,*], Hsing-Tao Kuo[4], Chao-Hung Hung[5], Kuo-Chih Tseng[6], Hsueh-Chou Lai[7], Cheng-Yuan Peng[7], Jing-Houng Wang[8], Jyh-Jou Chen[9], Pei-Lun Lee[9], Rong-Nan Chien[10], Chi-Chieh Yang[11], Gin-Ho Lo[12], Jia-Horng Kao[13,14], Chun-Jen Liu[13,14], Chen-Hua Liu[13,14], Sheng-Lei Yan[15], Ming-Jong Bair[16], Chun-Yen Lin[10], Wei-Wen Su[17], Cheng-Hsin Chu[18], Chih-Jen Chen[18], Shui-Yi Tung[7], Chi-Ming Tai[12], Chih-Wen Lin[12], Ching-Chu Lo[19], Pin-Nan Cheng[20], Yen-Cheng Chiu[20], Chia-Chi Wang[21], Jin-Shiung Cheng[22], Wei-Lun Tsai[22], Han-Chieh Lin[23], Yi-Hsiang Huang[23,24], Ming-Lun Yeh[2], Chung-Feng Huang[2], Meng-Hsuan Hsieh[2,3], Jee-Fu Huang[2], Chia-Yen Dai[2], Wan-Long Chung[2], Chiao-Li Khale Ke[25,], Ming-Lung Yu[2,**] (T-COACH Study Group)**

[1]Department of Internal Medicine, Chiayi Christian Hospital, Chiayi, Taiwan, [2]Hepatobiliary Section, Department of Internal Medicine, and Hepatitis Center, Kaohsiung Medical University Hospital; Hepatitis Research Center, School of Medicine and Cohort Research Center, Kaohsiung Medical University, Kaohsiung, Taiwan, [3]Health Management Center, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [4]Division of Hepatogastroenterology, Department of Internal Medicine, Chi Mei Medical Center, Tainan, Taiwan, [5]Division of Hepatogastroenterology, Department of Internal Medicine, ChiaYi Chang Gung Memorial Hospital, Chiayi, Taiwan, [6]Department of Gastroenterology, Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Chiayi, Taiwan, [7]Division of Hepatogastroenterology, Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan, [8]Division of Hepatogastroenterology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan, [9]Division of Gastroenterology and Hepatology, Chi-Mei Medical Center, Liouying, Tainan, [10]Division of Hepatology, Department of Gastroenterology and Hepatology, Linkou Medical Center, Chang Gung Memorial Hospital, Keelung, Taiwan, [11]Division of Gastroenterology, Department of Internal Medicine, Show Chwan Memorial Hospital, Changhua, Taiwan, [12]Division of Gastroenterology and Hepatology, Department of Medicine, E-Da Hospital, I-Shou University, Kaohsiung, Taiwan, School of Medicine, College of Medicine, I-Shou University, Kaohsiung, Taiwan, [13]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, [14]Division of Gastroenterology and Hepatology, National Taiwan University Hospital, Taipei, Taiwan, [15]Division of Gastroenterology, Department of Internal Medicine, Chang Bing Show-Chwan Memorial Hospital, Changhua, Taiwan, [16]Division of Gastroenterology, Department of Internal Medicine, Taitung Mackay Memorial Hospital, Taitung, Taiwan, [17]Division of Gastroenterology, Department of Internal Medicine, Changhua Christian Hospital, Changhua, Taiwan, [18]Division of Gastroenterology, Department of Internal Medicine, MacKay Memorial Hospital, Taipei, Taiwan, [19]Department of Internal Medicine, St. Martin De Porres Hospital, Daya, Chiayi, Taiwan, [20]Division of Gastroenterology and Hepatology, Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan, [21]Division of Gastroenterology, Department of Internal Medicine, Taipei Tzuchi Hospital, The Buddhist Tzuchi Medical Foundation, New Taipei, Taiwan, [22]Division of Gastroenterology and Hepatology, Department of Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, [23]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei, Veterans General Hospital, Taipei, Taiwan, [24]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [25]Department of Psychiatry, Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

Background/aims: Chronic hepatitis C (CHC) has been associated with major psychiatric disorders; meanwhile, interferon-based therapy for CHC may cause psychiatric sequelae. We aimed to evaluate the long-term effects of successful antiviral therapy (sustained virological response, SVR, undetectable HCV RNA 24 weeks after end-

of-treatment) on the incidence of major psychiatric disorders in a nation-wide Taiwanese CHC Cohort (T-COACH).
Methods: Of 15,836 CHC patients with interferon-based therapy enrolled in T-COACH from 23 hospitals in Taiwan between 2003 and 2015, 12,723 CHC patients (9690 SVR and 3033 non-SVR patients) were linked to Taiwan National Health Insurance Research Databases for the incidence of major psychiatric disorders, including affective psychoses and schizophrenia. Death before major psychiatric disorders was considered a competing risk event.
Results: Twenty-four patients developed new-onset major psychiatric disorders during 67,554 person-years follow-up (3.6 per 10,000 person-years), including 16 affective psychoses, seven schizophrenia, and one organic psychotic condition. The incidence of major psychiatric disorders and affective psychoses did not differ between SVR and non-SVR groups (3.2 versus 4.6 and 2.4 versus 2.0 per 10,000 person-years, respectively). However, the 5- and 10-cumulative incidence rates of schizophrenia was significantly higher in non-SVR than in SVR patients (0.14% and 0.04%, respectively, versus 0.02% and 0.04%, respectively; Gray's $p = 0.036$). Cox subdistribution hazards model showed that SVR and older age were associated with a significantly lower risk of schizophrenia (hazard ratio/95% confidence interval, 0.18/0.04–0.90 and 0.17/0.04–0.71, respectively). The benefits of SVR in decreased incidence of schizophrenia were majorly observed among younger patients (age < 45 year, $p = 0.02$).
Conclusions: Successful interferon-based therapy could reduce the incidence rate of schizophrenia among CHC patients, especially among the younger subpopulation.

Abstract #379

Abnormal hepatocellular organelles are still present in patients with sustained virological response (SVR)

Aoyagi Haruyo[1], Iijima Hiroko[2], Kikuchi Minami[1], Koyama Maiko[3], Matsuda Mami[1], Watashi Koichi[1], Suzuki Ryosuke[1], Masaki Takahiro[1,4], Saito Takeshi[5], Shimada Noritomo[6], Kato Keizo[7], Enomoto Masaru[8], Hayashi Kazuhiko [9], Tsubota Akihito[10], Mimata Ayako [11], Sakamaki Yuriko [11], Ichinose Shizuko[12], Muramatsu Masamichi [1], Wake Kenjiro[13], Wakita Takaji [1], Aizaki Hideki[1]

[1]Department of Virology II, National Institute of Infectious Diseases, Tokyo, Japan, [2] Department of Internal Medicine, Division of Hepatobiliary and Pancreatic Disease, Hyogo College of Medicine, Hyogo, Japan, [3] Department of Research and Development, Biomaster, Inc., Kanagawa, Japan, [4] Department of Laboratory Medicine, The Jikei University School of Medicine, Tokyo, Japan, [5] Department of Medicine, Division of Gastrointestinal and Liver Diseases, Keck School of Medicine, University of Southern California, Los Angeles, California, USA, [6] Division of Gastroenterology and Hepatology, Ootakanomori Hospital, Chiba, Japan, [7] Division of Gastroenterology and Hepatology, Shinmatsudo Central General Hospital, Chiba, Japan, [8] Department of Hepatology, Osaka City University, Osaka, Japan, [9] Division of Gastroenterology and Hepatology, Meijo Hospital, Nagoya, Japan, [10] Core Research Facilities for Basic Science, Research Center for Medical Sciences, The Jikei University School of Medicine, Tokyo, Japan, [11] Research Core, Tokyo Medical and Dental University, Tokyo, Japan, [12] Department of Plastic, Reconstructive and Aesthetic Surgery, Nippon Medical School hospital, [13] Liver Research Unit, Minophagen Pharmaceutical Co., Ltd., Tokyo, Japan

Introduction: Treatment of patients with chronic hepatitis C infection (CHC) has improved significantly. > 90% of patients treated with direct-acting antivirals (DAA) can achieve a sustained virological response (SVR). While the liver carcinogenesis after SVR significantly decreases, liver carcinogenesis in SVR patients with risk factors (e.g., age, male, liver fibrosis or steatosis) remains problematic.
Objective: In this study, we verified whether organelle alterations were observed in CHC, as found in HCV-infected cells. Furthermore, liver pathology after SVR was examined with the goal of improving the management of the increasing SVR-patients.
Methods: The viral genomes were analyzed by RT-PCR. Cellular ultrastructure was assessed using transmission electron microscopy (TEM) in liver biopsies of SVR patients.
Results: HCV RNA was detected in 5 of 70 samples of liver tissue after SVR. Latent HCV RNA was detected in 2 of 37 SVR-HCC patients. Organellar abnormalities, such as nuclear membrane disruption, cristae destruction in swollen mitochondria, and dilation and membrane vesicle formation of ER were observed in hepatocytes of both CHC and SVR patients. In further in vitro experiments, we confirmed that the organellar abnormalities found in HCV-infected cells were improved after elimination of the virus by IFN or DAA treatment. In vivo experiments for HCV clearance in mice have been attempted, but they are still under investigation.
Conclusions: Abnormal hepatocellular organelles in SVR patients indicate a persistent disease state ("post-SVR syndrome"). Long-term follow-up of patients after SVR is recommended.

Abstract #413

Correlation between hepcidin serum levels and liver fibrosis based on *Fibroscan* in patients with chronic hepatitis C

A. Danial[1], I.A. Nusi[2], U. Maimunah[2], U. Kholili[2], B. Widodo[2], H. Thamrin[2], A. Ashariati[3], P.B. Setiawan[2]

Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga – Dr.Soetomo Teaching Hospital, Surabaya, Indonesia, [2] Gastroenterohepatology Division, Department of Internal medicine, Universitas Airlangga – Dr.Soetomo Teaching Hospital, Surabaya, Indonesia, [3] Hematology and Oncology Division, Department of Internal medicine, Faculty of Medicine, Universitas Airlangga – Dr.Soetomo Teaching Hospital, Surabaya, Indonesia

Background: Chronic hepatitis C infection can progress to liver fibrosis, cirrhosis, and hepatocellular carcinoma. Iron overload in chronic hepatitis C is a cofactor that promotes the development of liver damage and increases the risk of liver fibrosis. Increased iron in hepatitis C infection is associated with decreased hepcidin serum levels, a major regulator of iron homeostasis. The relationship between hepcidin and liver fibrosis in patients with chronic hepatitis C drug naive patients is still controversial.
Objective: To analyze the correlation between hepcidin serum levels with liver fibrosis based on *fibroscan* in chronic hepatitis C patients in Gastroentero-Hepatology Clinic.
Materials and methods: A cross-sectional observational analytic study, involving all hepatitis C patients during July–September 2019. 34 patients fulfilling the inclusion and exclusion criteria were the subjects of the study. Patients were selected with consecutive sampling and were examined for serum hepcidin levels and degree of liver fibrosis was measured by *fibroscan*. Data analysis used spearman correlation test and was considered significant if $p < 0.05$.
Results: A total of 34 subjects (64.71% females with the mean age of 49.76 ± 9.52 years) were eligible for enrollment in this study. The average hepcidin level was 18,23 ± 5,35 ng/ml. The average *fibroscan* measurement result was 8,80 ± 4,53 kPa and most patients with stage F3 were 11 peoples (32.4%). The serum hepcidin levels

correlated negatively and significantly (r = -0788, P < 0.001) with degree of liver fibrosis.
Conclusion: There is a negative correlation between hepcidin serum levels and liver fibrosis based on *fibroscan* in patients with chronic hepatitis C.

Abstract #417

A program of hepatitis C Surveillance with linkage to care for inpatients from non-infectious departments in two tertiary hospitals from Jiangsu, China

Long-gen Liu[1], Yuxin Chen[2], Xiujun Zhang[1], Rui Huang[2], Bei Jia[2], Chao Wu[2]

[1]Department of Hepatology, The Third People's Hospital of Changzhou, Changzhou, Jiangsu, China, [2] Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China

Introduction: Preliminary data indicated a lack of knowledge of non-infectious departments (non-ID) physicians regarding the criteria of patients who needs HCV antibody screening, and an insufficient follow-up of patients with positive HCV antibody (Ab). Therefore, we designed a compressive hospital-led program for enhanced HCV surveillance with linkage to care in non-IDs of hospitals.
Methods: This hospital-based program was launched in two tertiary hospitals in Jiangsu province of China. The program consisted of an educational campaign to raise awareness of physicians from non-IDs to promote HCV surveillance, a new established HCV clinical algorithm responsible for follow-up of patients with positive HCV Ab, and comprehensive testing, diagnosis, and treatment.
Results: With our new launched program of hepatitis C Surveillance with linkage to care for the last 6 months (from Mar 2019 to Oct 2019), a total of 68.7% (64,111/93,291) of inpatients had HCV Ab test. Among them, 0.54% (343/64,111) of non-ID inpatients was found with positive HCV Ab. 81.9% patients agreed to enroll in our study. 100% (281/281) of patients with positive HCV Ab was followed up for HCV RNA PCR testing, and 42.5% (119/281) of patients were confirmed with CHC. Currently, 71.4% (85/119) of HCV patients were linked to care, 57.6% (49/85) started DAA treatment.
Conclusion: This program achieved enhanced HCV Surveillance with linkage to care, an important strategy in hospital setting to improve the hepatitis C care continuum by identifying individuals unaware of their HCV status and facilitating their access to HCV treatment.

Abstract #439

The study on consequence of HCV management in Mongolia

Oidov Baatarkhuu[1,5], Nyamsuren Naranzul[1], Radnaa Otgonbayar[2], Jazag Amarsanaa[3], Sevjid Badamjav[4]

[1]Department of Infectious Diseases, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [2]Department of Pediatrics, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [3] Mongolian Associations for Study of Liver Diseases, Ulaanbaatar, Mongolia, [4]Department of Gastroenterology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [5]Mongolian Academy of Medical Sciences, Ulaanbaatar, Mongolia

Introduction: Mongolia has a large burden of viral hepatitis, especially chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, which are associated with cancer and cirrhosis. Therefore, there is need of to assess policy implementation, milestones of diagnostic and treatment development of HCV in our country.
Objective: to determine situation and implementation of HCV policy management.
Methods: descriptive study, analyzed policy and strategic documents and statistics issued by government organizations, reviewed treatment result published studies.
Results: Since 2014, 19 policy documents were approved and updated national viral hepatitis guideline three times. In 2017 Mongolia established The Whole Liver Program (HPCE) 2017–2020. It aims to eliminate HCV in Mongolia by 2020 and to significantly reduce viral hepatitis induced liver cirrhosis and HCC related mortalities. Within the framework of the program, free general population hepatitis screening, two free-of charge HCV viral load testing and no-out-of-pocket-cost HCV treatment campaigns have been initiated nationwide. 959,320 people were screened viral hepatitis, 94,280 people were tested viral load, 19,896 people were treated.
Conclusion: The HPCE Program in Mongolia is serving as a model for other countries in their fight against viral hepatitis.

Abstract #441

Functional abnormalities of the liver in diabetic patients with and without viral hepatitis C in Mongolia

Otgonbayar Radnaa[1], Altantuya Idkhuu[1], Uranbaigali Enkhbayar[2], Badamjav Sevjid[3], Sainbileg Sonomtseren[4], Oidov Baatarkhuu[5,6]

[1]Department of Internal Medicine, University General Hospital, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [2]Department of Clinical Laboratory, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [3]Department of Gastroenterology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [4]Department of Endocrinology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [5]Department of Infectious Diseases, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [6]Mongolian Academy of Medical Sciences, Ulaanbaatar, Mongolia

Introduction: Diabetic patients with viral hepatitis have a high risk of liver cirrhosis. M2BPGi biomarker helps to determine the stage of liver fibrosis in those with fatty liver disease and viral hepatitis in Mongolia.
Objectives: We aimed to compare liver function of diabetes mellitus patients with and without viral hepatitis C using the non-alcoholic fatty liver disease fibrosis score, aspartate transaminase to platelet ratio index, Fibrosis-4 Index, Mac-2-binding protein biomarker and ultrasonic liver stiffness measurements.
Methods: The study was conducted based on convenience sampling of 123 patients from the General hospital outpatient clinic. Slightly more than half of the study participants were male (53%, n = 64). 33 of the diabetics with hepatitis (mean age 52.31 ± 9.8 years) and 90 diabetics without hepatitis (mean age 53.26 ± 8.58) agreed to participate. Anthropometric measurements, non-alcoholic fatty liver disease fibrosis score, aspartate transaminase to platelet ratio index, Fibrosis-4 Index, Mac-2-binding protein biomarker, and ultrasonic transient elastography measurements were compared using independent t-tests for continuous variables and Wilcoxon rank sum tests for ordinal variables.

Results: The median values of the Fibrosis-4 Index for those with hepatitis C and without were 1.3 vs 0.9 ($p < .05$), Mac-2-binding proteinbiomarker2.0 vs 1.3 ($p < .0001$), ultrasonic liver stiffness measurements 10.3 vs 6.9 ($p < .0001$),aspartate transaminase to platelet ratio 0.6 vs 0.3 ($p < .001$), and Non-alcoholic fatty liver disease fibrosis scores were -0.2 vs -0.9 ($p < .004$), respectively.
Conclusions: Diabetic patients with hepatitis had statistically significantly higher Mac-2-binding protein biomarker, NAFLD Fibrosis Scores than patients without hepatitis. However, other fibrosis test results were similar in diabetic patients with hepatitis and without hepatitis C.

Abstract #457

Fatty liver disease in hepatitis C patients after therapy with direct –acting antiviral drugs

E. Vashakidze, M. Moistrapishvili, E. Packoria, I. Mikadze, M. Kvitashvili, N. Kipiani, M. Djangavadze

Department of Infectious Disease Tbilisi State medical University, Tbilisi, Georgia

Background: Prevalence of Fatty Liver Disease achieved 25.2% worldwide and concomitant with C and B hepatitis became one of the common disease.
Materials/methods: The aim of the study was to assess the prevalence of steatosis and the stage of Fibrosis in Patients with chronic hepatitis C who achieved a sustained virological response (SVR) after Direct –Acting antiviral therapy (DAA). 125 Patients with chronic hepatitis C were included in the study. (GNT1–84%; GNT2–16%). The Patients had been treated for 12 weeks with Lediapasvir/sofosbuvir (Harvoni) GNT1 and with ledipasvir/sofosbuvir (Harvoni) + ribavirin-GNT2. Transient elastography with controlled attenuation parameter (CAP) was used to assess hepatic steatosis.
Results: The mean age of patients was 56 ± 10 year. Males were 100 (80%), Females – 25 (20%); The mean data of fibrosis was 7.41 ± 9 kPa. Genotype – 1 reveled in 105 cases (84%), genotype 2- in 20 cases (16%). Post SVR ALT and AST diminished and it was statistically significant (for ALT 17.81 ± 2.3 U/l and 103.16 ± 2.6 IU/l and for AST 21.58 ± 0 IU/ml, and 51.84 ± 1.1 U/L) . Steatosis was present in 46.4% of these patients. Patients with steatosis had higher body mass index, ALT, CAP score and fibrosis score. They also had history of Diabetes Mellitus type 2 and dyslipidemia. In these group of patients after DAA therapy BMI index and stage of fibrosis didn't change, however in the group of patients without steatosis stage of fibrosis decreased and it was statistically significant . Liver transaminases ALT, AST decreased in both groups.
Conclusion: Thus, post-SVR assessment of steatosis and fibrosis is very significant. It is necessary longitudinal follow-up, to provide appropriate patients care and advance our understanding of the long-term consequences of hepatic steatosis in post-SVR patients.

Abstract #464

Prevalence of occult hepatitis C virus infection in patients with chronic liver disease: a systematic review and meta-analysis

Shan Fu[1], MengMeng Zhang, NaiJuan Yao[1], YaLi Feng[1] Yingren Zhao[1], Jinfeng Liu[1]

[1]Department of Infectious Diseases, First Affiliated Hospital of Xi'an Jiaotong University, 710061 Xi'an

Introduction and objectives: Detectable hepatic HCV-RNA are associated with histological activity of the protracted liver disease and abnormal of liver enzymes. Whereas, no comprehensive evidence is available for assessing the prevalence of occult HCV infection. This meta-analysis aims to determine the epidemiology of this type of HCV infection in patients with chronic liver disease.
Methodology: Two reviewers independently searched relevant literature in MEDLINE, Embase, and Cochrane Library for studies from database inception to Sep 24, 2019. Eligible studies included those evaluating the occurrence of OCI and we also manually screened the reference lists of primary studies and review articles for additional references. Random effects model was used to estimate pooled estimate of OCI. Subgroup analysis was performed to determine the incidence of this type of HCV infection in different chronic liver disease.
Results: Overall, 2971 patients (2413 in chronic HCV infection after achieving sustained virologic response (SVR), 241 in cryptogenic liver disease, 48 in autoimmune hepatitis and 269 in patients with long-standing abnormal results of unknown origin of liver function) were included. The pooled incidence of OCI in HCV patients who have achieved SVR was 22% (95% CI 11%–35%), unfortunately, a significant increase in the pooled OCI rate was shown in those with abnormal level of serum aminotransferases in spite of SVR (89% (95% CI 67%–100%). OCI was estimated in patients with cryptogenic liver disease at rate 9% (95% CI 5%–13%). None of 48 included patients with autoimmune hepatitis had occult HCV infection. The estimated rate of OCI was 33% (95% CI 11%-61%) in patients with long-standing abnormal liver-enzyme levels.
Conclusion: The pooled prevalence of OCI differs greatly in chronic liver disease, especially when combined with abnormal aminotransferases levels. Careful attention must be paid to the surveillance of OCI. More nationwide prospective trails are still necessary for confirming the clinical implications of OCI and whether OCI need to be treated.

Abstract #472

Association between IL28B gene polymorphisms and outcome of treatment with direct acting antivirals in chronic HCV-infected Egyptian patients

Islam El-Garawani[1], Sobhy Hassab El-Nabi[1], Marwa Gadallah[1], Eman Abdelsameea[2]

[1]Zoology Department, Faculty of Science, Menoufia University, Egypt, [2]Hepatology and Gastroenterology Department, National Liver Institute, Menoufia University, Egypt

Background: Single nucleotide polymorphisms (SNPs) of the interleukin 28B (IL28B) gene are associated with viral clearance and treatment response in chronic hepatitis C virus (HCV) infection.
Aim: to assess whether specific IL28B gene SNP, known as rs12979860 (C > T), could predict the outcome of treatment with direct acting antivirals (DAAs) among Egyptian patients with chronic HCV genotype 4 infection.
Methods: Tetra-primer (ARMS-PCR) and PCR-RFLP methods were used for SNP genotyping.
Results: The CC (wild type) genotype of rs12979860 was identified in 20 patients, 50% of them achieved SVR. SNP genotype TT was found in 17 patients and only 2 of them (11.76%) were responders. The frequency of CT genotypes was significantly higher in responders than in non-responders ($p = 0.021$). In contrast, the frequency of TT genotypes was significantly higher in non-responders (42.85%, $p < 0.001$). On univariate and multivariate logistic regression analyses of the significant predictors of SVR, there were six predictive factors

(Age, diabetes mellitus [DM], AST, albumin, type of therapy and IL28B genotype).
Conclusion: The TT genotype and T allele were significantly associated with failure to achieve SVR. However, CT genotype of IL-28B (rs12979860) may be considered as a predictor for SVR in patients who received DAAs.

Abstract #478

Efficacy and tolerance of the first Moroccan generics of direct antiviral agents (DAAs) in the treatment of viral hepatitis C (VHC)

Soukaina Zertiti

Of all medical revolutions,the treatment of VHC will remain among the most prominent revolutions.The objective of this work is to evaluate the efficacy of generic DAAs (Sofosbuvir,Daclatasvir) made locally for the treatment of VHC.
Patients and methods: prospective,single-center study involving 89 patients treated for HCV infection,all genotypes combined,whatever the degree of fibrosis.The therapeutic diets proposed to our patients were:Sofo-Dacla, Sofo-Dacla-Riba and Sofo-Ledi.Our patients have benefited from a pre-therapeutic assessment.All patients had regular follow-up with clinical and biological tolerance monitoring and biochemical and virological response.
Results: Total number of patients placed on DAAs was 75.sex ratio F.H:1.78.The average age of our patients was56.61.Treatment-naive patients accounted for 53.93%, relapsers were 15.7%, non-responders were15.7%,5 patients were intolerant (INF,Rib).The risk factors for contamination were unknown in 81.33% of cases, related to non-medical dental care in 18.66%,transfusions in 17.33% and to surgery in 6.66%.Two patients had HVB co-infection treated with Tenofovir.Genotype 1 was predominant 60%,G2 in 26.6%patients,G45.3%,G3 in a patient and not specified at 5 patients.28% had minimal fibrosis (F0-F1),28% had moderate fibrosisF2,31.9% had severe fibrosisF3-F4. The therapeutic protocol proposed to our patients was:66 patients were under Sofo-Dacla,8 under Sofo-Dacla-Riba, and 1 under Sofo-Ledi.The virological response was100% for patients with F0-F1-F2, and 98.8% for those with advanced fibrosis F3-F4.No cases of discontinuation of treatment have been reported.
Conclusion: The almost constant efficacy of generic DAAs confirmed by 98% virological response,implies a reinforcement of screening and treatment of all infected patients before the stage of advanced fibrosis as part of a decrease morbidity, mortality and viral transmission, as well as the goal of eradicating VHC.

Abstract #494

Proposals from a follow-up survey of hepatitis C in Egypt for 30 years JICA group training course

Kazuhiro Sugi[1], Mohamed Sami Fiad[2], Mohamed Hassany[2], Noha Sobhy Mahmoud Abdeen[3]

[1]National Hospital Organization Kumamoto Medical Center Gastroenterology and Hepatology, [2]National Hepatology and Tropical Medicine Research Institute, [3]Viral Hepatitis Control Unit El Beheira Governorate

Introduction: Our hospital started a viral hepatitis group training course for developing countries at the request of JICA in 1988, and it was completed in 2018. 32 participants from Egypt and 20 in the last 3 years. Therefore, a follow-up survey was conducted on October 13 to 17, 2019 in Egypt.
Methods: The schedule was to visit Suez Canal University (Ismailia Governorate) on t day 1, visit hepatitis centers in Cairo on day 2, visit El Beheira Governorate Health Bureau and hepatitis centers on day 3, the symposium with the ex-participants at National Hepatology and Tropical Medicine Research Institute on day 4, to participate in the three-party meeting with WHO Egypt Ministry of Health and JICA Egypt on day 5.
Results and conclusion: The following was confirmed. (1) The action plan of the ex-participants was being achieved in a short period of time, (2) Hepatitis C in Egypt had been tested by more than 80% of the population of 100 million people in 1 year by the national campaign, and treatment had been started for positive people, (3) By 2030 the global elimination of hepatitis C, in Egypt it would be achieved within 2 years and could become a global model, (4)In addition to WHO assistance, our previous hepatitis training courses had been contributing significantly, (5) The expansion of the hepatitis B elimination campaign to African countries, mainly in Egypt, was considered, and the possibility of cooperation of our hospital in the launch and implementation of JICA third-party training was considered. The field survey found that Egypt had been taking measures against hepatitis C in a short period of time, and hepatitis C was being eliminated. In addition to examining how to support our hospital and JICA in the future, it was thought that it was necessary to further strengthen efforts to combat hepatitis in Japan.

Abstract #509

Hepatocellular carcinoma risk is not increased in patients with hepatitis C related liver cirrhosis treated with directly acting antiviral agents

Abdallah Mohamed[1,2], Hassany Mohamed[1,3], Alboraie Mohamed[1,4], Gamal Eldin Hadeel[5], Elshazly Yahia[1,6], Esmat Gamal[1,5], Doss Wahid[1,5]

[1]National Committee for Control of Viral Hepatitis, Ministry of Health and Population, Cairo, Egypt, [2]Medical Research Division, National Research Center, Giza, Egypt, [3]National Hepatology and Tropical Medicine Research Institute, Cairo, Egypt, [4]Department of Internal Medicine, Al-Azhar University, Cairo, Egypt, [5]Endemic Medicine and Hepatology Department, Faculty of Medicine, Cairo University, Cairo 11562, Egypt, [6]Department of Internal Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Background: Hepatitis C virus "HCV" related liver cirrhosis predispose to hepatocellular carcinoma "HCC". Whether directly acting antivirals agents "DAAs" can confer an increased risk for HCC incidence still a matter of debate.
Objective: We aimed to detect HCC incidence among patients with HCV related liver cirrhosis treated with DAAs in Egypt.
Methodology: HCV patients treated with DAAs and proven to have advanced fibrosis/ cirrhosis by ultrasonography or by FIB-4 ($\geq$ 3.25) were scheduled for surveillance visits. Patients were subjected to thorough clinical evaluation, α-fetoprotein (AFP) levels in serum and ultrasound evaluation of the liver to rule out hepatic focal lesions. Those proven to have hepatic focal lesions were further evaluated by a dynamic imaging studies and were referred to liver cancer treatment centers.
Results: Our study included 8070 patients with liver cirrhosis (44.9% females). Sofosbuvir/ Daclatasvir was the most commonly prescribed regimen (60%) followed by Sofosbuvir/ Daclatasvir/ Ribavirin. Hepatic focal lesions were detected by ultrasonography in 1519 (18.83%) patients. Further confirmatory dynamic studies showed that

1197 (14.83%) of the patients do not have evidence of HCC and 322 (4%) had evidence of HCC. Most of HCC lesions (91.4%) were single and less than 5 cm in diameter. Among HCC patients, 271 (84.16%) were eligible for treatment (curative or palliative) and only 25% had elevated AFP > 100 ng/ml.
Conclusion: Treatment of HCC with DAAs does not confer an extra risk for HCC occurrence but may even reduce it. AFP serum level is not reliable for HCC surveillance.

Abstract #544

Ledipasvir/sofosbuvir plus ribavirin regimen efficacy in HCV patients with genotype 2 and 3

Asatiani Magda[1,2]; Zhamutashvili Maia[3,4]; Rukhadze Tamar[2]; Sharvadze Lali[2], Dolmazashvili Ekaterine[2,3,4], Zaldastanishvili Maia[3]; Kipiani Nino[3]

[1]Ilia State University, Tbilisi, Georgia, [2]Georgian-French Joint Hepatology Clinic HEPA, Tbilisi, Georgia, [3]Infectious Diseases, AIDS & Clinical Immunology Research Center, Tbilisi, Georgia, [4]European University, Tbilisi, Georgia

Introduction: Direct-acting antiviral agents (DAAs) showed high efficacy in chronic hepatitis C treatment, in particular, Ledipasvir/Sofosbuvir demonstrated almost 100% cure rate on specific genotypes, but the treatment of HCV 2 and 3 genotype patients' with Ledipasvir/Sofosbuvir remains questionable due to the variable data.
Objectives: This study aims to evaluate the efficacy of Ledipasvir/Sofosbuvir plus ribavirin regimen on HCV genotype 2 and 3 patients (with/without cirrhosis).
Methods: Retrospective analysis of patients with HCV 2 and 3 genotypes was carried, which included patients within the National Hepatitis C Elimination Program of Georgia. The patients were treated for 12 or 24 weeks (depending on genotype and the presence of cirrhosis/decompensated cirrhosis).
Results: The data of 2095 patients were analyzed. They were treated in 2016–2018 and sustained virological response (SVR) was assessed 12 to 24 weeks after treatment. From them, 1382 were genotype 3; 713 – genotype 2 (82 were recombinant 1b/2 k). Overall SVR rate was 98.85% (2071 individuals); only 1.15% (24 patients) relapsed. According to genotypes, the SVR rate was 98.74% for genotype 2 and 98.91 for genotype 3. From relapsed patients 3 patients (from 9) with genotype 2 were cirrhotic, and only 1 from 15 with genotype 3 was cirrhotic.
Conclusion: Ledipasvir/Sofosbuvir combination demonstrated a high cure rate in HCV genotype 2 and 3 patients, but the impact of cirrhotic status needs to be evaluated.

Abstract #581

Utility of telemedicine in the treatment of patients with chronic HCV infection using DAAs in remote areas with limited resources

Abdallah Mohamed[1], Wahed Sherif[2], Ammar Islam[3], Kamal Ehab[1], Alboraie Mohamed[4], Abdel-razek Wael[5], Hassany Mohamad[6], El-serafy Magdy[7], Waked Imam[5], Doss Wahid[7]

[1]Medical Research Division, National Research Center, Giza, Egypt, [2]Al-Wahat Al-Bahariya Central Hospital, Giza, Egypt, [3]Gastroenterology, hepatology and infectious diseases, Al-Azhar University, Cairo, Egypt, [4]Department of Internal Medicine, Al-Azhar University, Cairo, Egypt, [5]National Liver Institute, Menoufia University, Shebin Elkom, Egypt, [6]National Hepatology and Tropical Medicine research Institute; Cairo, [7]Endemic medicine and hepatology department, Cairo, Egypt

Background: Telemedicine is a useful tool to reach patients in remote areas with lack of specialized physicians. Using telemedicine in management of Hepatitis C (HCV) therapy in remote areas in Egypt has not been done before.
Objective: We aimed to assess the utility of telemedicine in HCV management in remote and resource-limited areas.
Methodology: Enrollment was done to HCV patients who were discovered in an extremely remote area "Bahariya Oases". A place which is only served by a small medical facility. Patients were clinically evaluated by a trained GP. Laboratory investigations and abdominal ultrasound evaluation for treatment decision was done by a consultant in Cairo via video conference. All patients' data were recorded on an online database. GP had a 24/7 access to the supervising consultant.
Results: Two hundred HCV patients were discovered in the oases. Most patients were males (68.5%) and their mean age was 51 years (range 19–87). Baseline evaluation showed that 21 patients (10.5%) were cirrhotics and all (100%) were treatment naïve. All patients started treatment which was Sofosbuvir plus daclatasvir for 12 weeks in 184 patients (92%) while weight-based ribavirin were added to the previous regimen in the rest of the patients (8%). One hundred fifty patients finished the treatment course with sustained virologic response (100%). Anaemia was the only reported adverse event in 15 patients (7.5%) but easily controlled on haematinics.
Conclusion: Telemedicine is a successful treatment strategy for HCV that could be used in all unreachable and resource-limited areas.

Abstract #588

Evolving epidemiology of viral hepatitis in uremic patients in Taiwan: the FORMOSA-LIKE group

Wei Yu-Ju[1], Lee Jia-Jung[2,3], Huang Chung-Feng[1,3], Huang Ching-I[1,3], Yeh Ming-Lun[1,3], Chen Szu-Chia[2,3], Niu Sheng-Wen[2], Yang Lii-Jia[2], Dai Chia-Yen[1,3], Huang Jee-Fu[1,3], Hwang Shang-Jyh[2,3], Chuang Wan-Long[1,3], Chiu Yi-Wen[2,3], Yu Ming-Lung[1,3]

[1]Division of Hepatobiliary, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [2] Division of Nephrology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [3] Faculty of Internal Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

Introduction: Hepatitis B virus (HBV) and hepatitis C virus (HCV) are leading causes of liver disease in hemodialysis patients in Taiwan. The treatment of HCV was underappreciated even in directly acting antivirals era.
Objectives: Evolution of the seroprevalence of viral hepatitis and HCV treatment rate in uremic patients is elusive. We aimed to address the issue by performing consecutive surveillances upon the population.
Methods: The Formosan Coalition for the study of Liver Disease in Chronic Kidney Disease (FORMOSA-LIKE group) consisted of 18 and 22 hemodialysis centers in 2012 and 2019, respectively. A total of 490 uremic patients participated in both screens. All subjects were tested for HBV and HCV serology and virology.
Results: The seropositivity of anti-HCV, HBsAg and both HBsAg/anti-HCV were 15.7% (n = 77), 14.3% (n = 70) and 2.5% (n = 12), respectively in 2012, and 16.3% (n = 80), 13.3% (n = 65), and 3.1% (n = 15), respectively in 2019. The HCV viremic rate decreased from 71.4% in 2012 to 52.5% in 2019 (p = 0.015). 39 of the 55 HCV

viremic patients in 2012 had persistent viremia in 2019, whereas 16 patients became HCV RNA undetectable [12-antivirals, 4-spontaneous clearances]. The annual incidence of HCV infection was 0.24% (7/490). The HCV treatment rate was 5.2% and 21.1% in 2012 and 2019, respectively (p = 0.01). The annual incidence of HBsAg seropositivity were 0.07%.
Conclusion: The trend of HCV treatment in uremic patients increased over these years but it is still underutilized in this population. Link-to-care and outreach onsite treatment are mandatory to increase the treatment uptake of HCV.

Abstract #599

Comparison of sustained virological response rates of all oral direct antiviral agents regimens for genotype 2 hepatitis C patients in community hospital setting

Wei-Chun Cheng,[1] Tzu-Chun Chen,[2] Jing-Jhen Wu,[2] Jung-Jung Chen,[3]

[1]Department of Gastroenterology, Tainan Hospital, Ministry of Health and Welfare, Tainan, Taiwan, [2]Department of Medial Administration, Tainan Hospital, Ministry of Health and Welfare, Tainan, Taiwan, [3]Department of Nursing, Tainan Hospital, Ministry of Health and Welfare, Tainan, Taiwan

Introduction: Hepatitis C is a major cause of liver cirrhosis and hepatocellular carcinoma. In Taiwan, about 50% of chronic hepatitis C (CHC) cases were infected by genotype 2 (GT2) hepatitis C virus (HCV). APASL guideline recommended All oral direct-acting antiviral agents (DAAs) regimens including Sofosbuvir plus Ribavirin (SOF+RBV), Daclatasvir and Sofosbuvir (DCV+SOF), Ledipasvir and Sofosbuvir (LDV+SOF) and Velpatasvir and Sofosbuvir to treat GT2 CHC patients.
Objectives: To assess treatment efficacy and tolerability for APASL recommended regimens and Glecaprevir/Pibrentasvir (GP) combination in a non-medical center community hospital setting.
Methods: We did a retrospective analysis of patients who received all oral DAA regiments treatment in Tainan Hospital, MOHW, Tainan, Taiwan, a regional hospital in south Taiwan. The primary endpoint was undetectable HCV RNA at 12 weeks posttreatment (Sustained Virological Response, SVR12) by Intent-To-Treat (ITT) Analysis.
Results: Since 2017, a total of 281 GT2 CHC patients were treated in our hospital. 39 of them received Sofosbuvir plus weight based Ribavirin; 48 received DCV+SOF; 92 received LDV+SOF; and 102 were treated with GP regimen. The SVR12 rates of these regiments were 92.3%, 100%, 100% and 98% by ITT analysis and overall SVR12 rate was 98.2%. For cases failed to achieve SVR12, three cases (2 SOF+RBV and 1 GP) cannot complete full treatment course while other two cases completed whole regimen (1 SOF+RBV and 1 GP) but still experienced treatment failure.
Conclusion: All oral DAA regimens were highly effective and well tolerated for GT2 CHC patients treated in community hospital setting.

Abstract #601

All oral direct antiviral agents regimens are highly effective and well tolerated for hepatitis C patients treated in community hospital setting

Wei-Chun Cheng,[1] Tzu-Chun Chen,[2] Jing-Jhen Wu,[2] Jung-Jung Chen,[3]

[1]Department of Gastroenterology, Tainan Hospital, Ministry of Health and Welfare, Tainan, Taiwan, [2]Department of Medial Administration, Tainan Hospital, Ministry of Health and Welfare, Tainan, Taiwan, [3]Department of Nursing, Tainan Hospital, Ministry of Health and Welfare, Tainan, Taiwan

Introduction: Chronic hepatitis C (CHC) infection is a major global public health issue, with 170 million people chronically infected world widely. It also causes significant mortality and morbidity in Taiwan. All oral direct antiviral agents (DAAs) are the current standard treatment in Taiwan.
Objectives: To assess treatment efficacy of DAA Regimens for CHC patients and risk factors for treatment failure in a non-medical center community hospital in Taiwan.
Methods: We did a retrospective analysis of patients who received all oral DAA regiments treatment in Tainan Hospital, MOHW, Tainan, Taiwan, a regional hospital in south Taiwan. The primary endpoint was undetectable HCV RNA at 12 weeks posttreatment (Sustained Virological Response, SVR12) by Intent-To-Treat Analysis.
Results: Since 2017, a total of 524 CHC patients were treated in our hospital. The genotype of these patients and SVR12 rates by ITT analysis are: GT1a: 39 (97.4%), GT1b: 145 (94.5), GT2: 281 98.2%), GT3: 7 (100%), GT4: 4 (100%), GT6 (95.8%). 1 case (2.6%) in GT1a patients, 4 cases (2.8%) in GT1b, 3 cases (1.1%) in GT2 and 1 case in GT6 (2.1%) patients failed to complete the full treatment course. Multivariate logistic regression showed more than 75 y/o of age, female sex and Interferon treatment experience were risk factors for failure to achieve SVR12.
Conclusion: All oral DAA regimens were highly effective and well tolerated for patients treated in community hospital setting. Elder, female and Interferon treatment experienced patients were at risk of failure to achieve SVR12.

Abstract #602

Comorbidities and potential risk of drug-drug interactions with direct antiviral therapy among HCV patients: real-world multicenter study from China

Yaling Guo[1], Shumei Lin[2], Yujuan Guan[3], Liaoyun Zhang[4], Huanwei Zheng[5], Xiuli Chen[5], Yan Huang[6], Yuemin Nan[7], Xiaoyuan Xu[8], Caixia Yang[9], Ying Guo[10], Hong Ren[11], Zhongping Duan[12], Dongliang Yang[13], Minghua lin[14], Haibing Gao[14], Jia Shang[15], Fang Wang[16], Xiaorong Mao[17], Wen Xie[18], Ying Han[19], Yuexin Zhang[20], Zhiliang Gao[21], Xiaoguang Dou[22], Lai Wei[23]

[1]The Eighth Hospital of Xi'an, Shanxi, China [2]The First Affiliated Hospital of Xi'an Jiaotong University, Shanxi, China [3]Guangzhou Eighth People's Hospital, Guangzhou Medical University, Guangdong, China [4]The First Hospital of Shanxi Medical University, Shanxi, China [5]Shijiazhuang Fifth Hospital, Hebei, China [6]Xiangya Hospital, Central South University, Hunan, China [7]The Third Hospital of Hebei Medical University, Hebei, China [8]Peking University First Hospital, Beijing, China [9]Wuhai Infectious Disease Hospital, Neimenggu, China [10]Taiyuan No.3 Hospital, Shanxi, China [11]The Second Affiliated Hospital of Chongqing Medical University, Sichuan, China [12]Beijing YouAn Hospital, Capital Medical University, Beijing, China [13]Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Hubei, China [14]MengChao Hepatobiliary Hospital of Fujian Medical University, Fujian, China [15]People's Hospital of Henan, Henan, China [16]The Third People's Hospital of Shenzhen, Guangdong, China [17]The First Hospital of Lanzhou University, Gansu, China [18]Beijing Ditan Hospital, Capital Medical University, Beijing, China [19]Xijing

Hospital, Shanxi, China [20]The First Affiliated Hospital of Xinjiang Medical University, Xinjiang, China [21]The Third Affiliated Hospital, Sun Yat-Sen University, Guangdong, China [22]Shengjing Hospital of China Medical University, Liaoning, China [23]Beijing Tsinghua Changgung Hospital, Beijing, China

Introduction: Since direct-acting antiviral (DAA) regimens provide high sustained virological response (SVR) with fewer adverse events (AE), the drug-drug interactions (DDIs) becomes an important consideration for HCV patients with comorbidities that require concomitant medications.
Objectives: We performed an analysis concerning the comorbidities and DDIs possibly affecting the DAA regimens, on which quite a few Chinese hospitals and research centers collaborated.
Methods: Chronic hepatitis C (CHC) patients from 23 centers around China were recruited between Mar 2018 and Oct 2019. DDIs were assessed as per the Hepatitis Drug Interaction Database from The University of Liverpool.
Results: 711 CHC patients were included in the study and treated with DAA regimens, in which 48.5% were males, median age being 51 years, 54.6% being genotype 1, 28.3% diagnosed with cirrhosis. The top five comorbidities were hypertention, diabetes mellitus, chronic kidney disease, coronary heart disease, respiratory disease. The top three prescribed DAAs were velpatasvir/sofosbuvir (VEL/SOF) (30.9%), sofosbuvir+daclatasvir (SOF+DCV) (18.1%), and ombitasvir/paritaprevir/ritonavir+dasabuvir (OPrD) (15.3%). Potential DDIs were identified in 18.3% VEL/SOF prescribed patients, 21.6% SOF+DCV prescribed patients, and 32.9% OPrD prescribed patients.
Conclusions: Prevalence of comorbidities and DDIs is very common for DAAs treatment and more frequent in protease-containing regimens. The choice of the DAA regimens must carefully take into account the potential DDIs.

Abstract #604

Real-world multicenter experience of direct antiviral therapy among HCV patients with cirrhosis from China

Shumei Lin[1], Yaling Guo[2], Yujuan Guan[3], Liaoyun Zhang[4], Huanwei Zheng[5], Xiuli Chen[5], Yan Huang[6], Yuemin Nan[7], Xiaoyuan Xu[8], Caixia Yang[9], Ying Guo[10], Hong Ren[11], Zhongping Duan[12], Dongliang Yang[13], Minghua lin[14], Haibing Gao[14], Jia Shang[15], Fang Wang[16], Xiaorong Mao[17], Wen Xie[18], Ying Han[19], Yuexin Zhang[20], Zhiliang Gao[21], Xiaoguang Dou[22], Lai Wei[23]*

[1]The First Affiliated Hospital of Xi'an Jiaotong University, Shanxi, China [2]The Eighth Hospital of Xi'an, Shanxi, China [3]Guangzhou Eighth People's Hospital, Guangzhou Medical University, Guangdong, China [4]The First Hospital of Shanxi Medical University, Shanxi, China [5]Shijiazhuang Fifth Hospital, Hebei, China [6]Xiangya Hospital, Central South University, Hunan, China [7]The Third Hospital of Hebei Medical University, Hebei, China [8]Peking University First Hospital, Beijing, China [9]Wuhai Infectious Disease Hospital, Neimenggu, China [10]Taiyuan No.3 Hospital, Shanxi, China [11]The Second Affiliated Hospital of Chongqing Medical University, Sichuan, China [12]Beijing YouAn Hospital, Capital Medical University, Beijing, China [13]Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Hubei, China [14]MengChao Hepatobiliary Hospital of Fujian Medical University, Fujian, China [15]People's Hospital of Henan, Henan, China [16]The Third People's Hospital of Shenzhen, Guangdong, China [17]The First Hospital of Lanzhou University, Gansu, China [18]Beijing Ditan Hospital, Capital Medical University, Beijing, China [19]Xijing Hospital, Shanxi, China [20]The First Affiliated Hospital of Xinjiang Medical University, Xinjiang, China [21]The Third Affiliated Hospital, Sun Yat-Sen University, Guangdong, China [22]Shengjing Hospital of China Medical University, Liaoning, China [23]Beijing Tsinghua Changgung Hospital, Beijing, China

Introduction: Real-life data on direct acting antiviral (DAA) therapies for HCV patients with cirrhosis from China is limited.
Objectives: This prospective study sought to evaluate sustained virologic response (SVR) and adverse events (AE) in Chinese cirrhotic patients treated with DAAs.
Methods: HCV patients with cirrhosis from 23 centers around China were recruited between Mar 2018 and Oct 2019. Patient demographics, disease severity, DAA regimens, SVR, and AE were analyzed.
Results: 200 CHC patients with cirrhosis were included in the study and treated with DAA regimens, in which 50% were males, median age being 55 years, 50% being genotype 1, 71.5% diagnosed with compensated cirrhosis and 28.5% with decompensated cirrhosis. 96% were treated with interferon-free DAA regimens. The most wildly used regimen was velpatasvir/sofosbuvir (VEL/SOF) in compensated cirrhosis, also the same in decompensated cirrhosis. Of 42 patients with evaluable SVR data, the SVR12 rate were both 100% in compensated (39/39) and decompensated (4/4) cirrhosis. During treatment, one patient develped HCC, three patients develped ascites, and one patient develped bleeding of esophageal varices. Adverse events occurred in 8.0% of patients, but none of patients required treatment discontinuation.
Conclusions: In this multicenter study of Chinese patients, DAAs were highly effective and well tolerated in HCV patients with cirrhosis, even in the patients with decompensated cirrhosis.

Abstract #605

The impact of direct antiviral therapy on renal function in HCV patients: real-world multicenter experience from China

Yujuan Guan[1], Shumei Lin[2], Yaling Guo[3], Liaoyun Zhang[4], Huanwei Zheng[5], Xiuli Chen[5], Yan Huang[6], Yuemin Nan[7], Xiaoyuan Xu[8], Caixia Yang[9], Ying Guo[10], Hong Ren[11], Zhongping Duan[12], Dongliang Yang[13], Minghua lin[14], Haibing Gao[14], Jia Shang[15], Fang Wang[16], Xiaorong Mao[17], Wen Xie[18], Ying Han[19], Yuexin Zhang[20], Zhiliang Gao[21], Xiaoguang Dou[22], Lai Wei[23]*

[1]Guangzhou Eighth People's Hospital, Guangzhou Medical University, Guangdong, China [2]The First Affiliated Hospital of Xi'an Jiaotong University, Shanxi, China [3]The Eighth Hospital of Xi'an, Shanxi, China [4]The First Hospital of Shanxi Medical University, Shanxi, China [5]Shijiazhuang Fifth Hospital, Hebei, China [6]Xiangya Hospital, Central South University, Hunan, China [7]The Third Hospital of Hebei Medical University, Hebei, China [8]Peking University First Hospital, Beijing, China [9]Wuhai Infectious Disease Hospital, Neimenggu, China [10]Taiyuan No.3 Hospital, Shanxi, China [11]The Second Affiliated Hospital of Chongqing Medical University, Sichuan, China [12]Beijing YouAn Hospital, Capital Medical University, Beijing, China [13]Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Hubei, China 14MengChao Hepatobiliary Hospital of Fujian Medical University, Fujian, China [15]People's Hospital of Henan, Henan, China [16]The Third People's Hospital of Shenzhen, Guangdong, China [17]The First Hospital of Lanzhou University, Gansu, China [18]Beijing Ditan Hospital, Capital Medical University, Beijing, China [19]Xijing Hospital, Shanxi, China [20]The First Affiliated Hospital of Xinjiang Medical University, Xinjiang, China [21]The Third Affiliated Hospital,

Sun Yat-Sen University, Guangdong, China [22]Shengjing Hospital of China Medical University, Liaoning, China [23]Beijing Tsinghua Changgung Hospital, Beijing, China

Introduction: The real-world effectiveness and impact of direct-acting antivirals (DAAs) on renal function have not been fully elucidated.
Objectives: This prospective study assessed the sustained virologic response (SVR) and renal function changes in Chinese CHC patients treated with DAAs.
Methods: HCV patients from 23 centers around China were recruited between Mar 2018 and Oct 2019. Patient demographics, disease severity, DAA regimens, SVR, and renal fuctions were analyzed.
Results: 711 CHC patients were included in the study and treated with DAA regimens, in which 48.5% were males, median age being 51 years, 28.3% diagnosed with cirrhosis, 14.3% with estimated glomerular filtration rate (eGFR) 60–89 ml/min/1.73 m^2, 3.1% with eGFR 30–59 ml/min/1.73 m^2, 0.8% with eGFR $\leq$ 30 ml/min/1.73 m^2. Of 188 patients with evaluable SVR data, the overall SVR12 rate were 100%. There was no significant change during treatment or follow-up period in eGFR, irrespective of baseline eGFR status and DAA regimens. An improvement in eGFR (defined as an increase in baseline eGFR of at least 10 ml/min/1.73 m^2) was observed in 24 patients (12.8%). Serious adverse effects were very rare, and none of patients required treatment discontinuation..
Conclusions: In this multicenter study of Chinese patients, selected DAAs were highly effective and well tolerated in HCV patients with impaired renal function.

Abstract #606

Direct antiviral therapy for treatment of hepatitis C: real-world experience from the hepatitis C therapeutic registry of China

Ming Yang[1], Shumei Lin[2], Yaling Guo[3], Yujuan Guan[4], Liaoyun Zhang[5], Huanwei Zheng[6], Xiuli Chen[6], Yan Huang[7], Yuemin Nan[8], Xiaoyuan Xu[9], Caixia Yang[10], Ying Guo[11], Hong Ren[12], Zhongping Duan[13], Dongliang Yang[14], Minghua lin[15], Haibing Gao[15], Jia Shang[16], Fang Wang[17], Xiaorong Mao[18], Wen Xie[19], Ying Han[20], Yuexin Zhang[21], Zhiliang Gao[22], Xiaoguang Dou[23], Lai Wei[1]*

[1]Beijing Tsinghua Changgung Hospital, Beijing, China [2]The First Affiliated Hospital of Xi'an Jiaotong University, Shanxi, China [3]The Eighth Hospital of Xi'an, Shanxi, China [4]Guangzhou Eighth People's Hospital, Guangzhou Medical University, Guangdong, China [5]The First Hospital of Shanxi Medical University, Shanxi, China [6]Shijiazhuang Fifth Hospital, Hebei, China [7]Xiangya Hospital, Central South University, Hunan, China [8]The Third Hospital of Hebei Medical University, Hebei, China [9]Peking University First Hospital, Beijing, China [10]Wuhai Infectious Disease Hospital, Neimenggu, China [11]Taiyuan No.3 Hospital, Shanxi, China [12]The Second Affiliated Hospital of Chongqing Medical University, Sichuan, China [13]Beijing YouAn Hospital, Capital Medical University, Beijing, China [14]Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Hubei, China [15]MengChao Hepatobiliary Hospital of Fujian Medical University, Fujian, China [16]People's Hospital of Henan, Henan, China [17]The Third People's Hospital of Shenzhen, Guangdong, China [18]The First Hospital of Lanzhou University, Gansu, China [19]Beijing Ditan Hospital, Capital Medical University, Beijing, China [20]Xijing Hospital, Shanxi, China [21]The First Affiliated Hospital of Xinjiang Medical University, Xinjiang, China [22]The Third Affiliated Hospital, Sun Yat-Sen University, Guangdong, China [23]Shengjing Hospital of China Medical University, Liaoning, China

Introduction: Direct-acting antiviral (DAA) regimens exhibit high virologic efficacy and tolerability in patients with hepatitis C virus (HCV) infection in clinical trials.
Objectives: This prospective multicenter study sought to confirm these findings in real-world settings in China.
Methods: Chronic hepatitis C (CHC) patients from 23 centers around China were recruited between Mar 2018 and Oct 2019. Patient demographics, disease severity and comorbidities, DAA regimens, sustained virological response (SVR), and tolerability were analyzed.
Results: 711 CHC patients were included in the study and treated with DAA regimens. 48.5% were males, median age being 51 years, 54.6% being genotype 1, 20.1% diagnosed with compensated cirrhosis and 8.2% with decompensated cirrhosis. 86.6% were treated with interferon-free DAA regimens. The most wildly used regimens were velpatasvir/sofosbuvir (VEL/SOF) (30.9%), sofosbuvir+ daclatasvir (SOF+DCV) (18.1%), and ombitasvir/paritaprevir/ritonavir+dasabuvir (OPrD) (15.3%). Of 188 patients with evaluable SVR data, the overall SVR12 rate was 100%,while 100% (39/39)and 100% (4/4) in compensated and decompensated cirrhosis respectively. During treatment, one patient develped HCC, three patients develped ascites, and one patient develped bleeding of esophageal varices. Adverse events occurred in 7.2% of patients, but none of patients required treatment discontinuation.
Conclusions: In this large multicenter CHC cohort from China, DAAs were highly effective and well tolerated. Policies should encourage treatment for all CHC patients with DAAs in China with its heavy burden of HCV.

Abstract #632

Assessing the ethnic disparities in the HCV-related type 2 diabetes in an ethnically diverse large population-based cohort in British Columbia, Canada

Jeong, Dahn[1,2], Wong, Stanley[2,] Karim, Mohammad Ehsanul[1,3], Butt, Zahid[2,4], Binka, Mawuena[2], Adu, Prince Asumandu[1,2], Wilton, James[2], Abdia, Younathan[1,2], Yu, Amanda[2], Alvarez, Maria[2], Bartlett, Sofia[2,5], Pearce, Margo[1,2], Clementi, Emilia[1,2], Velasquez, Hector[2], Krajden, Mel[2,5], Naveed Zafar Janjua[1,2]

[1]School of Population and Public Health, University of British Columbia, Vancouver, British Columbia, Canada, [2]British Columbia Centre for Disease Control, Vancouver, British Columbia, Canada, [3]Centre for Health Evaluation and Outcome Sciences, St Paul's Hospital, Vancouver, British Columbia, Canada, [4]School of Public Health and Health Systems, University of Waterloo, Waterloo, Ontario, Canada,[5]Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, British Columbia, Canada

Introduction: There is increasing evidence that persons living with hepatitis C virus (HCV) infection are at higher risk of type 2 diabetes (T2D). Previous studies have shown an ethnic disparity in diabetes, with increased risk in non-White populations.
Objectives: We examined if the impact of HCV infection on incident diabetes varied by ethnicity, within a large population-based cohort in Canada.
Methods: In the British Columbia (BC) Hepatitis Testers Cohort including 1.7 million individuals tested or reported as a case of HCV, individuals were followed from HCV diagnosis to the earliest of 1) incident T2D, 2) death or 3) end of study. Propensity scores (PS) were estimated based on age at HCV diagnosis, duration of follow-up and key covariates. HCV-positive and negative individuals were matched 1:1. We used stratified Fine and Gray competing risk models

adjusting for mortality and potential confounders to estimate hazard ratios (HR) for incident diabetes across ethnic groups.
Results: Matched sample included 117,192 individuals. Stratified HR for Whites with HCV was 2.00 (95% CI 1.88–2.12), for South Asians, 2.60 (95% CI 2.11–3.20), and for East Asians, 3.21 (95% CI 2.58–4.01). Other characteristics associated with T2D varied across ethnicities, with obesity being significantly associated with increased risk of T2D in Whites but not in South and East Asians.
Conclusion: In BC, the impact of HCV infection on incident T2D was modified by ethnicity, with the risk amplified in Asians. This study highlights the need for continued care and screening for HCV-related diabetes in individuals living with HCV infection, especially among Asian populations.

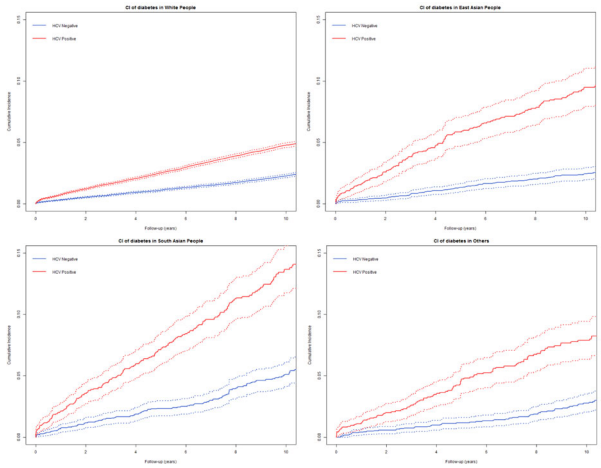


Figure 1. The 10-year cumulative incidence (CI) curves for diabetes by hepatitis C virus (HCV) infection status in the propensity score-matched dataset[a], by ethnicity, from the British Columbia Hepatitis Testers Cohort 1990-2015

Abstract #646

Efficacy and safety of sofosbuvir/velpatasvir in genotype 3 and 6 HCV patients in South China

Wu Zhe-bin

Introduction: Sofosbuvir/Velpatasvir (SOF/VEL) is a pangenotypic direct-acting antiviral drug (DAA) for chronic hepatitis C virus infectious patients, which has been available in China. Currently, In China, the real world data of SOF/VEL in patients with genotype 3b and 6 HCV infections is very limited.
Objective: To evaluate the safety and efficacy of SOF/VEL ± RBV in patients in South China with chronic HCV G3 and 6 infection.
Methods: This is a prospective, observational, multicenter, real-world study. Chronic hepatitis C patients were divided into 3 group, genotype 3a, 3b and 6 with 50 patients for each group. Genotype 3a and 6 patients were treated with Sofosbuvir/Velpatasvir, while genotype 3b was treated with Sofosbuvir/Velpatasvir + ribavirin for 12 weeks. The primary efficacy endpoint was sustained virological response (SVR12, HCV RNA < 15 IU/ml) at 12 weeks post-treatment.
Results: Interim analysis was performed on 55 patients who had completed 12 weeks treatment. Of 55 patients, 46 were male, 9 were female and 12 had compensated cirrhosis. Regard to genotype distribution,14 were genotype 3a, 8 were genotype 3b, 33 were genotype 6 (Table 1). At 4 weeks of treatment, 52 patients (n = 55, 96.36%) had HCV RNA below the lower limit of detection (Figure 1). At end of therapy (EOT), all patients (n = 55) had lower HCV RNA than the lower limit of detection (Figure 2).For patients who had completed post treatment 12 weeks follow up, the SVR12 (23/23) was 100% (Figure 3). Baseline characteristics did not affect the patient's efficacy, most adverse events (AE) were mild, 1 case of constipation occurred during treatment, 1 case of generalized rash, 2 cases of upper abdominal discomfort, 1 case of orthostatic hypotension, 2 cases of fatigue, 1 case of weight loss, 1 case of Ascites occurred 1 week after the end of treatment. No AE caused treatment discontinuation and no serious AE occurred.
Conclusions: Sofosbuvir/Velpatasvir regimen was highly effective and safe for Genotype3a,3b and 6 chronic hepatitis C patients in south China, with no virological failure, severe AE or treatment interruption.

Table 1 Patient baseline characteristics

Characteristic	Genotype 3a N=14	Genotype 3b N=8	Genotype 6 N=33
Male,n(%)	13 (92.9)	6 (75)	27 (81.8)
Age,median (range),years	40 (35-53)	42 (34-48)	42 (22-56)
HCV RNA,median(range), Log_{10} IU/ml	5.97 (3.30-7.03)	6.28 (5.19-7.35)	6.11 (1.28-7.63)
Without cirrhosis, n(%)	11 (78.6)	5 (62.5)	27 (81.8)

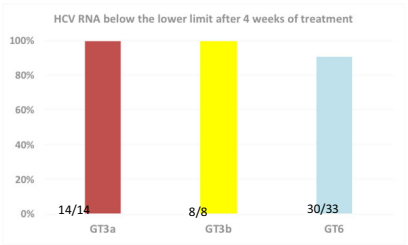


Figure 1 Comparison of HCV RNA below the detection limit for each genotype after 4 weeks of treatment

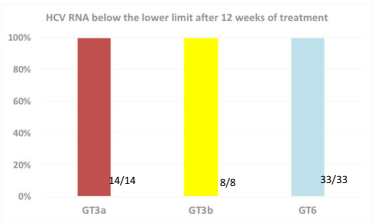


Figure 2 Comparison of HCV RNA below the detection limit for each genotype after 12 weeks of treatment

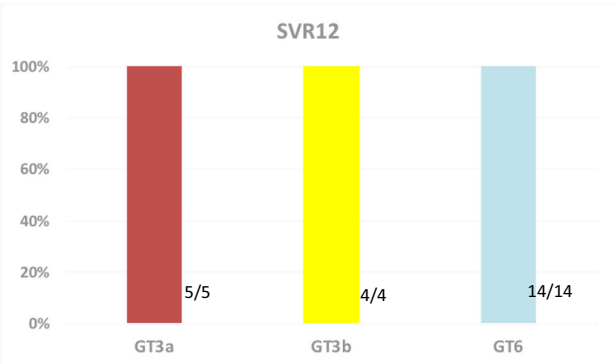


Figure 3 Comparison of each genotype of SVR12

Abstract #675

Community-based point-of-care hepatitis C testing and general practitioner initiated direct-acting antiviral therapy in Yangon, Myanmar (CT2 study)

Margaret Hellard

Introduction: The advent of direct-acting antivirals (DAAs) and near point-of-care testing for hepatitis C (HCV) facilitate improved community-based care. In many countries, access to DAAs is limited to tertiary hospitals but there is increasing recognition of the need for decentralizing care.
Objectives: This study demonstrates a decentralized hepatitis C care model in Yangon, Myanmar. It assesses feasibility, acceptability and effectiveness of model for people who inject drugs and general population.
Method: Rapid diagnostic test (SD Bioline) for anti-HCV antibodies was performed on-site; if reactive, GeneXpert HCV RNA test was performed. External laboratory investigations for liver staging were undertaken for viremic patients. Results were given to the participant at next appointment with GP; participants commenced DAA therapy if specialist review was not required. Outcome data on HCV test positivity, treatment uptake and SVR12 rates were collected.
Results: 634 participants were enrolled. 256 (40%) reported lifetime injecting drug use; other commonly reported risk factors included: family history (n = 87, 14%), surgery (n = 50, 8%), dental treatment (n = 32, 5%) and blood transfusion (n = 31, 5%). 607 (96%) were HCV antibody positive; all received an RNA test. 543 (89%) were RNA positive and proceeded to pre-treatment assessments. 462 were eligible for DAA therapy on initial assessment, 28 required specialist review and 489 (91%) were prescribed DAA therapy.
Conclusion: The study results suggest providing community based POC testing and treatment initiated by general practitioners is feasible in low/middle income settings. Evidence from this study will inform scale-up of HCV treatment programs in Myanmar and globally.

Abstract #678

Substantial difference between hepatitis C virus genotype 3a and 3b in the prevalence of natural resistance-associated substitutions

Xiaoqing Liu, Zhiwei Chen, Peng Hu

Department of Infectious Diseases, Institute for Viral Hepatitis, The Key Laboratory of Molecular Biology for Infectious Diseases, Chinese Ministry of Education, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China

Introduction: Patients with HCV genotype (GT)3 infection remains a difficult-to-cure population. GT3b had lower SVR rate than GT3a and RASs may impair HCV DAA treatment response. Nevertheless, there is little data about GT3 HCV RASs prevalence in Southwest China.
Objectives: The aim of this study was to investigate the prevalence of RASs in DAA treatment-naïve, GT3 infected patients in Southwest China.
Methods: A total of 136 DAAs treatment-naive hepatitis C genotype 3 patient serum samples were collected from southwest China and analyzed for RASs distribution by Sanger sequencing.
Results: In total, 41 patients were GT3a, 95 patients were GT3b. In the NS5A region, the presence of RASs found in GT3b (99%) were significantly higher than in GT3a (9%). But, RASs prevalence in GT3a (26%) were higher than GT3b (6%) in the NS3 region. The NS5B specific RASs were rare. In GT3b sequence, the NS5A A30k and L31M substitutions were the most common at 96% both. The A30K+L31M combination was found in 94% of GT3b isolates. However, A30K and L31M were not observed in any GT3a sequence. Interestingly, no Y93H was detected in both GT3a and GT3b stains. And there is also a difference in the prevalence of amino acid mutation between patients with cirrhosis and non-cirrhosis.
Conclusion: Huge differences was observed between GT3a and GT3b in the prevalence of RASs. The paired A30K+L31M substitutions occur in the vast majority of GT3b isolates. It seems that treatment of HCV GT3b patients is a greater challenge in DAA era.

Abstract #681

A real-world study on the efficacy and safety of sofosbuvir-based therapy in patients with HCV genotype 3 and 6 infection in a single center

Qiao Tang, Xiaoqing Liu, Peng Hu

Department of Infectious Diseases, Institute for Viral Hepatitis, The Key Laboratory of Molecular Biology for Infectious Diseases, Chinese Ministry of Education, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China

Introduction: A large number of studies have shown that sofosbuvir(SOF)-based regimens yield high sustained virological response(SVR)rates in patients with HCV infection except for GT3b patients with decompensated cirrhosis.
Objectives: The real-world study aims to explore efficacy and safety of SOF-based regimens in GT3 and GT6 patients, especially the impact of ribavirin (RBV) co-administration on SVR in GT3b patients with cirrhosis.
Methods: A retrospective cohort study included 147 patients initiated on SOF-based regimens. Main endpoint of treatment was sustained virological response at post-treatment week 12 (SVR12).
Results: 90 patients with sufficient follow-up were included. Overall, SVR12 rate was 93.3% (84/90), including 57 patients treated with addition of RBV to SOF-based regimens, given the inferior SVR12 rate (96.5%) than no-RBV regimens (87.8%). SVR12 rate of GT3 patients (41) and GT6 patients (27) was 95.1% and 96.3%. SVR12 was achieved in 96.4% in GT3b patients, 95.2% with RBV regimens and 100% without RBV. Among patients with cirrhosis (30), SVR12 rate was achieved in 100% treated with RBV regimens and 81.8% without RBV, comparing with 94.7% and 90.9% in patients without cirrhosis (60). Totally, 6 patients failed to achieve SVR12, including 1 GT1, 1 GT2, 2 GT3,1 GT6 and 1 genotype unknown patient, and 2 patients with cirrhosis. No sever adverse events occurred except for 1 patient with decompensated cirrhosis died unrelated to drugs.
Conclusion: Real-world data show that SOF-based regimens are effective and safe for patients with HCV GT3, 6 infection. Addition of RBV to SOF-based regimens improve efficacy in patients with cirrhosis.

Abstract #703

Community engagement in HCV treatment simplification and implementation guidelines in prison

C.N. Mone Iye[1], C. Thomas[1]

[1]Yayasan Koalisi Satu Hati

Background: HCV is transmitted through exposure to blood media and body fluids that are contaminated with HCV. The risk of contracting HCV is very high in injecting drug users (IDUs), where HCV transmission among IDUs dominates transmission of HCV, which is 60–80%. HCV with a lower incidence include unsafe sexual behavior

and unsafe use or personal equipment such as tattoo and piercing is also practiced in closed setting such as prison.
With the aforementioned conditions, Directorate General of Corrections of the Indonesian Ministry of Justice and Human Rights to make efforts related to testing and treatment of Hepatitis C in prisons/detention centers.
Methods: Development of guidelines and Pilot demonstration.
Results: Yayasan Koalisi Satu Hati work in collaboration with Ministry of Justice and Ministry of Health to develop implementation guidelines for HCV in prison, including determining the implementer and the activities. Activities included are refresher training for healthcare worker in 7 prisons, screening for 17,000 inmates, VL test for all patient with positive antibody, liver function test and CBC, treatment with DAA and SVR 12 to confirm the cure of HCV. All activities in the implementation guidelines had been piloted to all 7 prisons in Jakarta, resulting a possible micro elimination in Jakarta prison. Treatment is ongoing with result to be expected in early 2020.
Conclusion: Updating guideline from interferon based to DAA based is a long process for the community, especially when community was perceived as non experts. However, as community are becoming more knowledgeable in treatment of HCV, we have been seen as people who can provide meaningful input.

Abstract #714

Response and safety of direct-acting antiviral in hepatitis C related hepatocellular carcinoma patients

Kwan, Byung Soo[1], Kim, Jeong Han[1,2]

[1]Department of Internal medicine, Konkuk University School of Medicine, Seoul, Korea [2]Research Institute of Medical Science, Konkuk University School of Medicine, Seoul, Korea

Introduction: Chronic hepatitis C (CHC) treatment has dramatically improved since direct-acting antiviral (DAA) therapy was introduced. However, the use of DAA therapy in CHC patients with hepatocellular carcinoma (HCC) remains controversial.
Objectives: We investigated the DAA treatment response in CHC patients with HCC.
Methods: We retrospectively analyzed CHC patients treated with DAA from 2016 to 2018. Patients were divided into two groups based on their HCC history before DAA therapy. Baseline characteristics, sustained virologic response at 12 weeks (SVR 12), and HCC recurrence after DAA therapy were evaluated.
Results: A total of 192 patients were enrolled; 78.1% were treatment-naïve, and 34.9% had liver cirrhosis (LC). Among these patients, 168 did not have HCC, and 24 had HCC. The HCC group was older (57.0 vs 72.0 years, $P < 0.001$), had a higher incidence of LC (26.2% vs 95.8%, $P < 0.001$), higher Fibrosis-4 index (FIB-4) (2.6 vs 9.2, $P < 0.001$), higher Liver stiffness measurement (LSM) (7.0 vs 17.4 kPa, $P = 0.012$), and higher α-fetoprotein (AFP) (4.4 vs 8.2 ng/mL, $P = <$ 0.001). The SVR 12 rate was 97.0% in the non-HCC group and 91.7% in the HCC group ($P = 0.213$).
Conclusions: DAA treatment efficacy in CHC patients with and those without HCC were not significantly different, and HCC recurrence was relatively common.

Abstract #716

HCV microelimination project in 7 Jakarta prison

Thomas, Caroline[1], Widiastuti, Hetty[2]

Managing Director, Yayasan Koalisi Satu Hati, thomas135@gmail.com, Jakarta, Indonesia, [2] Head of Special Care and Rehabilitation Sub Directorate, Directorate of General Corrections, Ministry of Justice and Human Rights

Introduction: Hepatitis C in prison is more frequent than in the general population, proper treatment of chronic hepatitis C in prison is rare because most inmates with HCV infection remain unaware of their virological condition. While the response to antiviral treatment is similar in prisoners to that of the general population, it is unfortunate that treatment is administered less frequently. Nevertheless, when appropriate services are in place, periods of incarceration may provide an opportunity for the people in prison to be aware of their Hepatitis C status and to engage with the treatment provided in the prison. Looking at the similar response of antiviral treatment in general population and prison, micro elimination of Hepatitis C through screening, care and treatment services is becoming a cost effective way of reducing Hepatitis C burden as part of WHO Global Hepatitis Goals under the Sustainable Development Agenda 2030. With the aforementioned conditions, Directorate General of Corrections of the Indonesian Ministry of Justice and Human Rights to make efforts related to testing and treatment of Hepatitis C in prisons/detention centers.
Methods: Pilot demonstration.
Results: Yayasan Koalisi Satu Hati work in collaboration with Ministry of Justice and Ministry of Health to implement a series of activities to microeliminate HCV in prison. The results are: 28 healthcare worker in 7 prisons are trained, 16,063 people are screened, 991 VL test for all patient with positive antibody (88% viremic, n = 881) to complete treatment with DAA. All activities in the implementation guidelines had been piloted to all 7 prisons in Jakarta, resulting a possible micro elimination in Jakarta prison. Treatment is ongoing with result to be expected in early 2020.
Conclusion: While achieving the ambitious elimination goals set by WHO or set by the government will require full-scale resources, breaking down the larger elimination goals into smaller and achievable goals will provide a less intimidating and less complex goals. The effort to micro eliminate HCV in 7 prisons in Jakarta is a very targeted and will build national momentum by producing small victories that inspire more ambitious efforts.

Abstract #725

Development of a community-based long-term follow-up system for hepatitis B and C virus-positive individuals cooperating with healthcare providers

Kikuchi Minami[1,2], Yoshioka Kentaro [3], Aoyagi Haruyo [1], Hattori Satoru [4], Kawabe Naoto [3], Wakae Kosho [1], Watashi Koichi [1], Muramatsu Masamichi [1], Wakita Takaji [1], Sawabe Motoji [2], Aizaki Hideki [1]

[1]Department of Virology II, National Institute of Infectious Diseases, Tokyo, Japan, [2] Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, [3] Department of Hepatobiliary and Pancreatic Oncology, Fujita Health University Hospital, Aichi, Japan, [4] Okazaki City Health Center, Aichi, Japan

Introduction and objectives: In Japan, an estimated 500,000 hepatitis B virus (HBV) and 300,000 hepatitis C virus (HCV) inactive carriers have not yet noticed their infections. Moreover, approximately 500,000 to 1.2 million individuals with hepatitis B and C (HepBC) who were aware of their infections were not accessing care as of 2016. Although effective treatments are available, low levels of linkage to care (LTC) prevent viral hepatitis eradication. We aimed to promote LTC for HepBC individuals by understanding their current

situations and encouraging LTC cooperation between hepatologists and healthcare providers in local health centers that obtain the personal information of these patients.
Methods: In O City (population: 380,000), 504 HepBC individuals were detected through regional health examinations from 2008 to 2018. They were encouraged to obtain LTC through brochures and their LTC status was followed up by questionnaire to monitor their behavior modifications from 2012 to 2018.
Results: In the 2012 primary survey, the rate of HepBC individuals who visited hospitals was around 40% (n = 110). However, the rate significantly increased to over 80% (n = 181) by 2018, after the introduction of annual LTC encouragement. The proportion of individuals receiving treatment increased from 8.8% (n = 102) to 12.8% (n = 117) in HBV and from 30.8% (n = 78) to 47.7% (n = 65) in HCV over 7 years. The percentage of individuals attending hospitals also increased, with 40% of patients continuously attending hospitals.
Conclusion: By continuing LTC encouragement, we have successfully promoted LTC to individuals with hepatitis. It is also effective in accelerating regular attendance at hospitals.

Abstract #732

Eliminating HCV within prisons in Jakarta

Widiastuti Hetty[1], Sadrina Alima[2], Azhari Heri[3], Irna Irna[4], Ocnisari Istiqomah Nur[5], Sukmaputri Indri Oktaria[6], Regina T. Sidjabat[7], Thomas Caroline[8], Anartati Atiek[9], Kosasih Robert[10], Widyastuti Niken[11], Budiman Arief[12], Chan Yuhui[13], Fernandes Oriel[14], Christian B. Ramers[15], Caroline E. Boeke[16], A. Yusfachrudin[17]

[1]Directorate of Correction, Ministry of Law and Human Rights, Jakarta, Indonesia, [2]Pengayoman Hospital, Jakarta, Indonesia, [3]Directorate of Correction, Ministry of Law and Human Rights, Jakarta, Indonesia, [4]Directorate of Correction, Ministry of Law and Human Rights, Jakarta, Indonesia, [5]Directorate of Correction, Ministry of Law and Human Rights, Jakarta, Indonesia, [6]Head of section sub-directorate Hepatitis & Digestive Infection, MoH, Jakarta, Indonesia, [7]Head of sub-directorate Hepatitis & Digestive Infection, MoH, Jakarta, Indonesia, [8]Yayasan Koalisi Satu Hati, Jakarta, Indonesia, [9]CHAI, Jakarta, Indonesia, [10]CHAI, Jakarta, Indonesia, [11]CHAI, Jakarta, Indonesia, [12]CHAI, Jakarta, Indonesia, [13]CHAI, Boston, USA, [14]CHAI, Boston, USA, [15]CHAI, Boston, USA, [16]CHAI, Boston, USA, [17]Directorate of Correction, Ministry of Law and Human Rights, Jakarta, Indonesia

Introduction: In mid-2019, Directorate of Corrections/DGC collaborated with the national hepatitis program of Indonesia, Yayasan Koalisi Satu Hati and Clinton Health Access Initiative, to provide HCV treatment in 7 prisons in Jakarta.
Objectives: This project develop a model for HCV services in the prison setting which describes program set-up, outcomes and lessons learnt in the first 4 months of roll-out.
Methods: Screening was offered to all prisoners on-site. Blood samples of those with positive anti-HCV rapid tests were sent to a private laboratory for confirmatory viral load testing. A Jakarta-based hospital internist visited, diagnosed and initiated SOF+DCV therapy for viraemic patients. Bi-weekly coordination meetings allowed stakeholders to identify challenges and align on solutions.
Results: From July-October 2019, the program screened 16,063 prisoners, diagnosed 991 patients, and initiated 298 patients on treatment. Prevalence was 6.1% with a viraemic rate of 87.5%. Implementation challenges included drug nonadherence and linkage to care, the latter driven by limited drug stock and hospital capacity to treat patients prior to their release. The program is addressing these issues, and has engaged 135 peer educators to strengthen adherence and follow-up. In September, leveraging program success, Director General DGC announced an HCV elimination agenda in Indonesian prisons. Learnings from the implementation in Jakarta are expected to inform the broader elimination program.
Conclusion: With cross-sector collaboration, planning, and communication, a public health-oriented HCV program can be successfully implemented in the correctional setting. Programs such as this comprise a key pillar to comprehensive HCV elimination planning.

Abstract #750

Serum M2BPGi level as a novel fibrosis marker in treatment-naïve patients with HCV mono-infection and HCV/HIV co-infection

N. Chuaypen[1], S. Chittmittraprap[1], A. Avihingsanon[2], P. Tangkijvanich[1]

[1]Center of Excellence in Hepatitis and Liver Cancer, Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, Bangkok, 10330, Thailand, [2]The HIV Netherlands Australia Thailand Research Collaboration (HIV NAT), Bangkok, Thailand

Background: Serum Mac-2 binding protein glycosylation isomer (M2BPGi) has recently emerged as a novel marker for liver fibrosis, particularly in chronic hepatitis C virus (HCV) infection.
Objectives: This study was aimed at assessing the diagnostic role of serum M2BPGi levels in patients with HCV mono- and HCV/HIV co-infection.
Method: A total of 85 treatment-naïve HCV genotype 1-infected patients (59 mono- and 26 co-infected individuals) were included. Serum M2BPGi levels were measured by an automated lectin-antibody sandwich immunoassay. The diagnostic performance of serum M2BPGi was compared with AST/platelet ratio index (APRI) and transient elastography (TE) by using magnetic resonance elastography (MRE) as a reference.
Results: Among 85 patients, there were 63 male and 22 females, with mean age of 48.2 and 48.7 years, respectively. The correlations with MRE for TE, M2BPGi and APRI were r = 0.788, r = 0.703 and r = 0.564, respectively (all $P < 0.001$). Based on MRE as the reference, the area under the ROC curves (AUROC) for TE in differentiating significant fibrosis ($\geq$ F2), advanced fibrosis ($\geq$ F3) and cirrhosis (F4) were 0.89 [95% confident interval (CI); 0.82–0.96, $P < 0.001$], 0.93 (95% CI 0.88–0.99, $P < 0.001$) and 0.94 (95% CI 0.89–0.99, $P < 0.001$), respectively. The corresponding figures for M2BPGi were 0.84 (95% CI 0.76–0.93, $P < 0.001$), 0.92 (95% CI 0.86–0.98, $P < 0.001$) and 0.95 (95% CI 0.91–0.99, $P < 0.001$), respectively. For APRI, the corresponding values were 0.76 (95% CI 0.66–0.87, $P < 0.001$), 0.81 (95% CI 0.71–0.92, $P < 0.001$) and 0.89 (95% CI 0.80–0.98, $P < 0.001$), respectively. The optimal cut-off level of M2BPGi for diagnosing F2 based on the AUROC was 1.29 cutoff index (COI), with a sensitivity and specificity of 82.4% and 7.4%, respectively. For diagnosing F3, its best cut-off was 2.18 COI with 81.5% sensitivity and 89.7% specificity. For diagnosing F4, the corresponding figures were 2.92 COI, 91.7% and 89.0%, respectively.
Conclusion: Our results showed that serum M2BPGi was equivalent to TE in detecting advanced fibrosis and cirrhosis in patients with HCV mono- and co-infection. Compared to APRI, this novel marker had a better performance for the assessment of fibrosis. Thus, serum M2BPGi should be considered as a reliable non-invasive marker for the valuation of liver fibrosis in clinical practice.

Abstract #762

Crivalvir: universal screening HIV, HBV, HCV in primary care. First focus in Europe

Moises Diago

Background and aims: Current evidences suggest that an universal examination of all individuals 18–80 years old could be the most effective and profitable strategy from an individual and social perspective of HCV erradication. FOCUS began in 2010 in the United States as a public health initiative for HIV,HBV and HCV screening. FOCUS considered our Department as a pilot of the first FOCUS program in primary care outside the United States (CRIVALVIR).The aim was an universal screening in primary care of HIV,HCV and HCV to meet the objectives of UNAIDS and WHO in HIV and in HCV (90% diagnosed,80% treated and 65% reduction of deaths.
Method: Universal screening is performed in people aged 18–80 years of HIV, HBV and HCV viruses in primary care. The population assisted in our Department is 360,000 inhabitants (48% men, 186,365 "Baby boomers" and 50,000 foreign people). Training sessions and refresher knowledge of HBV,HIV and HCV destined for Doctors and Nurses of Primary care and Support Units were established. Posters and leaflets of the CRIVALVIR program were elaborated. The diagnosis of HCV is carried out in a single step and the telematics warning of the results and citation with the specialist in positive cases are activated immediately. The screening program is approved by the Research and Ethics Committee of the General Hospital and the informed consent is requested to carry out the test .
Results: These first data correspond to the first 8735 people tested, which correspond to different age ranges. In the total sample,11 HIV patients (0,13%), 43 HCV viremics (0,49%) and 56 HBV (0,64%) have been detected, 82%,63%y78% of them were new diagnoses. In the age range of 35–65 y/o: 6 HIV (0,12%; 28 HCV (0,55%) and 38 HBV (0,75%) have been detected. The prevalences according the age can be see in the figure. Fibroscan was performed in 32 / 43 (80%) of VHC viremic patients; F0–1 (50%) 16/32; F2 8/32 (25%), F3 3/32 (9%), F4 5/32 (16%) and in 26/56 of HBV patients (46%) F 0–1 23/26 (88%%);F21/26 (3%);F31/26 (3%) yF41/26 (3%).
Conclusion: The screening may be the most pragmatic and efficient strategy in diagnosis and prevention of HIV,HBV and HCV viruses. This program will allow to know which are the most favorable age ranges for an intensification of the screening in the territory in which is carried out.

Abstract #813

Genomic analysis of hepatitis B virus and its association with disease manifestations in Bangladesh HBV genome versus pathogenesis

[1]Ruksana Raihan, [2]Sheikh Mohammad Fazle Akbar, [3]Mamun Al Mahtab, [4]Kazuaki Takahashi, [2]Junya Masumoto, [5]Shahina Tabassum, [6,7]Kok Keng Tee, [1]Rosmawati Binti Mohamed

[1]Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia. Department of Microbiology, US Bangla Medical College, Narayanganj, Dhaka, Bangladesh [2]Department of Pathology, Ehime University Proteo-Science Center, Ehime University Graduate School of Medicine, Toon City, Ehime, Japan [3]Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh [4]Department of Medical Sciences, Tokyo-Shinagawa Hospital, Shinagawa, Tokyo, Japan [5]Department of Virology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh [6]Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia [7]School of Healthcare and Medical Sciences, Sunway University, Bandar Sunway, Selangor, Darul Ehsan, Malaysia

Background: Hepatitis B virus (HBV) has infected about 2 billion people and about 291 million are chronically infected. A significant proportion of those infected may progress to cirrhosis of liver (LC) and hepatocellular carcinoma (HCC), therefore, treatment is required for eligible patients to prevent or at least reduce liver disease progression. To date, the majority of chronic HBV-infected patients are diagnosed and it is estimated that only 4.8 million receive anti-HBV therapy. Most developed countries have implemented strategies to prevent and control chronic HBV-infected patients. In contrast, most of the developing and resource-constrained countries, although harbouring more than 80% chronic HBV-infected patients, lack national strategic plan to address this important public health issue. HBV possesses considerable heterogenicity in the viral genome, and HBV genotypes may contribute to the pathogenesis of liver disease progression in those chronically infected. In this study, we investigated the HBV genotype and mutations in HBV genome in Bangladesh, the 9th most populous nation of the world with 5.5% prevalence of CHB.
Design: HBV genotyping was performed in 360 patients. 195 patients were classified into 3 groups [Group 1: HBV DNA $<$ 2000 IU/mL and ALT persistently less than the upper limit of normal (ULN); Group 2: HBV DNA $>$ 2000 IU/mL and ALT persistently above ULN; Group 3: patients with LC and/or HCC)]. Full genome sequences of 38 isolates were performed. Partial sequencing of additional 73 isolates were accomplished to provide additional insights into the role of these mutations in liver damage.
Results: Three major HBV genotypes were prevalent among a total of 360 Bangladeshi chronic HBV-infected patients (Genotype A-18%, Genotype C-43% and Genotype D-39%). However, HBV genotype A and D were mostly found among patients of Group 1, whereas, genotype C predominates among patients of Group 2 (60.8%) and Group 3 (71.2%). Full genome sequences showed that mutations at T1762/A1764 were significantly higher in patients in Genotype C ($p < 0.001$). The T1762/A1764 mutations predominantly occurred in patients of Group 2 with high baseline HBVDNA and persistently raised ALT levels (60%) and Group 3 with LC or HCC (90%). Patients of Group 3 with HBV genotype C had T1762/A1764 mutations in 93.5% patients. Presence of Genotype C or mutations at T1762/A1764 is associated with 9 times higher risk of developing LC/HCC (OR 9.3, 95% CI 2.0–43.4, OR 9.0, 95% CI 2.3–50.9, respectively).
Conclusions: HBV genotypes C, D and A are prevalent among chronic HBV-infected patients in Bangladesh. HBV genotype C and mutation at T1762/A1764 was associated to the more advanced stages of chronic HBV-infections (CHB, LC, and HCC) with progression of HBV-induced liver diseases.

Abstract #814

Association of viral loads and ALT levels among HCV-infected bangladeshi patients with different genotypes

Sultana Nahida[1], Hossain Mohammad Enayet[2], Munshi SaifUllah[3], Tabassum Shahina[4]

[1]Research Assistant, Department Of Virology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka-1000, [2]Assistant Scientist Virology Laboratory & Infectious Disease Division (Emerging Infection), International Center for Diarrhoeal Diseases Research Laboratory, [3]Professor, Department Of Virology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka-1000, [4]Professor

and Chaiman, Department Of Virology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka-1000

Introduction: Hepatitis C virus (HCV) causes chronic infections that mainly affect the liver leading to hepatic fibrosis followed by development of cirrhosis and hepatocellular carcinoma (HCC). Several factors including HCV genotype have been proposed to associate with the clinical outcome of HCV infection.
Objectives: This study was aimed to determine whether there is any significant difference in HCV viral load and Alanine Aminotransferase (ALT) in relation to genotypes in HCV infected Bangladeshi patients.
Methods: A total of 534 Anti-HCV positive patients were enrolled in this study who provided blood at the Department of Virology, BSMMU for HCV RNA quantification. After HCV viral load quantification, 217 HCV RNA positive patients who had viral load > 600 IU/ml were selected and from them, 36 HCV RNA positive patients were randomly selected for genotyping and ALT measurement.
Results: The mean HCV viral load of genotype 1 infected patients was 14.11 ± 6.77 [$\log_{10}$ (copies/ml)] while it was 12.80 ± 2.05 [$\log_{10}$ (copies/ml)] for genotype 3 infected patients. The mean ALT level of genotype 1 and genotype 3 infected patients were 51.2 ± 34.4 U/L and 89.6 ± 86.6 U/L respectively. There was no significant statistical difference in serum ALT or plasma viral load between genotype 1 and genotype 3 infected patients.
Conclusion: In HCV infection, genotype may have no relation to viral load and serum ALT level among Bangladeshi patients.

Abstract #852

Wisteria floribunda agglutinin-positive Mac-2-binding protein is a useful prediction of hepatocellular carcinoma development after hepatitis C virus eradication

Shunsuke Sato, Hironori, Tsuzura, Takuya Genda

Juntendo University Shizuoka Hospital, Gastroenterology and Hepatology, Shizuoka, Japan

Objectives: Interferon (IFN)-free therapy of hepatitis virus C (HCV) has higher efficacy than previous IFN-based therapy, and a large number of patients currently achieve a sustained virological response (SVR). Although the eradication of HCV reduces the incidence of hepatocellular carcinoma (HCC), HCC development is not rarely observed even in patients achieved SVR. Wisteria floribunda agglutinin-positive Mac-2-binding protein (WFA+-M2BP) was recently developed as a noninvasive glycolbiomaker of liver fibrosis. However, it remains unclear the change of WFA+-M2BP level after viral eradication and its association with HCC development.
Method: A total of 522 patients achieved SVR (IFN-based therapy, 228; IFN-based therapy, 294) were included. Patients with follow-up period of < 0.5 year after the end of treatment (EOT) were excluded. Serum WFA+-M2BP levels were measured before treatment and at 24 weeks after EOT.
Results: During the median follow-up time of 2.9 years, 14 patients developed HCC. Multivariate analysis revealed that high WFA+-M2BP at SVR24 ($p = 0.020$), low platelet counts at pretreatment ($p = 0.036$) and elderly ($p = 0.011$) were independent risk factors for HCC development. From the receiver operator characteristics curve analysis, WFA+-M2BP level > 1.37 COI was identified as a cut-off value with an adjusted HR 12.2 (95% CI 3.41–43.91, $p < 0.001$). The 3- and 5-year cumulative incidence of HCC in patients with low WFA+-M2BP at SVR24 were 0.7% and 0.7%, respectively, whereas those of patients with high WFA+-M2BP were 4.8% and 12.4%, respectively ($p < 0.001$).
Conclusion: Post-treatment WFA+-M2BP is a useful predictor for HCC development after achievement of SVR, possibly even in IFN-free therapy era.

Abstract #861

Evaluation of true point of care molecular assay for diagnosis of Hepatitis C using fingerstick capillary whole blood

R. Agarwal[1], E. Gupta[1], G. Kumar[2], M. K. Sharma[2]

[1]Department of Clinical Virology, Institute of Liver and Biliary Sciences, New Delhi, India, 2Department of Biostatistics, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Currently available point of care (POC) molecular assays for hepatitis C are not considered as true POC due to additional sample collection and processing demanding minimal laboratory infrastructure. A new POC (Xpert HCV VL WB) precludes such requirements where specimen collected by simple fingerstick can be loaded directly into test cartridge with results available within 60 min.
Objectives: To evaluate new assay for RNA quantification using capillary whole blood (CWB) and venous whole blood (VWB) with Abbott Real Time HCV PCR (reference assay).
Methods: CWB via fingerstick and VWB via venipuncture collected from the enrolled participants were loaded into Xpert HCV VL WB for viral load estimation. Simultaneously Abbott Real time HCV PCR assay was also performed using plasma.
Results: Among the enrolled participants (n = 140), median age was 47 years and 63% were male. HCV RNA was detected in 65% with median 5.73 $\log_{10}$ (IQR: 5.21–6.36 $\log_{10}$) IU/ml on Abbott Real time assay. Xpert HCV VL WB showed 100% sensitivity and specificity using both CWB and VWB. The median viral load detected in CWB and VWB were 5.60 $\log_{10}$ (IQR: 4.78–6.16 $\log_{10}$) IU/ml and 5.52 $\log_{10}$ (IQR: 4.77–6.00 $\log_{10}$) IU/ml respectively. Excellent linear correlation was seen between the two assays. Perfect linear correlation and agreement (kappa = 1) was also observed between Xpert HCV VL WB using CWB and VWB.
Conclusion: The assay offer potential as true POC enabling diagnosis in a single visit, thereby reducing number of drop outs. However, further studies with larger sample size are warranted.

Abstract # 863

A model of micro-elimination of a hepatitis C hyperendemic aboriginal township in Taiwan

Dai Chia-Yen[1,2,3,4], Huang Ching-I[1], Yeh Ming-Lun[1,2], Huang Chung-Feng[1,2], Huang Jee-Fu[1,2],Chuang Wan-Long[1,2], Yu Ming-Lung[1,2,3]*

[1]Hepatobiliary Section, Department of Internal Medicine, Kaohsiung Medical University, Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [2]School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, [3]Department of Biological Science and Technology, College of Biological Science and Technology, National Chiao Tung University, Hsinchu, Taiwan, [4]Department of community Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

Introduction: In Taiwan, several hyperendemic townships with prevalence of anti-hepatitis C virus (HCV) more than 10% have been explored, including Tau-Yuan Township (TYT) in high mountain area of Kaohsiung.

Objectives: The aim of the study is to evaluate the effectiveness of an outreach people-centered screening and treater program for HCV micro-elimination in TYT.
Methods: In TYT, the project underwent with the goals: For the registered residents aged 30–75 years who live in TYT more than 6 months in a year (frequent living residents, FLR), the screening rate for HCV seromarkers more than 80%, and more than 80% of the definitely diagnosed viremic patients linked to receive DAAs therapy.
Results: Of overall 4317 registered residents, 1073 aged 30–75 years fulfill the criteria of FLR in TYT as the target population. By the end of Jan 2020, 1072 (99.9%) were completed for the screening (one resident expired), 127 anti-HCV positive patients were all tested for HCV RNA (100%) and 77 (61%) of the 127 patients were seropositive for HCV RNA. The overall treatment rate was 94.8%. Forty of the 42 patients (2 still with treatment) treated in TYT and 31 patients treated in other hospital have completed 12 weeks posttreatment follow-up and all achieved SVR12.
Conclusions: In this real-world micro-elimination project of a hepatitis C hyperendemic aboriginal township in Taiwan, the goal of HCV micro-elimination could be achieved by implementation of an people-centered outreach screening program to improve the ability of link-to-diagnosis and link-to-treat in local Health Center.

Abstract #879

Successful decentralization of HCV services to a district health facility in Vietnam

Nguyen Trang[1], Cao Thuy[2], Hanoi, Vietnam, Nguyen Thu[2], Chan Yuhui[3], Mai Hong[1], Ngo Dang[2], Boeke Caroline E[3], Tebor Jessica[3], Ramers Christian B[3], Nguyen Kinh[4]

[1]Nam Tu Liem District Health Center (DHC), [2]Clinton Health Access Initiative (CHAI), Hanoi, Vietnam, [3]CHAI, Boston, USA, [4]National Hospital of Tropical Diseases, Hanoi, Vietnam

Introduction: HCV service availability in Vietnam is limited to national and provincial health facilities. From July 2017-December 2018, Vietnam initiated a pilot to decentralize HCV services to Nam Tu Liem District Health Center (DHC), where HCV was integrated with existing primary care, HIV and methadone services. During this period, health insurance covered 100% of HCV diagnosis at provincial and national facilities, but did not cover treatment.
Objectives: This analysis describes the program set-up and treatment outcomes.
Methods: Screening by rapid tests and treatment via SOF+DCV ± RBV were offered on-site. Patients were referred to higher level facilities for viral load testing under health insurance. Data from 236 patients who initiated on treatment was collected via patient records and analyzed.
Results: 71.6% of patients were HIV co-infected, 2.5% were HBsAg positive, 83.9% reported ever injecting drugs, and 20.8% were cirrhotic. 94.4% of patients had access to health insurance. 94.5% of patients completed treatment; 5.1% were lost to follow-up while 0.4% died. 97.6% of patients with SVR12 results were cured. There was no statistically significant difference in cure rates between HIV/HCV co-infected and mono-infected patients, and between those with a history of injecting drugs and those without.
Conclusion: The high cure rate suggests that decentralization of HCV services to the district level may be an optimal approach to HCV service provision. This model achieved a lower rate of loss to follow-up compared to higher level facilities with specialized care, likely due to less travel, greater familiarity by patients, and integration with other primary care, HIV and methadone services.

Abstract #907

Ensuring free and fast access to hepatitis C testing and treatment for co-infected PLHIV in India

Haokip Elaine Chinrimoi,[1] El Kaim Jean Luc[2]

[1]Organization, The Delhi Network of Positive People, New Delhi, India, [2] Coalition PLUS, Paris, France

Introduction: India,the third highest Hepatitis C (HCV) prevalence country worldwide with 6–8 million chronically infected.Indian Government (Govt) recently addressed and responded to The Delhi Network of Positive People (DNP+) demand their "Right to Healthcare" to the Indian Govt. More than a decade,DNP+ contributes to elimination of HCV by 2030 through— (i) Advocacy campaign to the Govt,healthcare providers and (ii) providing service among PLHIVs.
Objectives: To advocate for free and fast access to HCV test and treatment in India. Linkage to HCV care and treatment among PLHIV.
Methods: Years ago, DNP+ provided support to PLHIVs and concentrate on HCV treatment advocacy.From grant received from Unitaid, Coalition PLUS provides financial support to DNP+ for HCV advocacy campaign.So,in 2017,project DAWN was implemented wherein during that time, HCV diagnostic,care and treatment was ignored by Govt.Through this project,DNP+ recognized that PWIDs legal and policy provisions are not in place to protect their "Right to Healthcare",so DNP+ intervened and filed PIL in High Court to push govt to provide Free HCV diagnostic and treatment for all in India and won the case in October 2019.
Result: In 28th July 2018, due to efforts of DNP+ and other NGOs and CBOs, Indian Govt launched National Viral Hepatitis Program with three guidelines. Through Support Group Meetings, strong, supportive and effective HCV community existed.
Conclusion: The project is highly effective in raising awareness and increasing knowledge on HCV care and treatment among PLHIVs, and if it replicates in other areas, the community itself believes that it will extensively contribute in elimination of HCV by 2030.

Abstract #917

Linkage to HCV Care And Treatment Among High Risk Behaviour Groups – PWIDs, MSM, FSW, HIV+ve, HCV+ve Person

Manitosh Ghildiyal

[1]The Delhi Network of Positive People, [2] The Delhi Network of Positive People, [3] The Delhi Network of Positive People

Background: India,the third highest HCV prevalence country in the world with 6–8 million chronically infected. Indian Government recently addressed and responded to this issue after The Delhi Network of Positive People (DNP+) demand their "Right to Healthcare" to the Indian Government. More than decade, DNP+ contributes to elimination of HCV by 2030 through—(i) Advocacy campaign to the Government, healthcare providers etc., and (ii) Providing service among high risk behavior / group – PWIDs, MSM, FSW, HIV+ve, HCV+ve person.
Description of model of care/intervention: Years ago, DNP+ provided support to PWIDs and concentrate on HCV treatment advocacy. From grant received from Unitaid, Coalition International Sida and International Treatment Preparedness Coalition provides financial supports to DNP+ for HCV advocacy campaign with a goal. So, in 2017, project DAWN and in 2018 project TREAT HCV NOW! was implemented wherein during that time, HCV diagnostic, care and

treatment was ignored by Government. Through this project, DNP+ recognized that PWIDs legal and policy provisions are not in place to protect their "Right to Healthcare", so DNP+ intervened and filed Public Interest Litigation to High Court to push government to provide Free HCV diagnostic and treatment for all in India.
Effectiveness: In 28th July 2018, due to the unbreakable efforts of DNP+ with other NGOs and CBOs, Indian Government launched the National Viral Hepatitis Program with three guidelines. Through Support Group Meetings, strong and effective HCV community existed where they support and educate each other on HCV, adherences, nutrition etc.
Conclusion and next steps: These projects are highly effective in raising awareness and increasing knowledge on HCV care and treatment among high risk behavior / group – PWIDs, MSM, FSW, HIV+ve, HCV+ve person with TB. People and if it replicates in other areas, the community itself believes that it will extensively contribute in elimination of HCV by 2030. Next step includes-1. Constant meeting with concern authority to ensure better forecasting and procurement system to prevent stockouts. 2.To investigate why PWIDs despite knowledge gained, would go ahead and engaged in risk behavior.

Abstract #962

An up-date of the distribution and circulation of hepatitis C virus genotypes and subtypes in China

Zhi-wei Chen, Xiao-qing Liu, Hu Li, Min Chen, Ming-li Peng, Hong Ren, Peng Hu

Department of Infectious Diseases, Institute for Viral Hepatitis, The Key Laboratory of Molecular Biology for Infectious Diseases, Chinese Ministry of Education, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China

Introduction: Hepatitis C Virus (HCV) is constantly mutating and evolving and presents global genotypic diversity. HCV genotyping is important in clinical management and epidemiological studies.
Objectives: To investigate the latest HCV genotypes and subtypes distribution and circulation in China.
Methods: We collected HCV infected patient's clinical data from 29 provinces and municipalities in China from August 2018 to July 2019. Each patient' region, age, gender, genotype and viral load was included for analysis.
Results: In total 10,751 HCV infected patients, four genotypes and 14 subtypes were identified. Five dominant subtypes were 1b (48.51%, n = 5215), 2a (22.38%, n = 2406), 3b (10.26%, n = 1103), 6a (10.14%, n = 1090) and 3a (6.16%, n = 662). Genotype 4, 5 and 7 and mixed subtypes were not detected. In geographic distribution, subtype 1b showed a pervasive high prevalence trend in China, especially in central and eastern China ($> 70\%$). Subtype 2a was more common in north of China but subtype 6a was opposite. Subtype 3a and 3b were shown similar distribution and mainly occurred in Zhejiang and Yunnan provinces. Males showed a lower percentage of subtype 1b and 2a but a higher percentage of subtype 3a, 3b and 6a than females. Notably, the proportion of subtype 1b and 2a presented an anti-parabolic trend with the age increasing, instead, the subtype 3a, 3b and 6a showed a parabolic trend. In addition, the average viral load among the subtypes were different, the rank was HCV 3a $>$ 1b $>$ 3b $>$ 6a $>$ 2a.
Conclusion: HCV genotype distribution patterns were complicated and differed by geography, gender, age and viral load in China.

Abstract #969

Effect of treatment with direct antiviral agents (DAAs) on glycemic control in patients with type 2 diabetes mellitus & hepatitis C virus genotype 4

Hassan Yousef Zied[1], Rasha Youssef Hagag[2], Amal Said El-Bendary[3], Nashwa Mohamed Abo Alnasr[2], Sherief Abd-Elsalam[4]

[1]Kafr-Elsheikh Liver Institute, Kafr-Elsheikh, Egypt, [2]Internal Medicine Department, Tanta University, Tanta, Egypt, [3]Clinical Pathology Department, Tanta University, Tanta, Egypt, [4]Tropical Medicine Department, Tanta University, Tanta, Egypt

Background: It is widely recognized that chronic hepatitis C is a metabolic disease that is strongly associated with type 2 diabetes mellitus (T2DM) and insulin resistance (IR). The evidence behind the effect of Direct Anti-Viral Agents (DAAs) therapy on T2DM is conflicting. The aim of the present study is to evaluate the effect of treatment with DAAs on glycemic control in patients with type-2 diabetes mellitus and chronic hepatitis C virus genotype 4.
Patients and methods: This study was a prospective study that conducted on 100 patients with chronic hepatitis C and Type-2 diabetes mellitus, selected from Kafr El-Sheikh Liver Research Center treated with Direct Anti-Viral Agents (DAAs) during the period from from 1st of September 2017 to last of August 2018. All patients in the study were subjected to the following: Full history taking, clinical examination and laboratory investigations. For quantitative data, mean and standard deviation (SD were calculated. For comparison between two groups, the independent samples (t) test was used. For all tests p value < 0.05 were considered significant. For all tests p value > 0.05 were considered insignificant.
Results: In the present study, there was significant decrease of HBA1c levels after treatment when compared with before treatment.
Conclusion: This study augments the importance of successful eradication of the world-wide problem ''HCV'', augmenting the secondary benefits of new Direct Anti-Viral Agents interferon free regimens in diabetic HCV infected patients.

Abstract #991

Patient response of direct acting antivirals vs traditional interferon therapy

Heeda Rozario

Introduction: The treatment goal of Chronic hepatitis C virus (HCV)infection is sustained virological response (SVR) which indicates HCV eradication. Traditionally pegylated-interferon-alpha (PEG-IFN) in combination with ribavirin was used but lately direct-acting antivirals (DAAs) which are specifically designed to target various stages of HCV life cycle.
Objective: To assess the physical and mental health related quality of life (HRQoL) before during and after treatment using EQ-5D-5L instrument.
Methods: 60 patients were included in our study.15 patients received direct acting antiviral agent (DAAs) plus pegylated alpha interferon (Peg-α-IFN) and the remaining 45 IFN free regimen.The EQ-5D-5L questionnaire and visual analog scale (VAS) were given to calculate coefficient's utility. Utility EQ index was calculated and statistical analysis were performed.
Results: The VAS score was negative in the IFN group indicating a poorer quality of life. The baseline EQ index were comparable however the post treatment EQ index was statistically better in group that received IFN –free therapy. Interferon and ribavarin treatment showed more adverse effect compared to DAAs. HRQOL had a

statistically significant correlation with age, sex, educational level, living type, employment status, monthly income level, and comorbidity status. Sofosbuvir and velpatasvir showed better tolerability among the DAAs.
Conclusions. DAAs are better tolerated by the patients and has a significant improvement in the quality of life. Education, compassion and health care needs to be tailored to improve the overall well being of patients with HCV.

Abstract #992

The genotypic association of hepatitis C associated oral lichen planus and its response to direct acting antivirals

Heeda Rozario

Objective: Oral Lichen Planus (OLP) is one of the extraneous manifestation of hepatitis C infection. Various genotypes may be associated with OLP. The genotypes vary in pathogenicity and response to direct-acting antivirals (DAAs). The study was done to assess the various genotypes linked with hepatitis C associated OLP.
Methods: Lichen Planus refractory to conventional steroid treatment was considered as an oral manifestation of HCV and it was confirmed by anti-HCV by ELISA (third generation). Genotyping was done using genotype specific core primers in nested polymerase chain reaction, NS5B sequencing and 5' non coding region based PCR restriction fragment length polymorphism. Eighteen patients with HCV-related OLP received Sofosbuvir with ribavirin for 24 weeks. Out of eighteen, ten were males with a mean age of 64. The patient response were assessed before and after treatment using escudier scoring system.
Result: Most common genotype associated with OLP was 3 (65%) followed by 1 (25%) and 4 (15%).In our sample the other genotypes were not seen. Sustained virological response was observed in all patients irrespective of the genotype OLP was associated with.There was no worsening of lichen planus in any of the treated patients. Clinically refractory lichen planus resolved with DAAs treatment.
Conclusion: HCV associated OLP responded to DDAs irrespective of the genotype corresponding to a reduction in escudier score.

Abstract #1016

Improvement of hemoglobin A1c (HbA1c) level after eradication of chronic HCV infection with direct antiviral agents

Zong-Sian Cai[1,2,3], Chi-Yu Lee[2,3,4], Tsang-En Wang[1,2,3], Ching-Wei Chang[1,2,3], Ming-Jen Chen[1,2,3]

[1]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan [2]MacKay Junior College of Medicine, Nursing and Management, Taipei, Taiwan. [3]MacKay Medical College, New Taipei, Taiwan. [4]Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan

Introduction: Epidemiological studies have shown that hepatitis C virus (HCV) infection is associated with a higher prevalence of type 2 diabetes mellitus (T2DM) and may worsen glycemic control in patients with T2DM.
Objectives: We aimed to investigate whether eradication of HCV improves glycemic control in patients with T2DM.
Methodology: From August 2016 to June 2018 in MacKay Memorial Hospital, Taipei and Tamsui branch, we retrospectively reviewed 145 patients with HCV infection who underwent HCV eradication therapy with interferon-free direct-acting antiviral (DAA) agents or not. Changes of hemoglobin A1c (HbA1c) level was compared between patients who achieved sustained virologic response at week 12 off therapy (SVR-12) and those who did not. We used Software for Statistics and Data Science for all statistical analyses.
Results: Among 145 patients with HCV infection, 40 patients underwent HCV eradication therapy with DAA agents and 105 patients did not undergo HCV eradication therapy. Among 40 patients who underwent DAA agents, 36 patients achieved SVR-12. The baseline characteristic of patients who were reviewed according to whether they achieved SVR-12 or not is listed as table 1. The ratio of change of HbA1c level before and after treatment (HbA1c level after treatment minus HbA1c level before treatment) to average HbA1c level before treatment was greater in those achieving SVR-12 than in those did not achieve SVR-12 (SVR-12 group: -0.734 ± 0.15; non-SVR-12 group: 0.003 ± 0.220, $P = 0.0313$).
Conclusion: DAA-based eradication of HCV is associated with improved glycemic control in patients with T2DM.

Table 1 Baseline characteristics of 145 patients with HCV infection

	Non-SVR-12 (N=109)	SVR-12 (N = 36)	P-value
Male (N, %)	52 (47.71)	15 (41.67)	0.529
Age, years (Mean, SD)	69.27 (9.37)	66.53 (8.52)	0.1226
Duration of DM, years (Mean, SD)	7.76 (6.13)	9.22 (5.06)	0.1989
Hypertension (N, %)	70 (64.22)	24 (66.67)	0.79
Hyperlipidemia (N, %)	28 (25.69)	8 (22.22)	0.1742
Alcoholism (N, %)	14 (12.84)	7 (19.44)	0.329
HBV infection (N, %)	15 (13.76)	5 (13.89)	0.985
Cirrhosis (N, %)	15 (13.76)	18 (50)	0.266
Fatty liver (N, %)	19 (17.43)	5 (13.89)	0.62
Treatment of HCV (N, %)	9 (8.26)	7 (19.44)	0.063
Family history of DM (N, %)	9 (8.26)	5 (13.89)	0.321
Hemoglobin, g/dL (Mean, SD)	11.02 (2.3)	12.63 (1.74)	0.0004
Platelet, 10^3/uL (Mean, SD)	152.046 (92.46)	136.8 (49.44)	0.347
AST, IU/L (Mean, SD)	76.68 (94.56)	64.44 (40.81)	0.4532
ALT, IU/L (Mean, SD)	58.44 (57.62)	63.94 (42.92)	0.6004
Total bilirubin, mg/dL (Mean, SD)	1.31 (1.1)	1.05 (0.51)	0.1649
Albumin, g/dL (Mean, SD)	3.49 (0.96)	4 (0.54)	0.026
Hemoglobin A1c, % (Mean, SD)	6.93 (1.86)	7.12 (1.17)	0.553
Fasting blood sugar, mg/dL (Mean, SD)	166.44 (105.75)	144 (47.84)	0.221
Triglyceride, mg/dL (Mean, SD)	126.71 (124.60)	123.06 (59.86)	0.8735
Cholesterol, mg/dL (Mean, SD)	148.9 (44.15)	165.42 (36.19)	0.0547
Creatinine, mg/dL (Mean, SD)	1.92 (2.25)	1.3 (1.94)	0.1428
eGFR, ml/min/1.73m^2 (Mean, SD)	67.01 (60.22)	74.92 (24.88)	0.4458

SVR-12, sustained virologic response at week 12 off therapy; DM, diabetes mellitus; HBV, hepatitis B virus; HCV, hepatitis C virus; AST, aspartate aminotransferase; ALT, alanine aminotransferase; eGFR, estimated glomerular filtration rate

Abstract #1028

Increased incidence of hepatic regeneration nodules in patients with Hep C treated by direct-acting agents

Metin Basaranoglu and Mustafa Serdar Usta

Gastroenterology Division, Internal Medicine Department, Bezmialem Vakif University, Istanbul, Turkey

Background and aim: Hepatitis C is one of the main causes of liver cancer. The recently discovered combinations of drugs changed everything. We analysed the patients whether any patient developed HCC during the follow-up.
Patients and methods: We evaluated 75 randomly selected patients who were treated between 01.06.2016-01.10.2017 in our gastroenterology out-patient clinic. Of the 75, 46 patients used the combination of Lepidoptera+ Sofosbuvir or 29 patients used the combination of Ombitasvir + Paritaprevir + Ritonavir/Dasabuvir.
Results: HCV-RNA levels were negative in all 46 patients by the combination of Lepidoptera+ Sofosbuvir. But, 3 patients were still positive after the Ombitasvir + Paritaprevir + Ritonavir/Dasabuvir combination threapy. More importantly, four patients developed displastic nodules immediately in the Lepidoptera+ Sofosbuvir group. Additionally, one patient developed HCC in the Ombitasvir + Paritaprevir + Ritonavir/Dasabuvir combination group.
Conclusion: The success of new treatment regimens proved in pratice by eliminating HCV-RNA. However, there are some issues need to

clarify: What the reason is *de novo* HCC development in some patients treated by new agents.

Table (1): Demographic characteristics of 135 studied patients

Characteristics	Summary statistics
Age (years) Mean ± SD (Range)	49.84±11.98 (21-70)
Gender ; Male/Female	90 (66.67%) / 45 (33.33%)
BMI (kg/m²) Mean ± SD	27. 4 ± 2.48
Cirrhotic patients: n (%) **Child Pugh A** **Child Pugh B**	31 (22.96%) 27 (20%) 4 (2.96%)
Diabetic patients: n (%) **HA1c:** Mean ± SD	21 (15.56%) 6 ± 1
Hypertensive patients: n (%)	10 (7.41%)

Table (2): Treatment characteristics in the 135 studied patients

Treatment data	Summary statistics
Type of treatment: n (%) Dual/ Triple	68 (50.37%) / 67 (49.63%)
PCR at baseline (IU/ml) Mean ± SD	1.59±3.26×10⁶
ETR: End of treatment response: n(%) **SVR 12/Relpser**	135 (100%) 133 (98.52%)/2 (1.48%)
Treatment naïve: n (%) **SVR 12** **Relapser**	120 (88.89%) 118 (98.33%) 2 (1.69%)
Treatment experienced* : n (%) **SVR 12**	15 (11.11%) **15 (100%)**

Table (3): Baseline laboratory investigations of studied groups

Baseline investigations	Dual therapy group N=68	Triple therapy group N=67	P value
WBCs (10^9/l) Mean ± SD	6.67± 2.37	6.03±2.69	0.406
Hamoglobin (g/dl) Mean ± SD	14.19±1.63	13.65±1.72	0.706
Platelets (10^9/l) Mean ± SD	228.88±69.65	171.86±68.44	0.671
T. bilirubin (mg/dl) Mean ±SD	0.78± 0.22	0.92±0.38	0.000***
ALT(IU/l) Mean ± SD	38.99±21.95	53.92±42.67	0.002**
AST(IU/l) Mean ± SD	36.45±15.84	56.10±46.49	0.000***
Serum albumin (g/dl) Mean ± SD	4.29±0.49	3.95±0.51	0.694
PT (sec) Mean ± SD	12.45±1.06	13.08±1.64	0.026*
PC Mean ± SD	89.99± 9.87	85.57±15.28	0.003**
INR Mean ± SD	1.06±0.10	1.09± 0.17	0.013*

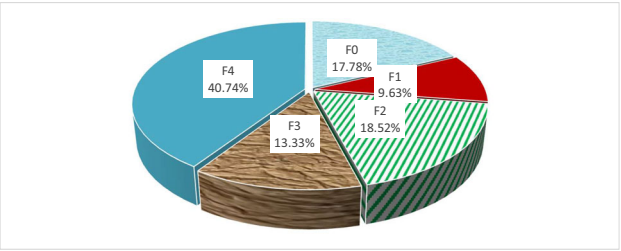


Figure (1): Distribution of stages of fibrosis measured by SWE at base line

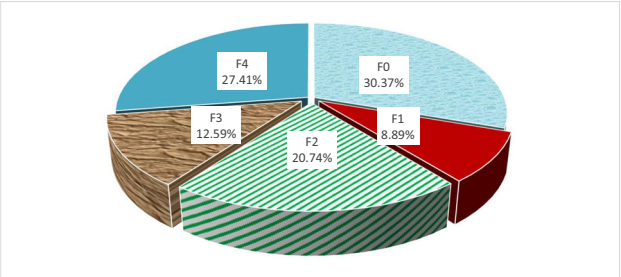


Figure (2): Distribution of stages of fibrosis measured by SWE at SVR12

Table (4): Liver stiffness measurements and other serum fibrosis scores at baseline and at SVR12

Investigation	Baseline	SVR12	Change (SVR12-baseline)	P value
LSM (m/sec) Median (IQR)	1.71 (1.3:2.6)	1.48 (1.17:2.08)	-0.19 (-0.46:0.02)	**0.0001*****
FIB4 Median (IQR)	1.58 (1.02:2.54)	1.14 (0.79:2.16)	-0.26 (-0.86:0.10)	**0.0001*****
APRI Median (IQR)	0.51 (0.33:0.85)	0.27 (0.19:0.46)	-0.23 (-0.54: -0.8)	**0.0001*****
AAR:Median (IQR)	0.97 (0.79:1.25)	0.84 (0.65:1.05)	-0.14 (-0.44:0.08)	**0.0001*****
Lok index Median (IQR)	0.39 (0.25:0.62)	0.36 (0.22:0.53)	-0.02 (-0.14:0.10)	0.20
Fibro Q Median (IQR)	2.79 (1.63:4.51)	2.92 (1.81:4.87)	0.22 (-0.57:1.21)	0.06
King score Median (IQR)	10 (5.34:18.90)	4.73 (3.0:8.80)	-4.4 (-11.26:-1.56)	**0.0001*****
CDS Median (IQR)	5 (4:6)	5.0 (4:6)	0 (-1.0:1.0)	0.69
AP index Median (IQR)	4 (3:6)	4 (3:6)	0 (-1.0:0)	0.14
GUCI Median (IQR)	0.52 (0.35:1.01)	0.26 (0.19:0.44)	-0.24 (-0.64:-0.08)	**0.0001*****

Table (5):Change in liver stiffness measurements and serum fibrosis marker at different stage of fibrosis

Investigation	Mild to moderate fibrosis N=62	Advanced fibrosis and cirrhosis N=73	P value
LSM (m/sec): Median(IQR)	-0.06 (-0.2:0.13)	-0.39 (-0.68:-0.1)	0.0001***
FIB4 :Median (IQR)	-0.16 (-0.47:0.09)	-0.37 (-1.16:0.10)	0.16
APRI : Median (IQR)	-0.18 (-0.30:-0.07)	-0.35 (0.67:-0.09)	0.02*
AAR: Median (IQR)	-0.14 (-0.54:0.05)	-0.16 (-0.40:0.10)	0.58
Lok index: Median (IQR)	-0.04 (-0.15:0.09)	0.01 (-0.12:0.10)	0.56
Fibro Q: Median (IQR)	0.15 (-0.55:1.09)	0.27 (-0.58:1.21)	0.34
King score :Median (IQR)	-2.91 (-7.30:-1.20)	-6.09 (-15.41:-1.77)	0.005**
CDS: Median (IQR)	0 (-1.0:1.0)	0 (-1.0:1.0)	0.22
AP index: Median (IQR)	0 (-1.0:0)	0 (0:0)	0.01*
GUCI : Median (IQR)	-0.21 (-0.41:-0.07)	-0.39 (-0.75:-0.09)	0.02*

Abstract #1063

Sustained virologic response among patients with HIV–HCV coinfection treated with sofosbuvir and daclatasvir at the HIV clinic in a private hospital: an observational cross-sectional study

Carolina Margaret Jo[1], Hendra Koncoro[1], Emon Winardi Danudirgo[1]

[1]Department of Internal Medicine, St. Carolus Hospital, Jakarta, Indonesia

Introduction: Direct-acting Antiviral Agents (DAA) are known to be effectively achieved a sustained virologic response (SVR) in hepatitis C Virus (HCV) infection.

Objectives: Describe the prevalence of HIV-HCV coinfection, rate of SVR, and profile of patients with HIV-HCV coinfection in our institution.
Methods: A 2-year observational cross-sectional study at the HIV clinic in a private hospital. Mean and standard deviation (SD), proportion in percentage (%) were calculated with Epi Info™ v7.1.4.0.
Results: The prevalence of HIV-HCV coinfection was 1.35%. A total of 45 patients were enrolled in sofosbuvir and daclatasvir treatment program. One patient was lost to follow up and two patients have not completed the treatment program. A total of 42 patients have completed the treatment and checked for HCV viral load 12 weeks after end of treatment with SVR rate of 88%. The majority of patients were male (90.48%) with average age of 36.9 years old (SD 6.57), IV drug users (69.05%). Mean duration of HIV antiretroviral therapy (ART) at the initiation of DAA was 4.29 years (SD 3.09), mean of recent CD4 was 363.07 cells/mm^3 (SD 208.29). Mean of HCV VL prior to DAA was 3043,142.26 IU/L (SD 3407,917.33). Mean of AST to Platelet Ratio Index (APRI) score was 0.69 (SD 0.78). The majority of liver function of patients were not in cirrhosis (n = 37 (88%)).
Conclusion: SVR rate among HIV-HCV coinfection patients with sofosbuvir and daclatasvir was quite good. Further analytical study may be needed to determine the predictor of SVR in patient with HIV/HCV coinfection.

Abstract #1069

Ombitasvir-paritaprevir-ritonavir + dasabuvir + ribavirin treatment experience in a newly diagnosed hepatitis C patient

Selçuk Aksöz[1]

[1]Adiyaman Training and Research Hospital, Clinic of Infectious Diseases, Adiyaman, Turkey

Objective: Hepatitis C is an inflammation of the liver caused by the RNA virus called Hepatitis C virus (HCV). The hepatitis C virus (HCV) is a member of the Flaviviridae family and its genome is highly variable. Viral genotype determination is of great importance in the choice of antiviral therapy, treatment duration and follow-up of treatment response. At least six different genotypes of the HCV virus have been identified and each genotype contains different subtypes. The prevalence of hepatitis C in the adult population in Turkey is around 0.5% and 80% of the patients are infected with the genotype 1b subtype. The aim of this study is to share the treatment experience in a newly diagnosed chronic hepatitis C patient with high liver enzymes.
Method: Case: In this study, we present a 30-year-old patient with a high level of liver enzyme and receiving Paritaprevir / Ritonavir / Ombitasvir 1 × 2 + Dasabuvir 2×1 + Ribavirin 2 × 3 for chronic hepatitis C. The patient was infected with Hepatitis C virus (HCV) genotype 1a and had not previously received treatment for HCV. The patient had no signs and symptoms of cirrhosis.
Findings: HCVRNA level was negative on the 13th day of treatment and ALT: 20 AST: 16. The patient did not develop any side effects during the treatment and continued treatment for 3 months.
Result: While Paritaprevir / Ritonavir / Ombitasvir + Dasabuvir + ribavirin, which is one of the newly developed treatment options in chronic hepatitis C cases, seems to be more effective and more tolerable in terms of side effect profile than the previous treatment options, it is important to support these findings through studies with larger patient groups.

Abstract #1089

Real-life dynamic evaluation of hepatic fibrosis after sustained virological response following DAA treatment in patients with chronic hepatitis C with advanced fibrosis before

H. Berak[1], J. Opoka-Kegler[1], G. Cholewińska[1], E. Marcinkowska[1], B. Szymańska-Kotwica[1], N. Gawron[2], A. Horban[1,3]

[1]Hospital for Infectious Disease in Warsaw, Poland, [2]The Insitute of Psyhology, the Maria Grzegorzewska University in Warsaw, Poland, [3]Medical University of Warsaw

Background: Transient elastography is acknowledged as a non-invasive method for assessing liver fibrosis in patients after an antiviral treatment, especially among individuals with the advanced fibrosis before. The aim of this observation was evaluation of fibrosis improvement in patient effectively treated with DAA.
Methods: Retrospective data base (N = 2765) of patients with CHC treated with DAA in Hospital for Infectious Diseases in Warsaw between 2015 and 2017 were reviewed. The observation include patients (n = 225) treated with ombitasvir/paritaprevir/ritonavir ± dasabuvir, ledipasvir/sofosbuvir or sofosbuvir ± ribavirin for 12 or 24 weeks according to the Summary of Product Characteristics and achieved a sustained virological response (SVR12). The first assessment was performed in different time of individual therapy. Liver stiffness was assessed with transient elastography (FibroScan) before DAA treatment and minimum 2 years after SVR. Before treatment, all patients had been diagnosed advanced fibrosis (LSM cut-off > 9,0 kPa) in Metavir stage: F3 (23.8%) and F4 (74.2%).
Results: We observed the changes in hepatic fibrosis in all patients, improvement: 202 pts (89,7%) and decrease: 23 pts (10,3%). In the group with improvement, the average kPa value before treatment was 22.9 ± 15.1, and after was 12.8 ± 7.9, which was significant ($p < .001$). On Metavir score change was also significant ($p < .001$). Among patents with initially F3 improved to F0/1 was observed in 12.9% and to F2: 7.9%. Among patents with initially F4 improved to F0/1: 5.9%; to F2: 15.3%; to F3: 17.8% respectively.
Conclusions: This real-life study indicated the high rate of improvement fibrosis in successfully treated patients with chronic hepatitis C.

Abstract #1093

Hypertensive patients associated with treatment failure in interferon based anti-Hcv therapy

Batbold Batsaikhan[1], Gantsetseg Gantumur[1], Sodgerel Batjargal[1], Chia-Yen Dai[2,3,4,5]

[1]Department of Internal Medicine, Institute of Medical Sciences, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [2]Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [3]Faculty of Internal Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, [4]Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, [5]Health Management Center and Department of Occupational and Environmental Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

Introduction: It is reported that patients with chronic hepatitis C (CHC) are more likely to have high blood pressure and other diseases related to glucose and lipid metabolism. High blood pressure is

considered as an extrahepatic manifestation of CHC. However, some studies revealed that there were no association between CHC and stroke or ischemic heart disease.

Aim: We aimed to investigate the sustained virological response (SVR) rate in hypertensive or non-hypertensive CHC patients.

Methods: The 440 treatment naïve CHC patients enrolled in this study. We have assessed hypertension by measuring blood pressure at the initiation of the therapy, also checked the patients who received antihypertensive drugs and appropriate statistical methods were performed for the analysis.

Results: One hundred and eighteen (26.8%) patients had high blood pressure or detected active use of antihypertensive drugs were enrolled in this retrospective analysis. Multivariate logistic regression analysis revealed that age (OR − 1.06; 95% CI 1.03–1.09; $p < 0.001$), body mass index (OR − 1.13; 95% CI 1.05–1.20; $p < 0.001$) and hyperlipidemia (OR − 4.48; 95% CI 2.05–9.80; $p < 0.001$) were significantly associated with hypertension in CHC patients and HCV RNA log (OR − 0.67; 95% CI 0.57–0.79; $p < 0.001$), total cholesterol (OR − 0.99; 95% CI 0.98–0.99; $p = 0.030$) level, HCV genotype non 1 (OR − 0.67; 95% CI 0.57–0.79; $p < 0.001$), hypertension (OR − 0.56; 95% CI 0.33–0.94; $p = 0.030$) and diabetes (OR − 0.45; 95% CI 0.24–0.82; $p = 0.009$) were significantly associated with SVR.

Conclusion: Hypertensive patients at the initiation of antiviral therapy was associated with treatment failure and patients who did not achieved SVR were associated with high viral load.

Abstract #1094

Effect of hepatitis C virus infection in renal function and clinical outcomes

Gantsetseg Gantumur[1], Batbold Batsaikhan[2], Hung-Pin Tu[3], Chia-Yen Dai[4,5,6,7]

[1]Mongolian Association of Family Medicine Specialists, Ulaanbaatar, Mongolia, [2]Department of Internal Medicine, Institute of Medical Sciences, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [3]Department of Public Health and Environmental Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, [4]Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, [4]Hepatobiliary Section, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [5]School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, [6]Health Management Center, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [7]Department of Biological Science and Technology, College of Biological Science and Technology, National Chiao Tung University, Hsin-Chu, Taiwan

Background: It is controversial that the association of hepatitis C virus (HCV) infection and chronic kidney disease (CKD). We wanted to investigate whether HCV really affect to renal function, also assess the association between clinical effects of CHC and decreased kidney function by estimated glomerular filtration rate (eGFR) level.

Methods: The 3360 patients with hepatitis C virus infection and 3360 age and sex matched community based control individuals without HCV were enrolled (1:1, case and control ratio) in this study between 2004 and 2016. We used Modification of Diet in Renal Diseases (MRDR) for calculate eGFR. Demographic and laboratory parameters were assessed and appropriate statistical methods were performed for the analysis.

Results: Multivariate logistic regression analysis revealed that serum GPT (OR − 0.998; 95% CI 0.997–0.999; $p = 0.001$) level, platelet (OR − 0.997; 95% CI 0.995–0.999; $p = 0.002$) count and hypertension (OR − 1.31; 95% CI 1.03–1.66; $p = 0.027$) were significantly associated with HCV infection and serum TG (OR − 1.001; 95% CI 1.00–1.002; $p = 0.005$) level, platelet (OR − 0.996; 95% CI 0.995–0.997; $p < 0.001$) count, BMI > 25 (OR − 1.43; 95% CI 1.23–1.67; $p < 0.001$), hypertension (OR − 1.69; 95% CI 1.42–1.99; $p < 0.001$), hyperlipidemia (OR 1.32; 95% CI 1.02–1.71; $p = 0.035$) and diabetes (OR − 1.33; 95% CI − 1.03 to 1.71; $p = 0.032$) were significantly associated with low eGFR (< 90 ml/min/m^3) in control subjects. The BMI > 25 kg/m^2, hypertension, and diabetes were associated with low eGFR interaction with the HCV infection by multivariate analysis.

Conclusion: Our study indicated that the patients with HCV infection are associated with low eGFR compared with non HCV infected patients. This association is consistent in obese, diabetic and hypertensive patients.

Table 1. Patient characteristics and safety profile of the 105 uremic patients

Patient characteristics	
Age, years (mean±SD)	66.2±10.0
Female, n (%)	51 (48.6)
BMI, kg/m^2 (mean±SD)	23.5±4.3
Hemodialysis duration, years (mean±SD)	8.9±8.5
Diabetes, n (%)	65 (61.9)
Hypertension, n (%)	75 (71.4)
HBsAg (+), n (%)	8 (7.6)
PWID history, n (%)	3 (2.9)
Major Thalassemia, n (%)	3 (2.9)
Hemophilia, n (%)	1 (1.0)
AST, IU/L (mean±SD)	25.4±14.7
ALT, IU/L (mean±SD)	24.3±15.2
r-GT, U/L (mean±SD)	53.5±78.2
Platelet count, x10^{3}u/L (mean±SD)	175.7±67.5
Albumin, g/dl (mean±SD)	3.7±0.3
Total bilirubin, mg/dL (mean±SD)	0.4±0.2
HCV RNA, logIU/mL (mean±SD)	5.6±1.2
HCV genotype, 1/2/6/unclassified, n (%)	46 (43.8)/53 (50.5)/5 (4.8)/1 (1.0)
FibroScan, kPa (mean±SD)	9.2±4.2
>9.5 kPa, n (%)	32 (30.5)
Liver cirrhosis, n (%)	22 (21.0)
Child-Pugh A, n (%)	21 (19.6)
Child-Pugh B, n (%)	1 (0.9)
Hepatocellular carcinoma, n (%)	7 (6.7)
Safety profiles	
DAA adherence, n (%)	
<20 %, n (%)	4 (3.8)
20-40 %, n (%)	1 (0.9)
40-60 %, n (%)	(3.8)
60-80, n (%)	4 (3.8)
>80 %, n (%)	92 (87.9)
Early treatment termination, n (%)	10 (9.5)
Treatment related*, n (%)	5 (4.8)
Not treatment related†, n (%)	5 (4.8)
Adverse event, n (%)	67(63.8)
Fatigue, n (%)	10 (9.5)
Pruritus, n (%)	9 (8.6)
Nausea, n (%)	7 (6.7)
Anorexia, n (%)	8(7.6)
Epigastric pain, n (%)	7(6.7)
Constipation, n (%)	7(6.7)
Rash, n (%)	6 (5.7)
Dizziness, n (%)	6(5.7)
Insomnia, n (%)	5(4.8)
Headache, n (%)	5 (4.8)

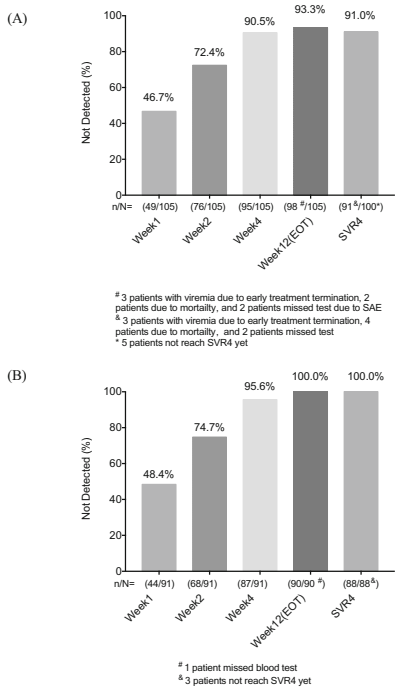


Figure. Treatment responses of the 105 uremic patients, (A) FAS; (B) mFAS

Abstract #1110

Elbasvir (EBR)/grazoprevir (GZR) is effective and tolerable for the treatment of HCV GT1-infected patients: a real world multicenter observatory study in Taiwan

Liu Chun-Jen[1], Cheng Pin-Nan[2], Chen Chi-Yi[3], Yu Ming-Lung[4], Lin Chun-Che[5], Lin Chun-Yen[6], Peng Cheng-Yuan[5], Tseng Kuo-Chih[7], Lo Ching-Chu[8], Tseng I-Hao[9]

[1]Department of Internal Medicine and Hepatitis Research Center, National Taiwan University College of Medicine and Hospital, Taipei City, Taiwan, [2]Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan, [3]Chia-Yi Christian Hospital, Chia-Yi City, Taiwan, [4]Kaohsiung Medical University Hospital, Kaohisung, Taiwan, [5]China Medical University Hospital, Taichung City, Taiwan, [6]Department of Gastroenterology and Hepatology, Chang Gung Memorial Hospital, Linkou Branch, Taoyuan City, Taiwan, [7]Division of Gastroenterology, Department of Medicine, Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Chia-Yi City, Taiwan, [8]Department of Internal Medicine, St. Martin de Porres Hospital, Chia-Yi City, Taiwan, [9]Department of Internal Medicine, Yuan's General Hospital, Kaohsiung, Taiwan

Introduction: Treatment of hepatitis C virus (HCV) by elbasvir/grazoprevir (EBR/GZR) was found to be efficacious and well tolerated in clinical trials.
Objectives: This study aimed to evaluate the effectiveness and tolerability of EBR/GZR in the treatment of HCV genotype 1 (GT1)-infected Taiwanese patients.
Methods: Chronic hepatitis C (CHC) patients infected with GT1b or 1a without resistance-associated substitution, and treated with 12-week EBR/GZR were enrolled from 10 hospitals in Taiwan between August 2017 and December 2018. All clinical and virologic data were collected at each participating center. Primary efficacy endpoint was sustained virologic response at week 12 (SVR12) after end of the EBR/GZR therapy, assessed in the per-protocol population, which excluded patients with important deviations from the protocol. Analysis was also performed based on the modified full analysis set (FAS), which included all allocated patients receiving at least 4-week medication. Virologic failure was recorded as breakthrough, nonresponse, or relapse. Safety was assessed through collection of adverse events (AEs), physical examination, vital signs, and standard laboratory evaluations.
Results: Per protocol SVR12 rates were 99.5% (1169/1175) for all HCV genotype 1 patients. Among patients with stage 4 or 5 chronic kidney diseases, 100% (107/107) achieved SVR12. In univariate analyses, variables associated with SVR12 were treatment duration ($P < 0.0001$) and treatment adherence ($P < 0.0001$). 22.3% of the patients experienced adverse effects during treatment. Seven patients did not complete the treatment, five due to liver-unrelated deaths, one due to AE and one due to epilepsy.
Conclusion: EBR/GZR treatment was highly effective and well tolerated.

Abstract #1126

Evaluation of depression and anxiety symptoms in HCV-infected patients effective treated with DAA

Bogna Szymańska-Kotwica[1], Natalia Gawron[2], Hanna Berak[1], Anna Kołakowska[1], Aleksandra Korczyńska[1], Grażyna Cholewińska[1], Jolanta Opoka-Kegler[1], Ewa Marcinkowska[1], Andrzej Horban[1,3] Tomasz Laskus[3]

[1]Hospital for Infectious Diseases in Warsaw, Poland, [2] The Institute of Psychology, The Maria Grzegorzewska University in Warsaw, Poland, [3] Medical University of Warsaw, Poland

Objective: Increased levels of depression and anxiety have been reported in approximately one-third of patients with hepatitis C virus (HCV). The aim of this study was to evaluate depression and anxiety symptoms in HCV patients treated with DAA.
Method: This observation is part of a bigger neuropsychological study (N = 71) conducted in the Hospital for Infectious Diseases in Warsaw. The measurements of depression and anxiety were done before and after DAA treatment (n = 50), using depression (BDI-II) and anxiety (STAI-X1) inventories. Initially, all patients had been diagnosed stage of fibrosis in Metavir scale: F0/1 (40%); F2 (18%); F3 (16%) and F4 (26%).
Results: Before DAA treatment mean BDI-II score was 8.2 ± 6.6 and mean STAI-X1 was 32.9 ± 7.7. At the time of the assessment, low mood was noticed among 28% of patients, mild depression in 14%, moderate in 4%, and severe in 2%. In the group with depression, 70% of individuals had fibrosis on F0/1 stage. After SVR, in the whole group average BDI-II was 5.7 ± 5.9 and average STAI-X1 was 32.5 ± 9.4. Low mood had 12% of participants, mild depression – 10%, and severe – 2%. After DAA treatment only BDI-II scores decreased significantly ($p < .001$), not anxiety. Participants' outcomes didn't differ in terms of sex.
Conclusion: This study has showed that depression was reduced after DAA treatment, however, the level of anxiety was similar. Such results differ from outcomes reported in other studies including patients treated Peg IFN/RBV. The above results might be used in advancing further research about mental health during treatment of HCV infection.

Abstract #1134

A survey on knowledge and testing rate of hepatitis C in the general population of South Korea

Gwang Hyeon Choi,[1] Eun Sun Jang,[1] Jin-Wook Kim,[1] Sook-Hyang Jeong[1]

[1]Departments of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Republic of Korea

Introduction: To eliminate hepatitis C virus (HCV) infection, improving the public knowledge of and accessibility to HCV screening and treatment is essential.
Objectives: To evaluate the knowledge and testing rate of HCV and the opinions about the inclusion of the HCV test in the Nation Health Examination (NHE) among the general population of South Korea.
Methods: A telephone interview survey was conducted by an independent research company using a 16 item-questionnaire (demographic, knowledge on HCV, testing rate and its result, necessity of screening) during May 2019. The sample population consisted of 1003 Korean adult residents adjusted by age, gender and area according to the standard Korean population in 2019.
Results: Among the 1003 participants (505 women, mean age of 47.9 years), 56.4% recognized HCV; 44.4% understood HCV is transmittable, and 56.8% thought HCV is curable by medication. The recognition rate tended to increase according to the increasing level of education. Testing for anti-HCV was reported by 91 people (9.1%); among them, 10 people (11.0%) reported a positive result, and 8 people were treated. The common reasons for HCV testing were a health check-up (58.5%), a physician's recommendation (11.0%) and elevated liver enzymes (10.7%). The majority (75.1%) agreed to HCV screening by integration into NHE.
Conclusions: The level of knowledge on HCV is suboptimal, and the self-reported testing rate of HCV is less than 10%, but once diagnosed, the treatment rate seems to be high in South Korea. More active campaigns and effective screening are needed.

Abstract #1166

A profile of patients with chronic hepatitis C infection: real-life data from Turkey

F. Tabak, S. Köse, B. Kurtaran, N.O. Cuvalci, S. Ocak, G. Yoruk, Y.K. Kaya, T. Yamazhan, A. Batirel, N. Ince, R. Karaali, E.Y. Zerdali, H.O. Cerik, F. Sarigul, Hep-C Study Group

Background: Chronic hepatitis C virus (HCV) infection is a challenging health care problem in Turkey with an approximately 1% of prevalence. We created an online database and collect data of patients with chronic hepatitis C (CHC) patients using in Turkey. We aimed to evaluate patient characteristics.
Patients and Methods: Between April 2017 and February 2019, 37 centers from Turkey recorded 2713 patients to the database. All patients older than 18 years with CHC under DAAs were enrolled in this non-interventional observational study. Demographics, clinical information were recorded. The study was approved by ethics committee and registered to clinicaltrials.gov (NCT03145844).
Results: Among the 2713 patients; 1333 (49.1%) were female and mean age was 54 ± 16 years (range 18–97) years. The most common HCV genotype was G1: 2265 (83.5%), followed by G3: 241 (9.1%), G2:105 (3.9%), G4:84 (3.1%), and G5:9 (0.3%). Among G1, 87% was G1b and 13.0% was G1a. Cirrhosis was detected in 334 (13.1%) and 206 (83.7%) were compensated (Child-Pugh A) and 40 were (16.3%) decompensated (Child-Pugh B-C). Liver biopsy was available in 1479 (56.7%); median histologic activity index (HAI) was 7 and fibrosis score was 2.
Conclusion: The study results which represent the HCV patient's profile in the country show that HCV patients are almost evenly distributed to both genders, in middle to advanced ages and infected with genotype 1b. Liver fibrosis is moderate to advanced in almost half of the patients. Diagnostic and therapeutic strategies should be effectively used for management of the patients in an early stage.

Abstract #1168

Efficiency and safety of direct-acting antiviral in cirrhotic hepatitis C infection patients: real-life data from Turkey

F. Tabak, Y. Tasova, S. Esen, N.C. Oztoprak, Y. Onlen, N.D. Sari, I.E. Yıldız, D. Inan, E.Y. Zerdali, R. Guner, S. Barut, H. K.Kumbasar, S. Kaya, N. Ince, I. Dokmetas, M. Namiduru, A. Batirel, O. Gunal, S.A. Coskuner, H. Karsen, I. Koksal, E. Akinci, G.G. Tosun, H.C. Gul, F. Sirmatel, K. Turker, F. Duygu, M. Sunnetcioglu, N. Erben, O. Karabay, A. Sener, E. Senates, G. Celebi, A.S. Tartar, N. Baykam, U. Aslihan, F. Sarigul, G. Yoruk, T. Yamazhan, Hep-C Study Group

Background: The development and approval of several DAAs in recent years has revolutionized antiviral therapy especially for cirrhotic patients. We created an online database and collect data of patients with chronic hepatitis C (CHC) patients using in Turkey. We aimed to evaluate effectiveness and safety of DAA in cirrhotic CHC patients.
Methods: Between April 2017 and February 2019, 37 centers from Turkey recorded 2713 patients to the database. Patients > 18 years with CHC under DAAs were enrolled in this non-interventional observational study. Efficiency and safety results are given for the patients with 12 weeks after end of treatment (SVR12) data. The study was approved by ethics committee and registered to clinicaltrials.gov (NCT03145844).
Results: Among the 2713 patients; 334 (13.1%) were cirrhotic. Of those, 159 (47.6%) were male and mean age was 64.4 ± 10.7 years. Among cirrhotics, 284 (87.7%) were compensated (Child-Pugh A) and 40 were (12.3%) decompensated (Child-Pugh B-C). The most common HCV genotype was G1: 295 (88.9%; among G1 91.9% G1b, 8.1% G1a). Previous treatment information was available for 325 patients: 143 out of the patients (44%) were treatment-experienced (58.7% relapser and 41.3% non-responder). DAAs given to the patients are shown in Table 1. Viral responses at the end of treatment and at SVR12 were 100% (188/188), and 98% (150/153) respectively (Figure 1).
Conclusion: Real-life data show that HCV treatment with DAA is highly efficacious and safe in cirrhotic patients as well. Being decompensated or decompensated, treatment-naïve or previously treated (relapse or non-responder) do not seem to affect the response rate.

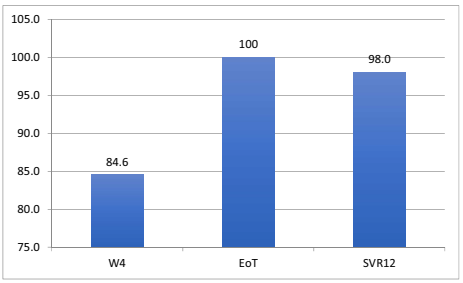


Figure 1. Virologic response rates on treatment week 4 (W4), end of treatment (EoT), and 12 weeks after the end of treatment (SVR12) (cut-off point <12 IU/mL)

Table 1. Direct-Acting Antivirals Used in the Treatment of Cirrhotic Patients

DAA	n	%
Sofosbuvir + Ledipasvir	159	48.2
Paritaprevir + Ritonavir + Ombitasvir + Dasabuvir	85	25.8
Sofosbuvir + Ledipasvir + Ribavirin	58	17.6
Paritaprevir + Ritonavir + Ombitasvir + Dasabuvir + Ribavirin	13	3.9
Sofosbuvir + Ribavirin	12	3.6
Paritaprevir + Ritonavir + Ombitasvir + Ribavirin	3	0.9

Abstract #1182

Changes of liver fibrosis in chronic hepatitis C patients with chronic kidney disease who had undergone hemodialysis after DAA therapy

M. Suryamin[1], S. Alwi[2]

[1]Division of Gastroentero-hepatology, Departement of Internal Medicine, Persahabatan Hospital Jakarta Indonesia, [2]Division of Nephrology, Departement of Internal Medicine, Persahabatan Hospital Jakarta Indonesia

Introduction: Hepatitis C infection is one of the major problems in the world, around 2.5% of the world's population has hepatitis C. Currently, treatment of chronic hepatitis C use Direct Acting Antiviral (DAA) drugs, including a special group of hepatitis C sufferers with Chronic Kidney Disease (CKD) who had undergone hemodialysis.
Objectives: This study assess the changes of liver fibrosis before and after DAA therapy in chronic hepatitis C patients with CKD undergone hemodialysis.
Methods: There were 14 chronic hepatitis C patients with CKD who had undergone hemodialysis (12 male and 2 female). Treated with Grazoprevir 100 mg and Elbasvir 50 mg for 3 months. At the end of treatment and 3 months after treatment, HCV RNA test was not detected. Transient elastographic examination was performed before and 8–9 months after completed therapy.
Results: Based on the Metavir score, 36% of patients had a decrease of liver fibrosis, 28% remained and 36% increased. Quantitatively based on kPa value, 57% of patients had a decreased of liver fibrosis and 43% increased.
Conclusions: Hepatitis C patients with CKD who had undergone hemodialysis, after being treated with DAA for 3 months based on Metavir scores showed only 36% of decreased fibrosis and based on kPa values showed 57% of decreased fibrosis.

Abstract #1188

Prevalence of pre-existing hepatitis C virus (HCV) variants resistant to DAAs in Vietnam

Chau Le Ngoc[2], Trinh Nguyen Mai[2], Thanh Tran Thi Thanh[2], Trang Nguyen Hoa[2], Phuong Nguyen Thi Ngoc[2], Ngoc Nghiem My[1], Man Dinh Nguyen Huy[1], Hung Le Manh[1], Chau Nguyen Van Vinh[1], Thuy Le[2], Motiur Rahman[2]

[1]Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam, [2]Centre for Tropical Medicine, Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam

Introduction: Treatment with direct-acting antiviral agents (DAAs) with or without interferon is the mainstay in the management of HCV infection. Pre-existing DAA resistance associated variants (RAVs) may result in treatment failure or require prolonged treatment.
Objectives: We examined the prevalence of 125 previously reported RAVs among treatment naïve first time diagnosed with jaundice and chronic HCV isolates from Vietnam and among different HCV genotypes.
Methods: Genotypes of the HCV positive plasma samples were determined by direct sequencing of 5'UTR, Core, NS5B regions. Non-ribosomal random PCR and next-generation sequencing based assay were performed for sequencing of HCV genomes. Consensus sequences were analyzed for RAVs.
Results: 167 HCV genomes including 56 from acute and 111 from chronic HCV patients were analyzed. Prevalence of genotype 1, 2, 3, 6 was 52.1% (87/167), 6.6% (11/167), 1.2% (2/167), 40.1% (67/167), respectively. 78.4% of sequences (131/167) harbored at least one resistance variant. RAV frequency in Genotype 1 was 60.9% and 100.0% in Genotype 2 and Genotype 6 sequences. Incidence of RAVs was 63.5% (106/167), 53.9% (90/167) and 31.7% (53/167) in the NS3, NS5A, NS5B regions. Prevalence of RAVs was higher in sequences from acutely infected patients (89.3% vs. 73.9%) compared to chronic patients. However, clinically relevant RAVs were higher in chronic patients than in acute patients (27.9% vs. 26.4%).
Conclusions: Clinically relevant and *in-vitro* RAVs were detected in highest prevalence in NS3 region of Genotype 6 isolates. The highest incidence of clinically relevant pre-existing RAVs was observed in chronically infected patients with HCV non DAA treatment.

Abstract #1231

The association between OATP variants and hepatocellular cancer risk in hepatitis C patients who treated with direct acting antivirals

Zuhal Mert Altintas[1], Engin Altintas[2]

Mersin University Faculty of Medicine, Medical Genetics[1], Gastroenterology[2], Mersin, Turkey

Introduction: We aimed to evaluate the association of genetic variants of organic anion-transporting polypeptide (OATP) between the risk of hepatocellular carcinoma (HCC) in hepatitis C patients treated with direct-acting antivirals (DAA).
Methods: 199 hepatitis C patients using DAA [ledipasvir / sofosbuvir (LS) or ombitasvir / paritaprevir / ritonavir ± dasabuvir (OPrD)] were included in the study. Patients were followed up with biochemistry and abdominal ultrasonography once a month during treatment and 3–6 months intervals end of treatment. 388 A > G, 521 T > C, 334 T > G and 699 G > A variants of OATP gene were studied by PCR-RFLP method.

Results: Ten patients developed HCC after treatment. The patients who developed HCC had a sustained viral response (12 weeks), mean age 55.5 years, 8 male and 2 female. 8 cirrhotic, 4 naive and all of them were genotype 1. Nine patients used LS and 1 patient used OPrD. There was no correlation between HCC development and 388 A > G, 521 T > C, 334 T > G and 699 G > A variants of OATP genes (respectively p = 0.815, p = 0.162, p = 0.898 and p = 0.624).
Conclusion: There is no correlation between the risk of hepatocellular cancer and genetic variants of OATP in hepatitis C patients who treated with direct-acting antivirals. Further work will be necessary to clarify the relationship between the OATP gene variants and susceptibility to HCC on larger populations of diverse ethnicity.

Abstract #1232

Role of the Sabadell NIHCED (non-invasive hepatitis C related cirrhosis early detection) index and right lobe diameter to albumin ratio in prediction of presence of varices in patient with liver cirrhosis

Ghada Mostafa Kamal[1], Amr Mohammed Zaghloul[2], Rania Ashraf Aref[3]

[1]Professor of Gastroenterology and Tropical Medicine, Sohag Univesity, Sohag Country, Egypt, [2]Associate professor of Gastroenterology and Tropical Medicine, Sohag Univesity, Sohag Country, Egypt, [3]Tropical Medicine and Gastroenterology Department, Sohag University Sohag Country, Egypt

Introduction: Portal hypertension in cirrhosis is a main cause of esophageal varices (OVs) leading to substantial morbidity and mortality. The gold tandard diagnosis of varices is esophagogastroduodenoscopy (EGD) and different non-invasive predictors are an alternative approach to perform selective screening endoscopy in high risk patients.
Objective: To evaluate whether the NIHCED score and the right lobe diameter to albumin ratio can predict the presence of OVS in cirrhotic patients.
Materials and methods: Seventy five cirrhotic patients with liver cirrhosis who underwent EGD and were administered NIHCED Score. Right lobe diameter to albumin ratio were calculated.
Results: In total 75 patients were included (51 males)with mean age 53.11 ± 9.89. They were segregated into two groups those with OVs and those without OVs. OVS were detected in 47 patients.
Roc curve analysis of NIHCED, at a cut-off point of 45, sensitivity was 70%, specifity was78%, and diagnostic accuracy of 74% with an AUC of 0.77 (95% CI 0.66–0.86) Roc curve analysis of right lobe diameter to albumin ratio, at a cut off point of 2.80. The sensitivity was 80% and specifity was 53%, and diagnostic accuracy of 67% with an AUC of 0.67 (95% CI 0.55–0.77).
Conclusions: The NIHCED score and right lobe diameter to albumin ratio were simple non-invasive predictors of presence of varices in patient with liver cirrhosis.

Abstract #1236

Correlation between hepcidin serum levels and liver fibrosis based on *Fibroscan* in patients with chronic hepatitis C

Ahmad Danial, Iswan A Nusi, Ummi Maimunah, Ulfa Kholili, Budi Widodo, Husin Thamrin, Ami Ashariati, Poernomo Boedi Setiawan

Background: Chronic hepatitis C infection can progress to liver fibrosis, cirrhosis, and hepatocellular carcinoma. Iron overload in chronic hepatitis C is a cofactor that promotes the development of liver damage and increases the risk of liver fibrosis. Increased iron in hepatitis C infection is associated with decreased hepcidin serum levels, a major regulator of iron homeostasis. The relationship between hepcidin and liver fibrosis in patients with chronic hepatitis C—drug naive patients is still controversial.
Objective: To analyze the correlation between hepcidin serum levels with liver fibrosis based on *fibroscan* in chronic hepatitis C patients in Gastroentero-Hepatology Clinic.
Materials and methods: A cross-sectional observational analytic study, involving all hepatitis C patients during July–September 2019. 34 patients fulfilling the inclusion and exclusion criteria were the subjects of the study. Patients were selected with consecutive sampling and were examined for serum hepcidin levels and degree of liver fibrosis was measured by *fibroscan*. Data analysis used spearman correlation test and was considered significant if $p < 0.05$.
Results: A total of 34 subjects (64.71% females with the mean age of 49.76 ± 9.52 years) were eligible for enrollment in this study. The average hepcidin level was 18,23 ± 5,35 ng/ml. The average *fibroscan* measurement result was 8,80 ± 4,53 kPa and most patients with stage F3 were 11 peoples (32.4%). The serum hepcidin levels correlated negatively and significantly (r = -0788, $P < 0.001$) with degree of liver fibrosis.
Conclusion: There is a negative correlation between hepcidin serum levels and liver fibrosis based on *fibroscan* in patients with chronic hepatitis C.

Abstract #1237

Correlation between serum ferritin levels and liver fibrosis based on *Transient Elastography* in chronic hepatitis C patients

M.B. Rizkiyanto[1], H. Purbayu[2], B. Widodo[2], A. Vidyani[2], M. Miftahussurrur[2], S.U.Y. Bintoro[3], P.B> Setiawan[2]

[1]Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga – Dr.Soetomo Teaching Hospital, Surabaya, Indonesia, [2]Gastroenterohepatology Division, Department of Internal medicine, Universitas Airlangga—Dr. Soetomo Teaching Hospital, Surabaya, Indonesia, [3] Hematology and Oncology Division, Department of Internal medicine, Faculty of Medicine, Universitas Airlangga—Dr.Soetomo Teaching Hospital, Surabaya, Indonesia

Introduction: Hepatitis C virus (VHC) infection is one of the leading causes of chronic liver disease worldwide, lead to severe fibrosis complications. VHC infection impaired hepcidin regulation, changes iron metabolism, indicated by an increase in serum ferritin levels. Some studies link the condition of impaired iron deposition in the liver with the degree of fibrosis. No research in Indonesia that proves relationship between serum ferritin levels and degree of fibrosis in patients with chronic hepatitis C, so this research needs to be done.
Objective: To analyze correlation between serum ferritin levels with liver fibrosis based on *transient elastography* in chronic hepatitis C patients.
Methods: A cross-sectional observational analytic study, involving all hepatitis C patients during May–September 2019. 30 patients fulfilling the inclusion and exclusion criteria were the subjects of the study. Ferritin examination carried out at the beginning of the examination. Data analysis used spearman correlation test and was considered significant if $p < 0.05$.
Results: The average age of patients was 51.17 ± 8.15, women (60%). Median of serum ferritin was 136.11 ng/mL, average of liver fibrosis based on *fibroscan* 17.39 ± 15.99 kPa and most patients with

stage F4 were 13 peoples (43.33%). A significant correlation was found between serum ferritin levels and the degree of liver fibrosis with value of r: 0.759 ($p < 0.01$).
Conclusion: There is a positive correlation between serum ferritin levels and liver fibrosis based on *transient elastography* in chronic hepatitis C patients.

Abstract #1306

HCV-RNA clearance after direct antiviral agent (DAA) therapy in chronic hepatitis C patients: preliminary study

Edi Mulyana, Nikko Darnindro, Annela Manurung, Arnold Harahap

Department of Internal Medicine, Fatmawati General Hospital, Jakarta, Indonesia

Background: Chronic Hepatitis C is associated with necroinflammation predisposes to fibrosis. Progression of necroinflammation and infection can be stopped and eliminated using DAA Therapy. Effectiveness and proportion of HCV RNA Clearance after DAA Therapy in Indonesia are still limited.
Objectives: To know proportion of HCV-RNA Clearance after DAA therapy.
Methods: We studied this proportion in 95 consecutive Hepatitis C patients referred to Fatmawati General Hospital from August 2017–2019. Sofosbuvir and Daclatavir were used as DAA, and Laboratory examination including HCV-RNA, and Fibroscan were tested before therapy. HCV-RNA SVR-12 was tested to evaluate the HCV-RNA elimination.
Results: Out of 95 patients who were admitted to clinic, median age was 44 (30–80) years-old. 67.4% patients were male. Median value of HCV-RNA was 1.35×10^6 IU/ml (311–$1.97.10^7$ IU/ml). 52.6% patients were diagnosed as cirrhosis. Median value of Fibroscan was 10.4 (3.3–75 kpa). HIV-HCV coinfection was detected in 30.5% patients. Proportion of HCV RNA clearance after DAA Therapy was 97.9%.
Conclusion: Proportion HCV-RNA clearance after DAA Therapy was high. This raises hopes for elimination of HCV Infection and improvement in liver cirrhosis in patients who have experienced it. Further research should be carried out in order to find improvement of liver status after viral eradication and reactivation of virus.

Abstract #1308

Glecaprevir and pibrentasvir for Japanese patients with human immunodeficiency virus and genotype 3 hepatitis C virus coinfection

Goki Suda[1], Takuya Sho, Masato Nakai[1], and Naoya Sakamoto[1] for the NORTE Study Group

[1]Department of Gastroenterology and Hepatology, Graduate School of Medicine, Hokkaido University, Hokkaido, Japan

The efficacy and safety of glecaprevir and pibrentasvir in Japanese patients with human immunodeficiency virus (HIV) and/or genotype 3 hepatitis C virus (HCV) infection is yet to be clarified. This is because none, or only a limited number of patients, were included in a Japanese phase 3 trial. We report for the first time the successful treatment of glecaprevir and pibrentasvir in three Japanese patients with HIV and genotype 3 HCV coinfection, and hemophilia. The first patient was a 48-year-old man with genotype 3a HCV and HIV coinfection. He had been treated with tenofovir alafenamide fumarate/emtricitabine + dolutegravir for HIV infection before initiation of glecaprevir and pibrentasvir therapy. The second patient was a 53-year-old man with genotype 3a HCV and HIV coinfection. He had been treated with abacavir sulfate/dolutegravir sodium/lamivudine + rilpivirine as antiretroviral therapy (ART) before initiation of glecaprevir and pibrentasvir therapy. The third patient was a 51-year-old man with genotype 3a HCV and HIV coinfection. He had been treated with tenofovir alafenamide fumarate/emtricitabine + dolutegravir as ART before initiation of glecaprevir and pibrentasvir therapy. Serum HCV RNA was negative at 12 weeks after the completion of glecaprevir and pibrentasvir therapy in all patients. All three patients completed 12 weeks of therapy without severe adverse events, and without any changes or dose reduction of ART. In conclusion, glecaprevir and piblentasvir treatment is safe and effective for Japanese patients with genotype 3 HCV and HIV coinfection.

Abstract #1341

TLL1 rs17047200 decreases the risk of hepatocellular carcinoma in Thai patients with chronic hepatitis C virus infection

N. Chuaypen[1], S. Chittmittraprap[1], A. Avihingsanon[2], P. Tangkijvanich[1,*]

[1]Center of Excellence in Hepatitis and Liver Cancer, Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, Bangkok, 10330, Thailand, [2]The HIV Netherlands Australia Thailand Research Collaboration (HIV NAT), Bangkok, Thailand

Background: A recent genome-wide association study showed that the *tolloid like 1 (TLL1)* rs17047200 single nucleotide polymorphism (SNP) might influence the development of hepatocellular carcinoma (HCC) in patients with hepatitis C virus (HCV) infection. This study was aimed to assess its correlation in Thai patients.
Method: A total of 655 patients with chronic HCV infection (307 mono-infection, 167 HCV/HIV co-infection and 187 HCC) were enrolled to determine the SNP distribution by allelic discrimination using real-time PCR with *Taq*Man probes.
Results: The frequencies of A and T alleles of rs17047200 in the HCV mono-infected group were 86.8% and 13.2%, respectively, while the corresponding figures in the HCV co-infected group were 89.5% and 10.5%. There was no difference in their distribution between the mono-infected and co-infected groups (OR = 0.77, 95%CI: 0.51–1.17, $P = 0.224$). The frequency of A and T alleles in the HCC group were 93.3% and 6.7%. Compared with the non-HCC group (HCV mono- and co-infection), the frequency of T allele was significantly lower in the HCC group (OR = 0.51, 95%CI: 0.32–0.80, $P = 0.004$). In addition, the distribution of AT+TT genotypes in patients with HCC were significantly lower than in patients without HCC (OR = 0.57, 95%CI: 0.35–0.93; $P = 0.023$).
Conclusion: Our results showed that rs17047200 was associated with a decreased risk of the development of HCV-related HCC. These data suggest that the SNP might have an influence on natural history of chronic HCV infection in Thai individuals.

Abstract #1371

Clinical performance evaluation of the Molbio Diagnostics Truenat™ HCV RNA assay: a near point-of-care test to strengthen Hepatitis C virus diagnostics

Vibha Mehta, Elena Ivanova, Beatrice Vetter, Sanjay Sarin, Babu Entoor Ramachandran, Ekta Gupta

Introduction: Point of care molecular testing is game changer for HCV diagnosis. One such assay is Truenat^{TM} HCV assay, by Molbio Diagnostics (Bangalore, India).
Objectives: Comparative analysis between Truenat^{TM} with Abbott (Illinois, USA) Real Time HCV viral load assay .
Study design: Three twenty archived plasma samples (152 HCV RNA positive, 168 HCV RNA negative) were randomly selected from -80 ° C . Limit of Detection (LoD) was 12 IU/ml for Abbott and 250 IU/ml for Truenat^{TM}. Samples were analysed on both assays simultaneously and quantitatively discrepant samples tested on 3rd HCV assay (GeneXpert HCV, LoD 10 IU/ml).
Results: Of total positive samples,13.2% had VL $< 10^4$ IU/ml, 14.5% had VL 10^4–10^5 IU/ml and 72.4% had VL $\geq 10^5$ IU/ml. Onehundredsix (69.7%) positive samples had genotype (GT) available, 36 (34%) were GT 1, 60 (62%) GT 3 and 2 (2%) GT4. Truenat^{TM} showed sensitivity of 94.98% (95% CI 89.06%–97.26%) and specificity of 98.81% (95% CI 95.77%–99.86%). 11 samples had discordant results (9 false negative and 2 false positive). Six of the 9 false negative on Truenat^{TM} had VL of < 250 IU/ml, below its LoD. By Bland Altman analysis, the average difference in Abbott – Truenat was 0.88 IU/ml, with 11 samples falling outside 1.96 SD . Excluding these outliers, the overall correlation of quantifiable viral loads between the Abbott HCV and Truenat HCV was $r^2 = 0.893$.
Conclusion: The study demonstrates excellent performance of the Truenat^{TM} HCV for viral load detection.

Abstract #1389

Remission of skin lesion after treatment of chronic hepatitis C virus infection with direct-acting antiviral (DAA) regimens

Caini He,[1] Yunyu Zhao,[1] Rong Gao,[2] Jiashu Liu,[2] Shen Li,[3] Longfei Zhu,[2] Wenjun Wang,[1] Zhengxiao Li,[1] Fanpu Ji,[1,4,5]

[1]Department of Infectious Diseases, the Second Affiliated Hospital of Xi' an Jiaotong University, Xi'an, China, [2]Department of Dermatology, the Second Affiliated Hospital of Xi' an Jiaotong University, Xi'an, China, [3]Shaanxi Provincial Centre for Disease Control and Prevention, Xi'an, China, [4]Shaanxi Provincial Clinical Research Center for Hepatic & Splenic Diseases, the Second Affiliated Hospital of Xi'an Jiaotong University, [5]National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, the Second Affiliated Hospital of Xi'an Jiaotong University

Background/aims: Hepatitis C virus (HCV) infection is a systemic disease with extrahepatic manifestations that include skin involvement, such as mixed cryoglobulinemia, lichen planus, and porphyria cutanea tarda. Remission of skin lesion has been associated with viral clearance, but its real-world DAA data is limited.
Methods: We performed a retrospective study of the effectiveness of interferon-free DAA regimens in patients with HCV infection and cutaneous manifestations. Clinical and laboratory features were recorded at baseline, the end-of-treatment, and 12/24 weeks afterwards.
Results: Five consecutive patients with HCV infection and skin lesion (age range, 25–57 years; 4 female; one cirrhosis; 3/2 with genotype 1b/2a) were recruited from our hospitals from 02/2016 to 09/2019. The cutaneous manifestations included eczema scrotum, prurigo nodosa, erythema nodosum, ulcerations and Sjogren's syndrome. They received sofosbuvir/velpatasvir (n = 3) or ledipasvir/sofosbuvir (n = 2) for 12 weeks. All 5 patients achieved sustained virological response at 12-weeks after completion of treatment. After treating with ledipasvir/sofosbuvir, eczema of scrotum had significant improvement and completed remission at 4 weeks treatment and post-treatment 12-weeks in patient 1# (Fig. 1). Significant improvement of prurigo nodosa (Fig. 1), erythema nodosum, and ulcerations after HCV clearance in patients 2–4#. Patient 5# was diagnosis as chronic HCV genotype 2a infection and secondary Sjogren's syndrome. Her symptoms had a completed remission 12 weeks after sofosbuvir/velpatasvir treatment. No patient had experienced a recurrence of skin damage during the follow-up.
Conclusions: In treating the skin lesion associated with HCV infection, the DAA regimens have been successful at achieving SVR and improving symptoms. Screening for HCV should be performed in patients with cutaneous manifestations.

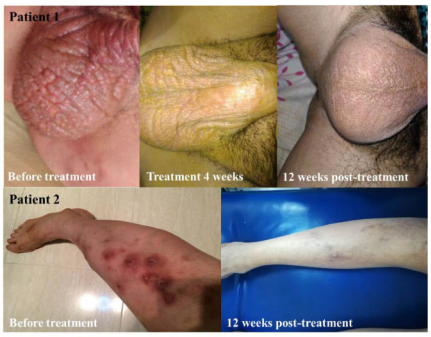


Fig.1 Remission of eczema scrotum and prurigo nodosa after DAA treatment for HCV

Abstract #1423

The efficacy of 12 week-elbasvir/grazoprevir as pan-genotype treatment in hemodyalisis hepatitis C patients

Harahap Arnold, Darnindro Nikko, Nugraha Mario Markus, Mulyana Edi, Manurung Annela, Sarwono Johannes, Purwanti Anggraini, Yohanes Aryan, Jasmine Elizabeth

Departement of Internal Medicine, Fatmawati General Hospital, Jakarta, Indonesia

Introduction: HCV Infection is found in 2–50% patients in Hemodyalisis. HCV infection in HD patients is associated with both increased morbidity and reduced survival. However, treatment of these patients remain difficult and challenging. Grazoprevir-elbasvir in Phase III C-SURFER study could achieved SVR 95% (ITT) and 99% (per-protocol).
Objective: To Know effectivenes of Elbasvir/Grazoprevir in HCV Pan-Genotype Hemodyalisis Patient.
Methods: We analyzed data in Hemodyalisis Hepatitis C Patients whom treat with 12 weeks-Elbasvor/Grazoprevir. Clinicodemographic data including SVR12 were obtained.
Results: Out of 20 Hepatitis C Hemodyalisis patients who were admitted to hepatology clinic, mean age was 44.3 ± 16 years-old. 75% patients were male. Mean of Trombocyte count was 214.500 ± 66.150 u/L Median value of ALT and AST were 36 (12–253) and 30 (14–237). Mean bilirubin and albumin level were 0.41 ± 0.12 g/dL and 3.87 ± 0.3 g/dL. Median value of HCV-RNA was 3.23 x 10^4 IU/ml (10–4.9 × 10^6 IU/ml). Median value of Fibroscan was 7.9 (4.4–24.3 kpa). Proportion of HCV RNA clearance 12 week after DAA Therapy (SVR12) was 100%.
Conclusion: Elbasvir-Grazoprevir for 12 weeks was highly effective in treating Pangenotype HCV Infection in Hemodyalisis Patients. SVR12 was achieved in all patients.

Abstract #1442

Well tolerability and highly effective treatment response for human immunodeficiency virus-hepatitis C virus coinfected patients treated by all oral direct acting antivirals

Su Pin-Shuo,[1] Su Chien-Wei,[1,2] Wu Sih-Hsien,[a] Chu Chi-Jen,[1,2], Huang Yi-Hsiang,[1,2], Hou Ming-Chih[1,2]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC, [2] Faculty of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan, ROC

Introduction: Human immunodeficiency virus (HIV)—hepatitis C virus (HCV) coinfection are associated with accelerated rates of hepatic fibrosis and higher incidence of hepatic decompensation. Poor treatment response for these patients by interferon (IFN)-based regimen was documented due to advanced liver disease, immune dysfunction and poor medical adherence.
Objectives: This study was aimed to investigate the efficacy and safety of all oral direct acting antivirals (DAAs) for HIV-HCV coinfection patients.
Methods: 50 consecutive HIV-HCV coinfection patients who treated with all oral DAAs (PrOD: 7, daclatasvir and asunaprevir: 1, glecaprevir and pibrentasvir: 15, sofosbuvir-based: 27) were enrolled. Selection of DAAs was based on genotype, patient characteristics, potential drug to drug interaction profiles and insurance reimbursement criteria.
Results: Mean age of patients was 42.1 ± 10.3 years, 92% of them was male, 20% have cirrhosis and 18% failed to previous IFN. Genotype distribution was as follows: 1a: 7, 1b: 22, 2: 14, 3: 1, and 6: 6. Baseline HCV RNA level was 6.53 ± 0.9 $\log_{10}$IU/mL. After DAAs, the distribution of week 4 HCV RNA was as follows: undetectable (< 15 IU/mL): 17 (89.5%) and 15 to 50 IU/mL: 2 (10.5%), respectively. Subjective and laboratory adverse events were generally mild and no patients early terminated therapy. End-of-treatment virological response was 100% and all 50 patients (100%) achieved SVR_{12} after post-treatment follow.
Conclusion: For HIV and HCV coinfection patients, which identified as a difficult-to-treat population by IFN-based therapy in the past with unmet medical needs, highly effective treatment response and well tolerability were achieved by all oral DAAs.

Abstract #1492

Hepatitis B and C Care in the opiate substitution setting—an integrated nursing model of care

Vincenzo Fragomeli

Background: Despite the availability of effective curative therapies for hepatitis C virus (HCV) in the form of Direct Acting Antivirals (DAA's) and viral suppressive therapies for hepatitis B virus (HBV), to date only a minority of infected patients attending an Opiate Substitution Therapy (OST) clinic have received treatment. Historically, attendees of these clinics have been reluctant to access viral hepatitis services and have often been termed "difficult to access/treat."
Model of care/intervention: Although current treatment guidelines suggest that active drug use should not preclude people from HCV treatment, uptake of therapy thus far has been low to say the least. Many barriers contribute to the low uptake of HCV/HBV treatment among OST patients and people who inject drugs (PWID) . Traditional means of managing HCV/HBV infection, that is, referral to a secondary or tertiary health centre, to date has proven to be an ineffective model for providing assessment and treatment options for this patient population. This paper will describe the creation and functioning of a multidisciplinary, nurse-led model of care that integrates viral hepatitis screening, assessment and treatment into the OST/PWID setting.
Conclusion/effectiveness: This nursing model of care has been effective in enhancing access to HBV/HCV services among the marginalized OST and PWID. This dynamic and innovative nursing model of care has facilitated improved access to viral hepatitis assessment and treatment for historically "difficult to access" patients.

Abstract #1524

Outcome of hepatitis C treatment

A. Samad

Introduction: Hepatitis C infection has a high prevalence in Pakistan.Treatment with direct acting antivirals is highly efficacious, but costly.In this study, we have enrolled patients with low socioeconomic status and treating them free of cost with combination of sofosbuvir, daclatasvir with or without ribavirin.
Objective: To determine the outcome of Hepatitis C treatment with direct acting antiviral therapy.
Methods: This is a retrospective study conducted in the outpatient department of Hepatology at Patel Hospital Karachi from 1st October to 31st December 2018. Sofosbuvir and daclatasvir with ribavirin was given to cirrhotic patients (Child class B and C), whereas non cirrhotic patients and Child A cirrhotic patients were treated with sofosbuvir and daclatasvir for a total duration of 12 weeks. Treatment outcome was assessed by checking rapid virological response (RVR), sustained virological response (SVR) at 12 weeks after completion of therapy and any treatment associated adverse effects.Results:A total of 100 patients received hepatitis C treatment during the study period.Out of these patients,63 were females and 37 were males.The mean age of patient was 41.62 (± 3.75).19 patients were cirrhotic.In cirrhotic,there were 6 Child A (31.5%),9 Child B (47.36%) and 4 Child C patients (21.05%).84 patients were treatment naïve,while 16 had experienced interferon treatment before. RVR was achieved in 96 patients out of 100 and SVR was achieved in 94 patients.Two patients developed ribavirin induced hemolysis managed conservatively. Conclusion:Hepatitis C treatment using combination of sofosbuvir and daclatasvir with or without ribavirin is highly efficacious.In resource limited setting, this combination is a good alternative to pangenotypic regimens.

Abstract #1532

AHFC therapy for controlling hepatic-fibrosis regression: descriptive study

Andri Sanityoso Sulaiman [1,2]

[1]Internal Medicine Department, Cipto Mangunkusumo Hospital Faculty of Medicine Universitas Indonesia, [2]Klinik Hati Prof. Ali Sulaiman, Jakarta, Indonesia

Introduction: Fibrosis is the end result of chronic inflammatory reactions induced by a variety of stimuli including persistent infections, autoimmune reactions, allergic responses, chemical insults, radiation, and tissue injury. Advances in the understanding of the cellular and molecular basis of hepatic fibrogenesis over the past 2 decades have allowed the emergence of a field dedicated to anti-

fibrotic therapy. AHFC is an extract of 10 defined herbs having the main ingredients such as: Salvia miltiorrhiza and Astragalus membranaceous and has showed its capability to reduce the incidence of complications in chronic hepatitis patients by blocking the development of fibrosis and preventing the emergence of it.
Objectives: To assess the efficacy and safety of AHFC consumption in patient with Fibrosis.
Methods: A retrospective case series was conducted among 22 patients receiving AHFC treatment in Prof. Sulaiman Liver Clinic. The liver stiffness was assessed by using Transient Elastography (TE).
Results: The average length of AHFC consumption among 22 patients was 3 $\pm$ 1.4 years. The study also found that there was significant decreasing of fibrosis level after treatment (32.2 kPA to 12.6 kPA, $p < 0.001$) that showed the presence of AHFC reaction towards controlling liver stiffness. In addition, the average patient experienced decreased levels of SGOT (p 0.02) and SGPT (p 0.53). Increased albumin value (p 0.008) and decreased levels of bilirubin also experienced by patients (p 0.62). Also, CHE score increased after therapy (p 0.001).
Conclusion: These results indicate that AHFC treatment could increase albumin levels and reduce bilirubin levels in fibrosis patients.

Abstract #1552

Novel virus isolation method and nested-PCR protocols to identify NS5A-ISDR/PKR-BD mutations of HCV genotypes 1a, 3, and 4 in Indonesian patients with HCV-HIV coinfection

Juferdy Kurniawan[1], Rino Alvani Gani[1], Samsuridjal Djauzi[1], Anugrah Dwi Handayu[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Hepatitis C virus (HCV) mutation in nonstructural protein 5A (NS5A)-interferon sensitivity determining region (ISDR)/ protein kinase R-binding domain (PKR-BD) is associated with improved outcomes in mono-infected patients treated with pegylated-interferon/ribavirin. Study analyzing NS5A-ISDR/PKR-BD of HCV genotypes 1a, 3, and 4 in patients with HCV-human immunodeficiency virus (HIV) coinfection has not been done in Indonesia.
Objectives: This study was done to establish a novel virus isolation method and nested—polymerase chain reaction (PCR) protocols to identify NS5A-ISDR/PKR-BD mutations of HCV genotypes 1a, 3, and 4 in Indonesian patients with HCV-HIV coinfection.
Methods: Plasma samples were obtained from treatment-naïve HCV-HIV coinfected patients from January to November 2018. Samples with HCV RNA $> 1 \times 10^4$ IU/mL were analyzed. Ribonucleic acid (RNA) was extracted from plasma and analyzed using spectrophotometer. RNA template underwent reverse transcription-PCR to produce NS5A region complementary deoxyribonucleic acid (cDNA). cDNA was amplified through nested-PCR. Amplification results were analyzed by electrophoresis and documented. All amplicons were purified and sequenced with direct nucleotide sequencing.
Results: 21 plasma samples were studied. Total concentration of RNA was 114–286 ng/μL and purity in the ratio 260/280 was 3209–3769. Clean and visible electrophoregrams that cover the entire NSA5A-ISDR/PKR-BD were obtained. Compared with GeneBank's consensus sequence, alignment of sequencing is AF009606, HQ912957, and AFN53800 for HCV genotype 1a, 3, and 4 respectively.
Conclusion: NS5A-ISDR/PKR-BD mutations of HCV genotypes 1a, 3, and 4 in HCV-HIV coinfected Indonesian patients can be identified through the novel virus isolation method and nested-PCR protocols established in this study.

Abstract #1557

Disentangling the life-spans of hepatitis C virus infected cells and intracellular vRNA replication-complexes during direct acting antiviral therapy

E. Fabian Cardozo[1], Dong Ji[2], George Lau[2,3], Raymond F. Schinazi[4], Guo-feng Chen[2], Ruy M. Ribeiro[5,6], Alan S. Perelson[5]

[1]Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA, [2] The Fifth Medical Center of Chinese PLA General Hospital (302 Hospital)-Hong Kong Humanity and Health Hepatitis C Diagnosis and Treatment Centre, Beijing, China, [3]Humanity and Health Clinical Trial Center, Humanity & Health Medical Group, Hong Kong SAR, China, [4]Center for AIDS Research, Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA, [5]Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, NM, USA, [6]Laboratório de Biomatemática, Faculdade de Medicina da Universidade de Lisboa, Portugal

Background: The decay rate of hepatitis C virus (HCV) infected cells during therapy had been used to determine the duration of treatment needed to attain a sustained virologic response, but with direct acting antivirals (DAA) this rate was difficult to estimate. Here we showed that it was possible to estimate it, by simultaneously analyzing the viral load and alanine aminotransferase (ALT) kinetics during combination DAA therapy.
Methods: We modeled the HCV RNA and ALT serum kinetics in 26 patients with chronic HCV genotype 1b infection, under four different sofosbuvir based combination treatments.
Results: In all patients, ALT decayed exponentially to a set-point in the normal range by 1–3 weeks after initiation of therapy. The model indicates that the ALT decay rate during the first few weeks after initiation of therapy reflects the death rate of infected cells, with an estimated median half-life of 2.5 days in this patient population. This information allows independent estimation of the rate of loss of intracellular replication complexes during therapy. Our model also predicts that the final ALT set-point is not related to the release of ALT by dying HCV infected cells.
Conclusions: Using ALT data, one can separately obtain information about the rate of "cure" of HCV infected cells versus their rate of death, something not possible when analyzing only HCV RNA data. This information can be used to compare the effects of different DAA combinations, and to rationally evaluate their antiviral effects.

Abstract #1586

Sofosbuvir-based regimen is effective and safe for HCV Genotype 6 in Hainan Island of China: a real world study

Tao Wu[1,2], Jiao Wang[1,2], Biao Wu[1,2], Ming Liu[1,2], Jun Ge[1,2], Furong Xiao[1,2], Feng Lin[1,2]

[1]Department of Infectious Disease,Hainan General Hospital, [2]Hainan Affiliated Hospital of Hainan Medical University

Background and objective: Our previous studies have shown that 6a is the main subtype in the distribution of HCV genotypes in Hainan Island of China, and it is not rare to find other subtypes of HCV genotype 6 and special unidentified virus strains . At present, the pan genotype drugs in small molecule antiviral drugs (DAA) are mainly

based on sofa and GP, which have achieved good results in the treatment of common HCV genotypes (including 1a / 1b / 2a). However, there are few reports in the real world on the treatment of other subtypes of HCV genotype 6 and special unidentified virus strains. In this study, we focused on the real world study of Sofosbuvir-based regimen for HCV genotype 6 in Hainan Island of China.
Methods: The sera of 32 patients with chronic hepatitis C with HCV genotype 6 from January 2018 to October 2019 were sequenced to determine the genotype. None of these patients had cirrhosis. They were treated with SOF based regimens (SOF + RBV for 24 weeks or SOF / VEL for 12 weeks), and HCV-RNA / liver function were detected during the treatment (4 W) / at the end of the treatment / after the treatment (12 Weeks) to evaluate the virological response. This article mainly carries on the retrospective research to the above patient data.
Results: The distribution of HCV genotypes in 32 patients with chronic hepatitis C was as follows: 22 patients were 6a, 2 patients were 6 W, 2 patients were 6 V, 6 patients were unclassified genotypes. HCV-RNA was not detected in all patients (24 weeks of SOF + RBV or 12 weeks of SOF / VEL) during the treatment (4 W) / at the end of the treatment / after the treatment (12 W), suggesting that all patients had a good virological response.
Conclusion: Sofosbuvir-based regimen can not only get high response rate in the treatment of HCV 6a subtype, but also get good virological response to the rare epidemic gene subtype and special virus strain in HCV genotype 6.

Genotype	N	DAAs(n)	ETVR(%)	SVR12(%)	Combined disease (n)	Drugs (n)
6a	22	SOF+RBV 24W: 6 SOF/VEL 12W:16	100(22/22)	100(22/22)	No 11 1kind 5 2kinds 3 3kinds 3	No 18 1kind 4
6w	2	SOF/VEL 12W:2	100(2/2)	100(2/2)	0	
6v	2	SOF/VEL 12W:2	100(2/2)	100(2/2)	0	
undetermined genotypes	6	SOF/VEL 12W:6	100(6/6)	100(6/6)	0	
Total	32	SOF+RBV 24W: 6 SOF/VEL 12W:26	100(32/32)	100(32/32)	No 11 1kind 5 2kinds 3 3kinds 3	No 18 1kind 4

Abstract #1616

Comparison of hepatitis B & C disease burden in Asia Pacific and global

H. Razavi, S. Blach, E. Dugan, C. Estes, I. Gamkrelidze, R. Dunn, D. Razavi-Shearer

Center for Disease Analysis Foundation, Lafayette, Colorado, USA

Introduction: Globally, hepatitis B & C represent a large burden, and an understanding of the regional burden is needed to develop regional strategies for hepatitis elimination to achieve the WHO 2030 elimination targets.
Objective: Quantify the burden of HBV and HBV in Asia Pacific and how the region is performing relative to the rest of the world.
Method: Data from the Polaris Observatory was aggregated for Asian Pacific countries (APAC) and compared to the global estimates.
Results: 67% of all HBV infections are in APAC with 82% of all diagnosed cases and 92% of all treated patients residing in the region. 52% of all HCV infections are in APAC with 43% of all diagnosed and 47% of all treated patients residing in the region. 74% of all HBV and 54% of all HCV liver related deaths are in APAC. While APAC accounts for 53% of all births globally, 69% of HBV birth dose vaccinations and 55% of all 3 dose vaccinations are in APAC. China, India, Indonesia and Philippines account for most of HBV infections in the region and globally. China, Pakistan, India, Bangladesh and Indonesia account for most of HCV infections.
Conclusion: Globally, the APAC region is ahead of global averages for HBV diagnosis, treatment and vaccination. However, HCV cascade of care lags behind global averages. Although HBV vaccination has brought down HBV incidence in the region, diagnosis and treatment are way below the required levels to achieve the WHO 2030 hepatitis elimination targets.

Abstract #1627

Comparison end of treatment response of hepatitis C patients at Saiful Anwar Hospital in Malang

Somarnam[1], Bogi Pratomo[2], Syifa Mustika[2], Supriono[2]

[1]Resident of Internal Medicine, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia, [2]Gastroenterohepatology Division, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia

Introduction: Hepatitis B infection is a major public health concern. Little is known about the knowledge status among hepatitis B patients in Indonesia.
Background: The latest therapy using Direct Acting Antiviral (DAA) gives hope for better recovery. This study want to see how the end of treatment response (ETR) of hepatitis C patients in Malang.
Method: Design of this study is cross-sectional survey, sampling of patients receiving hepatitis C therapy at Saiful Anwar Hospital Malang. Collection of medical record data is carried out from December 2017 to February 2018. Statistical analysis using poison tets and Chi Square test with significance $p < 0.05$. Data is processed using SPSS version 16.
Results: The study sample was 106 patients, each treatment regimen carried out the Poison Test to see the significance of the success of therapy with the results of 35 patients who received a combination of Sofosbufir-Daclatasvir (p: 0.000), 6 patients with Sovosbufir-simeprevir (p: 0.014), 5 patients Sofosbuvir + Ribavirin (p: 0.014), 6 patients with Sofosbuvir-peginterferon-ribavirin (p: 0.025) and 54 patients with Pegilated Interveron + Ribavirin therapy (p: 0.000). From each of these regimens were then divided into 3 groups and Chi square tests were performed with the results: Combination of two DAA (Sofosbuvir-Daclatasvir or Sofosbuvir-Simeprevir) compared to one DAA + Non DAA (Sofosbuvir-Ribavirin or Sofosbuvir-PegIFN-Ribavirin) p: 0.601, two DAAs compared to non DAA (PegIFN-Ribavirin) p: 0.743, and one DAA + non DAA therapy compared to non DAA p: 0.517. There is no difference in ETR between Hepatitis C patients treated with a combination of Two DAAs, One DAA+ non DAA and non DAA therapy.
Conclusion: Each treatment regimen shows good ETR.

Abstract #1630

APRI Score Analysis in C Hepatitis Patients Achieving SVR with DAA Treatment in RSSA

Bobi Sewow[1], Reni Ary[1], Supriono[2], Syifa Mustika[2], Bogi Pratomo[2]

[1]Participants in the Internal Medicine Specialist Medical Education Program in Brawijaya University, [2]Consultant of Gastroenterohepatology Division, Lab / SMF Internal Medicine, FK Brawijaya University Malang-RSUD Dr. Saiful Anwar Malang

Introduction: C Hepatitis virus infection is one of the main causes of chronic liver disease. Patients who use DAA experience higher Sustained Virological Response (SVR), shorter duration of treatment, easy use orally and fewer side effects. APRI score is one of the

noninvasive serological tests to assess the degree of easy and validated liver fibrosis.
Objective: The inclusion criteria were patients aged > 18 years, with all stages of fibrosis and cirrhosis, naïve patients or who had previously undergone treatment, completed and completely underwent treatment with DAA (Sofosbuvir-Daclatasvir).
Method: This study was an observational analytic cross sectional approach at Dr. Saiful Anwar Malang, the sample in this study was taken by purposive sampling, in the period of 2015–May 2019.
Results: Analysis of APRI scores with characteristic data revealed a decrease in mean APRI scores in the cirrhosis group of patients ($1.0111 \pm 1.27 \rightarrow 0.4568 \pm 0.52$), the results were not statistically significant with the P value 0.103.
Conclusion: There was a decrease in APRI scores in patients infected with HCV who had achieved SVR with DAA treatment in RSSA Malang.

Abstract #1632

Therapy with direct acting antivirals in chronic hepatitis C is associated with reduction in hepatic fibrosis on LSMs and noninvasive fibrosis indexes

Xiaojing Liu[1], Xiaocui An[1], Lei Shi, Xi Zhang, Xueliang Yang, Yunru Chen, Feng Ye, Shumei Lin

Department of Infectious Diseases, the First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, China

Backgrounds and aims: Hepatitis C virus (HCV) infection is a major public health problem worldwide. Direct acting antivirals (DAAs) therapy is currently the main treatment for patients with chronic hepatitis C virus (CHC). However, the liver fibrosis is still a key determinant of disease progression in patients with cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma. Due to the invasive nature of liver biopsy, we have applied non-invasive fibrosis indices such as aspartate aminotransferase/platelet ratio index (APRI), FIB-4 and liver stiffness measurements (LSMs), which has evolved to assess the stage of hepatic fibrosis. The antiviral efficacy and dynamic changes of hepatic fibrosis stage in Chinese patients with CHC treated with DAAs are limited. The purpose of this study was to investigate the changes of LSMs and non-invasive fibrosis indexes in patients with CHC after DAA treatment.
Methods: 254 patients with hepatitis C virus infection admitted to the first affiliated Hospital of Xi'an Jiaotong University from January 2018 to May 2019 were studied. All patients were newly diagnosed and then treated with DAA antiviral treatment. HCV RNA levels were measured at baselines, 4 weeks, 8 weeks, end of therapy, and then 12 weeks after the completion of DAA treatment, HCV genotype and biochemical parameters (ALT, AST, ALB, TBIL) were detected at the same time. Transient elastography is used to measure LSMs at baseline and the end of DAAs treatment.
Results: (1) A total of 254 patients with CHC were included, with an average age of 54.17 ± 12.12 years, of whom 54.17% were women. The distribution of HCV genotypes in 254 patients was: 1b (56.9%), 2a (35.7%), 3b (3.7%), undetectable genotype (3.7%). (2) The patients in the group were given DAAs drugs according to the HCV genotype, including Sofosbuvir (SOF) and Daclatasvir (DCV), which accounted for 51.99%, Sofosbuvir-based combination of ribavirin (RBV), accounting for 1.9%, Sofosbuvir/velpatasvir (SOF/VEL) in 24.1%, Paritaprevir/Ritonavir-Ombitasvir combined with Dasabuvir united in 11.1%, Elbasvir/Grazoprevir in 11.1%. (3) The average level of hepatitis C virus RNA at baseline is 6.21 ± 0.80 $\log_{10}$IU/ml, the non-detection rate of HCV RNA was 100% at 4 weeks and the end of treatment. The SVR rate was 100% at 12 weeks after the completion of DAA treatment. (4) The average platelet count increased at 12 weeks after the completion of DAA treatment compared with baseline ($p = 0.032$). The ALT levels decreased significantly at the 12 weeks after the completion of DAA treatment compared to Baseline ($p < 0.001$). (5) The average APRI decreased from 2.1 (0.26–16.85) at baseline to 0.26 (0.26–5.37) at 12 weeks after the completion of DAA treatment ($p = 0.004$). The same trend was found in FIB-4 and LSMs, decreased from 4.40 (0.35–21.48) to 3.07 (0.32–18.26) and 15.78 ± 8.85Kpa to 10.42 ± 6.33Kpa respectively, compared at baseline with at 12 weeks after the completion of DAAs treatment ($p < 0.001$).
Conclusions: DAAs antiviral therapy has a high curative effect on patients with chronic hepatitis C. It can not only effectively control hepatitis C virus, but also improve the degree of hepatic fibrosis and help reduce the incidence of cirrhosis and hepatocellular carcinoma.

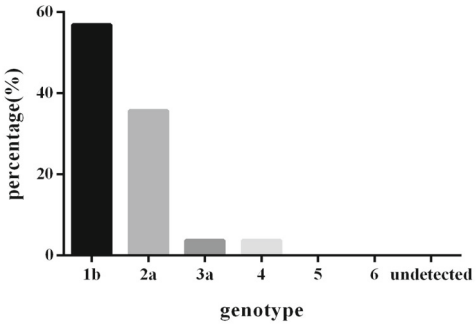


Figure1: Genotype Distribution

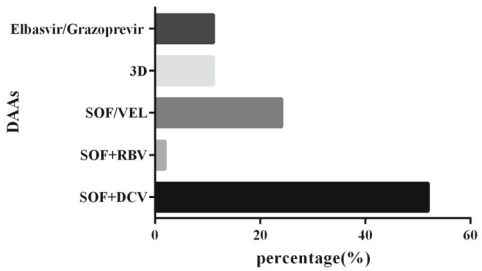


Figure 2: DAAs Distribution

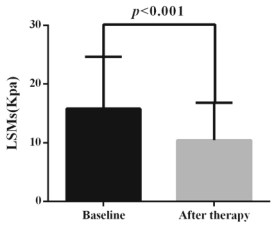


Figure 3: LSMs at baseline and at 12 weeks after completion of therapy in chronic hepatitis C patients treated with DAAs

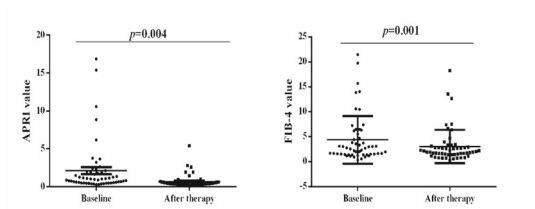


Figure 4: APRI value and FIB-4 value at baseline and at 12 weeks after completion of therapy in chronic hepatitis C patients treated with DAAs

Abstract #1639

Real world experience of treating hepatitis c patients with generic DAAs and minimal investigations in a resource limited country

Shoukat Ali Samejo

Introduction: With the availability of pan genotypic treatment it is possible to cure hep c in more the 90% of patients. In our country genotype is genotype 3 in about 80% patients which is consider to be difficult to treat we hereby share our real experience for treating hepatitis C patients with minimal investigations.
Methods: Anti HCV positive pt visiting the liver clinic were further evaluated by complete blood count, liver function test, HCV RNA qualitative, u/s abdomen and fib 4 score. Patients were classified into different category: (1) treatment naïve without cirrhosis patients. (2) Treatment naïve pt with cirrhosis. (3) Treatment experienced pt without cirrhosis. (4) Treatment experience with cirrhosis. (5) Patient with decompensated liver disease. Treatment offer to these patients were sofosbuvir + daclatasvir and ribavirin for 12 to 24 weeks, sofosbuvir + velpatasvir with and without ribvarin for 12 to 24 weeks. The decision of duration and addition of ribavirin was made according to the previous treatment status and fib 4 score. The qualitative PCR was repeated at the end of 12 weeks post treatment period.
Results: Total number of patients were 225, The mean age of presentation was 46 ± 12.66, and most (84.9%) were treatment naïve with and without cirrhosis. 66.7% (150/225) were male and 33.3% (75/225) were female. Patients were treated in groups, 112 patients were treatment naïve without cirrhosis, 79 patients were treatment naïve with cirrhosis, 15 patients were treatment experienced without cirrhosis, 19 patients were treatment experience with cirrhosis and 70 patients were decompensated liver disease. Sustained virolgical response was seen in 95% group, 112 treatment naïve without cirrhosis patients were achieved SVR, 78/79 treatment naïve with cirrhosis patients achieved SVR, 31/34 treatment experienced patients with or without cirrhosis were achieved SVR. Patients non serious adverse event leading to hospitalization. Patients who did not achieve SVR were treatment experience 1.3% (3/225) patients. The cost of DAAs for hepatitis C treatment, who were treated with sofosbuvir+daclatsvir+ribavirin for 12 and 24 week was 39$ and 77$ respectively. The cost of DAAs for hepatitis C treatment, who were treated with Sofosbuvir+Velpatasvir ± Ribavirin for 12 or 24 weeks was 145$ and 290$ respectively.
Conclusion: Low cost treatment with generic DAAs is effective in treating hepatitis c patients in resource constraint countries with comparable.

Abstract #1645

Successful hemostasis of duodenal variceal bleeding with N-butyl-2-cyanoacrylate Injection in a cirrhotic patient with massive upper GI bleeding: a case report

Carlos Paolo D. Francisco[1], Zcharmaine Yumang[2], Roxanne Mae Butal[2], John Pangilinan[2]

[1]Institute of Digestive and Liver Diseases, St. Luke's Medical Center – Bonifacio Global City, Taguig City, Metro Manila, Philippines,
[2]Institute of Digestive and Liver Diseases, St. Luke's Medical Center – Quezon City, Metro Manila, Philippines

Introduction: Duodenal variceal bleeding is a rare cause of gastrointestinal (GI) bleeding in patients with liver cirrhosis. It accounts for 1%-5% of all gastrointestinal bleeding in patients with portal hypertension with a mortality rate of up to 40%. In these cases, expeditious decision making on its management should be done to improve patient prognosis.
Clinical presentation: We report a case of a 57 year old male diagnosed with liver cirrhosis secondary to chronic hepatitis C complicated by alcoholic liver disease who was admitted due to episodes of hematochezia resulting to hypovolemic shock..
Management: Intravenous fluid resuscitation and somatostatin IV infusion were given. After achieving a stable hemodynamic status, upper GI endoscopy was done which showed esophageal and gastric varices with gastric lumen filled with clotted blood. A large duodenal varix at the D3 junction with a spurting vessel was seen upon further advancement of the gastroscope. Complete hemostasis was achieved after deploying a hemoclip and N-butyl-2-cyanoacrylate injection (Histoacryl®) directly into the duodenal varix. No bleeding recurrence noted on serial follow-up.
Recommendations: Due to the rarity of this case, no treatment guideline has been established yet and the choice of treatment modality should be individualized based on the location of varices, patient's condition, extent of disease and facilities available.

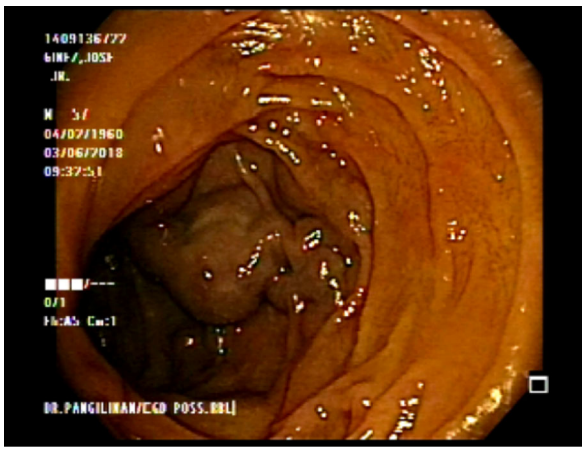


Figure 1. Large intestinal varix at the D3 junction

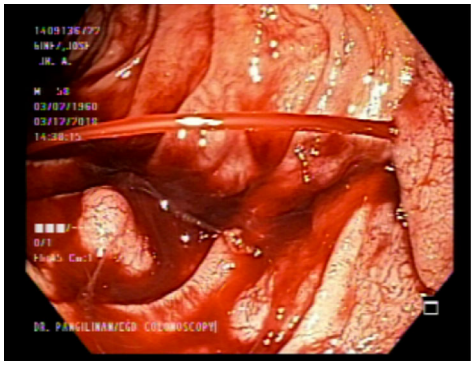


Figure 2A. Large, tortuous varix at the D3 segment, spurting with blood

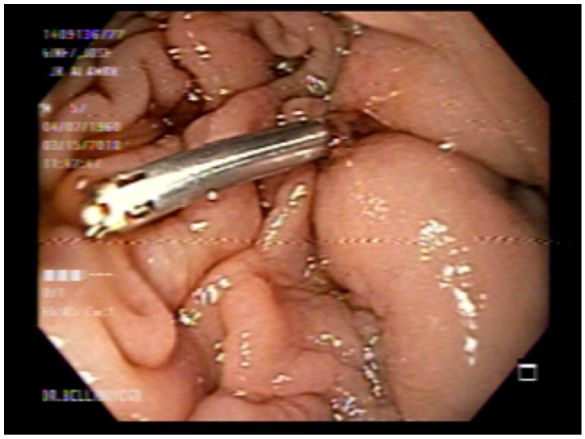


Figure 2B. deployment of a hemoclip

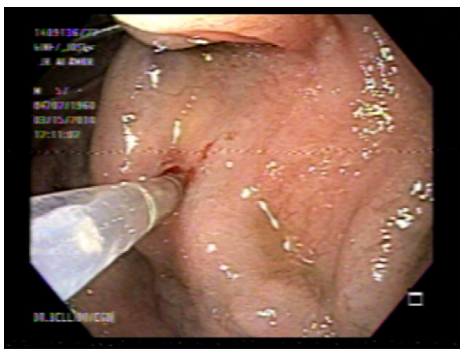


Figure 3. N-butyl-2 cyanoacrylate (Histoacryl ®) injection into the varix.

Abstract #1661

Surgical resection for hepatocellular carcinoma in patients with chronic hepatitis C virus infection: a Chinese multicenter experience

Hao Xing[1], BA Li-Yang Sun[1,2], Lei Liang[1], Chao Li[1], Ming-Da Wang[1], Ya-Hao Zhou[3], Wei-Min Gu[4], Hong Wang[5], Ting-Hao Chen[6], Yong-Yi Zeng[7], Meng-Chao Wu[1], Feng Shen[1], Tian Yang[1]

[1]Department of Hepatobiliary Surgery, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, China, [2]Department of Clinical Medicine, Second Military Medical University, Shanghai, China, [3]Department of Hepatobiliary Surgery, Pu'er People's Hospital, Yunnan, China, [4]The First Department of General Surgery, the Fourth Hospital of Harbin, Heilongjiang, China, [5]Department of General Surgery, Liuyang People's Hospital, Hunan, China, [6]Department of General Surgery, Ziyang First People's Hospital, Sichuan, China, [7]Department of Hepatobiliary Surgery, Mengchao Hepatobiliary Hospital, Fujian Medical University, Fujian, China

Background and aims: There are very few studies on surgical resection for HCC in patients with HCV infection from China. Based on a multicenter database, we aimed to analyze clinical characteristics, short-term and long-term prognosis after HCC resection in Chinese patients with chronic HCV infection.

Methods: The records of all patients with HCV infection who underwent curative resection for initial HCC between 2004 and 2015 were reviewed. Perioperative mortality and morbidity, long-term overall survival (OS) and recurrence-free survival (RFS) were evaluated.

Results: Of the enrolled 382 patients, nearly half (46.1%) did not know their history of HCV infection before HCC diagnosis, and only 14.6% had received anti-HCV therapy before surgery. The 30-day morbidity and mortality were 44.8% and 2.9%, respectively. The 5-year OS and RFS rates were 45.0% and 34.4% respectively. Multivariable analyses showed that concurrent HBV infection, portal hypertension, tumor size $>$ 5 cm, macrovascular and microvascular invasion, and none of postoperative anti-HCV therapy were independently associated with OS, while concurrent HBV infection, preoperative AFP level $>$ 400ug/L, tumor size $>$ 5 cm, multiple tumors, and macrovascular and microvascular invasion were independently associated with RFS after curative resection for HCC in patients with chronic HCV infection.

Conclusions: The proportion of patients with HCV infection receiving anti-HCV therapy is low in China. Although perioperative morbidity and mortality are acceptable, the long-term outcomes are unsatisfactory, which may be related to high concurrent HBV infection rate, aggressive liver- and tumor-related characteristics, and low proportion of postoperative anti-HCV therapy.

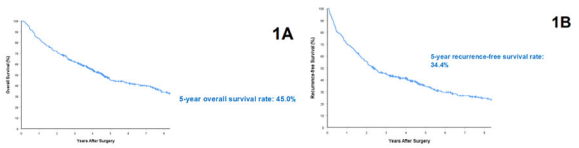


FIGURE 1. Overall survival (A) and recurrence-free survival (B) curves in patients with chronic HCV infection after curative liver resection for hepatocellular carcinoma

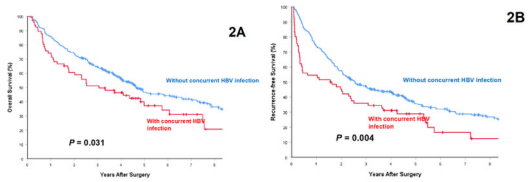


FIGURE 2. Comparisons of overall survival (A) and recurrence-free survival (B) curves in patients with chronic HCV infection after curative liver resection for hepatocellular carcinoma between patients with and without concurrent HBV infection

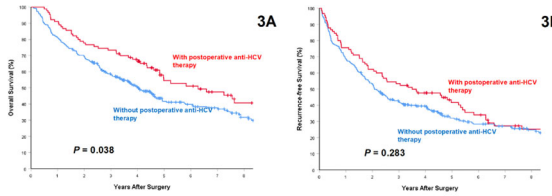


FIGURE 3. Comparisons of overall survival (A) and recurrence-free survival (B) curves in patients with chronic HCV infection after curative liver resection for hepatocellular carcinoma between patients with and without postoperative regular anti-HCV therapy

Abstract #1675

PIVKA-II additional marker for HCC detection in HCV-infected patients after SVR in resource-limited setting

Sargsynats Narina[1]

[1]Infectious Diseases, Elit-Med Medical Centre, Yerevan, Armenia

Introduction: Despite success is considered a major breakthrough in HCV therapy, there have been several alarming reports of increased incidence of HCC in patients who achieved SVR with oral DAAs. Management of HCC in resource-limited countries is huge challenge. US was less effective for detecting early-stage HCC, with a sensitivity of only 63%.
Objectives: HCC biomarkers should be used only for risk-assessment of HCC development. PIVKA-II (Protein Induced by Vitamin K Absence or Antagonist-II) or DCP (Des-γ-carboxy-prothrombin) in combination with AFP as an early biomarker of HCC for risk stratification.
Methods: 50 HCV-infected patients with F3 (22%) and F4 (78%) from 33 to 73 years old (70% male, 56.0 ± 9.1 years old, BMI 27.6 ± 5.9 kg/m2, treated with DAA-contain regimens with/without IFN (4/45). AFP checked in all patients (normal ≤ 8.78 ng/mL). PIVKA-II checked in patients with elevated AFP or liver nodules on US. Serum levels of PIVKA-II were measured using the chemiluminescent assay of the Architect 1000i System, Abbott with cut of < 50.9mAU/mL.
Results: AFP in average 15.2 ± 3.7 ng/mL (range 1.4–135.3) was elevated in 42% of patients. In majority of patients, AFP decreased after antiviral therapy. HCC suspected in 10 patients with F4 (90% male) despite SVR, in 5 patients diagnosis conformed, in 2 – rejected by dynamics of AFP, PIVKA-II and Imaging. Data concerning HCC suspected patients in Tab 1 with dynamics of AFP and PIVKA-II.
Conclusions: Despite SVR, awareness to HCC development is mandatory in all patients with F3-F4. Serum levels of PIVKA-II in combination with AFP and imaging technics can help in early detection of HCC.

Table 1. Main characteristics of the patient with SVR with/without HCC and dynamics of AFP and PIVKA-II

Patient	Age	BMI	Geno-type	Fibrosis	Co-morbidities	Previously treated	DAA	AFP, ng/mL			PIVKA-II, mAU/mL	
								before	SVR 12	repeated	first	repeated
1.	58	36	3	F4 (Child-Pugh A)	obesity, metabolic syndrome, dyslipidemia, NAFLD, alcohol abuse	Experienced	PEG-IFNα-2a +RBV+SOF	8.56	5.08	20.55/ 76.7/ 441.37/ 74.64/ 2446.81	**577.18**	**1080.26/ 988.49/ 164.27/ 353.41**
2.	58	34	1b	F4 (Child-Pugh A)	obesity, alcohol abuse	Naive	SOF/LDV+ RBV	26	51.6	77308	**95658**	-
3.	52	34	1b	F4 (Child-Pugh B)	alcohol abuse	Naive	SOF/LDV	4.2	3.3	2.76	**100226. 28**	-
4.	52	18	3	F4 (Child-Pugh B)	alcohol abuse	Naive	SOF+DCV+ RBV	9.31	4.97	13.46	**243.28**	**2387.06**
5.	64	33	1	F4 (Child-Pugh A)	diabetes, obesity, psoriasis, vitiligo, metabolic syndrome, NAFLD, alcohol abuse	Experienced	ambitasvir/ paritaprevir /ritonavir+ dasabuvir (3D)	-	5.83	6.87	**56.80**	**51.70**
6.	49	25	1	F4 (Child-Pugh A)	anti-HBc+, with testicular cancer, radiation 7-8 years ago, acute pancreatitis 6-7 years ago	Naive	SOF/LDV	54.47	2.44	1.19	**36.6**	-

Abstract #1679

Vitamin D deficiency in patients with chronic liver diseases

Sargsyants Narina

Elit-Med Medical Center, Yerevan, Armenia

Introduction: According to recent studies vitamin D has immunomodulatory, anti-inflammatory and anti-fibrotic activities. In patients with chronic liver diseases, especially in patients with liver cirrhosis serum 25-hidroxyvitamin D [25 (OH)D] deficiency or insufficiency are quiet common. There is no consensus on serum required levels of 25 (OH)D in patients with chronic liver diseases; most experts suggest deficiency less than < 20 ng/ml and insufficiency 20–30 ng/ml.
Objectives: The aims of this report is evaluation of Vitamin D deficiency and insufficiency in patients with chronic liver diseases.
Methods: Vitamin D-25OH level was checked in 47 patients (55.3% male) from 32 to 70 years old (49.7 ± 9.4), BMI 30.4 ± 6.5 kg/m^2. Among them 23 patients with NAFLD, 25 patients with chronic hepatitis C (53.2%), 2 with autoimmune live disease involved in the study. For evaluation of Vitamin D-25OH we use by Immunochemical assays analyzed on Abbott Architect i-2000 Statistical analysis was done by SPSS11.0.
Results: Diabetes mellitus had 32% of patients, 43% had obesity, 26% overweight. Vitamin D-25OH 12.2–73.1 nmol/L (35.0 ± 15.5); 21 patients had level less 30 ng/ml, 6 of them (12%) – less than < 20 ng/ml and 15 patients (30%) 20–30 ng/ml. Among them 13 patients with low level had HCV-infection (62%), majority with advanced fibrosis/cirrhosis (8 with F4, 1 with F3). In patients with NAFLD without HCV-infection 7 had deficiency of Vitamin D-25OH and one female patients with NASH-cirrhosis/diabetes had insuffiency.
Conclusions: Deficiency of Vitamin D-25OH revealed in 12% of patients with chronic liver diseases and insufficiency – in 30%. Low level of Vitamin D-25OH observed mainly in patients with HCV-cirrhosis.

Abstract #1742

Direct acting antiviral (DAA) resistance in a low-resource setting with high burden of hepatitis C infection: a case series

H. Hassaan Zahid[1], Elin Hoffman Dahl[2],Khawar Aslam[1], Nasir Hassan Luck[3]

[1]Medical Department, Médecins Sans Frontières, Pakistan, [2]Medical Department Médecins Sans Frontières, Norway, [3]Department of Gastroenterology and Hepatology, Sindh Institute of Urology and Transplantation

Globally, approximately 71 million people are living with Hepatitis C virus (HCV) infection and Pakistan bears 10% of this burden. The advent of Direct Acting Antivirals (DAAs) has revolutionized the treatment of HCV, opening the door to the ambitious World Health Organization HCV infection elimination strategy by 2030. However, emerging resistance to DAAs may jeopardize achieving these targets. We present a case series of nine patients with treatment failure to first-line treatment regimens, all of whom were found to have Resistance Associated Substitutions (RAS). To avoid the spread of refractory HCV within the existing epidemic, we call for improved access to pan-genotypic, second- and third line DAAs in high-burden low- and middle-income countries.

Abstract #1766

The role of secondary structure transformation of NS5A region and virological response in patients coinfected with HCV-HIV with Peg-IFN/RBV therapy

Juferdy Kurniawan[1], Rino Alvani Gani[1], Samsuridjal Djauzi[1]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Hepatitis C virus-human immunodeficiency virus (HCV-HIV) coinfected patients are suspected to have mutations particularly associated with the secondary structure transformation of nonstructural protein 5A (NS5A)-interferon sensitivity determining region (ISDR)/protein kinase R-binding domain (PKR-BD), that plays a role in successfulness of pegylated interferon and ribavirin (Peg-IFN/RBV) therapy.
Objectives: This study was done to determine the presence and role of the secondary structure transformation of HCV NS5A-ISDR/PKR-BD mutation and host single nucleotide polymorphism (SNP) interleukin 28B (IL-28B) on the successfulness of Peg-IFN/RBV therapy in HCV-HIV coinfected patients.
Methods: Prospective cohort was performed in this study. Plasma samples were collected from 134 subjects with HCV-HIV co-infection prior to therapy. All of them were treated with Peg-IFN/RBV for 48 weeks. The examination of HCV RNA was performed 24 weeks after the end of therapy to assess treatment response (sustained virological response/SVR).
Results: In genotype 1a, there is no significant association between the secondary structure transformation of NS5A-ISDR/PKR-BD with SVR in patients with HCV-HIV coinfection (p = 1.00). The secondary structural transformation is found in the NS5A protein in 21 patients out of 30 patients (70%), but this does not affect the therapeutic response. Bivariate analysis in this study found no significant association between SNP IL-28B polymorphism and HCV NS5A mutation associated secondary structure transformation (p = 0.43). The structure of the NS5A HCV binding site in non-SVR HCV-HIV coinfected patients does not differ greatly from consensus (wild type), whereas the structure of the binding site in patients that achieve SVR is different from consensus.
Conclusion: Transformation in protein secondary structure was not associated with SVR achievement in coinfected patients, but changes in binding site structure were found in HIV-HCV coinfected patients who achieved SVR.

Abstract #1772

REAL C-long term outcomes impact of SVR on HCC incidence in real-world chronic hepatitis C (CHC) patients: results of the REAL-C registry from Hong Kong, Korea, Japan and Taiwan

Yasuhito Tanaka[1], Hidenori Toyoda[2], Dae Won Jun[3], Masaru Enomoto[4], Chung-Feng Huang[5], Eiichi Ogawa[6], Satoshi Yasuda[2], Etsuko Iio[1], Shinji Iwane[7], Hiroaki Haga[8], Chia-Yen Dai[5], Grace Wong[11], Dong-Hyun Lee[12], Hirokazu Takahashi[7,13], Jee-Fu Huang[5], Hansen Dang[14], Mayumi Maeda[14], Ramsey Cheung[14,15], Yoshiyuki Ueno[8], Yuichiro Eguchi[7], Jun Hayashi[16], Norihiro Furusyo[6], Akihiro Tamori[4], Takashi Kumada[2], Ming-Lung Yu[5], Mindie Nguyen[14], For the REAL-C Investigators

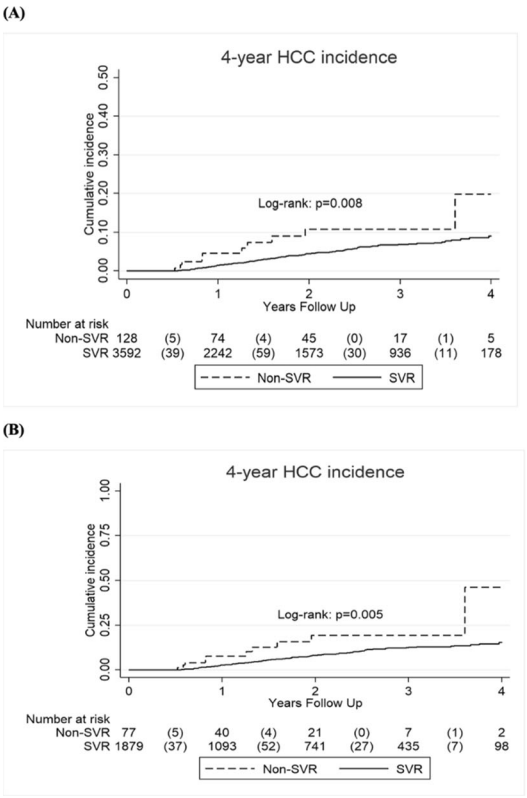
[1]Department of Virology and Liver Unit, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan, [2]Department of Gastroenterology, Ogaki Municipal Hospital, Ogaki, Japan, [3]Department of Gastroenterology, Hanyang University, Seoul, South Korea, [4]Department of Hepatology, Osaka City University Graduate School of Medicine, Osaka, Japan, [5]Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [6]Department of General Internal Medicine, Kyushu University Hospital, Fukuoka, Japan, [7]Liver Center, Saga University Hospital, Saga, Japan, [8]Department of Gastroenterology, Yamagata University Faculty of Medicine, Yamagata, Japan, [9]Department of Internal Medicine, Hanyang University College of Medicine, Guri Hospital, Guri, South Korea, [10]Department of Internal Medicine, Inje University Haeundae Paik Hospital, Busan, South Korea, [11]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, [12]Department of Gastroenterology, Good Gang-An Hospital, Busan, Korea, [13]Division of Metabolism and Endocrinology, Saga University Faculty of Medicine, Saga, Japan, [14]Division of Gastroenterology and Hepatology, Department of Medicine, Stanford University Medical Center, Palo Alto, CA, USA, [15]Division of Gastroenterology and Hepatology, Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA, [16]Kyushu General Internal Medicine Center, Haradoi Hospital, Fukuoka, Japan

Background: DAA update in Asia is more recent than in the West and long-term outcome data of treated patients are more limited. We aimed to compare cumulative HCC incidence in IFN-free DAA-treated East Asians who achieved SVR (SVR group) with those who did not (non-SVR group).
Methods: Patients were recruited from the multinational REAL-C registry of IFN-free DAA treated CHC Asians (immunosuppressed and co-infected cases excluded). We estimated HCC incidence (HCC within 6 months of DAA initiation excluded) using Kaplan-Meier methods and examined factors associated with HCC using multivariable Cox regression modeling.
Results: We analyzed 3744 patients: 132 non-SVR and 3612 SVR patients. Non-SVR patients were more likely cirrhotic and had higher AFP but similar to SVR patients in regards to age, sex, genotype (1 vs. non-1), and CPT class. SVR patients had lower 4-year cumulative HCC incidence rates than the non-SVR group: 9.1% vs 19.8%, p = 0.008 in total cohort and 15.5% vs 46.3%, p = 0.005 among the

cirrhotic subgroup (Figures). In unadjusted analysis, SVR, age, baseline cirrhosis and AFP were significantly associated with HCC but not sex and diabetes. In multivariable analysis (adjusted for age, baseline cirrhosis and AFP), SVR was significantly associated with a 58% reduction in HCC incidence (adjusted hazard ratio = 0.42, 95% CI 0.22–0.81, $p = 0.010$).

Conclusion: SVR was independently and strongly associated with lower risk of HCC development in East Asians. However, the post-SVR risk for HCC is still notable, especially in cirrhotic patients, highlighting the need for continued surveillance of high-risk patients after SVR.

Figure 1. Four-year HCC incidence (A) Overall cohort (B) Cirrhotic patients who achieved SVR or failed to achieve SVR with DAAs



Abstract #1828

Correlation of platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio with virological response in chronic hepatitis C patients treated with sofosbuvir and daclatasvir

D.N. Adriana[1], W. Metacita[1], B. Widodo[2], I.A. Nusi[2], P.B. Setiawan[2], H. Purbayu[2], T. Sugihartono[2], U. Maimunah[2], U. Kholili[2], H. Thamrin[2], A. Vidyani[2], M. Miftahussurur[2]

[1]Residents of Internal Medicine Department, Universitas Airlangga, Dr.Soetomo General Academic Hospital, Surabaya, Indonesia, [2]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Universitas Airlangga, Dr.Soetomo General Academic Hospital, Surabaya, Indonesia

Introduction: Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Lymphocyte Ratio (NLR) are two important systemic inflammatory biomarkers. Both PLR and NLR are immune response-related indicators. Chronic Hepatitis C (CHC) itself is an inflammatory liver disease and its high degree of chronicity associated with disorders of immune function. The association of PLR and NLR with Direct Acting Antivirals (DAAs) treatment outcomes however has not yet been established.

Objectives: The aim of this study was to evaluate the clinical value, virological response in particular, of the PLR and NLR in CHC patients treated with DAAs (Sofosbuvir-Daclatasvir) in order to provide new indicator parameters for CHC treatment.

Methods: A total of 31 naïve patients with CHC were enrolled to this cohort prospective study by total sampling from February to April 2019. All subjects were then treated with Sofosbuvir-Daclatasvir regimen for 12 or 24 weeks depending on the cirrhosis. Sustained Virological Response (SVR) by PCR HCV RNA was then evaluated in 12 weeks after end-of-treatment.

Results: From all 31 subjects, 23 subjects were treated for 12 weeks while 8 subjects received 24 weeks treatment due to cirrhosis. Only 5 subjects did not achieve SVR-12 (non-SVR) and all of them were subjects with cirrhosis. Based on Lambda correlation test we found that both NLR and PLR have strong significant correlations with SVR in CHC patients (p = 0.0.015, r = 1.00; p = 0.0.015, r = 1.00 respectively).

Conclusions: Both NLR and PLR are closely related to the virological response in CHC patients and therefore might be used as indicator parameters for CHC treatment.

Abstract #1829

Platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio as a predictor of liver fibrosis in chronic hepatitis C

R.A. Hakim[1], W. Mettacita[1], B. Widodo[2], I.A. Nusi[2], P.B. Setiawan[2], H. Purbayu[2], T. Sugihartono[2], U. Maimunah[2], U. Kholili[2], H. Thamrin[2], A. Vidyani[2], M. Miftahussurur[2]

[1]Resident of Internal Medicine Department, Universitas Airlangga – Dr.Soetomo General Academic Hospital, Surabaya, Indonesia, [2]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Universitas Airlangga, Dr.Soetomo General Academic Hospital, Surabaya, Indonesia

Introduction: Liver fibrosis is one of the complications of Chronic Hepatitis C (CHC). Liver biopsy remains the gold standard for fibrosis despite being invasive. Transient elastography using FibroScan is one of the noninvasive approaches despite its limitations. Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Lymphocyte Ratio (NLR) are easily accessible systemic inflammatory markers obtained from complete blood count. These ratios have been evaluated as noninvasive diagnostic tools of hepatic fibrosis.

Objectives: The aim of this study was to evaluate the clinical value of the PLR and NLR in naïve CHC patients in order to provide new indicator parameters for the degree of hepatic fibrosis.

Methods: A total of 31 naïve patients with CHC were enrolled to this cross-sectional study by total sampling from February to April 2019. Degree of hepatic fibrosis, reflected by liver stiffness measured with transient elastography (FibroScan) and complete blood count were obtained from all subjects. Statistical computation was done using statistics software SPSS version 17.

Results: Blood samples were drawn from all 31 subjects to calculate the PLR and NLR, and all subjects underwent transient elastography (FibroScan) to determine the degree of liver stiffness. Based on Spearman's rho analysis we found that PLR correlated with liver stiffness (p = 0.0012; r = − 0.446), while NLR was not found to correlate with degree of liver stiffness (p = 0.058; r = 1.00).

Conclusion: There is a weak correlation between PLR and the degree of hepatic fibrosis, as reflected by liver stiffness measured with transient elastography; while NLR does not show significant correlation with the degree of hepatic fibrosis.

Abstract #1846

Promoting recognition of hepatitis-positive patients contributes to higher notification and referral rate

Yuki Haga

Background: Screening for Hepatitis B virus antigen (HBsAg) and Hepatitis C virus antibody (HCVAb) is usually performed before patient admission, invasive examinations, and operations. In our medical center, test results are given to the attending doctors who ordered the tests. The results can be viewed by all the departments, but not all doctors appropriately deal with these test results; thus, not all patients who test positive for hepatitis are properly followed-up.
Methodology: Our center's hepatologists comprehensively listed all the patients who tested positive for hepatitis and provided recommendations in their medical records for hepatology referral, if necessary.
Results: From August 2018 to September 2019, 193 patients were found to be HBsAg positive and 248 patients were HCVAb positive. Among them, 25 HBsAg positive patients and 85 HCVAb positive patients were newly recognized or not followed-up appropriately. Within 3 months after recording recommendations, head doctors noticed that 72 cases tested positive for hepatitis and referred 36 cases to hepatologists. Despite the recommendations, no change was observed in the medical records in 38 cases.
Discussion: Physicians who identify hepatitis-positive patients should provide appropriate medical care depending on the cirrhotic and carcinogenic risk of the patients. Hepatologists should guide those who test positive for hepatitis to receive appropriate follow-up. Adding reminders in medical records of patients allows doctors from departments other than hepatology, to give proper follow-up to patients.

Abstract #1851

Correlation of HCV RNA titers and biochemical markers with liver fibrosis in hepatitis C infection

San Rio Tonapa*, Nu'man AS Daud, Fardah Akil, Muhammad Luthfi Parewangi, Rini Rachmawarni Bachtiar, Susanto H Kusuma, Amelia Rifai

Centre of Gastroenterology-Hepatology HAM Akil/DR.Wahidin Sudirohusodo General Hospital, Division of Gastroenterology-Hepatology, *Department of Internal Medicine, University of Hasanuddin, Makassar-Indonesia

Introduction: A variety of biological makers are useful for clinical outcome and monitoring of hepatitis C virus chronic (CHC) infection. Different blood-based parameters have been found could reflect the extent of liver damage as an alternative to liver biopsy. In CHC patients, the relation between serum biochemical markers, HCV RNA titers and histological liver injury remain controversial.
Objectives: To investigate the correlation between HCV RNA titers and biochemical markers with degree of liver fibrosis in CHC patients.
Methods: This cross-sectional study using 122 HCV patients between year 2017–2018. Demography and laboratory (biochemical/virology) data were collected. Grading of liver fibrosis divided into F0F1/F2F3/ $>$ F3: no or mild fibrosis/significant fibrosis/advance fibrosis or cirrhosis (by Fibroscan-TE). One-way ANOVA and Pearson's correlation coefficient test with logistic regression analysis were calculated ($p < 0.05$ significant).
Results: Of them 31 (25.4%)/25 (20.5%)/66 (54.1%) had liver fibrosis grading F0F1/F2F3/ $>$ F3 respectively. Median of laboratory data: PLT 192.5 $\times$ 10^3/mm3, alanine aminotransferase (ALT)/aspartate aminotransferase (AST) 49.5/46U/L, albumin 3.8 g/dl, billirubin 0.7 mg/dl, HCV-RNA 5.8$\log_{10}$IU/ml, TE 11.6 kPa. Liver fibrosis grading were significantly correlated with ALT (coefficient-r:0.073,p = 0.018), AST (coefficient-r:0.330,p = 0.000), albumin (coefficient-r $-$ 0.272,p = 0.004) and bilirubin (coefficient-r:0.069,p = 0.003) levels but no correlation with HCV RNA titers (p = 0.576). It was observed that ALT/AST/bilirubin were higher with lower albumin levels in advance fibrosis as compared with the initial stage ($p < 0.05$). Logistic regression analysis revealed that AST and bilirubin level at diagnosis correlated with liver fibrosis grade (OR 3.806;95%CI:1.598–9.067;p = 0.002 and OR 14.524;95%CI:1.849–109.890; p = 0.000).
Conclusion: Our study suggests that AST/ALT/albumin/bilirubin correlate with liver damage and AST/bilirubin are independent risk factors of liver fibrosis in CHC.

Abstract #1898

Effectiveness of hepatitis C treatment within National "Roadmap on prophylaxis, diagnostics, treatment and prevention of consequences of viral hepatitis" in the Republic of Kazakhstan

Alexander Nersesov, Almagul Jumabayeva, Jamilya Kaibullayeva, Elmira Kuantay, Gulsana Nuraliyeva

Department of Gastroenterology, Asfendiyarov National Medical University, Almaty, Kazakhstan

Introduction: In accordance with National "Roadmap on prophylaxis, diagnostics, treatment and prevention of consequences of viral hepatitis" in the Republic of Kazakhstan (Roadmap), antiviral therapy (sofosbuvir and daclatasvir generics $\pm$ ribavirin) of chronic hepatitis C (CHC) is reimbursed since 2018 and its efficacy need to be evaluated.
Objectives: To characterize epidemiology, patient profile, and efficacy of antiviral therapy of CHC in Kazakhstan.
Methods: Retrospective and prospective study of virological status (genotype), liver disease stage (transient elastography) of all the registered patients with chronic hepatitis C and evaluation of sustained virologic response on week 12 (SVR) in all the patients treated within Roadmap since 2018.
Results: 28,415 patients with CHC are currently registered in Kazakhstan. 55% of them have 1b genotype, 35% and 10%—3 and 2 genotype respectively. 22% have stage F0 of liver disease, 20%—F1, 19%—F2, 14%—F3, 14%—F4/compensated cirrhosis, 1%—decompensated cirrhosis; in 10% of patients fibrosis stage is not defined. To the moment 15,389 patients have been treated or are on the treatment (sofosbuvir plus daclatasvir in F0-F3 stages and genotype 1 and 2 with F4/compensated cirrhosis, and sofosbuvir plus daclatasvir combined with ribavirin in decompensated cirrhosis and in genotype 3 with F4/compensated cirrhosis). SVR 12 was documented in 8094 from 8164 patients (99,1%), and 70 patients (0,9%) turned to be non-responders.
Conclusion: CHC is characterized by prevalence of 1b genotype, predominant F0-F2 disease severity and high SVR 12 rate (more than 99%) within National Roadmap in Kazakhstan.

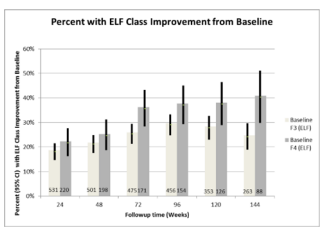
Abstract #1911

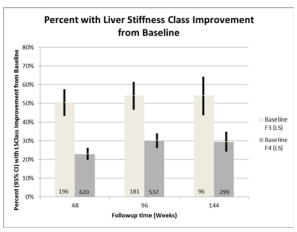
Long-term course of cirrhosis regression: lessons from patients with HCV cirrhosis following successful sofosbuvir-based treatment

I. Jacobson[1], A.J. Muir[2], E. Lawitz[3], E. Gane[4], B. Conway[5], P.J. Ruane[6], Z. Younes[7], F. Chen[8], M. Camargo[8], A. Chokkalingam[8], A. Gaggar[8], R.P. Myers[8], W.Y. Lu[8], B. Leggett[9], J.L. Calleja[10], K. Agarwal[11], K.R. Reddy[12], A. Mangia[13]

NYU Langone Health, New York, NY, USA, [2] Duke University, Durham, NC, USA, [3] Texas Liver Institute, University of Texas Health San Antonio, TX, USA, [4] New Zealand Liver Transplant Unit, Auckland City Hospital, Auckland, New Zealand, [5] Vancouver Infectious Diseases Centre, Vancouver, BC, [6] Ruane Medical & Liver Health Institute, Los Angeles, CA, USA, [7] GastroOne, Germantown, TN, USA, [8] Gilead Sciences, Inc., Foster City, CA, USA, [9] School of Medicine, University of Queensland, Brisbane, Australia, [10] Hospital Universitario Puerta de Hierro, Madrid, Spain, [11] Kings College Hospital NHS Trust Foundation, London, UK, [12] University of Pennsylvania, Philadelphia, PA, USA, [13] Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo, Italy

The aim of this study was to evaluate changes in noninvasive tests of fibrosis (NITs) to understand the natural history of cirrhosis regression following removal of the causative exposure.In this ongoing, prospective cirrhosis registry study, 1574 subjects with HCV cirrhosis who achieved SVR via sofosbuvir (SOF)-based regimens were enrolled. Routine assessments included semi-annual Child-Pugh-Turcotte (CPT) scoring and measurement of the Enhanced Liver Fibrosis (ELF) test, as well as annual liver stiffness measurement by transient elastography (LS by TE). Logistic regression was used to identify predictors of fibrosis improvement as defined by NITs.As of May 2019, median duration of follow-up was 123 weeks (IQR 96, 168). At week 144, 49% of those with baseline CPT class B/C had improved CPT class, while 98% of those with baseline CPT class A remained in CPT class A. During follow-up, changes in ELF and LS by TE suggested fibrosis improvement in an increasing proportion of patients with both F3 and F4 fibrosis at enrollment (Figure). ELF score improved by $\geq$ 0.5 units at week 144 in 27% and 47% of patients with baseline F3 (ELF 9.8–11.3) and F4 (ELF $>$ 11.3) fibrosis, respectively. Predictors of ELF improvement included higher ELF ($p < 0.001$) and AST ($p = 0.049$), and lower platelets ($p = 0.02$) and BMI ($p = 0.10$) at registry baseline. In patients with cirrhosis in whom HCV has been eradicated by SOF-based therapy, NITs suggest significant fibrosis improvement in 25–50% of patients within 3 years. Associations between reductions in these NITs and improvements in clinical outcomes require evaluation during longer-term follow-up.





Abstract #1937

Use of sofosbuvir and daclatasvir with or without ribavirin as an oral treatment option for cirrhotic patients with hepatitis C virus genotype 3 infection

Juferdy Kurniawan[1], Hikmat Pramukti[2]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Background: Hepatitis C virus (HCV) genotype 3 infection is a challenging disease in need of effective therapies. The combination of daclatasvir (DCV) and sofosbuvir (SOF) for 24 weeks, with or without ribavirin (RBV), is recommended for HCV genotype 3 infection with cirrhosis in several guidelines, but there are few empirical data comparing the effectiveness between those regimens.
Objectives: To compare sustained virological response at 12 weeks post treatment (SVR12) of hepatitis C genotype 3 cirrhotic patients treated with SOF-DCV-RBV or SOF-DCV.
Methods: Online search of PubMed, Google Scholar, and Cochrane databases yielded 1 relevant study. Clinical or cohort studies published within the last 5 years and written in English were included.
Results: 246 cirrhotic patients received antiviral treatment: 15.4% (38/246) SOF-DCV for 12 weeks, 2.8% (7/246) SOF-DCV-RBV for 12 weeks, 59.8% (147/246) SOF-DCV for 24 weeks, and 22% (54/246) SOF-DCV-RBV for 24 weeks. SVR12 was achieved in 83% (204/246) of patients. Patients receiving SOF-DCV-RBV for 12 weeks had lower SVR12 compared to patients receiving SOF-DCV for 24 weeks (57% vs 88%); meanwhile, patients receiving SOF-DCV-RBV for 24 weeks had similar SVR12 compared to patients receiving SOF-DCV for 24 weeks (83% vs 88%). SOF-DCV-RBV for 12 weeks and 24 weeks were associated with greater $\geq$ 1 serious adverse event compared to SOF-DCV for 24 weeks (25% and 21% vs 11%).
Conclusion: SVR12 was similar between both regimens; however, adding RBV was associated with serious adverse events. SOF-DCV for 24 weeks may be preferred for HCV genotype 3 infected patients with cirrhosis.

Abstract #2016

High SVR rates of elbasvir/grazoprevir in Thai patients with HCV genotype 1 infection

N. Chuaypen[1], S. Chittmittraprap[1], A. Avihingsanon[2], P. Tangkijvanich[1]

[1]Center of Excellence in Hepatitis and Liver Cancer, Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, Bangkok, 10330, Thailand, [2]The HIV Netherlands Australia Thailand Research Collaboration (HIV NAT), Bangkok, Thailand

Background: Elbasvir/grazoprevir is a new generation direct acting antiviral (DAA) for chronic hepatitis C virus (HCV) genotype 1.
Objectives: This study was aimed at assessing its efficacy in Thai patients with HCV mono- and HCV/HIV co-infection.
Method: Total 101 HCV genotype 1-infected patients (65 mono- and 36 co-infection) were recruited in a clinical trial. There were 80 treatment-naïve patients received elbasvir/grazoprevir for 12 weeks and 21 treatment-experienced patients treated with the combination plus ribavirin for 16 weeks. HCV RNA level $<$ 12 IU/mL was considered undetectable.
Results: There were 79 male and 22 females, with mean age of 46.2 and 48.7 years, respectively. Of them, 22 (19.8%) had baseline cirrhosis (defined by transient elastography $>$ 14.0 kPa). Overall

sustained virological response (SVR)12 and SVR24 rates were 98% and 95%, respectively. SVR12 rates in the mono- and co-infected groups were 98.5% and 97.2%, respectively, while the corresponding figures for SVR24 rates were 93.8% and 97.2%, respectively. The therapeutic effects were not related to factors such as age, sex, HIV status, previous HCV treatment, baseline HCV RNA level, duration of therapy and underlying cirrhosis.
Conclusion: Elbasvir/grazoprevir for 12 or 16 weeks, with or without ribavirin, was highly effective in Thai patients with HCV genotype 1.

Abstract #2034

HCV screening in three settings in the general population in Delhi, India: the HEAD-Start project

Ekta Gupta[1], Kavita Aggarwal[1], Reshu Agarwal[1], Archana Ramalingam[2], Babu Entoor Ramachandran[3], Sanjay Sarin[3], Jessica Markby[3], Sonjelle Shilton[3], Ankur Jindal[4], Manoj Kumar Sharma[4], Shiv Kumar Sarin[4], Sundeep Miglani[5]

[1]Department of Clinical Virology, Institute of Liver and Biliary Sciences (ILBS), New Delhi, India, [2]Department of Epidemiology, ILBS [3] Foundation for Innovative New Diagnostics (FIND) [4]Department of Hepatology, ILBS. [5]Directorate of Health Services, Government of National Capital Territory of Delhi

Introduction: An estimated 12–18 million people are infected with HCV in India, accounting for a significant proportion of the global HCV burden. The HEAD-Start Project in Delhi aimed to enhance HCV diagnosis and treatment pathways in the general population at District Hospitals, Polyclinics and screening camps.
Objective: To assess feasibility of decentralized Hepatitis C Virus (HCV) testing and treatment services.
Methods: HCV rapid diagnostic tests (RDTs) were used to screen the general population at 5 district hospitals, 15 polyclinics and 62 screening camps. Seropositive patients were referred to linked hospital for confirmatory testing and treatment. HCV prevalence, retention in the HCV care cascade and turn-around time were measured.
Results: Between January and September 2019, 38,853 patients were screened for HCV. Of those, 22,756 were screened at hospitals, 5774 at polyclinics, and 10,323 at screening camps. 49.9% were female and the mean age was 38.3 years (SD $\pm$ 14.6) with HCV risk factors including: 3.9% surgery, 2.3% MSM, 1.8% blood transfusion, 1.8% PLHIV, and 0.2% PWID. Of those screened, 2.2% (837) were seropositive and 86.7% (726) received confirmatory testing in a median time of 1 (IQR 0–2) days. Of the 626 (86.2%) patients with confirmed HCV infection, treatment was initiated in 506 (80.83%) patients in a median time of 8.5 (IQR 4–20) days. To date, 318 (62.85%) have completed treatment, with a 94.74% (126) cure rate among 133 tested for SVR.
Conclusion: This hub and spoke model of decentralized HCV care provision at point of care (PoC) proved to be effective in resource limited Indian scenario. Introduction of a simplified testing algorithm resulted in a higher yield and better retention.

Abstract #2069

Serum ferritin and aspartate aminotransferase to platelet ratio index as markers for liver fibrosis based on *Transient Elastography* in patients with chronic hepatitis C virus

Poernomo Boedi Setiawan[1], Muhammad Bagus Rizkiyanto[2], Iswan Abbas Nusi[1], Herry Purbayu[1], Titong Sugihartono[1], Ummi Maimunah[1]

[1]Gastroenterohepatology Division, Department of Internal medicine, Universitas Airlangga – Dr.Soetomo Teaching Hospital, Surabaya, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga – Dr.Soetomo Teaching Hospital, Surabaya, Indonesia

Introduction: Hepatitis C virus (VHC) infection is one of the leading causes of chronic liver disease worldwide, lead to severe fibrosis complications. Liver fibrosis is a dynamic procedure that results from an irregularity between fibrogenesis and fibrolysis. After time this procedure can lead to cirrhosis of the liver. VHC infection impaired hepcidin regulation, changes iron metabolism, indicated by an increase in serum ferritin levels. Some studies link the condition of impaired iron deposition in the liver with the degree of fibrosis. AST to Platelet Ratio Index (APRI) score is the most common used to assess indirectly the degree of liver fibrosis.
Objective: To analyze correlation between serum ferritin levels and APRI score with liver fibrosis, based on *transient elastography* in chronic hepatitis C patients.
Methods: A cross-sectional observational analytic study carried out during May–September 2019. 30 patients fulfilled the inclusion and exclusion criteria. Ferritin examination carried out at the beginning of the examination. APRI score were calculated. Data analysis used spearman correlation test.
Results: Significant correlation was found between serum ferritin levels and APRI score liver fibrosis with liver fibrosis with value of r: 0.759 and 0.601 conscutively ($p < 0.01$).
Conclusion: There is a positive correlation between serum ferritin levels and APRI score with liver fibrosis based on *transient elastography* in chronic hepatitis C patients.

Abstract #2124

Mortality related to hepatitis C treatment in hepatitis B+C coinfection: a case report

Ahmet Uyanikoglu, Mehmet Onder Ekmen

Harran University, Medical Faculty, Gastroentrology, Sanliurfa, Turkey

Introduction: HBsAg may be positive in 2–10% of anti-HCV positive patients. In the literature, in HBV + HCV co-infection treatment-related reactivation has been reported. We present a patient who developed fulminant hepatitis B reactivation during HCV treatment.
Case: A 64-year-old female patient was followed up with HBV + HCV co-infection in an external center, dasabuvir, ombitasvir, paritaprevir, ritonavir treatment for HCV, 2 months ago. When transaminases and bilirubin were found to be high in the second month of therapy. In the physical examination he had mild disorientation, flapping tremor (+) and grade I encephalopathy. Hemogram was normal, ALT: 2000 IU, AST: 2500 IU, total bilirubin: 20 mg / dl, direct bilirubin: 9 mg / dl, INR: 2. HBsAg: positive, anti HBc-IgM: negative, and anti-HCV: positive. Hepatobiliary ultrasonography, liver size was increased, and perihepatic fluid was present. She was internalized in the internal intensive care unit and entecavir 0.5 mg 1

× 1 and supportive therapy was started. Following: ALT: 2700 IU, AST: 3386 IU, total bilirubin: 27 mg / dl, direct bilirubin: 11.7 mg / dl, INR: 6.37, blurred consciousness, encephalopathy deepened (grade 3 encephalopathy). As the patient was preparing for emergency liver transplantation, her vitals worsened. On the second day of follow-up was exıtus.

Conclusion: HCV treatment planned each patients should be screened for HBV and should be considered oral antiviral prophylaxis against HBV if necessary. In HBV + HCV co-infection, fulminant hepatitis B reactivation may develop during hepatitis C treatment and mortality as in our patient.

Abstract #2166

Treatment efficacy and safety of sofosbuvir/velpatasvir for chronic hepatitis C among uremic patients under maintenance hemodialysis-an interim report of ERASE-C

Ming-Lung Yu, Chung-Feng Huang, Yu-Ju Wei, Ming-Lun Yeh, Ching-I Huang, Wen-Yi Lin, Yi-Hung Lin, Po-Cheng Liang, Ta-Wei Liu, Chia-Yen Dai, Jee-Fu Huang, Wan-Long Chuang

Background/aims: Hepatitis C virus (HCV) prevails in uremic patients in Taiwan. However, treatment uptake is underappreciated in the special population. The current study aimed to address the efficacy and tolerability of sofosbuvir (SOF)/velpatasvir (VEL) in treating chronic hepatitis C (CHC) patients in the HD units.

Methods: An outreach treatment strategy using 12-week SOF/VEL was adopted in 18 hemodialysis units.

Results: A total of 105 CHC uremic patients were included (mean age 66.2 years, female 48.6%, hepatitis B virus dual infection 7.6%, pre-existing hepatocellular carcinoma 6.7%, liver decompensation 0.9%). By the end of October 2019, the rate of undetectable HCV RNA at treatment week 1, week 2, week 4, end-of-treatment (EOT) and post-treatment 4 weeks (SVR4) was 46.7% (49/105), 72.4% (76/105), 90.5% (95/105), 93.3% (98/105) and 91.0% (91/100), respectively, in full-analysis-set population, and was 48.4% (44/91), 74.7% (68/91), 95.6% (87/91), 100% (90/90) and 100% (88/88), respectively, in modified full-analysis-set population. There was no relapse between EOT and SVR4 assessment. Ten patients discontinued therapy before the end-of-treatment. Of them, 5 were considered treatment related (dizziness [n = 1], nausea/vomiting [n = 2], epigastric pain [n = 2]), whereas the other 5 serious adverse events were unrelated to treatment regimen (sepsis [n = 3], acute myocardial infarction [n = 1] and pneumonia [n = 1]). The most common adverse event was fatigue (9.3%), followed by pruritus (8.4%).

Conclusions: 12 weeks of SOF/VEL was highly effective in uremic CHC patients in the interim analysis. A satisfactory final treatment outcome may be anticipated in the full patient set.

Table 1. Patient characteristics and safety profile of the 105 uremic patients

Patient characteristics	
Age, years (mean±SD)	66.2±10.0
Female, n (%)	51 (48.6)
BMI, kg/m^2 (mean±SD)	23.5±4.3
Hemodialysis duration, years (mean±SD)	8.9±8.5
Diabetes, n (%)	65 (61.9)
Hypertension, n (%)	75 (71.4)
HBsAg (+), n (%)	8 (7.6)
PWID history, n (%)	3 (2.9)
Major Thalassemia, n (%)	3 (2.9)
Hemophilia, n (%)	1 (1.0)
AST, IU/L (mean±SD)	25.4±14.7
ALT, IU/L (mean±SD)	24.3±15.2
r-GT, U/L (mean±SD)	53.5±78.2
Platelet count, x10^{3}u/L (mean±SD)	175.7±67.5
Albumin, g/dl (mean±SD)	3.7±0.3
Total bilirubin, mg/dL (mean±SD)	0.4±0.2
HCV RNA, logIU/mL (mean±SD)	5.6±1.2
HCV genotype, 1/2/6/unclassified, n (%)	46 (43.8)/53 (50.5)/5 (4.8)/1 (1.0)
FibroScan, kPa (mean±SD)	9.2±4.2
>9.5 kPa, n (%)	32 (30.5)
Liver cirrhosis, n (%)	22 (21.0)
Child-Pugh A, n (%)	21 (19.6)
Child-Pugh B, n (%)	1 (0.9)
Hepatocellular carcinoma, n (%)	7 (6.7)
Safety profiles	
DAA adherence, n (%)	
<20 %, n (%)	4 (3.8)
20-40 %, n (%)	1 (0.9)
40-60 %, n (%)	(3.8)
60-80, n (%)	4 (3.8)
>80 %, n (%)	92 (87.9)
Early treatment termination, n (%)	10 (9.5)
Treatment related*, n (%)	5 (4.8)
Not treatment related†, n (%)	5 (4.8)
Adverse event, n (%)	67(63.8)
Fatigue, n (%)	10 (9.5)
Pruritus, n (%)	9 (8.6)
Nausea, n (%)	7 (6.7)
Anorexia, n (%)	8(7.6)
Epigastric pain, n (%)	7(6.7)
Constipation, n (%)	7(6.7)
Rash, n (%)	6 (5.7)
Dizziness, n (%)	6(5.7)
Insomnia, n (%)	5(4.8)
Headache, n (%)	5 (4.8)

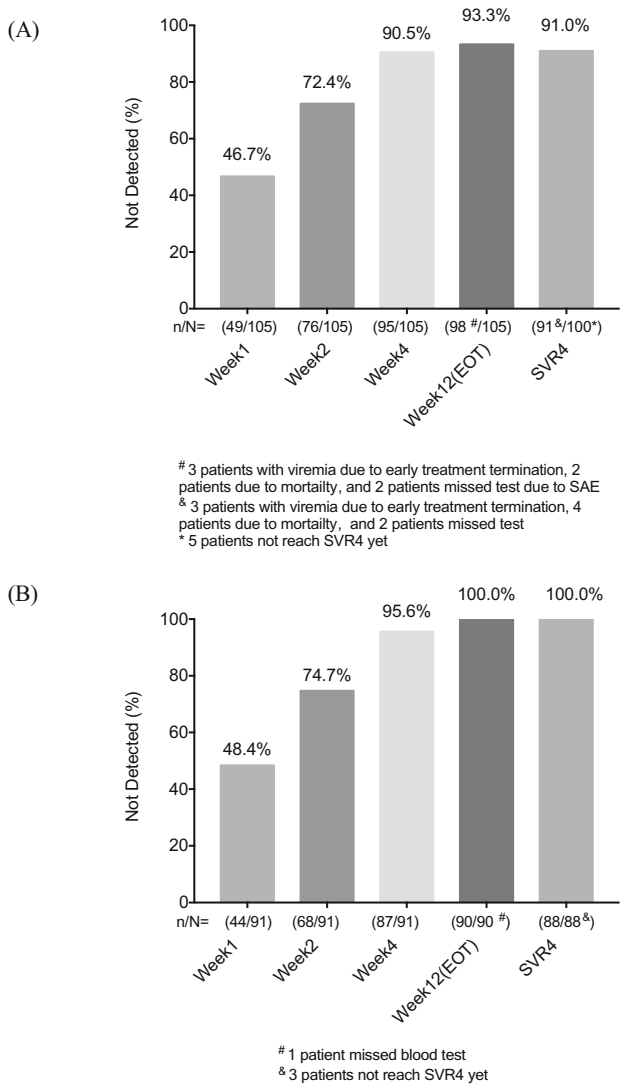


Figure. Treatment responses of the 105 uremic patients, (A) FAS; (B) mFAS

Abstract #2171

Hepatitis C infection is associated with high skin sympathetic nerve activity

Shu-Ling Chang[1], Mu-Chun Cheng[1], Tien-Chi Huang[1], Shien-Fong Lin[2], PhD Wen-Ter Lai[1], Chia-Yen Dai[3,4,5], Ming-Lung Yu[4,5], Wei-Chung Tsai[1]

[1]Division of Cardiology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [2]Institute of Biomedical Engineering, National Chiao-Tung University, Hsin-Chu, Taiwan, [3]Department of Community Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [4]Division of Hepatology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [5]Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

Introduction: Hepatitis C virus (HCV) infection was associated with extra-hepatic manifestations including autonomic dysregulation. Direct-acting antiviral therapy (DAA) is effective in treating HCV infection. neuECG is an innovative method to evaluate autonomic function by measuring skin sympathetic nerve activity (SKNA).
Objective: To test the hypothesis that SKNA is increased in patients with HCV infection and reduced after successful DAA.
Methods: We recorded neuECG in 21 patients with HCV infection and 89 controls. The neuECG recordings were made from conventional electrocardiogram in Lead I (SKNA-I) and right neck (SKNA-N). The data were then bandpass filtered between 500 and 1000 Hz to display SKNA. Data were analyzed to determine the average SKNA (in μV) per digitized sample during baseline, stress and recovery phases.
Results: The SKNA-I at baseline and recovery phases were 1.28 ± 0.58 and 1.18 ± 0.48 μV in HCV group, which were higher than 0.85 ± 0.29 ($p < 0.001$) and 0.91 ± 0.35 ($p = 0.002$) μV, respectively, in the controls. After adjusting for age, gender, diabetes, dyslipidemia and hypertension, HCV infection was independently associated with increased SKNA at baseline (β = 0.489, 95% CI 0.294–0.694) and recovery phases (β = 0.360, 95% CI 0.155–0.551). Regarding the DAA effect, SKNA before and after successful HCV eradication by DAA was recorded in 8 HCV patients. The baseline SKNA-N was reduced from 1.03 ± 0.31 to 0.69 ± 0.16 μV ($p = 0.025$) after DAA therapy.
Conclusion: HCV infection is independently associated with high SKNA at baseline and recovery phases. The high SKNA induced by the HCV infection could be reversed by successful HCV eradication via DAA.

Abstract #2194

Enhance leadership amongst the HCV community members to strengthen national HCV program

Qafarian Mehrdad

Project Manager, IP & Access to Medicine Project, The Delhi Network of Positive People (DNP+) Organization, Delhi, India

Introduction: According to the Indian Association for Study of Liver, in India alone, there are around 8 million people chronically infected with HCV, out of which 0.7% are in Viremia and require immediate attention. The data indicate an urgent need for government's intervention with the support of community-based networks to create an enabling environment for testing and treatment.
Objectives: Considering the current scenario, the government of India geared up to eradicate this epidemic by 2030 in India and as the first milestone to achieve, the government launched the National Viral Hepatitis Control Program (NVHCP) on the 28th 2018 with three guidelines as Operational Guidelines, Diagnosis and Management Guidelines and the Laboratory Testing Guidelines. However, the government cannot meet the needs of the hour alone without the community's approach.
Methods: Like HIV, a community-led approach is needed to sustained demand and an improved environment for simplified diagnostics and treatment of HCV through intensifying community's engagement and strengthen the capacity of HCV activists at national, and sub-national levels.
Conclusion: The strengthened community will advocate for better diagnostics and treatment of HCV at different levels including at the grassroots, depending on the requirement. Knowledge alone by the Government is not sufficient, and can only be transferred into power, only when combined with action and unity of the community!

Abstract #2213

A real-world study: efficacy of SOF combined with RBV in the treatment of chronic hepatitis C in Guangzhou population

Zhang Chunlan, Feng Qianchang, Xu Min, Li Jianping

Department of Liver Disease, Guangzhou the Eighth People's Hospital, Guangzhou Medical University, Guangzhou City, Guangdong Province, China 510060

Introduction: China is a high-incidence area for chronic infection of HCV, there is a total people of about 10 million. HCV infection is highly chronic and the onset is concealed. It is one of the important causes of active hepatitis, cirrhosis and hepatocellular carcinoma. If not treated in time, 15% to 30% of patients will progress to cirrhosis within 20 years.
Objectives Since the introduction of the first generation of direct-acting antiviral agents (DAAs) in 2011,anti-HCV treatment has shifted from IFN-based regimens to full oral drug regimens.This study investigated the efficacy and safety of Sofosbuvir (SOF) combined with Ribavirin (RBV) in the treatment of chronic hepatitis C in 30 patients from the real world of Guangzhou (multiple chronic disease and predominantly genotype 6a).
Method: 30 chronic hepatitis C (CHC) patients combined chronic diseases were analyzed retrospectively, who took treatment of SOF combined with RBVfor 12–24 weeks and followed-up for 12–24 weeks from outpatient between December 2017 and July 2019. Virological response at end of treatment(ETVR)and sustained virologicalresponse (SVR) were observed at the 12-week follow-up after drug withdrawal.
Result: The genotype, ETVR, SVR12, combined diseases and drugs in 30 patients with CHC are shown in Table 1.20 cases were received complicated 1 to 3 kinds of drugs, no drug-drug interaction (DDI) occurred.
Conclusion: SOF combined with RBV treatment is effective (100%) in the real-world multiple combined diseases and predominantly 6a genotype in Guangzhou, and it is safe.

Table. 1 The genotype, ETVR, SVR12, combined diseases and drugs in 30 patients with CHC

Genotype	N	ETVR（%）	SVR12（%）	Combined disease (n)	drugs(n)
6a	11	100 (11/11)	100(11/11)	5 kinds	5kinds
1b	9	100 (9/9)	88.89 (8/9)	5 kinds	5 kinds
2a	8	100 (8/8)	100(8/8)	3 kinds	3kand
3a	1	100 (1/1)	100 (1/1)	1 kind	1 kind
3b	1	100 (1/1)	100 (1/1)	1 kind	1 kind
Total	30	100(30/30)	96.67(29/30)	1 kind(16) 2kinds(3) 3kinds(1)	1 kind(16) 2kinds(3) 3kinds(1)

Abstract #2235

Efficacy and safety of sofosbuvir and daclatasvir regiments in chronic kidney disease

Andri Sanityoso Sulaiman[1,2]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Klinik Hati Prof. Ali Sulaiman. Jakarta, Indonesia

Introduction: The rapid development of hepatitis C anti-viral drugs has led to the discovery of a new class of anti-virus, namely Direct Acting Antivirals (DAA), an anti-viral agent that works directly in the replication phase of the hepatitis virus. However, some contraindications or special attention need to be given to the management of DAA-based therapies, especially related to liver and kidney function. In this case, any sofosbuvir-based regimen is not recommended if there is a condition of kidney failure with eGFR $<$ 30 ml / min / 1.73m2.
Objectives: This study aimed to review the efficacy and safety of sofosbuvir and daclatasvir regiments in Chronic Kidney Disease.
Methods: Literature searching was conducted by using database Pubmed, Scopus, dan Cochrane. The keywords, inclusion criteria were also applied. The selected article was appraised to discuss the validity, importance, and applicability, which led to four relevant articles.
Results Akhil, et al. (2018) study found out of 22 patients with genotype 3, 72.72% attained sustained SVR12 . Y. L. He,et al. (2017) study showed all 33 patient (100%) achieve a SVR at 12 weeks end of treatment. Sanjay, et al. (2017) showed total of 62 treatment-naïve patients, 59 patients (95.2%) had a sustained viral response (SVR) of the therapy. Goel, et al. (2018) study showed 37/41 patient who undergone therapy achieved SVR 12 (90.2%).
Conclusion: This study concluded sofosbuvir-daclatasvir therapy is efficacious for HCV Patients with chronic kidney disease or under maintenance haemodialysis. The therapy also found reasonably save and not make any major adverse effect.

Abstract #2255

The combination therapy of glecaprevir/pibrentasbir for HCV infected patients with or without CKD

Tatsuo Kanda, Hiroshi Takahashi, Masayuki Honda, Shuhei Arima, Reina Sasaki, Mariko Kumagawa, Shinni Kanezawa, Ryota Masuzaki, Tomotaka Ishii, Tomohiro Kaneko, Yoichiro Yamana, Taku Mizutani, Naoki Matsumoto, Kazushige Nirei, Hiroaki Yamagami, Masahiro Ogawa, Shunnichi Matsuoka, Mitsuhiko Moriyama

Division of Gastroenterology and Hepatology, Department of Medicine, Nihon University School of Medicine, Tokyo 173-8610, Japan

Backgrounds: We here reported that the results of the combination therapy of NS3/4A inhibitor glecaprevir and NS5A inhibitor pibrentasbir for HCV infected patients in daily clinical practice of Japanese Hospital.
Methods: Total 106 HCV infected patients were treated with glecaprevir/pibrentasbir for 8 or 12 weeks. HCV RNA was measured by TaqMan RT-PCR. Sustained virologic response (SVR) was evaluated at 12 or 24 weeks after the stoppage of therapy.
Results: In all patients, patients with or without chronic kidney disease (CKD), end of treatment response rates were 100%, 100%, or 100%, respectively; SVR12 rates were 99%, 100%, or 99%, respectively; and SVR24 rates were 99%, 100% or 98%, respectively. Severe adverse events were observed in total 3 patients without CKD: 1 cerebral hemorrhage and 2 hyperbilirubinemia, but these patients achieved SVR12. Only one treatment-naïve patient with HCV genotype 1b had relapse at 12 weeks after the 8-week combination of glecaprevir/pibrentasbir. This patient without CKD had polypharmacy of at least 7 drugs including proton pump inhibitor.
Conclusion: SVR rates were excellent in the 8 or 12-week combination therapy of glecaprevir/pibrentasbir for HCV infected patients with or without CKD. Attention should be paid to the unexpected adverse events.

Other Viral Hepatitis

Oral Presentations

Abstract #577

Prevalence and risk factors of de novo HEV infection in solid organ transplant patients

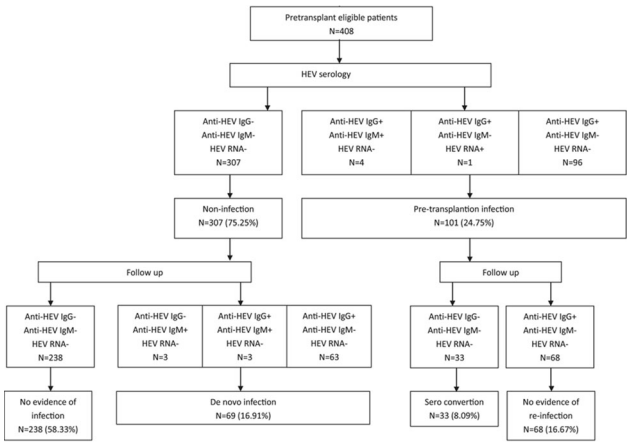
Yijin Wang

Background and aims: Hepatitis E virus (HEV) infection is endemic in developing and developed world. It is a common cause of acute viral hepatitis. Chronic HEV infection has commonly been described in immunocompromised patients, especially in solid organ transplant (SOT) recipients. However, the prevalence and risk of HEV infection after transplantation remains unclear. This study aimed to clarify the prevalence of HEV infection in Chinese SOT recipients and identify the independent risk factors for de novo HEV infection after transplantation.

Method: Organ transplantation recipients who admitted in the 5th Medical Center, Chinese PLA General Hospital between January 2006 and May 2018 were enrolled in this study. HEV parameters, including HEV RNA, HEV immunoglobulin M and HEV immunoglobulin G were tested. Clinical symptoms, laboratory data and clinical outcomes were reviewed from patients' records. Chronic HEV infection was defined as HEV RNA positive more than 6 month. Patients who had negative HEV parameters before transplantation and showed positive HEV parameters during follow up were considered to have a de novo HEV infection.

Results: A total 408 patients meeting the eligible criteria were included in this study. Median age was 50 (range 9–72) and median follow up time was 54.71 (range 1–621.71) weeks. 331 (81.13%) of the patients were men. Viral hepatitis and viral related liver disease (74.75%) were the most cause of liver transplantation. 307 (75.25%) patients had no evidence for pre-infection. 101 (24.75%) patients had positive HEV serological findings before transplantation, including 4 patients with positive anti-HEV IgM and IgG, 1 with positive anti-HEV IgG and HEV RNA, and 96 with positive anti-HEV IgG. Among the remaining 307 patients who had no experience of HEV infection, 238 (58.33%) patients showed no evidence for post infection and 69 (16.91%) patients had de nove infection, including 3 with positive anti-HEV IgM, 3 with both positive anti-HEV IgM and IgG, and 63 with positive anti-HEV IgG. For de novo infection, 56 (81.15%) patients only developed acute HEV infection without evidence for chronic HEV infection. Of the 101 patients who had HEV infection before transplantation, 33 (8.09%) achieved HEV parameters conversion and 68 (16.67%) remained to keep positive anti-HEV IgG after transplantation. Multivariate analysis demonstrated alcoholic cirrhosis (OR, 5.324; p = 0.0164; 95% CI 1.36–20.982), and liver failure (OR, 23.762; p = 0.0038; 95% CI 2.78–203.084, at transplantation, graft rejection (OR, 0.217; p = 0.0151; 95% CI 0.063–0.744) after transplantation were associated with HEV de novo infection in 3 years.

Conclusion: As the first prevalence analysis study for HEV infection in SOT patients in China, our data demonstrated that alcoholic cirrhosis, graft rejection and liver failure were the risk of de novo HEV infection. Additional work with large cohort study with longer follow up time is needed to corroborate the finding.



Abstract #598

Hepatitis A related severe acute liver injury complicated by hemolytic anemia and secondary hemophagocytic lymphohistiocytosis: a case report

Mehtani Rohit[1], Premkumar Madhumita[2], Dhiman R. K[3]

[1]Senior Resident, Department of Hepatology, Postgraduate institute of Medical Education and Research, Chandigarh, India, [2]Assistant Professor, Department of Hepatology, Postgraduate institute of Medical Education and Research, Chandigarh, India, [3]Professor and Head, Department of Hepatology, Postgraduate institute of Medical Education and Research, Chandigarh, India

Introduction: Virus-associated hemophagocytic syndrome (VAHS) is a life-threatening hematological disorder related to some viral infections. It is most commonly associated with Epstein Barr Virus, Cytomegalovirus, Human Herpesvirus type 6. Hemophagocytic lymphohistiocytosis due to hepatitis A virus is very rarely described with only few cases reported in literature.

Case: A 22 year old gentleman presented with high grade fever, vomiting, right upper quadrant abdominal pain and jaundice since 15 days. He had tachycardia, fever and scleral icterus with hepatosplenomegaly. His serum bilirubin was 4.1 mg/dL, AST 942 U/L, ALT 913 U/L and INR was 1.68. He was positive for IgM HAV. He was given IV ceftriaxone and IV N-acetyl cysteine for 5 days. After 8 days of index presentation, he again had high grade fever with severe anemia and thrombocytopenia. He had raised LDH (1102 U/L), raised plasma Hemoglobin, elevated ferritin and serum triglyceride level with normal G6PD levels and coomb's test. Bone marrow examination revealed mildly hypercellular marrow with increase in erythroid cells and histiocytes with few of them showing hemophagocytosis. A diagnosis of HLH was made and he was started on Intravenous Immunoglobulin (IVIg) 2 mg/kg over 5 days. However, his fever and anemia persisted. He was then given IV dexamethasone for 1 week to which he responded.

Conclusion: Hepatitis A associated HLH is a rare disease and treatment protocols are not well defined. A strong clinical suspicion is needed to diagnose it early and institute treatment early to improve patient outcomes.

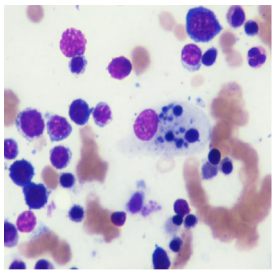


Figure 1: Bone marrow biopsy of the patient showing increased histiocytes with evidence of hemophagocytosis

Abstract #693

Efficacy of pegylated interferon-alpha-2a in chronic hepatitis D infected patients. Experience from the Tertiary Care Hospital in Karachi

Nazish Butt, Riaz Hussain, Lajpat, Sabir, Hanisha Khemani, Ali Khan

Jinnah Postgraduate Medical Centre, Karachi

Background and aims: Hepatitis Delta Virus (HDV) is a unique virus because it needs Hepatitis B Virus (HBV) for its replication hence, survival. Pegylated Interferon-Alpha-2a (PEG-alfa-2a) is the only option available for the treatment of HDV. In the present study, we aimed to assess the efficacy of PEG-alfa-2a in patients with HDV infection.
Method: We enrolled all 165 patients with chronic HDV at Gastroenterology section of medical unit IV, Jinnah Postgraduate Medical Centre On presentation, all patients were positive for both Anti-HDV and HBsAg, who were treated for 48 weeks with PEG-alfa-2a. Evaluation of HBV and HDV infection through Polymerase chain reaction (PCR) was done at 6-month, and 12-month intervals. All laboratory values were repeated on regular intervals to assess the efficacy and side effects of therapy.
Results: From total 165 patients, Eighteen patients lost to follow up, 20 patients stopped treatment due to side effects of Interferon and 20 patients were excluded from the study due to liver cirrhosis, rest of 107 patients, 76 (71%) were male while 31 (29%) were female with a mean age of 27.84 ± 10.52 years. Baseline investigations showed: Hemoglobin, 13.12+2.04 g/dL; platelets, 200.73 ± 91.31 x10^9/L; and On PCR, HDV DNA was confirmed in every collected sample, with a mean value of 10,786,066.28 ± 31,826,055.19 iu/ml, while HBV DNA was detected in 44 (41%) patients. Duration of treatment was 12 months, 25 (23%) patients achieved the 48-weeks End Treatment Response (ETR), 27 (25%) patients showed partial response to Peg-INF, while 54 (50%) had treatment failure (Null response or Non-responders).
Conclusion: Interferon therapy in patients with CHD shows a sub-optimal outcome. Only 23% achieved ETR. Patients with treatment failure or null response should urgently be given an effective alternative option.

Abstract #1113

Altered fecal microbiota on the expression of Th Cells responses in the exacerbation of patients with hepatitis E infection

Jian Wu, Xiaowei Shi, Jiaqi Zhu, Hongcui Cao

State Key Laboratory for the Diagnosis and Treatment of Infectious Diseases, National Clinical Research Center for Infectious Diseases, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, 79 Qingchun Rd., Hangzhou 310003, China

Introduction: Fulminant hepatitis E that leads to acute liver failure (ALF) are possible. Perturbations of intestinal microbiota are related to severe liver disease.
Objectives: To study the correlations between fecal microbiota and the occurrence and exacerbation of HEV infection.
Methods: We assessed the characterization of 24 fecal samples from 12 patients with AHE and 12 patients with HEV-ALF using high-throughput sequencing.
Results: Both the alpha and the beta diversity index showed no significant differences between the AHE and HEV-ALF groups. Several predominant taxa were significantly different between the AHE and HEV-ALF groups. Most notably, the HEV-ALF group had increased levels of Gamaproteobacteria, Protebacteria, Xanthomonadceae and Stenotrophomonas but reduced levels of Firmicutes, Streptococcus, Subdoligranulum, and Lactobacillus than in the AHE group. The levels of Lactobaciliaceae and Gamaproteobacteria could be used to distinguish the patients with HEV-ALF from those with AHE. In addition, the level of Th lymphocytes in HEV-ALF group was significantly lower than in AHE group. The relative abundance of Lactobaciliaceae were positively correlated with Th lymphocytes, the serum INR and severity of HE, while Gamaproteobacteria were positively correlated with the Th lymphocytes, serum INR, and severity of HE. Moreover, the surviving patients had higher levels of the Lactobacillus _mucosae than decreased patients.
Conclusion: The altered fecal microbiota was associated with the exacerbation of HEV infection, which might be useful to explore the interactions among fecal microbiota, immune responses, the mechanism of the exacerbation of patients with HEV infection, and shed light on novel diagnosis and therapy for them.

Abstract #1403

Etiological profile and characterization of hepatocellular carcinoma according to metabolic biomarkers

Hasmik Ghazinyan[1], Aregnaz Mkhitaryan[2], Mher Davidyants[1], Lyudmila Niazyan[1], Lusine Navoyan[2], Ruzanna Safaryan[2]

[1]Nork Infection Clinical Hospital, [2]Yerevan State Medical University

Background: The lack of effective biomarkers for the early detection of HCC results in unsatisfactory curative treatments.
Aims: The study was aimed at the description of etiological profile and diagnostic utility of biomarkers in different stages of HCC in Armenian patients.
Methods: In 2018–2019,420 patients with cirrhosis were involved in the study. 15,2% (64) of them were diagnosed with HCC, of which 27 (42%) and 37 (58%) patients in early and advanced stages of disease, respectively. Investigations included biochemical, serological, virological, instrumental parameters and metabolic biomarkers (Protein-induced by vitamin-Kabsence-II (Pivka II) and Alpha-fetoprotein (AFP)). Histological HCC diagnosis was performed in 15,6% (10) of the patients.
Results: The mean age of HCC-patients was 58,7 ± 7,99 with the predominance of male 56 (87,5%). The main risk factors were Hepatitis C virus 50% (32) following by cryptogenic (probably nonalcoholic steatohepatitis) in 31,25%, Hepatitis B virus 15,6% (10), alcohol abuse 3,1% (2).Total bilirubin 57,25 ± 101, albumin 34,32 ± 8,1, PLT 176 ± 90,46, GGT 275,3 ± 214, ALP 220 ± 181.
Pivka II and AFP were assessed in early and advanced stages diagnosed groups distinctly. In the first group PIVKA II was 80% and

AFP was 41,17%, while in the second group PIVKA II was 97,3% and AFP was 81,25%, respectively.
Conclusions: Our study results revealed that HCV is a leading risk factor (50%) of HCC in Armenia. The PIVKA II is more sensitive diagnostic marker than AFP, especially in early stage of HCC. It has been shown that the combination of both markers significantly increases the diagnostic and prognostic accuracy for HCC.

Abstract #1624

Epidemiological and clinical problems of Hepatitis Delta in Azerbaijan

Gulnara Aghayeva

Head of the Department of Liver Diseases, Baku Health Centre, Sechenov University, Baku, Azerbaijan

Introduction: The problem of hepatitis Delta is very acute all over the world. There are several reasons for this: firstly, it is considered a rare disease, secondly, lack of awareness of this disease is not only among the population, but also among medical personnel. This leads to the fact that the patient that has been observed for years as a patient with hepatitis B, it is not checked for the presence of hepatitis Delta, which ultimately leads to the development of serious complications, primarily liver cirrhosis and hepatocellular carcinoma.
Objectives: In Azerbaijan, in 2010–2011, in Baku and 8 regions of the country, testing for heparitis B and C was carried out, 8951 people were tested, but Delta hepatitis wasn't checked. However, specialists working in this field, who checking patients for the presence of hepatitis Delta, reveal a significant number of patients.
Methods: We collected data for 2169 patients with chronic hepatitis B admitted to clinics between January 2008 and June 2018 from four largest private hospitals in Baku, Azerbaijan. Since the initiation of Supersonic Aixplorer SWE and Fibroscan use in 2012, the degree of fibrosis was determined and recorded in all patients. Abbot Laboratory and Cobas Tagman equipment were used for evaluation of viral load of both hepatitis B and D.
Results: By combining data from 4 large private clinics in Baku, we identified 11.9% of HBsAg-positive patients with hepatitis Delta.
Data on possible routes of transmission of the virus: blood transfusions and the use of intravenous drugs, as well as iatrogenic causes, are the most common causes of infection, as well as surgical manipulations. At the first admission, 42% of the patients presented with advanced liver disease (compensated cirrhosis), 27% with 1 or more episode of hepatic decompensation and 2,3% with hepatocellular carcinoma (HCC). The data on the percentage of cirrhotic patients in different age groups were presented. So in the group of patients over 50 years old, it is 80%, but more importantly, that the most active and young patients had cirrhosis is observed in 57% in the group from 30 to 50 years and more than one-third in the group up to 30 years.
Conclusion: Dual HBV/HDV infection is one of the most rapidly progressive cause of advanced liver disease that can end up with dangerous complications such as cirrhosis and HCC. The prevalence on HDV infection is 11,9% in Azerbaijan. In summary, our analysis provides a preliminary estimate of the epidemiology of hepatitis D virus infection in Azerbaijan and points to several important gaps in knowledge and directions for future research. Results suggest that co-infection with hepatitis B and D viruses could represent an important cause of liver disease in some populations. Improved and systematically collected epidemiology data are needed, as is identification of risk factors for hepatitis D virus transmission.

Abstract #2111

The morphofunctional changes in liver of experimental animals when exposed to radio frequency electromagnetic radiation (RFEMR)

G. Ibadova[1], G. Tashpulatova[1], G. Khamidova[1], Sh. Sadirova[2], L. Maksudova[1]

[1]Tashkent Institute of Postgraduate Medical Education, Tashkent, Uzbekistan, [2]Scientific Research Institute of Virology, Tashkent, Uzbekistan

Introduction: WHO included the scope of electromagnetic contamination of environment in a number of the global problem. Therefore, studying the morphofunctional response of liver being under the exposure to RFEMR is an important problem.
Objective: The goal of the research was defined, i.e. to reveal the profile and dynamics of the morphological and functional changes in liver of rats in experiment with their exposure to RFEMR.
Method: The experiment was made on 72 white rats who were divided into 4 groups with exposed to 50mcV/cm^2, 500mcV/cm^2, 1000mcV/cm^2 and control group, consisted of acute and chronic stages.
Results: The morphological changes arising in the liver tissue were characterized by different severity level and developed both in hepatocytes and the vascular-stromal renal structures. The RFEMR exposure lasting 30 days in the dose of 50mcW/cm^2 characterized by microcirculation impairments manifesting themselves in non-uniform plethora of the renal parenchyma of diffuse or mosaic character, emptying the portal part and sinusoids, impairment of hepatocyte complexes, moderate hyperchromia and degenerations of hepatocytes' nucleus. However, we have not found out lymphoid-plasmocytic infiltration and fibrosis. More considerable changes were observed after RFEMR exposure at 500mcW/cm^2 and 1000 mcW/cm^2. After 3 months exposure we observed the further increase in the signs of liver architectonics impairment occurred due to critical microcirculation defects and accruing proteinosis.
Conclusion: The RFEMR effect was shown to manifest itself by pathological changes in the structure of the liver with the critical impact of the micro-vascular bed impairment on morphological, metabolic and homeostasis shifts that occurred.

Poster Presentations

Abstract #76

Evaluation of hepatitis A seroprevalence in Ege University Faculty of Medicine

Isıkgoz Tasbakan Meltem[1], Akyol Deniz[1], Altuglu Imre[2], Pullukcu Hüsnü[1]

[1]Ege University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Izmir, Turkey, [2]Ege University Faculty of Medicine, Department of Clinical Microbiology, Izmir, Turkey

Introduction: Medical students are in the same risk group as other health workers. In this group, vaccination is recommended for diseases that can transmitted through blood, body fluids and droplet-contact. However, screening usully are missing and the test results are not evaluated. A 21-year-old male student was followed for acute hepatitis A in our clinic and liver transplantation were prepared due to fulminant hepatitis. After 25 days of hospitalization in intensive care unit, the patient was discharged fully recovered. In this report, we

aimed to evaluate the seroprevalence of hepatitis A infection for the internship students.
Methods: Students who have been studying in the medical faculty between 2008 and 2019 were included in the study. We were retrospectively reviewed records of serology results of cases. Hepatitis A IgG detection was perfomed using Architect Anti-HAV IgG Chemiluminescence Microparticle Immunoassay Assay kit (Abbott, USA).
Results: A total of 1867 people (47.7% male) (term 1–6) were included in the study. Hepatitis A IgG was studied in 1597 (85.5%) medical students. The rate of anti-HAV seropositivity was 29.4% (471/1597).
Conclusion: Infections that can be prevented by vaccination in health workers cause serious costs as well as medical consequences. The screening results should be evaluated carefully. In the early stages of the faculty, medical students should be screened serologically, informed about protection from risky behaviors and vaccination programs should be established. Vaccines of seronegative students reported to Workers' Health and Safety Centre are applying by our clinic.

Abstract #99

A case of subchorionic hematoma caused by viral hepatitis A infection during pregnancy

Hyuk Soo Eun[1,2], Hyeon Seok Lee[2], Byung Seok Lee[1,2], Seok Hyun Kim[1,2], Eaum Seok Lee[1,2], Jong Seok Joo[1,2], Woo Sun Rou[1,2], Hee Sung Lee[1,2], Min Young Shin[1,2], Sung Hun Kang[1,2], Sang Ok Jung[1,2], Min Ji Cho[1,2], In Ki Min[2]

[1]Department of Internal Medicine, Chungnam National University College of Medicine, Daejeon, Republic of Korea, [2]Department of Internal Medicine, Chungnam National University Hospital, Daejeon, Republic of Korea

Introduction: Hepatitis A virus (HAV) is an enterovirus of the family Picornaviridae that is transmitted primarily via the fecal-oral route. Most affected age is in 20–40 years and most patients have experienced benign course without severe complication. In addition, HAV infection is rarely associated with severe outcomes or complications during pregnancy and maternal-infant HAV transmission is thought to be very uncommon. Recently, we experienced and introduce a case of pregnant woman with HAV associated with subchorionic hematoma.
Methods: This review is based on electronic medical records including laboratory data, liver ultrasonographic findings. Authorization for the review of these clinical data for case report was obtained from the Institutional Review Board of Chungnam National University Hospital (IRB number: 2016-05-059).
Results: A 36-year-old woman visited our hospital at 8 weeks with gestational age (Parity: 1-0-3-1). She visited to our emergency department and presented with fever lasting 2 days and vaginal bleeding about 35 ml. Esperically, vaginal sonographic examination revealed that she had subchorionic hematoma at our obstetrics and gynecology department. Considering previous abortion history, we doubted that this clinical sign was related with lupus anticoagulant and antiphospholipid antibody syndrome. However, almost autoimmune antibodies were all negative on the laboratory examination. On the other hand, the mild elevation of total bilirubin and striking elevation of liver enzymes were observed on the laboratory examinations. Moreover, HAV IgM antibody was positive and finally, acute viral hepatitis A was confirmed. As a result of abdominal ultrasonography, she had mild hepatomegaly, fatty liver, and diffuse edematous wall thickening of gallbladder, suggesting acute hepatitis. We suggested to her for admission and taking a rest on the hospital for a period of several days. After several days of observation, elevated liver enzyme and total bilirubin were improved and discharged.
Conclusion: It has been reported previously that maternal hepatitis A infection has caused several problems, such as premature birth in the 2nd and 3rd trimester of pregnancy. However, there was no report of subchorionic hematoma on 1st trimester of pregnancy. Therefore, it is the first case of presenting subchorionic hematoma in pregnant woman with acute viral hepatitis A.

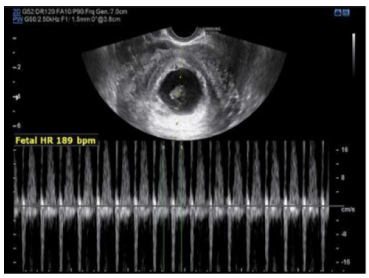


Fig 1. Transvaginal Sonography : Subchorionic hematoma

Table 1. Laboratory data (viral marker & autoimmune antibody)

HBs Ag	Negative	Anti PL IgG (U/mL)	1.4	ACA IgG	Negative	PR-3 Ab	Negative
HBS Ab	Negative	Anti PL IgM (U/mL)	5.1	ACA IgM	Negative	MPO Ab	Negative
HCV Ab	Negative	Anti DNA Ab (IU/mL)	Negative (9.65)	LMK Ab	Negative		
Anti HAV IgG	Negative	ANA titer	Negative (< 1:80)	ASMA	Negative		
Anti HAV IgM	Positive	Anti β2-GP Ab IgG	Normal (3.0)	AMCA	Negative		

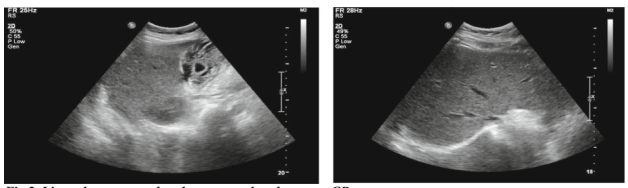


Fig 2. Liver ultrasonography : hepatomegaly, edematous GB

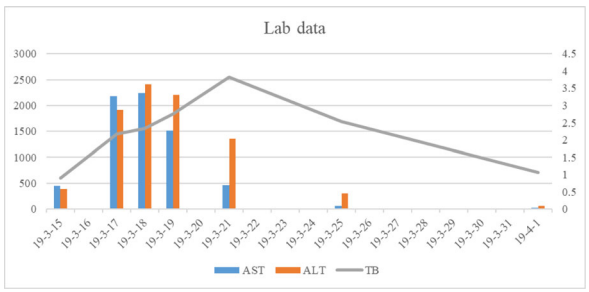


Fig 3. Summaries of laboratory data (AST/ALT/TB)

Abstract #130

Stable HEV IgG seroprevalence in Belgium between 2006–2014

Erwin Ho[1,3], Julie Schenk[6,7], Veronik Hutse[4], Vanessa Suin[4], Amber Lizroth[5], Stéphanie Blaizot[7], Sereina A. Herzog[7], Vera Verburgh[4], Marjorie Jacques[4], Abbas Rahman[2], Peter Michielsen[1,3], Pierre Van Damme[2], Steven Van Gucht[4], Heidi Theeten[2], Niel Hens[6,7], Thomas Vanwolleghem[1,3]

[1]Antwerp University Hospital, Department of Gastroenterology and Hepatology, Edegem, Belgium, [2] Centre for the Evaluation of Vaccination, Vaccine & Infectious Disease Institute, Faculty of Medicine and Health Sciences, University of Antwerp, Belgium, [3] Laboratory of Experimental Medicine and Paediatrics, Faculty of Medicine and Health Sciences, University of Antwerp, Belgium, [4] National Reference Centre for Hepatitis Viruses, Scientific Directorate Infectious Diseases in Humans, Sciensano, Belgium, [5] Scientific Directorate Epidemiology and Public Health, Sciensano, Belgium, [6] Interuniversity Institute for Biostatistics and statistical Bioinformatics, Data Science Institute, Hasselt University, Hasselt, Belgium, [7] Centre for Health Economic Research and Modelling Infectious Diseases, Vaccine & Infectious Disease Institute, Faculty of Medicine and Health Sciences, University of Antwerp, Belgium

Introduction: Recent studies have shown an increase in seroprevalence of hepatitis E virus (HEV) over time in younger age cohorts in Europe, but substantial regional differences are found and knowledge of the overall HEV burden of disease is lacking.
Aim: We evaluated time trends in birth cohort-specific HEV seroprevalence and regional differences in Belgium.
Methods: We analysed HEV IgG seroprevalence on two Belgian national serum banks consisting of residual samples collected in 2006 and 2014 using the Wantai anti-HEV IgG ELISA. Reflex testing with the Wantai HEV antigen (Ag) and subsequent Altona HEV RNA PCR were performed on HEV IgG positive samples. Sex, region and birth cohort specific proportions were compared in SPSS 25 using Chi square analysis or Fisher's Exact Test. Subsequently, a generalized additive model with a complementary log-log link was used to model observed seroprevalence and then weighted by province to retrieve the age-specific proportion positive for HEV IgG for the whole of Belgium.
Results: No significant differences between birth cohorts or sexes were found. The best fitting generalized additive model identified the individual's age and province (person's residence or lab location) as the relevant factors. The probability of HEV (sero-)infection (the prefix 'sero-' refers to the IgG positivity as a proxy of past or present infection) increases significantly with increasing age (p-value $<$ 0.001). An estimated total of 434,819 (sero-)infections or a yearly rate of 54,352 (sero-)infections was found between 2006 and 2014. Overall HEV IgG seroprevalences were 4.1% (64/1579, 95% CI 3.1–5.1, when standardized for province, sex and age: 4.1%, 4.1%, 4.4%, respectively) and 5.8% (121/2087, CI 4.8–6.9, when, standardized for province, sex and age: 5.7%, 5.8%, 6.1%, respectively) in 2006 and 2014; respectively. Observed HEV antigen seroprevalence was 0.027% (1/3666) for the entire cohort.
Conclusions: This first Belgian nationwide study showed stable birth cohort specific HEV IgG seroprevalences based on 2006 and 2014 serial serological data. Probability for HEV (sero-)infection rises with increasing age, with an overall estimated yearly (sero-)infection rate of 54,352 new infections in Belgium.

Abstract #202

HAV IgG seroprevalence among chronic liver disease patients in South Korea

Dae Jin Kim

Daegu fatima hosptial, Daegu, South Korea

Introduction: Coinfection of hepatitis A can aggravate liver damage in chronic liver disease patient. HAV IgG seroprevalence is low in young generation because of good hygine.
Method: We checked HAV IgG in 40 patients who have chronic liver disease from 2017 to 2018. Hepatitis B patients were 15, Hepatitis C patients were 5 and alcoholic liver disease patients were 20. Seroprevalence of HAV Ig G was analyzed retrospectively.
Result: Seropositivity of HAV IgG is 70% (28/40). According to age, 10–19 years 25% (1/4), 20–29 years 25% (2/8), 30–39 years 33% (4/12), 40–49 years 87% (14/16). Seropositivity of IgG is increasing as age becomes higher ($p < 0.05$). Seropositivity of patients below 40 years old is 29% (7/24) and above 40 years old is 87% (14/16). Seropositivity is high in patient above 40 years old ($p < 0.05$). Seropositivity of IgG among underlying disease (HBV, HCV, alcoholic liver disease) was not different ($p > 0.05$).
Conclusion: Seropositivity of HAV IgG was not high in young generation. HAV vaccination can be reasonable for chronic liver disease under 40 years old in South Korea.

Abstract #280

Long-term outcome of hepatitis D virus among chronic hepatitis B patients who received nucleos (t)ides analogues therapy

Tyng Yuan Jang[1,2]

[1]Hepatobiliary Division of Department of Internal Medicine in Kaohsiung Medical University Hospital, [2]Department of Internal Medicine in Pingtung Hospital Ministry of Health and Welfare

Introduction: Reports regarding the prevalence of hepatitis D virus (HDV) infection among chronic hepatitis B (CHB) patients vary worldwide. The seroclearance of HDV seromarkers in the HBV treated cohort is also elusive.
Plan: We aimed to address the seroprevalence of HDV by recruiting a large HBV cohort who received antiviral therapy on clinical demands. We also sought to elucidate the incidence and factors potentially associated with HDV seroclearance by following the characterized cohort constantly.
Background/aims: Reports regarding the prevalence of hepatitis D virus (HDV) infection among chronic hepatitis B (CHB) patients vary worldwide. The seroclearance of HDV seromarkers in the HBV treated cohort is also elusive.
Methods: CHB patients receiving nucleotide/nucleoside analogues (NUCs) were tested for anti-HDV and HDV RNA at the time of initiating anti-HBV therapy and consequently during the followed-up period.
Results: The seropositive rate of anti-HDV and HDV RNA was 2.7% and 0.9%, among 2850 CHB patients, respectively. Factor associated with anti-HDV seropositive were platelet counts (odds ratio [OR]/95% confidence intervals [CI]: 0.995/0.992–0.999, P = 0.006), hepatitis B virus (HBV) DNA levels (OR/CI: 0.81/0.70–0.94, P = 0.005) and hepatitis B e-antigen (HBeAg) seropositivity (OR/CI: 0.22/0.05–0.95, P = 0.04). The only factor associated with HDV RNA positivity among anti-HDV seropositive patients was age (OR/CI: 0.95/0.90–1.00, P = 0.03). The spontaneous clearance rate of serum anti-HDV antibody was 2.0 per 100 person-years with a median

follow-up period of 3.5 years (range 2–15 years), whereas the seroclearance rate of HDV RNA was 4.3 per 100 person-years among anti-HDV seropositive patients after a median follow-up period of 6.0 years (range 2–11 years). Baseline Anti-HDV titer < 0.5 cut-off index (C.O.I.) was the only factor predictive of anti-HDV seroclearence (Hazard ratio [HR]/CI: 20.00/2.07–193.37, P = 0.01).
Conclusions: HDV infection was not common among HBV treated patients in Taiwan. Seroclearance of anti-HDV and HDV RNA did occur over time, albeit the chance is rare.

Abstract #437

Prognosis and risk factors of acute viral hepatitis D in Mongolia

Badamnachin Batsukh[1,2], Ganbold Sarangua[2], Badarch Gansaikhan[2], Jamyan Ariunbileg[2],Sosorbaram Ariunaa[2], Oidov Baatarkhuu[1,3]

[1]Department of Infectious Diseases, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [2]Department of Hepatology, National Center for Communicable Diseases, Ulaanbaatar, Mongolia, [3]Mongolian Academy of Medical Sciences, Ulaanbaatar, Mongolia

Introduction: Hepatitis D virus (HDV) infection is considered to cause more severe hepatitis such as liver cirrhosis and HCC. Mongolia has the highest prevalence (> 15%) of HCV (> 10%) HBV infection and HDV 75–100% of HBsAg carriers.
Objectives: To investigate prognosis and risk factors acute viral hepatitis D in Mongolia.
Methods: A total of 86 patients with acute viral hepatitis D were enrolled and their data collected 2016–2017.
Results: The mean age of patients was 29.7 ± 7.17. 52 (60.4%) of them were males and 34 (39.6%) were females. Risk factors were unprotected sexual contact 41 (47.67%), dental care 11 (12.8%), tattooing 8 (9.3%), admit hospital 42 (48.83%), history of surgery 13 (15.1%), acupuncture 12 (13.9%), share with nail clipper 74 (86%) and family contacts with viral hepatitis B 23 (26.7%). Anti-HDV IgM and anti-HD total Ab tests were both positive in 34/86 samples, anti HDV IgM was the only positive delta marker in 65/86 samples and anti-HD total Ab was the only marker in 61/86 samples. During follow-up, three of 5 (4.9%) patients with co D infection showed HBsAg loss and 58 patients with super D infection (100%) showed persistent hepatitis B and D viremia.
Conclusions: Risk factors for hepatitis D virus infection were unprotected sexual contact, admitted hospital, share with nail clipper and family contacts with viral hepatitis B.During follow-up, three of 5 (60%) patients with co D infection showed HBsAg loss and 58 patients with super D infection (100%) showed persistent hepatitis B and D viremia.

Abstract #567

Poor outcomes of acute hepatitis E in patients with cirrhotic liver diseases regardless of etiology

Yijin Wang

Background and aims: chronic liver diseases (CLD) have been documented to exacerbate clinical outcomes of acute hepatitis E (AHE). However, CLDs vary largely in their etiology and disease stages and the course of AHE with different CLDs is unclear. This study aimed to uncover the role of etiology and status of CLD in the adverse outcomes of AHE.
Method: Patients diagnosed of AHE were consecutively retrieved from January 2015 to October 2017 and interviewed of the demographic information, clinical symptoms and laboratory data, complications, extra-hepatic manifestations and clinical outcomes in the 5th Medical Center, Chinese PLA General Hospital. Chronic liver diseases were defined with presence of one or more of the following diseases: chronic hepatitis B, C, alcoholic liver disease, moderate to severe fatty liver, autoimmune liver diseases, and all etiology related cirrhosis.
Results: A total of 227 patients were eligible for the study, including 56 of cirrhotic CLD, 47 of non-cirrhotic CLD and 124 of no-CLD patients. Alcoholic liver disease and CHB were the predominant CLDs in both cirrhotic and non-cirrhotic groups. Compared with no-CLD HEV patients, HEV patients with CLD were more commonly to present ascites, pleural effusion and peritonitis. The frequency of liver failure was also significantly higher in HEV patients with CLD than solely HEV infected patients. Of great interest, there revealed no significant difference between HEV patients without CLD and with non-cirrhotic CLD in regard of all the liver function tests, complications and outcomes, suggesting that non-cirrhosis is unlikely to be involved in poor outcomes of AHE. An even worse but non-significant trend of some complications, including ascites, pulmonary infection, peritonitis renal injury and liver failure, were observed in HEV patients without CLD compared to HEV patients with non-cirrhotic CLD. In contrast, most complications and outcomes were worsen in AHE patients with cirrhotic CLD, compared to AHE patients with non-cirrhotic CLD and AHE patients without CLD. In multivariate analysis, cirrhosis was found to be the only independent risk factor of development of liver failure. However, etiology of CLD was not associated with liver failure.
Conclusion: The overall status of liver, other than specific etiology of CLD, is more pivotal for determinant of risk of liver failure in patients with AHE. Additional work with large cohort study is needed to corroborate the finding and identify the variants for predicating poor outcome of HEV infection and provide recommendations for intensive surveillance of liver cirrhotic patients against HEV infection.

Abstract #727

Long-term renal and bone safety of tenofovir disoproxil fumarate in chronic hepatitis B patients

N. Butt[1], L. Rai, R.H. Channa, H. Khemani, S.A. Soomro, A. Abbasi[2]

[1]Gastroenterology Department, Jinnah Postgraduate Medical Centre, Karachi, Pakistan, [2]Medical Unit II, Dow University of Health Sciences, Ojha Campus, Karachi, Pakistan

Introduction: Tenofovir disoproxil fumarate (TDF) is one of the approved drugs for chronic hepatitis B (CHB) management. Although not curative, it inhibits viral replication, requiring long-term administration. It is generally considered safe but there is a strong risk of loss of bone mineral density and renal function.
Methods: This cross-sectional study was started in January-2019 at the Department of Gastroenterology, Jinnah-Postgraduate-Medical-Centre, Karachi, Pakistan. A total of 120 patients with CHB started on TDF therapy, having age more than 18 years to 60 years were recruited till date. Bone mineral density and renal functionas were assessed on the basis of pre and post Dual-Energy X-ray Absorptiometry (DEXA) scan & eGFR, respectively. Dexa score (T-Score) of less than − 1.0 of left hip & spine and eGFR of less than 90 ml/min was considered abnormal. Patients were assessed at the time of recruitement then after three and 6 months for comparison.

Results: Out of 120 patients, 61% were males and 39% were females, with a mean age of 32.50 ± 12.01 years. The T and Z scores were normal at the end of 3 months, but it was significantly reduced after 6 months (Z-score 33% at hip and 37% at hip site, $p < 0.05$). While T score of 14% was at the lumbar & 5% at hip sites after 6 months (p value > 0.05) was found. Comparing with baseline a significant reduction of eGFR has been observed at the end of three and 6 months (p value < 0.05).
Conclusion: The results of this study conclude that the use of TDF is associated with reductions in renal function and bone density in patients with CHB having no prior renal or bone disease.

Abstract #848

Recent trend of acute hepatitis E virus infection in Japan

Fukada Hiroo, Yamashina Shunhei, Someya Shuunin, Morinaga Maki, Nakadera Eisuke, Uchiyama Akira, Fukuhara Kyoko, Kon Kazuyoshi, Ikejima Kenichi

Department of Gastroenterology, Juntendo University School of Medicine, Tokyo, Japan

Introduction: Though water-borne, pandemic infection of hepatitis E virus (HEV) has never been reported in Japan, we sometimes experience sporadic acute HEV infection following consumption of undercooked pork or wild game meat such as boar and deer.
Objectives: We retrospectively surveyed the recent cases of acute hepatitis E in our institution located in Tokyo metropolitan area.
Methods: We identified 30 patients with IgA-HEV antibody positive from January 2013 through December 2018. Clinical characteristics (age, sex, route of infection), blood examinations (AST, ALT, Prothronbin Time (PT), Total Bilirubin (T-Bil)) and clinical course of these patients were evaluated.
Results: The median age was 53 year-old (range 24–75 year-old), and 24 cases (80%) were male. Estimated routes of infection were unknown (24), meat (3) and travelling overseas (3). Seven patients had no symptom, others had fatigue (9, 30%), appetite loss (7, 23.3%), fever (5, 16.7%), jaundice (4, 13.3%) or abdominal pain (3, 10%). The average value of blood examinations after first vistit were as followes; AST 311 (26-4876) U/L, ALT 662 (37-3839) U/L, PT 95 (31-107) % and T-Bil 1.10 (0.35–15.8) mg/dL. Sixteen patients were hospitalized with the median length of 14 (4–60) days. One patient requred plasmapheresis, but unfortunately died on the 60th hospital days.
Conclusion: The spread of testing methods and understanding of HEV may be the cause of increasing HEV in Japan. Sporadic infection of HEV is increasingly observed in Tokyo metropolitan area. HEV infection needs attention for the differential diagnosis of acute liver injury even in non-pandemic area.

Abstract #891

HBV, HCV and HIV infections and vaccine-induced seroprotection against HBV in healthcare professionals of the Wroclaw Medical University, Poland

Justyna Janocha-Litwin [1,2,3], Iwona Buczynska [1,2], Sylwia Serafinska [1,2], Anna Szymanek-Pasternak[1,2,3], Krzysztof Simon [1,2]

[1]Department of Infectious Diseases and Hepatology, Wroclaw Medical University, Wroclaw, Poland, [2]1st Department of Infectious Diseases, Regional Specialistic Hospital in Wroclaw, Poland, [3]Novum Clinic, Kielczow/Wroclaw, Poland

Background: Hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infections may occur through exposure to infected blood and body fluids which poses occupational risk for healthcare workers.The aim of the study was to assess the prevalence of markers of HBV, HCV and HIV infection and to evaluate vaccine-induced seroprotection against HBV among 4th year students of the Faculty of Medicine and Dentistry and employees of the Faculty of Medicine and Dentistry, Wroclaw Medical University, Poland.
Materials and methods: 141 people were examined: 53 students and 88 employees. The following serological tests were performed: HbsAg, total anti-HBc Ab, anti-HBs Ab, anti-HCV Ab and HIV Ag/Ab.
Results: In 4 (7.55%) students serological markers of hepatotropic virus infection were detected: 1 (1.9%) was anti-HCV positive, 3 (5.66%) – anti-Hbc total positive. Among them only 1 student (1.9%) confirmed active HBV infection with positive serum HBV DNA and positive HbsAg, while other students had serological markers of past HBV and past HCV infections. All students received complete HBV vaccine series in the past, but 6 had unprotective anti-HBs concentrations (< 10 mIU/ml). In the group of employees, serological features of past HBV infection were detected in 5 people (5.68%). All were vaccinated against HBV, but 16 (18.18%) had anti-HBs levels $<$ 10 mIU/ml. 1 person was found to have false positive HIV Ag/Ab test result (the test was verified by a negative confirmation test). No anti-HCV Ab were detected.
Conclusions: No HCV or HIV infection was detected. Only 1 case of active HBV infection was detected, most likely acquired in infancy (before obligatory childhood vaccination program in Poland was introduced).

Abstract #1061

Changes in the clinical features of the patients with acute hepatitis A for 20 years in Korea

Suk Bae Kim, Kwang Woo Nam, Ki Bae Bang, Jun Ho Choi, Hyun Deok Shin, Jung Eun Shin, Hong Ja Kim, Il Han Song

Department of Internal Medicine, Dankook University Hospital, Cheonan, Korea

Background/aims: This study aim to analyze the clinical features of acute hepatitis A patients in a single hospital for 20 years.
Methods: Patients with acute hepatitis A who had been hospitalized at Dankook University Hospital from 1998 to 2017 were included. We reviewed patients' medical records and analyzed the data such as the number of inpatients, age, symptoms, length of hospital stay, recovery rate, liver function test.
Results: For 20 years, total 676 patients had admitted with acute hepatitis A. The mean age of the patients was 25.8 ± 11.9 years in 1998 and gradually increased to 39.6 ± 11.0 years in 2017. The mean peak AST and ALT were 1329.2 IU/L and 1539.6 IU/L in 1998, and increased to 2838.2 IU/L and 2926.9 IU/L in 2017, respectively. However, other parameters such as total bilirubin, WBC, platelet, serum Cr, and albumin did not show meaningful change by year. The mean duration of hospital stay was 7.14 ± 1.8 days without significant changes for 20 years. The number of acute hepatitis A patients was highest in 2008 and 2009. There were 5 patients who were transferred to other center for consideration of liver transplantation. They are all male and their mean age was 38.4 ± 18.5 years old.
Conclusions: The average age of patients with acute hepatitis A has increased as 13.8 years. AST and ALT of the patients were higher than past, and INR was also increased, indicating severe liver

dysfunction. Therefore, hepatitis A vaccination for middle-aged people should be actively considered.

Abstract #1241

Acute liver failure due to viscera leishmaniasis

Hasmik Ghazinyan[1], Aregnaz Mkhitaryan[2], Mher Davidyants[1], Lyudmila Niazyan[1], Tigranuhi Asatryan[1], Lusine Navoyan[2]

[1]Nork Infectious Clinical Hospital, [2]Yerevan State Medical University

Background: Acute-liver-failure is an uncommon condition which results in loss of liver functions, that occurs rapidly after the first signs of liver disease. Leishmaniasis is an emerging infectious disease of protozoan origin. Visceral Leishmaniases (VL) is the most severe clinical form of the diseases and it is endemic in Armenia. Hepatomegaly is common in VL patients, however, rapid acute progressive hepatitis as a presenting feature is rare.
Case presentation: We present an unusual immunocompetent 1-year-old female case of acute liver failure due to visceral leishmaniasis, following a prolonged fever of unknown origin for 14 days and 2-day history of jaundice. Laboratory test results showed aspartat-aminotransferase (403U/L), alanine-aminotransferase (879U/L), alkaline-phosphatase (339U/L), gamma-glutamyle-transferase (116U/L). Bilirubine was 231mcmol/l, with predominance of direct (158 mcmol/l), albumin was 29.9 g/l, PT-39 s, hemoglobine—76 g/l, leukocites—10.54 $\times$ 10^3/µl and platelets—85 $\times$ 10^3/µl. Chest-radiography revealed hydrothorax, ultrasound-examination-ascitis (300–400 ml), hepatosplenomegaly. Microbiology investigations were negative for Human-immunodeficiency-virus, viral-hepatitis (A, B, C,), Epstein-Barr-virus. IgM for Leishmania was negative, but IgG and rK39 antigen was positive. Bone marrow aspiration and microscopic examination turned out positive for the amastigotes of Leishmania spp. Diagnosis of Visceral Leishmaniasis was confirmed. Despite pathogenetic and symptomatic treatment, disease was rapidly progressing and on the second day of hospitalization, the patient died because of hepatorenal acute failure. Histopathological examination showed the liver involvement in VL appeared as a diffuse hepatitis process (necroinflamatory pattern), which was caused by toxic injure of liver.
Conclusion: In case of acute hepatitis leading to acute-liver-failure leishmaniasis should be considered as differential diagnosis.

Abstract #1349

Hepatitis A seroprevalence in an intermediate endemic country and impressions for vaccination policy

Celal Ulasoglu[1], Abdüllatif Sirin[1], Feruze Enc[1]

[1]Medeniyet University, Goztepe Education and Research Hospital, Department of Gastroenterology

Introduction: In recent years, local fatal outbreaks due to Hepatitis A (HAV) as a non-enveloped picornaviridae RNA virus in western countries are reported.
Objectives: We aimed to assess the features of HAV seropositivity in all age groups in Western Turkey with dta of hospital-based, cross-sectional study.
Methods: Hepatitis A serology in last 2 years (2018–2019) were retrospectively collected in terms of all age groups and genders.
Results: The data of 16,932 patients (50,1% female and 49,9% male) were evaluated retrospectively for AntiHAV-IgG serology and antibody titer. Overall seropositivity was 58,0% (56,7% for women, 59,4% for men, $p < 0.001$). The rate of seropositivity was 61,0% in children under 9 years old. The seropositivity of HAV for age groups were: age 0–4, 5–9, 10–14, 15–24, 24–44, 45–64 and > 64 had 78,8%, 51,4%, 31,2%, 30,8%, 69,0%, 95,9% and 98,6% seropositivity, respectively. The titer of antibody was 4,5 ± 4.4 mIU/ml for females and 5,06 ± 4,4 mIU/ml for males ($p < 0.001$).
Conclusion: The seropositivity graphic of HAV had a convex curve (Figure 1) due to low immunity in adolescents and young adults, lower than children and older group. Besides the routine childhood vaccination schedule, all risk groups and especially young population should be vaccinated, a least one vaccination instead of double vaccination with 6 months interval.

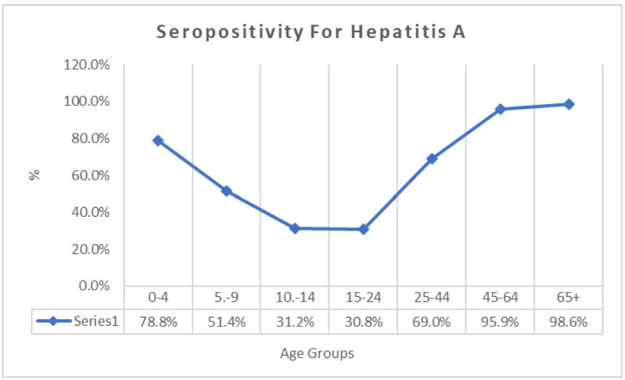


Figure 1: Seropositivity ratio according to age groups.

Abstract #1463

Characterization of pathomorphological features of the oral mucosa in patients with HBV, HCV and HIV infections

V.Yu. Azatyan[1], L.K. Yessayan[1], H.L. Ghazinyan[2], M.V. Shmavonyan[2], A.H. Hovhannisyan[2], A.G. Heboyan[3], G.E. Manrikyan[1], G.G. Melik-Andreasyan[4]

[1]Yerevan State Medical University (YSMU), Department of Therapeutical Stomatology, Yerevan, Armenia, [2] Norq Clinical Hospital of Infectious Diseases, Yerevan, Armenia, [3]Yerevan State Medical University (YSMU), Department of Prosthodontics, Yerevan, Armenia, [4]National Center of Disease Control and Prevention, The Ministry of Health of Republic of Armenia, Yerevan, Armenia

Introduction: Oral clinical manifestations can be observed in patients infected by the HIV, HBV and HCV viruses and may indicate an impairment in the patient's general health status. Aim of this study is assessment of pathomorphological features of oral mucosa in patients infected with HIV, HBV and HCV.
Methods, objectives: This cross-sectional study was conductedin Stomatology Policlinic 1 of Yerevan State Medical University after M.Heratsi, Yerevan, Armenia. A total of 60 patients with HBV (n = 20), HCV (n = 20) and HIV (n = 20) were enrolled in the study. Biopsy of the oral mucosa followed by histological examination was performed. Statistical analyses were conducted using Excel 2013 and R software.
Results: Pathomorphological examination revealed inflammatory infiltrations in all samples. Circulatory disorders were detected in 98.3% of samples,fibrinous overlay on the surface of erosions and ulcers of the mucous membrane in 1.7%, fibrosis of mucous membrane in 70%, dystrophy of squamous epithelium in 93.3% and bone sequestration in 3.3%. Comparison of pathomorphological features revealed mainly lymphoplasmocytic infiltration in case of HBV and

HCV versus neutrophils infiltration and absence of plasmocytes in case of HIV.
Conclusion: Abnormal pathomorphological changes of oral mucosa were typical for all patients with HBV, HCV and HIV. Obvious difference in the character of inflammation in case of HIV illustrated destruction of humoral immune system. Understanding of the character of inflammation could be useful for timely differential diagnoses and management of the patients.

Abstract #1600

Clinical profile and outcome of patients admitted with acute viral hepatitis, an experience of a Tertiary Care Centre

A. Samad

Introduction: Acute viral hepatitis is a global health problem and in developing countries like Pakistan, it affects a large number of people. Most of the patients make uneventful recovery, however few patients can develop fulminant hepatic failure.
Objective: To determine the clinical profile and outcome of patients with acute viral hepatitis at Patel Hospital Karachi.
Methods: Our study is a retrospective study that included a total of 396 patients admitted with acute viral hepatitis from January 2015 till December 2019. Only patients with hepatitis secondary to viruses (A, B, C, D and E) are included.
Results: Out of total 396 patients with acute viral hepatitis, 150 were males and 246 were females. The mean age of patients was 23.46 ($\pm$ 15.65). 250 patients (63.63%) were found to be positive for hepatitis E, followed by hepatitis A in 137 patients (34.84%), 8 patients were hepatitis B positive (2.02%) and only one patient with Hepatitis C (0.25%). The mean SGPT of patients was 1586.74 ($\pm$ 25.67), SGOT was 1390 ($\pm$ 14.68) and bilirubin 7.32 ($\pm$ 2.35). The mean INR of patients on admission was 1.36.The average length of stay in hospital was 3 days. Fulminant hepatic failure leading to death developed in only 12 patients (3.03%), out of which 7 had Hepatitis E, 3 had Hepatitis A and 2 had Hepatitis B. Conclusion: Hepatitis E is the most common etiological agent causing acute hepatitis followed by Hepatitis A. Most of these infections can be prevented by improving hygienic measures.

Abstract #1644

Comorbidity of hepatitis A infection and Gallbladder Polyp

Margono Jacqueline Tasha[1], Jonathan Kent Setiawan[1], Kurniawan Andree[2]

[1]Faculty of medicine, Pelita Harapan University, Tangerang, Indonesia, [2]Internal Medicine, Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia

Introduction: Hepatitis A is a self-limited illness caused by Hepatitis A Virus that confers a lifelong immunity and is preventable via vaccination. Most of the gallbladder polyps are benign in nature (cholesterol polyps, inflamatory polyps, adenoma, and fibroma), but some polyps are malignant (gallbladder carcinomas). The initial symptoms of the gallbladder polyp which was characterized by increased bilirubin can worsen the jaundice in patient with hepatic problem comorbidity.
Case illustration: A 34-year-old male presented with chief complaints of fever and jaundice for 3 days. On physical examination we found icteric sclera and skin with right upper quadrant abdominal pain. Laboratory findings showed slight leukocytosis (11.02 $\times$ 10^3/µl), increased in total bilirubin (5.55 mg/dL) and direct bilirubin (5.23 mg/dL), highly elevated SGOT (1266 U/L) and SGPT (2156 U/L), and reactive anti HAV IgM. Abdominal ultrasonography showed hyperechoic lesion in gallbladder suggestive a 0.9 cm in diameter polyp. After a few days of hospital stay, total bilirubin and direct bilirubin, SGOT and SGPT decreased signifcantly, his symptoms improved and he was discharged the next day. 3 days after discharged, patient came to the clinic with the lab result of total bilirubin 1.68 mg/dL, indirect bilirubin 0.97 mg/dL, SGOT 54 U/L, and SGPT 167 U/L.
Conclusion: We reported a case in which a patient presented with symptoms of Hepatitis A infection. Although there is comorbidity with gallbladder polyp, the physical and laboratory abnormalities resolves with in 1 week.

Abstract #1861

Performance of two commercial Hepatitis E Virus RNA assays and HEV Ag assay in WHO HEV RNA reference standard and patients with hepatitis E

Haiying Zhang

Background and aim: Results obtained from different anti-HEV IgM assays are usually inconsistent. It is important to diagnose HEV infections by detecting HEV RNA and HEV Ag.
Methods: We assessed the performance of the Jinhao and Aikang assays, the two newly commercially available HEV RNA assays, and the diagnostic accuracies of serum HEV Ag and HEV RNA, using serial dilutions of WHO HEV RNA reference standard. We compared the correlation between two HEV RNA detection methods by testing 52 patients in both acute and chronic hepatitis E.
Results: The Jinhao assay was linear from 250 to 250,000 IU/ml, and the Aikang assay was linear from 500 to 250,000 IU/ml. Reproducibility was estimated from the CT values for each dilution. The mean standard deviations were 0.7 CT (range: 0.4 to 1.6 CT) for the Jinhao RT-PCR and 0. 9CT (range: 0.6 to 1.8 CT) for the Aikang RT-PCR. The Jinhao assay detected 8/10 250 IU/ml samples, while the Aikang assay detected 1/10. The Jinhao and the Aikang RT-PCR results were correlated. HEV Ag demonstrated good consistency with WHO HEV RNA standards detected by Jinhao and Aikang assay, respectively ($k = 0.949$, $P < 0.001$; $k = 0.923$, $P < 0.001$).
Conclusions: Two HEV RNA detection methods and HEV Ag assay show good consistency in patients with acute and chronic genotype 4 hepatitis E and WHO HEV RNA standard. We therefore recommend these two HEV RNA detection methods and HEV Ag assay.

Abstract #2163

Severity of acute viral hepatitis in patients with Glucose-6-phosphate dehydrogenase deficiency: a case control study

Om Parkash

Background/ aim: Viral hepatitis is known to be one of the significant causes of morbidity and mortality globally. In patients with glucose 6 phosphate dehydrogenase deficiency (G6PD), acute viral hepatitis may be associated with complications such as severe anemia, hemolysis, renal failure, hepatic encephalopathy and even death. In this study we will compare the parameters of morbidity and outcomes in patients of acute hepatitis with and without co-existing G6PD deficiency.
Materials and methods: Nine patients with acute viral hepatitis and diagnosed G6PD deficiency were compared with 27

matched control patients presented with acute viral hepatitis, from January 2012 to December 2018.
Results: The patients with G6PD deficiency had a significantly raised mean total bilirubin levels as compared to controls (23.8 ± 17.4 vs 10.0 ± 8.8 mg/dl, respectively, P < 0.01), Direct and indirect bilirubin levels were also significantly raised in patients with G6PD deficiency. Mean Hemoglobin levels were low in G6PD patients in comparison to the control group (12.0 ± 2.6 vs 14.07 ± 2.6 g/dl, respectively, P = 0.05). Hemolysis was seen in 22.2% of G6PD group. Anemia was more prevalent in G6PD patients as compared to controls (66.7% vs 7.4%, respectively, P < 0.02). Acute kidney injury in G6PD group was significantly high as compared to control group (55.8% vs 3.7%, respectively, P < 0.02). Only one patient in each group required hemodialysis. The most common etiology was hepatitis A in both group (66.7% vs 44.4%) followed by hepatitis E. The average duration of stay was prolonged in G6PD patients (9.1 ± 12.2 vs 3.5 ± 1.5 days, respectively, P < 0.05). No significant difference was seen in symptoms, prothrombin time, liver enzymes and outcome in both groups i.e. recovery was seen in both groups.
Conclusion: Acute viral hepatitis in patients with G6PD has a more severe clinical course due to complications leading to prolonged hospital stay but no difference was seen on overall clinical outcome of patients.

Abstract #2247

Acute motor axonal neuropathy following acute hepatitis-A-A rare presentation

Jha Ashish Kumar,[1] Dayal Vishwa Mohan[1]

[1]Department of Gastroenterology, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Bailey Road, Patna, Pin- 800014, Bihar, India

Introduction: A variety of neurological syndromes have been reported in hepatitis A viral (HAV) infection. Usually these patients suffer from acquired demyelinating polyradiculoneuropathy, but a few cases showed acute motor axonal neuropathy.
Objective: We describe a rare case *of acute motor axonal neuropathy following HAV infection*.
Methods: A 19-year-old female presented with jaundice of 2-weeks duration and weakness of all four limbs since 1-week. Examination revealed icterus, decreased muscular power (2 to 3/5) in all four-limbs and hyporeflexia. Labs showed anaemia (9.8 gm/L), leukocytosis (22,400/cumm), hyperbilirubinemia (15 mg/dL), transaminesemia, hypokalemia (2.4 mEq/L), elevated serum ammonia (144μ/mol/L) and deranged PT-INR (1.55). Serology was positive for anti-HAV (IgM). Ultrasonography revealed hypoechoic parenchyma, gallbladder wall thickening and small peri-portal lymph node. Supportive treatment including correction of hypokalemia was done, but her weakness did not improve. *Nerve conduction velocity showed generalized motor axonal neuropathy*. The patient was diagnosis as acute liver failure with acute motor axonal neuropathy caused by HAV infection. Use of intravenous immunoglobulin and plasmapheresis have been described, *however we treated our patient with supportive therapy due to presence of acute liver failure.*
Results: The patient had improvement in her symptoms and liver function after 2-weeks. She was discharged after 3-weeks. Follow-up after a month showed improved serum bilirubin (4.5gm/dL) and muscular power (4 to 5/5).
Conclusions: Acute motor axonal neuropathy may be one of the neurologic manifestations of HAV infection; however, whether it is a coincidence or a causal relationship remains a question.

Alcoholic Liver Disease

Oral Presentations

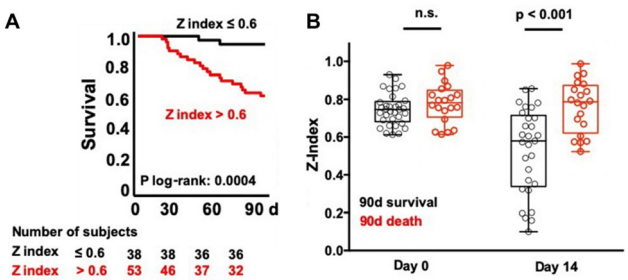
Abstract #670

A novel lipoprotein-based Z-index robustly predicts 90-day mortality in severe alcoholic hepatitis

Perez-Matos Maria Camila[1], Garcia Erwin[2], Shalaurova Irina[2], Landeen Lee[3], Otvos James D[2], Connelly Margery A[2], Jiang Z. Gordon[1]

[1]Division of Gastroenterology and Hepatology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215, [2]Laboratory Corporation of America Holdings (LabCorp), Morrisville, NC 27560, [3]Vital Therapies, Inc., San Diego, CA 92128

Introduction: Severe alcoholic hepatitis (AH) is associated with high mortality, while accurate prognostication remains difficult, which complicates transplant candidate selection. We recently discovered that AH patients have profoundly impaired lipoprotein metabolism characterized by the accumulation of lipoprotein Z (Lp-Z), an abnormal LDL-like particle rich in free cholesterol.
Objective: To test the utility of Z-index, a score that captures the degree of impairment to hepatic lipoprotein metabolism, in predicting outcomes in severe AH.
Method: We identified 91 subjects from the phase 3 log-rank Liver Assist Device (ELAD) trial for AH (VTI-208E) and measured lipoprotein profiles on a Vantera NMR spectroscopy analyzer to calculate the Z-index at baseline and day 14.
Results: ELAD subjects (n = 91) had a mean MELD of 26 (IQR 24–28) and 90-day mortality of 26%. The baseline Z-index was strongly associated with 90-day mortality with a hazard ratio of 120 (95% CI 7.8–1850, p = 0.001) in the Cox proportional hazard model. Kaplan Myer survival analysis using Z-index cutoff of 0.6 significantly differentiates subjects with high 90-day mortality (P log-rank < 0.001). Only two subjects with Z-index < 0.6 died, whereas 20 out of 53 died within 90 days. Among the subjects with Z-index ≥ 0.6 at baseline, repeat Z-index measured at day 14 was significantly lower among 90-day survivors (0.53 vs. 0.76, p < 0.001 by T-test) independent of the treatment group.
Conclusions: A Z-index calculated from circulating Lp-Z in severe AH subjects was shown to outperform MELD and more robustly prognosticated 90-day mortality.



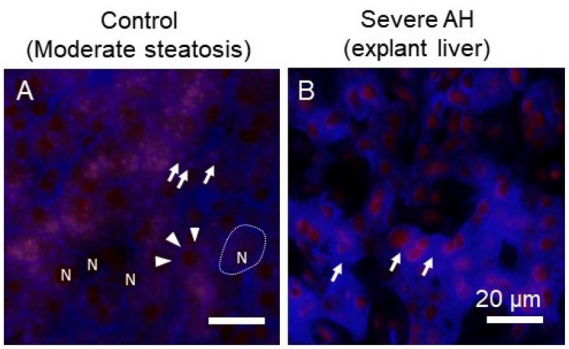
Abstract #673

Abnormal lipoprotein Z drives cholesterol-mediated toxicity in alcoholic hepatitis: a novel pathogenic pathway

Hu Kunpeng[1,2], Perez-Matos Maria C[1], Deng Huiyan[1], Cai Huimei[1], Tran Stephanie[1], Sun Zhaoli[3], Jiang Z. Gordon[1]

[1]Division of Gastroenterology and Hepatology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, United States, [2]Department of General Surgery, The Third Affiliated Hospital of Sun Yat-Sun University, Guangzhou, China, [3]Department of Surgery, John Hopkins University, Baltimore, Maryland, United States

Introduction: We recently found that alcoholic hepatitis (AH) patients carry a distinctive profile of circulating lipoproteins characterized by a remarkable accumulation of Lipoprotein-Z (Lp-Z), a low density lipoprotein (LDL)-like particle rich in triglyceride and free cholesterol (FC). High levels of FC is known to cause cytotoxicity, which raises the possibility that LpZ contributes to liver failure in AH.
Objectives: To determine the impact of Lp-Z on hepatocytes relevant to AH.
Methods: Liver tissue and serum samples from AH patients were analyzed for FC and Lp-Z. Synthetic Lp-Z-like emulsion particles (rLpZ) were reconstituted in vitro to study its impact on HepG2 and PXB primary human liver cells.
Results: Fluorescent microscopy of frozen liver explant tissues from AH patients illustrated a remarkable accumulation of FC and disruption of its normal distribution in hepatocytes. These changes were associated with a decrease in the expression of Acyl-CoA Acyltransferase 2 (ACAT2), a hepatocyte-specific enzyme that converts FC to cholesterol ester. To test the impact of Lp-Z on hepatocytes, we reconstituted rLpZ using the lipid compositions seen in AH patients. Upon incubation with rLpZ labeled with TopFluor cholesterol, hepatocytes were infiltrated by TopFluor cholesterol tracer in a time-dependent manner in both HepG2 and PXB cells. Upon treatment of hepatocytes with rLpZ in vitro, HepG2 cells underwent a FC-dose dependent cell death within 6 h. The rLpZ induced cell toxicity was exacerbated upon the inhibition of ACAT2.
Conclusion: A high concentration of Lp-Z seen in AH patients causes FC-mediated hepatotoxicity. Targeting cholesterol-toxicity may be a viable strategy to treat AH.



Blue: FC stained by Filipin (arrow); red: nucleic acid (N) stained by propidium iodide

Abstract #712

Up-regulation of Fgl2 induced by chronic ethanol consumption combined with HBV promotes hepatic macrophage M1-polarization and lipid metabolism disorder

PengWang[1], Xue Hu[1], DanQing Hu[1], Yaqi Wang[1], Xiaoping Luo[1], HongWu Wang[1], Qin Ning[1]

[1]Department and Institute of Infectious Disease, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Introduction: As an important immuno-inflammatory regulator, fibrinogen-like protein 2 (FGL2) play a key role in HBV-related liver diseases. However, its role in alcoholic liver disease combined with HBV persistence (ALD-HP) remains unclear.
Objectives: To investigate the mechanism of Fgl2 in ALD-HP using a new mouse model.
Methods: 6-week-old male C57BL/6 mice with Fgl2 status (+/+ or −/−) were hydrodynamically injected with a pAAV-1.2 HBV vector and then fed an ethanol diet for 6 weeks. Serum biomarkers and liver histology, liver fat levels, macrophages polarization and lipid metabolism related molecules were measured. In vitro assays primary bone marrow cells were stimulated to be M1 or M2 macrophages and then co-cultured with Hepa1–6 cells cells to examine the difference of lipid metabolism-related genes between *Fgl2*+/+ and −/− groups.
Results: Compared with *Fgl2*−/− mice, *Fgl2*+/+ mice showed significant hepatic steatosis and increasing TG and TC contents in ALD-HP group. Both alcohol and HBV persistence led to increased hepatic Fgl2 expression, increased M1 and reduced M2 proportions, respectively. The trend was more significant in ALD-HP group and blunted after gene knockout of *Fgl2*. In vitro assay also demonstrated that Fgl2 promoted macrophage differentiation to M1, thus up-regulating crucial lipid metabolism-related genes in Hepa1–6 cells, including Srebp-1, NF-κB, Srebp-2 and HMGCR.
Conclusion: Alcohol and HBV infection could up-regulate hepatic Fgl2 expression, promote macrophage towards M1, and thus result in an abnormal hepatic lipid metabolism. The condition was significantly improved by knock-out of *Fgl2*.

Abstract #1212

Dietary copper plays an important role in maintaining intestinal barrier integrity during alcohol induced liver disease through regulation of intestinal HIF-1a signaling pathway

Yongping Chen[1], Hongwei Lin[1]

[1]Department of Infectious Diseases, the First Affiliated Hospital of Wenzhou Medical University, Zhejiang Provincial Key Laboratory for Accurate Diagnosis and Treatment of Chronic Liver Diseases, Wenzhou Key Laboratory of Hepatology, Hepatology Institute of Wenzhou Medical University, Wenzhou 325000, China

Introduction: Impaired intestinal barrier function and oxidative stress injury play critical roles in the pathogenesis of alcoholic liver disease (ALD) and recent investigations reveal a role of dietary copper in the liver and intestinal barrier function.
Objectives: The current study is to investigate the mechanisms and role of dietary copper on alcohol induced liver diseases.
Methods: C57BL/6 mice were used to create alcoholic liver disease model with Lieber-DeCarli diet containing 5% alcohol and fed with different concentrations of dietary diets adequate copper (6 ppm, Cu A), marginal copper (1.5 ppm, Cu M)or supplemental copper (20 ppm, Cu S).Caco-2 cells were also employed to expose to ethanol and different concentrations of copper. Damages of the liver and intestine were evaluated by transaminases and histology staining, as well as cell proliferation, oxidative stress and mitochondrial membrane potential.
Results: Alcohol diet causes liver injury and disruption of intestinal barrier function as well as decreases genes expression such as hypoxia-inducible factor-1a (HIF-1a), Superoxide dismutase 1 (SOD1), and glutathione peroxidase 1 (GPX1). However, supplemental dietary copper can revert these changes, but marginal dietary copper can worsen these changes. In animal experiments, marginal dietary copper or low level of dietary copper showed detrimental effects on intestinal barrier function and genes expression.
Conclusion: Supplemental dietary copper has benefial effects on the liver and intestinal barrier function as well as gene expression.

However, marginal dietary copper shows detremental effects on these paremeters.

Abstract #1219

Modified Lille score incorporating the neutrophil-to-lymphocyte ratio (NLR)—a novel score for predicting prognosis in severe alcoholic hepatitis

Pb. Sriram[1], A.R. Venketeshwaran[1]

[1]Institute Of Medical Gastroenterology, Madras Medical College, Chennai, India

Background: Use of Prednisolone which is considered the cornerstone treatment for severe alcoholic hepatitis (AH) is limited by the increased risk of infection in these patients. Day-4 Lille score is a widely employed prognostic model used to identify non-responder subgroup. The present study evaluates the prognostic ability of the inflammatory marker, the neutrophil-lymphocyte ratio (NLR), as a stand-alone model and in conjunction with the day-4 Lille score.
Methods: A total of 200 patients diagnosed with AH were included. Demographic and biochemical data at diagnosis were collected to calculate Maddrey's discriminant function (MDF) and model for end-stage liver disease (MELD) score upon admission and also on day 4. Receiver operating characteristic (ROC) curves were plotted for day-4 NLR and day-4 Lille score for prediction of 90-day mortality, and optimal cut-off values were determined.. We then performed a multivariate analysis for prediction of 90-day mortality using day-4 Lille score and day-4 NLR, constructing a new prediction score based on the odds ratio (OR). The ROC curve of the new score was plotted and the area under a curve (AUC) was reported and compared with previously validated scores.
Results: Based on our analysis, both day-4 NLR and Lille score individually predicted 90-day mortality with statistical significance (p: 0.049, $p < 0.001$, respectively.)The ROC analysis of day-4 Lille score for the prediction of 90-day mortality revealed an AUC of 0.859 with an optimal cut-off value of 0.45 (sensitivity: 83.3%, specificity: 76.1%). Day-4 NLR had an AUC of 0.786 with an optimal cut-off value of 11.5 (sensitivity: 66.7%, specificity: 78.1%) The combined day-Lille-NLR model with a cut-off of 0.55 had an AUC of .889, which was higher than day-4 Lille score and NLR independently).
Conclusion: Combining Lille score with NLR to create a "modified" Lille score adds increased performance characteristics to the prediction of outcomes/mortality in patients with severe alcoholic hepatitis.

Abstract #1705

Temporal change in the plasma metabolome profile is indicative of outcome in severe alcoholic hepatitis

Jaswinder Singh Maras[1], Adil Bhat[1], Gaurav Yadav[1], Arun Thakur[1], Shiv kumar Sarin[1,2]

[1]Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi, 110070, [2]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, 110070

Background and aims: Severe alcoholic hepatitis (SAH) has a high mortality, and corticosteroid therapy is effective in reducing 28 day mortality in about 60% patients. There is limited data on the serial metabolomic profile of SAH patients on corticosteroid therapy and clinical outcomes (responder, R, Lille score < 0.45 at day 7, or non-responder, NR) till 60 days.
Methods: We analyzed plasma metabolome at baseline, day 4,7,14 and 28 using ultra-high performance liquid chromatography and high-resolution mass spectrometry. Multivariate projection analysis identified metabolites in the discovery cohort (n = 35,R = 23, NR = 12) which were evaluated in the validation cohort of 100 patients (70 R, 30 NR).
Results: A total of 671 features were annotated by using metabolomic/spectral databases. SAH plasma showed significant increase in 181 metabolites linked to tryptophan metabolism, bile acids, butanoate metabolism, nitrogen metabolism and others, whereas significant decrease in 199 metabolites linked to glutathione metabolism, TCA cycle, pyruvate metabolism and others as compared to healthy subjects (FC $\pm$ 1.5, $p < 0.05$). Corticosteroid exposure for 4 days increased plasma metabolites linked to tryptophan metabolism, bile-acids, nitrogen metabolism and reduced metabolites linked to sphingolipid metabolism, biosynthesis fatty-acids, glutathione metabolism, energy metabolism in NRs compared to R (FC $\pm$ 1.5,$p < 0.05$). Similarly, corticosteroid exposure for 7, 14 or 28 days significantly increased plasma metabolites linked to inflammation; tryptophan, butanoate, arachidonic/leukotriene metabolism and decreased metabolites associated to antioxidant pathway (glutathione metabolism), biosynthesis of fatty acids and alternate energy pathways in NR (FC > 1.5, $p < 0.05$). Increased plasma levels of 3-hydroxyanthranilate, L-kynurenine, 3-Indoleacrylic acid (tryptophan metabolism) and arachidonate, lecithin, leukotriene-C4, prostaglandin-B1 (arachidonic/leukotriene metabolism) significantly correlated to severity and mortality ($r > 0.4$; $P < 0.01$). Upon validation, baseline levels of L-kynurenine (OR, 2.1 (1.5–3.2) Indoleacrylic acid (OR, 3.0 (2.4–8.2), lecithin (OR, 1.5 (1.2–2.9) and prostaglandin B1 (OR, 3.5 (1.8–9.2) were the most significant predictors of non-response and non-survival (AUROC > 0.80; $p < 0.05$) in our study cohort.
Conclusion: Corticosteroid over exposure has hazardous effect particularly on non-responsive patients. Temporal changes in plasma metabolome signatures associated with tryptophan and arachidonic/leukotriene metabolism can reliably predict at baseline steroid response and disease outcome in SAH patients.

Abstract #2027

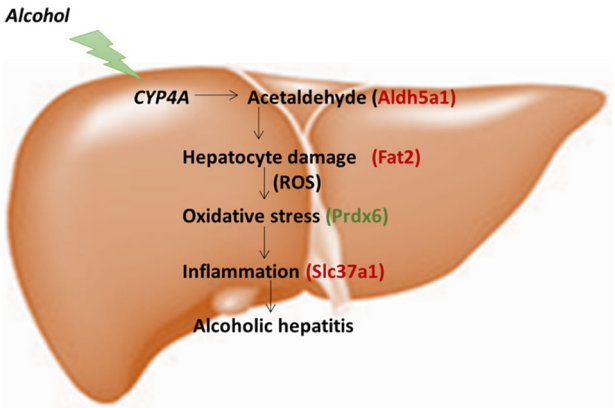
Proteomic variations presented with chronic dose of alcohol can be captured in low and early exposure

Chaudhary Sudrishti[1], Bhat Adil[1], Kumari Anupama[1], Tandon Suchita[1], Kadyan Sonia[1], Rastogi Archana[2,] Maras Jaswinder Singh[1], Sarin Shiv K[1,3], Sharma Shvetank[1]

[1]Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi, India, [2]Department of Histopathology, Institute of Liver and Biliary Sciences, New Delhi, India, [3]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Chronic or high dose of ethanol has been studied in detail but there is limited information regarding the effects of early or low dose of alcohol on hepatic proteome. This study investigated the kinetics of proteins in low and high chronic exposure to alcohol.
Methods: C57/B6J male mice (n = 20) were pair-fed isocaloric Lieber-DeCarli liquid diet containing 5% and 25% ethanol for 12 weeks. Liver was harvested at 4 and 12 weeks and studied for histology, injury markers, and biochemical parameters. After protein isolation, label free quantitative proteomic analysis was performed by high resolution mass spectrometry.
Results: 5% alcohol showed 1677 differentially expressed proteins (DEPs) (> 693up, > 482downregulated) whereas 25% group had

1797 DEPs (> 349up, > 1195 downregulated; fold change ± 1.5p > 0.05). Unique pathways in 5% ethanol dose were associated with ABC transporters, bile metabolism and with 25% ethanol group HIF-1 signaling and glycerophosholipid metabolism pathways were linked. However, the common pathways associated with differentially regulated proteins (Protocadherin-Fat2 (Fat2), Glucose-6-phosphate exchanger (Slc37a1) and aldehyde dehydrogenase-5 (Aldh5a1) (FC > 1.5;p < 0.05) in both low and chronic high dose ethanol were related to fatty acid metabolism, drug metabolism, inflammation and tight junction assembly. Whereas common downregulated proteins in both groups (chaperonin-containing-TCP1 (Cct3), dihydrodiol-dehydrogenases (Dhdh) and Peroxiredoxin-6 (Prdx6) (FC < 1.5;p < 0.05) were associated with glutathione metabolism, amino acid metabolism and PPAR signaling pathways. Expression of these target proteins detected in chronic stage were reflected even in low dose, early ethanol exposure.
Conclusion: Our data implicates key proteins/pathways that can be captured even after low dose ethanol exposure and as early markers of alcoholic liver disease.



Poster Presentations

Abstract #320

Critical roles of conventional dendritic cells in autoimmune hepatitis via autophagy regulation

Xiaoli Fan, Ruoting Men, Chen Huang, Mengyi Shen, Tingting Wang, Tinghong Ye, Li Yang

Background: Autoimmune hepatitis (AIH) is a necroinflammatory disease associated with interactive cell populations of the innate and adaptive immune systems. The contribution of conventional dendritic cells (cDCs) to AIH and the underlying mechanism remain poorly understood.
Methods: Peripheral blood samples and liver were collected from AIH patients and healthy controls. In vitro, immature DCs were generated from mice bone marrow (BMDC). Under ConA treament, the autophagy-related proteins were measured as well as the maturation of DCs. 3-MA and bafilomycin A1 were added, respectively, to observe the effects on the expressions of antophagy markers and the phenotypic change of DCs. The electron microscopy and immunofluorescence method were also used to evaluate the process of autophagy flux.
Results: The frequency of peripheral mature cDCs increased in AIH patients and was positively correlated with disease severity. In EAH mice, hepatic accumulation of mature cDCs was observed, along with an increase in the periphery. Sequentially, BMDC from EAH mice exhibit more proinflammatory function than those from control mice. In vitro, ConA treatment promotes the maturation of BMDCs. ConA also induced the expression of autophagy-related protein and the formation of autophagosomes in DCs. 3-MA and bafilomycin A1 inhibited the mature status and proinflammatory cytokine secretion and diminished the proliferation and differentiation of CD4+ T cells when ConA-induced BMDCs cocultured CD4+ T cells.
Conclusion: We demonstrated that cDCs contribute to the pathogenesis of AIH through excessive maturation. Aberrant autophagy flux plays a vital role in the immunogenic maturation of cDCs in AIH.

Abstract #488

Role of TGF-β in alcohol-induced liver disease

Le Thi Thu Hien-[1], Le Quoc Tuan[2], Tran Viet Tu[3], Nguyen Ba Vuong[3]

[1]Thai Nguyen University of Medicine and Pharmacy, [2]Thanh Ba Hospital, [3]103 Military Hospital

Introduction: Transforming growth factor-β (TGF-β) is a vital molecule that promotes the stimulation of collagen I and an important cytokines involved in the fibrotic and cirrhotic transformation of the liver and HSCs transformation. Understanding the role of TGF-β, and inhibiting TGF-β release in alcoholic liver disease (ALD), as well as identifying key biological pathways and mechanisms for suppressing alcohol-induced stem cell injury will be critical for enhancing patient care and the employment of new therapeutic approaches.
Objectives: To determine the clinical significance of the serum levels of TGF-β in ALD.
Methods: A total of 95 patients with a pathologically confirmed diagnosis of ALD were enrolled into this study. Serum TGF-β concentrations were determined by the solid-phase sandwich ELISA method. Liver biopsy was required for the diagnosis of histologic ALD. Evaluate the stage of liver fibrosis according to Metavir classification.
Results: TGF-β levels of the ALD patients were significantly lower than those in the control group ($p < 0.001$). TGF-β levels of the liver fibrosis of F3-F4 group were significantly higher than those in the liver fibrosis of F1-F2 group (median values 1289.92 ng/L–1390.94 ng/L vs. 1136.33 ng/L–1172.28 ng/L, respectively; $p < 0.001$). TGF-β levels of alcoholic cirrhosis group were significantly higher than those in the alcoholic hepatitis group ($p < 0.05$).
Conclusions: There was a relationship between TGF-β with disease stage and liver fibrosis stage. It may be a biomarker used to assess the stage of liver fibrosis and to predict disease severity in clinical practice.
Keywords: Transforming growth factor-β, Alcoholic liver disease.

Abstract #490

The role of GGT levels and AST/ALT ratio in alcoholic liver diseases

Le Thi Thu Hien[1], Le Quoc Tuan[2], Dong Duc Hoang[1]

[1]Thai Nguyen University of Medicine and Pharmacy, [2]Thanh Ba Hospital

Introduction: Alcoholic liver disease (ALD) is one of the most frequently diagnosed liver problems in the hospitalized patients in most tertiary care hospitals all over the world. The diagnosis of ALD is most of the time clinical. GGT (Gamma glutamyle transferase), AST/ALT (Aspartate/Alanine aminotransferases) ratio is a useful and reliable biochemical marker of liver injury due to alcohol.

Objectives: To assess the value of enzymes GGT, AST and ALT as diagnostic indicators of ALD.
Methods: This study was conducted at Thai Nguyen Hospital. A total of 95 patients diagnosed as ALD since January 2016 to December 2018 were analyzed. Serum levels of AST, ALT and GGT were analyzed using standard. The data was analyzed using software SPPSS 16 version.
Results: The mean values of GGT in ALD patients (749.10 ± 116.18) was markedly increased as compared to healthy group (31.25 ± 12.36). The mean values of AST (198.19 ± 55.05) was found to be highly increased in comparision to ALT (85.86 ± 71.06) leading to significatinly higher AST/ALT ratio (2.99 ± 2.01). The mean values of deritis ratio in ALD patients which was markedly increased as compared to the ratio of controls. There were significant differences in the AST/ALT ratio between two groups. Patients with ALD had AST/ALT ratio > 1.5
Conclusion: High AST/ALT ratio suggests advanced ALD. GGT and AST/ALT ratio of ≥ 1.5 together are good indicators of alcohol as the cause of liver disease. AST/ALT ratio > 2 indicates advanced liver disease in alcoholics.

Abstract #883

Role of single nucleotide polymorphisms (SNPs) in hydroxysteroid 17-β dehydrogenase 13 (HSD17B13) gene in patients with alcoholic ACLF

Bakshi Neha[1], Bihari Chhagan[1], Rastogi Archana[1], Baweja Sukriti[2], Sarin Shiv K.[3]

[1]Department of Pathology, Institute of liver and biliary sciences, New Delhi, India, [2]Department of Molecular and cellular medicine, Institute of liver and biliary sciences, New Delhi, India, [3]Departmen of Hepatology, Institute of liver and biliary sciences, New Delhi, India

Introduction: SNPs in HSD17B13 have been linked with protection from chronic liver disease, better liver histology in NASH and lower serum ALT in hazardous drinkers.
Objectives: To evaluate association between SNPs in HSD17B13 and (a) histopathologic (liver biopsy) features (b) treatment (steroid) response (c) short term outcome in alcoholic ACLF.
Methods: 100 liver biopsies (n = 100) reported as severe alcoholic hepatitis compatible with ACLF were analyzed for predetermined histologic parameters and HSD17B13 IHC; DNA isolated from liver biopsies was genotyped for HSD17B13 SNP **rs72613567, rs62305723 and rs10433879**. SNP status was correlated with histologic and IHC findings, clinical parameters, treatment response and survival.
Results: rs72613567:TA showed less severe lobular inflammation [LI] (p = 0.019), lesser parenchymal necrosis [PN] (p = 0.040), lower AHHS score (p = 0.031) and trend towards lower total bilirubin, ALT, AST and MELD score (p > 0.05). rs62305723:GA and rs62305723:A showed lesser LI (p = 0.413), absence of neutrophilic satellitosis [NS] (p = 0.022), lower serum bilirubin (p = 0.048) and trend towards lower AST, ALT, GGT, MELD score (p > 0.05). rs10433879:GC genotype showed lower serum GGT (p = 0.015), trend towards lower ALT and ALP (p > 0.05) but did not significantly influence histology. Steroid response was better for rs72613567: TA (100% vs 76.5%; p = 0.221) and rs10433879:GC (83.3% vs 77.7%; p = 0.321). Response rate was 80% for rs62305723:A (vs 80.3%; p = 0.302). 90 day survival was 100% in rs72613567:TA (vs 72.3%; p = 0.336), 100% for rs62305723:A (vs 68.3%; p = 0.1077) and 72.7% for rs10433879:GC (vs 74.3%; p = 0.998).
Conclusion: SNPs (rs72613567:TA; rs62305723:A) in HSD17B13 are associated with better liver histology and lower AHHS score in severe alcoholic hepatitis.

Abstract #922

SIBO is prevalent in patients of Alcoholic liver disease even after complete abstinence

Nikhil Gupta[1], Vivek Kumar Mishra[2], S. P. Misra[3], M. Dwivedi[4]

[1]Senior Resident, Department of Gastroenterology, MLN Medical College Allahabad, India, [2]Assistant Professor, Department of Gastroenterology, MLN Medical College Allahabad, India, [3]Professor and Head, Department of Gastroenterology and Hepatology, MLN Medical College Allahabad, India, [4]Professor, Department of Gastroenterology and Hepatology, MLN Medical College Allahabad, India

Background: Small intestinal Bacterial overgrowth is prevalent in patients with liver cirrhosis predisposing to remote liver injury and various complications.
Aim: To determine the prevalence of SIBO in patients with alcoholic liver disease on complete abstinence and to compare the prevalence with other etiologies.
Methods: 102 patients with liver cirrhosis were assessed for presence of SIBO by glucose hydrogen breath test. A basal breath-hydrogen > 20 ppm or a rise by ≥ 12 ppm above baseline following glucose administration was taken as positive test. Prevalence of SIBO was compared in patients with alcoholic liver disease (who were in complete abstinence for 6 months) with cases with other etiologies of CLD.
Results: Of the 102 cirrhotic cases, highest number of SIBO positive cases were found to have alcoholic cirrhosis (83.34%) percentage SIBO positivity in cases with HBV, HCV, autoimmune hepatitis, cryptogenic cirrhosis as etiologies of CLS were 70.83%, 46.15%, 42.85% and 54.54% respectively. On directly comparing the percentage positivity of S9.2534; p = 0.0023IBO in patients with alcoholic liver disease with other etiologies as a whole the association of SIBO with alcoholic liver disease was statistically significant (Chi square = 9.2534; p = 0.0023).
Conclusion: Small intestinal bacterial overgrowth was highly prevalent in patients with alcoholic liver disease as compared to cirrhotic patients of other etiologies.

Abstract #1543

Clinical features of alcoholic liver disease with chronic viral hepatitis: a single-center, retrospective, cross-sectional study

Youwen Tan[1], Xingbei Zhou[1]

[1]Department of Hepatology, The Third Hospital of Zhenjiang Affiliated Jiangsu University, Zhenjiang, 212003 Jiangsu Province, China

Objective: To examine the status and clinical characteristics of alcoholic liver disease (ALD) in patients with chronic viral hepatitis.
Method: This was a single-center, retrospective, cross-sectional study. Clinical data were collected from patients diagnosed with ALD who were hospitalized from the 1st of January 2012 to the 1st of January 2019 in the Third Hospital of Zhenjiang Affiliated to Jiangsu University.
Results: The study included 725 cases of ALD, including 381 cases of ALD alone, 226 cases of ALD complicated with chronic hepatitis

B (CHB), and 118 cases of ALD complicated with chronic hepatitis C (CHC). There were differences in age, sex, history of alcohol consumption, hospitalization time, main biochemical parameters, and platelet count (PLT) among the three groups (P all < 0.05). Among all ALD patients, 141 patients were diagnosed with cirrhosis, while 584 patients had disease that was not accompanied by cirrhosis. Multiple logistic (binary) regression analysis suggested that alcohol consumption, prealbumin (PALB), creatinine (CR), cholesterol (CHOL), and PLT levels were associated with cirrhosis, while ascites and chronic hepatitis B are also known risk factors for cirrhosis. Among all patients, 68 were diagnosed with hepatocellular carcinoma (HCC), while 657 had no diagnosis of HCC. Multiple logistic (binary) regression analysis suggested that alpha-fetoprotein, alkaline phosphatase, and cirrhosis were risk factors for HCC.

Conclusion: We found that a considerable proportion of patients with ALD were infected with either hepatitis B or hepatitis C virus. Compared with patients with ALD alone, patients with viral hepatitis had a younger hospitalization age, reduced history of alcohol consumption, and a higher incidence of cirrhosis.

Abstract #1816

The value of early dynamic improvement of acute-on-chronic liver failure on the mortalities of patients with alcoholic liver cirrhosis

Eileen L. Yoon[1], Do Seon Song[2], Jin Mo Yang[2], Hee Yeon Kim[2], Chang Wook Kim[2], Sung Won Lee[2], Han Ah Lee[3], Young Kul Jung[3], Hyung Joon Yim[3], Jeong-Ju Yoo[4], Soung Won Jeong[4], Sang Gyune Kim[4], Jae Young Jang[4], Seong Hee Kang[5], Moon Young Kim[5], Jung Gil Park[6], Won Kim[7], Baek Gyu Jun[8], Ki Tae Suk[9], Dong Joon Kim[9], on behalf of Korean Acute-on-Chronic Liver Failure (KACLiF) Study Group

[1]Department of Internal Medicine, Inje University, [2]Department of Internal Medicine, The Catholic University of Korea, [3]Department of Internal medicine, Korea University, [4]Department of Internal Medicine, Soonchunhyang University, [5]Department of Internal Medicine, Wonju College of Medicine, Yonsei University, [6]Department of Internal Medicine, Yeungnam University College of Medicine, [7]Department of Internal Medicine, Seoul Metropolitan Government Seoul National University Boramae Medical Center, [8]Department of Internal Medicine, University of Ulsan College of Medicine, [9]Department of Internal Medicine, Hallym University College of Medicine

Background/Aims: We aimed to investigate the relationship between early dynamic improvement (EDI) of ACLF and mortalities in alcoholic LC patients.

Methods: A total of 1156 alcoholic LC patients admitted for acute decompensation were prospectively enrolled from 33 academic hospitals in South Korea (male 927, median age 54 years) since 2015. EDI was defined as improved ACLF down to grade 0 on day 7 following the diagnosis among CLIF-C ACLF patients. Patients were divided into 3 groups; group 1, no ACLF (n = 866); group 2, ACLF with EDI (n = 112); group 3, ACLF without EDI (n = 110).

Results: During the median follow-up of 8.4 months (IQR 2.0–16.6 months), 1-year mortalities of group 2 (HR 1.57, 95% CI 1.24–2.00, $P < 0.001$) and group 3 (HR 3.09, 95% CI 2.47–3.86, $P < 0.001$) were higher than that of group 1. Group 3 showed significant higher mortality than that of group 2 (HR 1.92, 95% CI 1.42–2.59, $P < 0.001$). Among ACLF patients, higher ACLF grades (≥ 2) at baseline (HR 2.07, 95% CI 1.21–3.55, $P = 0.008$) and presence of EDI at day 7 (HR 0.22, 95% CI 0.12–0.40, $P < 0.001$), but not the MELD at baseline or at day 7, were significant predictors for 28 days mortality. Meanwhile, older age and higher MELD at day 7 (≥ 15), but not the ACLF grade at baseline and presence of EDI at day 7, were significant predictors of 1-year mortality.

Conclusions: The presence of EDI in ACLF was significant predictor for short-term mortality. However, MELD at day 7 was better predictor for 1-year mortalities among ACLF patients with alcoholic LC.

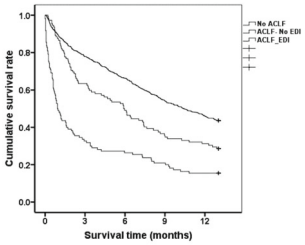


Figure 1. One-year mortalities of patients in group 1 (No ACLF), group 2 (ACLF with EDI), and group 3 (ACLF without EDI)

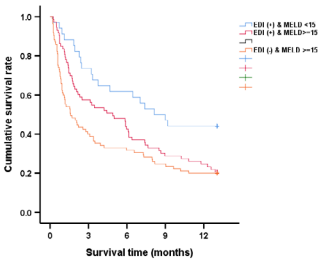


Figure 2. One-year mortalities of ACLF patients based on the early dynamic improvement (EDI) of ACLF and MELD at day 7 following ACLF diagnosis.

Abstract #2225

A young female with alcoholic liver cirrhosis: case report

Muhammad Iqbal[1]

[1]Internsip Doctor in Asembagus General Hospital, Situbondo Regency, East Java Province, Indonesia

Introduction: Alcoholic liver cirrhosis is a disease due to excessive alcohol consumption that manifest as fatty liver, alcoholic with fibrosis or liver cirrhosis.

Case Illustration: Female, 26 years old complaints of bloody vomiting, black tarry stool, abdominal distention and history of alcohol consumption for 10 years. Physical examination revealed anemic conjunctiva, ascites, hepatosplenomegaly, and bilateral legs edema. Laboratory examinations showed thrombocytopenia and hypoalbuminemia. AST, ALP and Bilirubin level were increased. Abdominal USG revealed hepatomegaly with coarse heterogenic ecoparenchym, portal vein dilatation, and splenomegaly. Diagnosis of alcoholic liver cirrhosis was made based on clinical, laboratory, and radiologic findings, while biopsy result did not confirm the pathology.

Discussion: Diagnosis of alcoholic liver disease was made based on the presence of excessive alcohol consumption history, presence of sign and symptoms of liver disease, and absence of other etiology of liver injury. Physical examination may range from normal to the presence of signs of cirrhosis. There is no single definite laboratory marker which can determine alcohol as the etiology of liver disease. Imaging studies did not have specific role in determining alcohol as the specific etiology of liver disease. Cessation of alcohol consumption is the most important thing in therapy and early management of alcohol abuse in patients with alcoholic liver disease.

Conclusion: Alcoholic liver disease can happen in patient who consumed alcohol excessively. The success of management depends on the integration of all competencies in public health, epidemiology, addiction behaviour, and alcohol-induced organ injury.

Autoimmune and cholestatic disease

Oral presentations

Abstract #564

Progression of portal hypertension in primary biliary cholangitis: single center report from Kazakhstan

Aiymkul Ashimkhanova[1,2], Damesh Orazbayeva[2], Marzhan Zhanasbayeva[2], Yura Prokopenko[2], Aibar Agynbay[2]

[1]Nazarbayev University School of Medicine, Nur-Sultan, Kazakhstan. [2]National Research Center for Oncology, Hepatology and Gastroenterology Unit, Nur-Sutan, Kazakhstan

Introduction: Primary biliary cholangitis is one of the most common autoimmune diseases worldwide with a female prevalence after age of 45–50's. In Kazakhstan the prevalence of disease is not known currently, but with the development of autoimmune markers in the labs, advancement in pathology and specialist training in tertiary care centers the confirmatory diagnosis has been improved in the country.
The Aim: It has been observed during routine clinical practice that signs of portal hypertension in Primary biliary cholangitis patients occur faster before the synthetic dysfunction of the liver can be observed or the progression into cirrhosis is established. In order to assess this hypothesis we decided to analyze the role of ultrasound Doppler characteristics in 23 patients with confirmed diagnosis of primary biliary cholangitis admitted from 2018 at National Research Oncology Center, Liver Unit. The chief specialist has the major role in assessing the Doppler measurements to keep the validity of the results.
Results: Total of 476 patients were admitted to the Liver Unit for the duration of 2018 January to 2019 October with variety of etiologies including: NASH, alcoholic/toxic liver injury, Liver cirrhosis decompensation, AIH, post-transplant rejection, primary portal hypertension, thrombophilia's, and other Liver injuries, among them 23 patients had been diagnosed with primary biliary cholangitis. Following established criteria used to diagnose: AMA-M2 antibodies, Liver histology and ALP/GGTp elevation together with bilirubinemia and transaminase elevations. Female to male ratio was 21:2, AMA-M2 negative, but gp210 and sp100 antibodies positive patients were observed in 6 female patients with confirmatory features of bile duct inflammation and concurrent ALT/AST elevation. Among them there were 3 patients with an Overlap syndrome with IgG increase more than 20 g/L and gamma globulin fraction of more than 20% together with AMA-M2 high titers and increase of ALT/AST more than 300 IU/ml. Mean age for the onset of disease was 47 y.o. (s.d. ± 8.98), mean ALP of 475 (s.d. ± 289.92), GGTp mean was 315 (s.d. ± 228.49), mean cholesterol was 6.7 mmol/l (s.d. ± 2.67), total bilirubin of 33.51 (sd ± 35.17), direct bilirubin of 26.11 (sd ± 32.29). Ultrasound Doppler characteristics for this cohort was following: mean portal vein size of 1.14 cm with sd ± 0.2, mean velocity was 21 cm (sd ± 12.87), V.lienalis diameter mean of 0.8 cm (sd ± 0.28), with a velocity of 21.31 cm (sd ± 7.9), the diameter of hepatic artery propria was 0.42 cm (sd ± 0.06), with a mean velocity of 98.57 cm (sd ± 25.28), mean IR of 0.67 (sd ± 0.05), splenic artery diameter of 0.56 cm (sd ± 0.1), with an increased velocity of 125 cm (sd ± 31.5), IR 0.64 (sd ± 0.07), the averaged area of the spleen was calculated to be 66.94 cm^2 (sd ± 37.15) and with the following platelet average of $229*10^9$/L (sd ± 93), WBC average $5.31* 10^9$/L (sd ± 1.34) and a mean hemoglobin of 112 g/L (sd ± 27). Other synthetic function tests measured by total protein (mean = 75.68), albumin (mean = 36.93), fibrinogen (mean = 2.97), INR (mean = 1.07) were not affected.
Conclusion: According to the results of the Doppler measurements of portal system among patients with confirmed primary biliary cholangitis, there is a tendency in increasing velocity in splenic artery as a first sign of portal hypertension progression in patients with Ishak fibrosis stage 3–4/6 without apparent signs of liver cirrhosis. Another finding is the splenomegaly which appears also earlier and might further progress into hypersplenism with platelet trapping and worsening of the disease. This could be helpful in adding earlier management in this patient treatment of PH decreasing medications such as non-selective beta-blockers, as well as optimize timing to add statin treatment to decrease portal inflammation along with UDCA. In order to validate the role of Doppler in follow up of disease progression the proper design needs to be established with detailed criteria and other inflammation markers added in order to validate that PH progression develops further more faster in this category of patients due to high autoimmune inflammation where the portal vein and its tributaries are highly involved.

Abstract #904

Acute autoimmune hepatitis: an uncommon mimicker of acute viral hepatitis, difficult to diagnose and treat

Taneja Sunil[1], De Arka1, Verma N[1], Premkumar M[1], Duseja A[1], Singh V[1], Das A[2], Dhiman RK[1]

Department of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh, India, [2]Department of Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Introduction: Acute autoimmune hepatitis (AIH) can mimic acute viral hepatitis and acute liver failure especially in absence of autoantibodies and hypergammaglobulinemia.
Objective: To determine the clinical, laboratory, histopathological characteristics, treatment and outcome of acute AIH patients.
Methods: A retrospective analysis of 24 patients with acute AIH diagnosed over a period of 11 years (2008–2019).
Results: Out of the 207 patients diagnosed with Autoimmune liver disease, Acute AIH was present in 24 (11.6%) patients including four with acute liver failure. Male: Female ratio was 11:1 with a median age of 36 (15–44) years. Fifteen (62.5%) patients had Type 1 AIH and 9 (37.5%) patients were diagnosed with seronegative AIH. All 24 (100%) patients had jaundice at presentation. The median bilirubin was 4.6 mg/dl (range 2.2–35), AST was 548 IU/L (range 336–908), ALT was 456 IU/L (range 257–1026) and SAP was 395 IU/L (range 112–890) during symptomatic period. Histopathological examination showed Chronic hepatitis in 17 (70.8%) patients, Cirrhosis with activity in 3 (12.5%) and Central venulitis with necrosis in 4 (16.7%). Twenty (83.3%) patients were treated with a combination of steroids and azathioprine. Four (16.7%) were treated as acute liver failure out of which one patient received plasmapheresis and steroids. 16 (66.6%) achieved complete biochemical remission and 4 (16.7%) achieved partial remission. Four (16.7%) patients succumbed to illness, three with fulminant presentation and one with complications of cirrhosis.
Conclusion: Acute AIH can mimic acute viral hepatitis and acute liver failure. Treatment with immunosuppression can be beneficial in majority of patients.

Abstract #1214

The protective effect and mechanism of hPMSCs-derived exosomes on in vitro model of primary sclerosing cholangitis

Chen Wenyi[1], Qiaoling Pan[1], Jinfeng Yang[1], Cao Hongcui[1]

[1]State Key Laboratory for the Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China

Introduction: Primary sclerosing cholangitis (PSC) is an incurable cholangiopathy of little known etiopathogenesis which character as cholangiocyte senescence. As human placenta mesenchymal stem cells (hPMSCs) have been proven to have protective effect upon several diseases. We develop and characterize the three-dimensional (3D) model of senescent cholangioids from adult mouse, to clearly test whether hPMSCs-derived exosomes have protective effect to senescent cholangioids induced by oxidative stress in vitro.
Methods: We identified the growing features of cholangioids by light microscope and confocal microscopy. The exosomes were introduced concurrent with H_2O_2 to the senescent cholangioid models. By immunohistochemistry and immunofluorescence staining we assessed the expression of senescence markers. We determined chemokine profiles and senescence-associated secretory phenotype (SASP) by qRT-PCR and culture medium cytokine analysis.
Results: Senescent cholangioids expressed significantly more senescence-associated $p16^{INK4a}$, $p21^{WAF1/Cip1}$ and SA-β-gal. The aging process of cholangioids became faster after inducing by oxidative stress compared to exosomes treated and control group, while SASP components (i.e. IL-6, IL-8, CCL2) and several chemokines were attenuated by exosomes treated group.
Conclusion: hPMSCs-derived exosomes can elicit protective effects against oxidative stress induced senescent cholangioids by postponing aging progress and reducing the SASP components and several chemokines, which considered a potential therapeutic approach for PSC.

Abstract #1268

Seroprevalence of AIH-related autoantibodies in patients with acute hepatitis E viral infection: a prospective case–control study in China

Jian Wu[1], Hongcui Cao[1]

[1]State Key Laboratory for the Diagnosis and Treatment of Infectious Diseases, National Clinical Research Center for Infectious Diseases, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, 79 Qingchun Rd., Hangzhou 310003, China

Introduction:The seroprevalence of hepatitis E virus (HEV) is significantly higher in autoimmune hepatitis (AIH) patients, but the prevalence of AIH-related antibodies in patients, particularly Asians, with acute hepatitis E (AHE) is unclear.
Objectives: In this study, we investigated whether acute HEV infection is associated with the seroprevalence of AIH-related autoantibodies and assessed their impact on the disease characteristics.
Methods: AIH-related autoantibodies were detected by indirect immunofluorescence in 198 AHE patients and 50 type 1 AIH patients (controls).
Results: The positivity rates of against nuclear antigen (ANA) and smooth muscles antibody (SMA) in AHE patients were 37.4% and 22.7%, respectively, and the total positivity rate was 50% (99 of 198). Compared to those in AIH patients, the positivity rates of ANA-H and SMA-AA were significantly lower (35.1% vs. 82.1%, $P < 0.05$; and 4.4% vs. 88.4%, $P < 0.05$, respectively). Female gender and the alanine aminotransferase level, but not immunosuppressive or antiviral drugs, were independently predictive of the presence of AIH-related autoantibodies in AHE patients. Fifty-two patients positive for AIH-related autoantibodies were followed up for 12 months. During this period, 33 of them became negative and 19 remained positive, albeit with significantly decreased titers.
Conclusion: The seroprevalence of AIH-related autoantibodies in AHE patients was elevated, particularly in females, but their subspecificities and titers differed from those of type 1 AIH. Acute HEV infection may be related to AIH.

Abstract #1419

Significant anticholestatic effects of elafibranor, a peroxisome proliferator-activated receptor (PPAR) alpha/delta agonist, in primary biliary cholangitis (PBC) patients with inadequate ursodeoxycholic acid (UDCA) response

Schattenberg Jörn[1], Albert Pares[2], Kris V. Kowdley[3], Michael Heneghan[4], Stephen Caldwell[5], Daniel Pratt[6], Alan Bonder[7], Gideon M. Hirschfield[8], Cynthia Levy[9], John Vierling[10], David Jones[11], Sophie Megnien[12], Remy Hanf[13], David Magrez[13], Pascal Birman[13], Zhou Zhou[14], Joy Zhou[14], Velimir Luketic[15]

[1]I.Medizinische Klinik und Poliklinik, Johannes Gutenberg Universität, Mainz, Germany, [2]Hospital Clínic, University of Barcelona, Liver Unit, Barcelona, Spain, [3]Swedish Medical Center, Seattle, United States, [4]King's College Hospital, Institute of Liver Studies, London, United Kingdom, [5]University of Virginia Health System, Charlottesville, United States, [6]Massachusetts General Hospital, Gastrointestinal Unit, Boston, United States, [7]Beth Israel Deaconess Medical Center (BIDMC), Boston, United States, [8]University Hospitals Birmingham NHS Foundation Trust, The Medical School, University of Birmingham, Birmingham, United Kingdom, [9]University of Miami, Center for Liver Diseases, Miami, United States, [10]Institute for Clinical and Translational Research, Baylor College of Medicine, Houston, United States, [11]Newcastle University, Newcastle upon Tyne Hospitals, Newcastle, United Kingdom, [12]GENFIT CORP, Cambridge, MA, United States, [13]GENFIT SA, Loos, France, [14]Terns China Biotech, Shanghai China, [15]Virginia Commonwealth University, Division of Gastroenterology, Hepatology and Nutrition, Richmond, United States

Introduction: UDCA is first line treatment for PBC. Treatment options are limited for Asian-Pacific patients with inadequate UDCA response. Elafibranor (ELA), a dual PPARα/δ agonist, has treatment potential for these patients.
Objectives: Assess anticholestatic response and safety of ELA in PBC patients with inadequate UCDA response
Methods: A double-blind phase 2a study randomized non-cirrhotic UDCA-treated PBC patients with alkaline phosphatase (ALP) $\geq 1.67 \times$ upper limit of normal (ULN) to 12 weeks of once daily ELA 80 mg, ELA 120 mg or placebo (PBO) (n = 15/group). The primary endpoint was ALP change at Week (W) 12.
Results: 45 patients were treated (43 women, mean age 59 years). Mean ALP decreases at W12 were − 48% for ELA 80 mg, − 41% for ELA 120 mg, and + 3% for PBO ($p < 0.001$ for both ELA groups). 67% of patients at 80 mg and 79% patients at 120 mg achieved composite ALP $< 1.67 \times$ ULN, ALP decrease $> 15\%$ and total bilirubin $<$ ULN compared to 6.7% of PBO ($p = 0.002$ and $p < 0.001$, respectively). Both ELA doses were well tolerated and

showed improvements in GGT, bile acid intermediate C4, serum lipids, IgM, CRP, and haptoglobin versus PBO. Among patients with pruritus at baseline (10/group), median pruritis changes at W12 were − 24% in ELA 80 mg, − 49% in ELA 120 mg, and − 7% in PBO.
Conclusion: In PBC patients with inadequate UDCA response, ELA was well-tolerated, demonstrated anticholestatic effects, and improved pruritis, inflammatory biomarkers and serum lipids. Further ELA studies in PBC patients are warranted.

Abstract #1453

Rational pharmacotherapy of primary biliary cholangitis. Own experience

Ilyassova BS[1]

[1]National Scientific Center of Surgery of the Ministry of Health of the Republic of Kazakhstan, Asfendiyarov Kazakh National Medical University Almaty, Republic of Kazakhstan

Introduction: In Kazakhstan, PBC takes the 2nd place in the frequency of liver diseases in recipients who underwent liver transplantation. Five years of experience in monitoring patients in the post-transplant period showed that this disease has a tendency to develop recurrent primary biliary cholangitis in patients in the distant period after transplantation. The purpose of this study was to evaluate the clinical efficacy and safety of therapy using UDCA with a modified release of Dezursolen at a dose of 15 mg/kg per day for 6 months in patients with stage I–III stage III.
Material and research methods: The "Dezursolen" drug was tested in the format of an open single-center clinical trial, in which 30 patients with PBC of I-III morphological stages took part, including 2 patients with recurrent PBC after liver transplantation. All patients have taken Dezursolen at a dose of 15 mg/kg body weight for 6 months. Before the appointment of therapy, baseline patient information was collected, including demographic data (gender, date of birth, body weight, height), medical history, results of an initial medical examination; also conducted a physical examination with an assessment of the inclusion/exclusion criteria established in the study.
Results: The use of the drug "Dezursolen" in the treatment of patients with stage I–III PBC at a dose of 15 mg/kg per day for 180 days is accompanied by a statistically significant decrease in the levels of biochemical parameters: ALT, AST, alkaline phosphatase, GGT, total and direct bilirubin, improving the emotional, psychological and physical condition of patients.
Conclusion: The results of the study confirm the effectiveness, safety and good tolerance of the drug "Desursolen" in the treatment of patients with morphological stages I-III PBC. Good tolerance of the drug, the absence of adverse events, are of great importance for the formation of the patient's commitment to taking the drug and achieving a stable response to therapy.

Abstract #1505

Treatment of patients with atypical primary biliary cholangitis and studying its prognostic indicators

Jian-Dan Qian[1], Tian–Tian Yao[1], Yan Wang[1], Gui-Qiang Wang[1,2,3]

[1]Department of Infectious Diseases and the Center for Liver Diseases, Peking University First Hospital, Beijing 100034, China, [2] The Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Zhejiang University, Hangzhou 310003, Zhejiang Province, China, [3]Peking University International Hospital, Beijing 102206, China

Introduction: Primary biliary cholangitis (PBC) is considered an autoimmune disease, UDCA was the first drug approved for the treatment of patients with PBC. However, some patients have no response to UDCA. There is no proven treatment for UDCA -refractory PBC or the effect on long-term outcome.
Objectives: We reviewed the medical records of atypical primary biliary cholangitis (PBC) patients which diagnosed by liver biopsy, treated with corresponding treatment. Therapeutic effect and long-term prognosis indicators were evaluated.
Methods: A total of 80 patients were enrolled. Corresponding treatment was prescribed. We analyzed the biochemistries, immune parameters, noninvasive assessments for liver fibrosis as well as the treatment efficacy, long-term outcomes and adverse effects at baseline and each visit point. Assess indicators which can affect prognosis.
Results: 38 PBC patients received UDCA mono-therapy (group A), and another 42 patients received UDCA, prednisolone and immunosuppressant triple therapy (group B). After therapy, biochemical parameters, immunoglobulin and liver fibrosis were markedly improved. Triple therapy was more effective, there was significantly different between two groups. We also found that positive anti-gp210 antibody, negative AMA, higher alkaline phosphatase, TBIL and globulin levels, progressive fibrosis at baseline were independent predictors of a poorer prognosis.
Conclusions: The results of this study suggest that triple therapy was a choice in UDCA -refractory patients, and it has more effectivity in improvement of liver biochemical, immune and non-invasive fibrosis indicators than UDCA mono-therapy. Anti-gp210 antibody positive, AMA negative, higher alkaline phosphatase and TBIL level and progressive fibrosis at baseline were associated with poor prognosis.

Abstract #1920

Analgesic Efficacy of ultrasound: guided Erector Spinae plane Block for percutaneous biliary drainage—a randomized control trial

Swati[1], Deepak[2]

[1]Department of Anesthesiology, Indira Gandhi Institute Medical Institutes, Patna, Bihar, India, [2]Department of Gastroenterology, Patna Medical College and Hospital, Patna, Bihar, India

Background and Aims: To determine the analgesic efficacy and safety of ultrasound guided erector spinae plane block for percutaneous biliary drainage.
Materials and methods: In this double-blind study 40 age and sex matched patients who were to undergo percutaneous biliary drainage because of malignant biliary obstruction were randomly assigned to the true—block group (30 ml 0.5% bupivacaine block) or placebo—block group all had access to a patient controlled analgesia (fentanyl pump). Self-medication, Pain reports, blood pressure, heart rate and oxygen saturation were monitored during and until 8 h after drainage. The Mc Gill Pain Questionnaires was administered 1 h after biliary drainage.
Results: Patients in the placebo group self administered statistically significantly more fentanyl than did patients in the true-block group ($P = 0.008$). Peak pain scores (10-point scale) and McGill Pain Questionnaire scores were statistically significantly higher for the placebo group patients ($P = 0.017$ and $P = 0.001$, respectively). There

were no differences between groups in terms of blood pressure, heart rate, and oxygen saturation. There was no complication reported in any patient.
Conclusion: Ultrasound guided—erector spinae plane block was effective in decreasing pain and opioid requirements during and after percutaneous biliary drainage and did not compromise the cardiopulmonary status of the patient.

Poster Presentations

Abstract #116

Comparison of outcomes among decompensated and compensated cirrhosis with autoimmune hepatitis treated with steroids

Agarwal S[1], Sharma S[1], Kaushal K[1], Gunjan D[1], Poudel S1, Anand A1, Gopi S[1], Mohta S[1], Kante B[1], Vajpai T[1], Ranjan M[1], Singh N[1], Saraya A[1]

[1]Department of Gastroenterology and Human Nutrition, All India Institute of Medical Sciences, New Delhi, India 110029

Introduction: Patients with autoimmune hepatitis (AIH) related decompensated cirrhosis have poor outcomes with steroids, but limited data is available in this regard. We evaluated treatment response in this group and compared it with patients of compensated AIH related cirrhosis.
Methods: In this retrospective analysis, clinical data, laboratory parameters, liver biopsy indices, Child-Turcot-Pugh (CTP) and model for end stage liver disease (MELD) scores at baseline were compared between the patients with compensated (n = 32) and decompensated cirrhosis (n = 62) treated with steroids. The primary outcome was transplant free survival at 12 months. Biochemical remission and clinical improvement were also assessed. Predictors of outcomes were identified in the decompensated cirrhosis subgroup.
Results: CTP and MELD were significantly higher in patients with decompensated (n = 62) compared with compensated cirrhosis (n = 32). Transplant free survival was 96.8% and 54.2% at 12 months ($p < 0.001$) and biochemical remission occurred in 53.1% and 20.9% of compensated and decompensated cirrhotics (p = 0.002) respectively (Figure). Among patients with decompensated cirrhosis, those with transplant free survival had better prognostic scores, lesser post-treatment infections and more frequent biochemical remission than those who did not. On multivariate analysis, MELD score [subdistributional Hazards Ratio [sHR] (95%CI) – 1.153 (1.07–1.24); $p < 0.001$] and ascites [sHR: 2.556 (1.1565–5.65); p = 0.002] predicted survival. Baseline serum albumin [sHR: 2.699 (1.1459–6.359); p = 0.023] and absence of post-treatment infection [sHR: 0.107 (0.012–0.916); p = 0.041] predicted biochemical remission. MELD score of 17 had best performance characteristics [86 (65–97) % sensitivity and 70 (53–83) % specificity] for predicting survival.
Conclusion: AIH related decompensated cirrhosis with better prognostic scores may have good response to steroids. MELD score and ascites remain the most important predictors of survival in these patients.

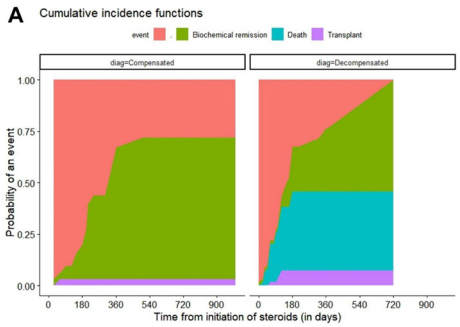


Figure: Competing risks plot demonstrating rates of biochemical remission, death and liver transplant over duration of follow-up in compensated and decompensated AIH related cirrhosis

Abstract #233

Successful single-step approach for cholelithiasis with rare silent choledocholithiasis

Dian Daniella[1], Wifanto Saditya Jeo[2]

[1]General Practitioner, Siloam Hospitals Kebon Jeruk, Jakarta, Indonesia. [2]Digestive Surgeon, Siloam Hospitals Kebon Jeruk, Jakarta, Indonesia

Introduction: Choledocholithiasis happen in 10–15% cholelithiasis patient. Silent choledocholithiasis carries a risk of concurrent cholangitis and pancreatitis and treatment is recommended. For patient with cholelithiasis and choledocholithiasis, there are two interventional options such as single-step approach with laparoscopic cholecystectomy and Common Bile Duct (CBD) exploration or two-stage approach with laparocopic cholecystectomy with Endoscopic Retrograde Cholangiography Pancreatography (ERCP) before or after surgery. In this case report, patient was managed with single-step approach.
Objectives: Objective of this case report is to increase physician awareness of silent choledocholithiasis in cholelithiasis patient and interventional options.
Case report: A 52 year old male came to the hospital with abdominal pain, especially in epigastric area around 2 weeks. Magnetic Resonance Cholangiopancreatography (MRCP) showed 1.86 cm × 1.36 cm stone in distal CBD and multiple stone in gall bladder was found (0.9 cm and 1.95 cm). His laboratory values showed slight higher than normal total and conjugated bilirubin (2.7 and 2.07 mg/dL). Single-step approach (laparoscopy cholecystectomy and CBD exploration) was done. Due to limited resources, CBD stone was extracted using flexible cystoscopy. The operation was successful and patient was discharged three days after.
Conclusion: It is important to recognize high risk cholelithiasis patient for choledocholithiasis to evaluate further and manage accordingly, such as dilated CBD on ultrasound and bilirubin total > 1.8 mg/dL. Single-step approach is safe and well tolerated with short hospital stay. Multiple studies showed two-step approach has a higher number of hospitalization days and the number of anesthetic and surgical events.

Abstract #234

Clinical courses of mirizzi syndrome with porcelain gallbladder in cholelithiatic patient managed with laparoscopic cholecystectomy

Dian Daniella[1], Sandra Utami[2], Ferica Valentine Kuhuwael[3], Wifanto Saditya Jeo[3]

[1]General Practitioner, Siloam Hospitals Kebon Jeruk, Jakarta, Indonesia, [2]Internist, Siloam Hospitals Kebon Jeruk, Jakarta, Indonesia, [3]Internist, Siloam Hospitals Kebon Jeruk, Jakarta, Indonesia, [3]Digestive Surgeon, Siloam Hospitals Kebon Jeruk, Jakarta, Indonesia

Introduction: Gallbladder cancer often coincidence with Mirizzi Syndrome (MS) (28%) and porcelain gallbladder (PGB) (15%) as a consequence of chronic inflammatory process. Mirizzi syndrome is a benign mechanical obstruction of the hepatic duct caused by an impacted gallstone in the gallbladder neck (0.5%–1.4%). Porcelain gallbladder characterized by rare calcification of the gallbladder wall (0.06% to 0.8%). Due to high possibility of gallbladder cancer, cholecystectomy should be done. Laparoscopic cholecystectomy (LC) remains controversial for MS due to scarring and inflammatory tissue near Calot's triangle causing difficulty in dissection and in PGB patient due to brittle nature with conversion rate to open until 25%, hence the rarity of their study. There is no case report discussing clinical course of MS with PGB in cholelithiatic patient managed with laparoscopic cholecystectomy.
Aim: To present a clinical courses of MS with PGB in cholelithiatic patient managed with laparoscopic cholecystectomy and biliary stent.
Case report: Eighty-three years old male came to hospital due to yellow discoloration of skin 1 weeks prior. He had high ALT (149 U/L), AST (70 U/L), GGT (1343 U/L), total bilirubin (14.0 mg/dL) and direct bilirubin (10.7 mg/dL). Abdominal CT scan showed porcelain gallbladder with multiple cholelithiasis. Magnetic resonance cholangiopancreatography (MRCP) showed dilatation to intrahepatic biliary duct, common hepatic duct, cystic duct and with no stone in common bile duct (CBD), hence diagnosis MS was made. Patient undergone LC with stone extraction from cystic duct. In 6 days after operation, bilirubin value was increasing. Pathologic anatomic examination resulted in chronic cholecystitis with calcification. Due to this result, Endoscopic Retrograde Colangiopancreatography (ERCP) was done and showed biliary stricture. This stricture was managed with stent and bilirubin value decreasing day by day.
Conclusion: Laparoscopic cholecystectomy in MS with PGB in cholelithiatic patient is feasible to be done with post-cholecystectomy syndrome due to biliary stricture can be managed with biliary stent.

Abstract #321

The treatment response to corticosteroid therapy was predicted by GGT, CHOL and fibrosis in patients of PBC-AIH overlap syndrome: a Real-World Study

Fan Xiaoli

Background and Aims: The aim of this study was to elucidate the response to corticosteroid therapy and the associated factors in primary biliary cholangitis—autoimmune hepatitis (PBC–AIH) overlap syndrome.
Methods: A cohort study was performed to evaluate the treatment response to immunosuppressive therapy and ursodesoxycholic acid (UDCA) combination in this unique group. This cohort study was performed by a retrospective analysis of prospectively documented data between October 2013 and January 2019 and included 101 patients. The primary endpoints were treatment response at 6 months. Logistic regression analysis was performed to identify factors significantly associated with treatment response.
Results: 55.4% of patients did not respond to treatment. The baseline values of serum total bilirubin, alkaline phosphatase, gamma-glutamyl transpeptidase (GGT), globulin, IgG, cholesterol (CHOL) and positivity for anti-mitochondrial antibody differed significantly between the responders and non-responders ($P < 0.05$). After multivariate analysis, high GGT levels ($P = 0.036$; odds ratio = 1.003), high CHOL levels ($P = 0.005$; odds ratio = 1.639) and presence of cirrhosis ($P = 0.005$; odds ratio = 6.424) were associated with lack of response to corticosteroid therapy. The responders have a better liver-related adverse event-free survival, compared with non-responders according to the Kaplan–Meier estimate (Log-Rank: $p < 0.001$). Second-line immunosuppressive agents (mainly mycophenolate mofetil and tacrolimus) led to biochemical remission in 65.0% of patients who did not respond to initial immunosuppression.
Conclusion: 55.4% of patients of PBC-AIH overlap showed poor prognosis to corticosteroid therapy in a university hospital. Early identification of no-response may allow timely intervention to prevent clinical deterioration. Second-line immunosuppressive agents lead to 65.0% of response.

Abstract #343

A validation study of the UDCA response score in a Japanese PBC cohort

Yagi Minami[1], Matsumoto Kosuke[1], Tanaka Atsushi[1]

[1]Department of Medicine, Teikyo University School of Medicine, Tokyo, Japan

Introduction: Although ursodeoxycholic acid (UDCA) is a first-line treatment in patients with primary biliary cholangitis (PBC), 20–30% of patients with PBC exhibit incomplete response to UDCA. Recently, Carbone et al. demonstrated the UDCA Response Score (URS), which predict UDCA response using pre-treatment parameters of UK PBC patients.
Objectives: In the current study, we validated the URS in Japanese PBC patients.
Patients and methods: We took advantage of PBC patients' registry data in Japan (n = 873). Among this registry, we selected patients who provided all clinical parameters required for calculation of the URS, including liver chemistries and age at baseline, treatment time lag from diagnosis to treatment, and the difference of ALP levels between diagnosis and starting treatment. The endpoint was UDCA response, defined as ALP less than 1.67 times the upper limit of normal (ULN) after 12 months of treatment, as the original study. When bezafibrate was commenced within 12 months of UDCA treatment, we defined the endpoint was not met.
Results: Among 873 patients in the Japanese cohort, all parameters were available in 804 patients (male/female = 120/684, age 58.9 ± 11.0). Bezafibrate was commenced within 12 months of UDCA in 78 patients. The endpoint was achieved in 651 (1.67 xULN, 81%). The AUROC of the URS with the original model was 0.74 (95% CI 0.70–0.79), which was 0.83 (0.79–0.87) in the original publication.
Conclusion: The validity of the URS was acceptable but slightly lower in Japanese cohort, presumably because of early intervention with bezafibrate before judgement of UDCA response in Japanese clinical practice.

Abstract #419

Lipid peroxidation of intrahepatic biliary epithelial cells in primary biliary cholangitis

Jiang Ting[1], Zheng Mengyao[1], Yu Jiankun[2], Tai Wenlin[1], Yang Jinhui[1]

[1]Hepatology Center, The Second Affiliated Hospital of Kunming Medical University, Kunming, China, [2]Institute of medical biology, Chinese Academy of Medical Sciences, Kunming, China

Background: Enhanced lipid peroxidation of small bile ducts in Primary Biliary Cholangitis (PBC) has recently been reported, but its role for pathological initiation and progression has remained unclear. Herein, we carried out a comparative analysis of the lipid peroxidation in various stages PBC and HBV controls.
Method: Liver biopsies of 33 treatment-naïve PBC patients with positive anti-AMA2 immunoglobulin and abnormal obstruction enzymes were performed. 27 paraffin embedded livers of matched HBV control patients were collected. Immunofluorescent staining of 4-hydroxynonenal (HNE) protein adducts was performed, histological stages and hepatic function were evaluated.
Result: Immunofluorescent staining of liver biopsies showed that HNE was significant increase in PBC than HBV ($p < 0.001$). Notably, correlation analysis showed that the HNE were closely associated with Ludwig stages ($r^2 = 0.5931$, $P < 0.001$). HNE in intrahepatic bile ducts can be used to discriminate between treatment-naïve PBC patients from HBV controls (Area under curve = 0.867).
Conclusion: These results validate that enhanced lipid peroxidation of small bile ducts in PBC. Moreover, we also found that lipid peroxidation of small bile ducts may play a vital role in the pathological initiation and progression of liver, the detailed pathogenic molecular mechanism is worth further study.

Table 1. Demographic characteristics of study subjects.

	PBC			HBV controls	
	Ludwig I-II (n=20)	Ludwig III-IV (n=13)	P Value^	(n=27)	P Value*
Age	48.35±10.55	48.23±11.51	0.976	45.07±9.88	0.235
Gender, Female/Male	16/4	12/1	0.625	21/27	0.496
ALT, U/L	61.40±26.74	47.62±27.59	0.163		
AST, U/L	41.80±19.11	43.46±18.44	0.806		
ALP, U/L	238.25±257.73	287.00±193.04	0.564		
GGT, U/L	342.20±401.87	372.15±227.23	0.809		

*Wilcoxon rank-sum test was used to compare age between naïve PBC (n=33) and HBV controls (n=27); Fisher's exact test was used to compare gender distribution between PBC and HBV controls. ^Paired Wilcoxon rank-sum test was used to compare clinical liver enzymes of PBC (n=37) from various stages of Ludwig liver biopsy. ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, γ-glutaryltransferase; PBC, primary biliary cholangitis; HBV, Hepatitis B.

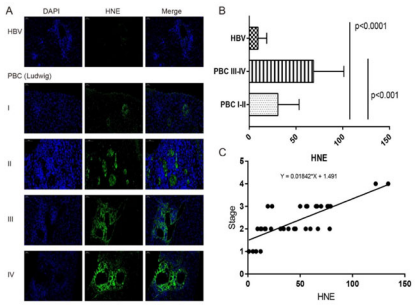


Figure 1. Immunofluorescent staining of hepatic HNE protein adducts in patients with PBC and HBV.
(A) Immunofluorescent staining of hepatic HNE protein adducts in patients with various stages PBC and HBV. HNE, 4-hydroxynonenal protein adducts; DAPI, 4',6-diamidino-2-phenylindole. (B). Differentially expression of HNE in each group were captured by a fluorescence microscope. P< 0.0001, HBV&PBC; P< 0.001, PBC I-II&PBC III-IV. (C) Correlation between the HNE and the Ludwig stages.

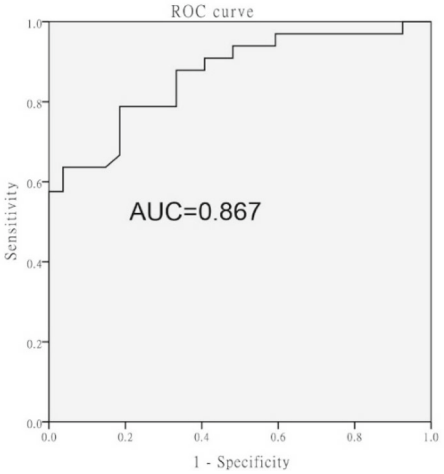


Figure 2. Disease discrimination based on the HNE.

Abstract #482

Factors associated with osteoporosis in patients with primary biliary cholangitis (PBC)

Soukaina Zertiti

Introduction: PBC is a chronic autoimmune hepatopathy leading to cholestasis and an increased risk of osteoporosis. The aim of this work is to study the factors associated with osteoporosis in patients with PBC compared to those with isolated osteopenia.
Patients and methods: 22-year retrospective study. All patients who did not receive bone mineral density BMD were excluded as well as those with normal BMD. Statistical analysis of the data was done using the SPSS software. Osteopenic and osteoporotic patients comparisons were performed using the Chi square and the Mann–Whitney tests.
Results: Among 90 patients followed for PBC, 49 patients met our inclusion criteria, sex ratio F.M was 2.35. 59.2% of patients had isolated osteopenia and 40.8% osteoporosis isolated or associated with osteopenia. The mean age of osteopenic patients was 43.41 ± 9.77 and that of osteoporosis was 51.6 ± 11.9 with a statistically significant difference ($p = 0.012$) 0.23.9% of women were postmenopausal, 42.1% of whom had osteoporosis, while only11.1%had osteopenia with a statistically significant difference ($p = 0.032$) 0.63.2% of osteoporotic patients had a chronic liver disease (CLD) and 36.8% had a normal liver versus 24% of osteopenic patients with CLD and 76% with a normal liver with a difference statistically significant ($p = 0.025$). There is a statistically significant difference in the UK-score at 5, 10, and 15 years ($p = 0.03$) between the osteopenic and osteoporotic patients. We found no evidence of an effect of sex decrease in vitamin D and calcium, response to Paris 2 and degree of cholestasis about osteoporosis.
Conclusion: advanced age, menopause, CLD and the elevation of the UK-score, seems to be factors associated with osteoporosis in PBC. In order to have evidence to support this link, we need large multicentric randomized clinical trials with high methodological quality.

Abstract #507

Decreased frequency and regulatory effects of double-negative T cells in primary biliary cholangitis

Tingting Lv[1,2,3], Yaning Wang[4,5,6], Chunpan Zhang[1,2,3], Shuxiang Li[1,2,3], Dan Tian[4,5,6], Guangyong Sun[4,5,6], Xinyan Zhao[1,2,3], Lu Yang[3], Sha Chen[1,2,3], Hong Ma[1,2,3], Yuanyuan Kong[3], Hong You[1,2,3], Xiaojuan Ou[1,2,3], Dong Zhang[3,4,5,6] and Jidong Jia[1,2,3]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, 100050, [2]Beijing Key Laboratory on Translational Medicine on Cirrhosis, Beijing, China, 100050, [3]National Clinical Research Center for Digestive Disease, Beijing, China, 100050, [4]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, 100050, [5]Beijing Clinical Research Institute, Beijing, China, 100050, [6]Beijing Key Laboratory of Tolerance Induction and Organ Protection in Transplantation, Beijing, China, 100050

Background: There is an increasing interest in the role of double-negative T cells (DNT) in autoimmunity, transplant rejection, and tumor immunity due to their importance in maintaining immune tolerance. However, the function of DNT in the immunopathogenesis of primary biliary cholangitis (PBC) is poorly understood.

Methods: We comprehensively evaluated the immunobiology of DNT in the peripheral blood of PBC patients via flow cytometry and performed transcriptome analysis to identify the potential mechanisms.

Results: The number and frequency of circulating strictly defined DNT, from which CD1d-restricted NKT cells had been excluded, were significantly decreased in PBC patients when compared with those in healthy controls and CHB patients. In addition, peripheral DNT from PBC patients showed decreased proliferation, increased apoptosis, and an enhanced capacity for homing to secondary lymphocyte organs. Furthermore, the suppressive function of DNT was impaired in PBC patients, which promoted the proliferation and effector molecule expression of B cells. Finally, the downregulation of the T cell receptor signaling pathway, especially the reduction of *PIK3R1* expression, was associated with the reduced quantity and defective function of DNT in PBC.

Conclusions: The frequency and immunosuppressive function of circulating strictly defined DNT were both decreased in PBC patients, which might result in the loss of immune regulation in $CD19^{+}$ B cells and the aggravation of the pathogenesis of PBC. The downregulation of *PIK3R1* expression on DNT accounts for these defects in PBC patients.

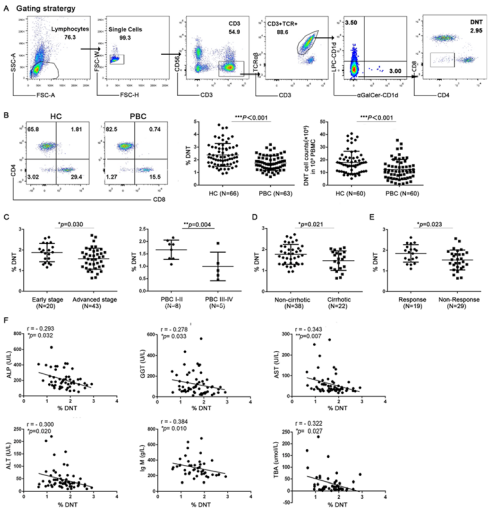


Figure 1. The frequency and absolute number of circulating DNT were decreased in PBC patients and were inversely correlated with disease severity.

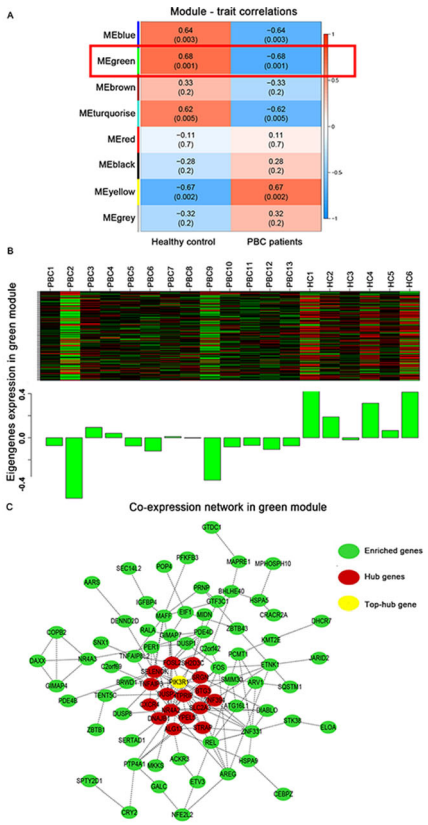


Figure 2. Identification of key module and top-hub gene correlated with clinical traits of DNT cells through WGCNA.

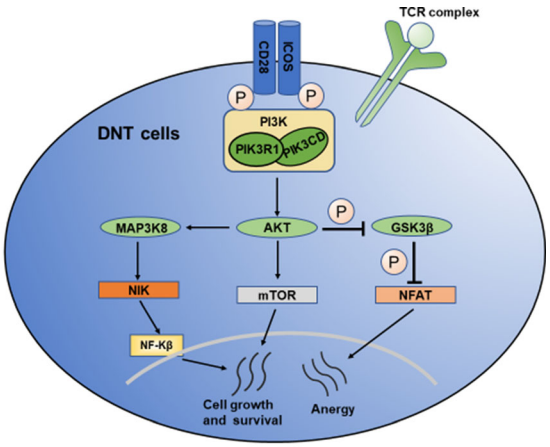


Figure 3. mode pattern of T cell signal receptor pathway

Abstract #610

Analysis of clinical and pathological features of idiopathic non-cirrhotic portal hypertension

Li Yue, Zhou Xin-gang, Yang Kun, Zhang Liang, Ma Zhi-yuan, Wang Qi, Wang Peng

[1]Department of Pathology, Beijing Ditan Hospital, Capital Medical University, 100015 Beijing, [2]Center of Liver Diseases, Beijing Ditan Hospital, Capital Medical University, 100015 Beijing

Objective: To analyze and observe the clinical and pathological features of idiopathic non-cirrhotic portal hypertension (INCPH).
Methods: A retrospective review of 42 cases of INCPH diagnosed by ultrasound-guided liver biopsy from January 2008 to October 2019 in Beijing Ditan Hospital, Capital Medical University. The diagnosis was based on diagnostic criteria established by the INCPH Research Committee of the Ministry of Health and Welfare of Japan. The first symptoms, signs, laboratory tests, imaging, endoscopy and pathology were analyzed and summarized.
Results: The ratio of gender was the same. The average age of onset was 39.3 ± 12.7 years; the most common first symptom of liver discomfort, splenomegaly or hematological abnormalities; nearly 1/2 patients had no obvious positive signs, and splenomegaly was more common signs; 42.9% of patients with liver function tests were normal, and the rest of the patients had mild to moderate liver damage; leukopenia and thrombocytopenia were the most common in blood routine tests; In pathological aspects, false leaflet and complete fibrous septum formation were not found in all of the patients, but irregular expansion of the portal vein between the interlobes, abnormal portal veins, cavernous neovascularization in the portal area, and "insertion" into the surrounding hepatic plate and hepatic nodular hyperpl can exist in a large proportion of patients. The imaging of liver cirrhosis is more common in imaging diagnosis, and may be combined with splenomegaly; gastroscopic examination can be seen in esophagogastric varices.
Conclusion: At present, the understanding of the clinical features of INCPH is limited. This study provides new data for further expanding the number of cases and exploring INCPH from the pathological and clinical manifestations.

Abstract #684

A time trend of improvement in long-term outcome of patients with primary biliary cholangitis in Japan

Matsumoto Kosuke[1], Hirohara Junko[2], Nakano Toshiaki[2], Tanaka Atsushi[1]

[1]Department of Medicine, Teikyo University School of Medicine, Tokyo, Japan, [2]The Third Department of Internal Medicine, Kansai Medical University, Osaka, Japan

Introduction: Primary biliary cholangitis (PBC) is a chronic cholestatic liver disease, potentially leading to cirrhosis and liver failure without appropriate treatment. In Japan, a prospective, large-scale nationwide cohort of PBC patients has been established, and 9919 patients with PBC have been registered to date. In the current study, we took advantage of this cohort and investigated changes in presentation, treatment and long-term outcome pf patients with PBC over time in Japan.
Patients and Methods: The Japanese PBC cohort is established by the nation-wide surveys, initiated in 1980 and updated every 3 years by the Intractable Hepato-Biliary Diseases Study Group (Japan PBC Study Group).
Results: In this study, 8180 patients without missing data regarding age at diagnosis, gender, outcome and final follow-up date were included: mean age at diagnosis 56.9 years and 1104 males (14%). The number of patients diagnosed in -1980, -1990, -2000, -2010 and 2010- was 192, 1494, 2612, 2596 and 1286, respectively. The proportion of patients with any liver-related symptom (jaundice, varices, ascites, encephalopathy and hepatocellular carcinoma) at presentation was decreased until 2000 (89%, 46%, 20%, 26% and 24%), and the proportion of those with histological stage 4 on biopsy at presentation was also decreased; 9%, 6%, 4%, 3%, and 3%. The liver transplantation-free survival was significantly improved over time; 59.3%, 85.1%, 90.0%, 92.8% and 94.3%. The proportion of patients treated with ursodeoxycholic acid (UDCA) was 6%, 56%, 88%, 91%, 91%, and with bezafibrate (BZF) was 0%, 2%, 7%, 16% and 17%, respectively.
Conclusion: Long-term outcome of patients with PBC has significantly improved in Japan, probably due to both earlier diagnosis and treatment with UDCA and BZF.

Abstract #771

Autoimmune pancreatitis presenting with gastric carcinoma: a case report and literature review

Butt N[1], Khemani H[1], Rai L[1], Channa RH[1], Soomro SA[1]

[1]Gastroenterology Department, Jinnah Postgraduate Medical Centre, Karachi, Pakistan

Introduction: Autoimmune Pancreatitis (AIP) is defined as inflammation of the pancreas with an autoimmune process. Type-1 AIP is associated with positive immunoglobulin (Ig)-G4 levels and cellular infiltration. It is one of the manifestations of IgG4 related multisystemic autoimmune disease. Concurrent presentation of type-1 AIP and different malignancies have been reported in the literature. We present a case of a female with AIP, later diagnosed as having. AIP and gastric carcinoma.
Case Presentation: A 33-year-old female with no known comorbidities, presented with complaints of vomiting, weight loss, and epigastric pain. Abdominal examination revealed ascites, while respiratory examination showed right-sided basal crepts with decreased air entry on the left side. The antinuclear antibody was homogenous

positive. Serum IgG4 levels were raised. A chest x-ray showed left-sided pleural effusion. Ultrasound abdomen revealed mild hepatomegaly with an enlarged pancreas. Echogenicity was increased with no focal mass or duct dilation. Computed tomography scan of abdomen with contrast also showed mild hepatomegaly and massive abdominal ascites, with pancreas appearing hypodense and mildly swollen, associated with mild adjacent fat stranding. These findings were suggestive of
acute pancreatitis. Diffuse thickening of walls of stomach was seen along with multiple enlarged paraaortic lymph nodes. Esophagogastroduodenosopy revealed diffuse ulcerated gastric mass. Histopathological examination revealed adenocarcinoma of the stomach (with signet ring cells). A final diagnosis of AIP along with adenocarcinoma of stomach was made.
Conclusion: Type-1 AIP is a rare IgG4 related autoimmune disorder. It is associated with different malignancies. Gastric malignancy is also part of its wide spectrum. Genetic studies should be done to evaluate their associations with different malignancies.

Abstract #857

The high rates of biochemical remission of high-dose urosodeoxycholic acid in treatment of autoimmune liver diseases

Soo Hyung Ryu[1], Dong Hoon Lee[1], Youn Jae Shin[1], Si Hyeung Lee[1], Tae Young Park[1], Jeong Seop Moon[1]

[1]Department of Internal Medicine, Seoul Paik Hospital, Inje University College of Medicine, Seoul, Republic of Korea

Backgrounds/aim: Autoimmune liver diseases including autoimmune hepatitis and primary liver cirrhosis have been known to be very rare, however its prevalence is now increasing. The adverse effects of steroid treatment has been a limitation for its treatment. We evaluate the success rates of high dose ursodeoxycholic acid in autoimmune liver diseases.
Methods: We retrospectively analyzed the biochemical remission rates of autoimmune liver diseases diagnosed by autoantibodies and/or liver biopsy at Seoul-Paik hospital. They had no underlying liver diseases and causes of chronic liver diseases such as viral hepatitis, alcohol abuse, and toxic drug history. A total of 50 patients who had autoimmune antibodies and/or liver biopsy (M:F = 7:43; mean age: 67.1 years; mean serum ALT level 174.0 IU/L) were subjected. Percutaneous liver biopsy was performed in 31 patients.
Results: High dose ursodeoxycholic acid treatment was done in 46 patients and steroid was started in 4 patients. The biochemical response after 1 year high dose ursodeoxycholic acid was noted in 22 patients, no response was found in 4 patients, and response could not be evaluated in 20 patients because of follow up loss and normal ALT levels at the beginning of treatment. The biochemical remission rates of high dose ursodeoxycholic acid in autoimmune liver diseases were 84.6% (22/26). Among 14 patients of biopsy proven autoimmune hepatitis, biochemical remission was noted in 10 patients, no response in 1, and could not evaluated in 3.
Conclusions: High dose ursodeoxycholic acid treatment for autoimmune liver diseases showed very high biochemical remission rates.

Abstract #868

Autoimmune hepatitis patients with histological confluent necrosis had more severe liver injury but similar response rate and clinical outcomes to standard immunosuppressive therapy

Sun Xiaoyi[1], Zhang Jingqi[1], An Wen[1], Wang Qianyi[1], Zhao Xinyan[1], Jia Jidong[1]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, National Clinical Research Center for Digestive Diseases, Beijing, China

Introduction: Autoimmune hepatitis (AIH) has a variety of clinical and histological severity. Whether degree of histological necroinflammation would affect disease severity and response to standard immunosuppressive therapy (IS), deserved to be further studied.
Objectives: To compare disease severity, biochemical response to standard IS-therapy and clinical outcomes between AIH patients with or without confluent necrosis.
Methods: AIH-patients with thorough follow-up data in our hospital during 2007–2018 were included. Demographic, laboratory data were retrieved. Histological features were assessed. Disease severity, response rate to standard IS-therapy and clinical outcomes were compared between patients with and without confluent necrosis (Ishak confluent necrosis score > 3) by T and Chi square Test.
Results: 41-AIH patients were enrolled. Average age: 53.3 ± 12.8-year-old and male/female ratio, 1:4.9. 25/41 patients had confluent necrosis and 12/41 patients had advanced fibrosis (Ishak stage > 4). The confluent necrosis group had significantly lower albumin (32.97 ± 3.77 g/L vs 35.63 ± 5.37 g/L), platelet ($141.29 \pm 48.82 \times 10^9$/L vs $178.38 \pm 83.91 \times 10^9$/L) and higher Child–Pugh-score (6.87 ± 1.54 vs 6.09 ± 0.92) than that in non-confluent necrosis group (All P value < 0.05). After standard IS-therapy, confluent necrosis group had similar rate of transaminase normalization at 1-, 3-, 6-and 12-month (47.8%, 60.9%, 65.2%, 73.9%) compared to non-confluent necrosis group (40.0%, 53.3%, 66.7%, 80%, $P > 0.05$). Similarly, patients with advanced fibrosis also had similar rate of transaminase normalization at 1-,3-,6- and 12-month (54.5%, 72.7%, 72.7%, 72.7%) compared to patients without advanced fibrosis (40.7%, 51.9%, 63.0%, 77.8%, $P > 0.05$). Non decompensated cirrhosis occurred in both groups and one liver cancer developed in each group.
Conclusion: AIH patients with histological confluent necrosis had significantly more severe liver injury but similar rate of transaminase normalization and clinical outcomes after standard immunosuppressive therapy.

Abstract #972

Prognosis of probable autoimmune hepatitis patients diagnosed by international autoimmune hepatitis group criteria

Koji Fujita[1], Takashi Himoto[2], Tsutomu Masaki[1]

[1]Department of Gastroenterology and Neurology, Faculty of Medicine, Kagawa University, [2]Department of Medical Technology, Kagawa Prefectural University of Health Sciences

Introduction: Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease which, if untreated, often leads to cirrhosis, liver failure or hepatocellular carcinoma. AIH is diagnosed using the international scoring system and classified into definite AIH and probable ones. While management and prognosis of definite AIH have been already established, those of probable cases have not been well investigated.

Objectives: Prognosis of probable AIH was evaluated in comparison to definite AIH.
Methods: Among patients who underwent percutaneous liver biopsy examinations in a clinical practice between 1987 and 2018, those who were diagnosed as AIH, PBC or NASH were enrolled in a retrospective cohort study. According to the International Autoimmune Hepatitis Group (IAIHG) criteria revised in 1999, 72 definite cases and 49 probable ones were included in a retrospective study. Median follow up period was 4 years.
Results: Liver fibrosis stage at baseline was more advanced in the definite cohort than the probable cohort. Similarly, median albumin bilirubin score at baseline was greater in the definite cohort. In the follow up period, six patients in the probable cohort died. In the definite cohort, 4 four patients died and two patients were pointed out hepatocellular carcinoma. Univariate and multivariate analysis revealed that younger age and noncirrhotic status at baseline were the predictive factors for hepatocellular carcinoma-free survival. No significant prognostic difference was indicated between the definite and probable cohorts.
Conclusion: Prognosis of probable AIH was not different from that of definite cases, which was determined by baseline age and liver fibrosis stage.

Abstract #1058

Complexity on clinical significance and correlative factors of positive antimitochondrial antibody: a large-scale clinical data

Rui Jin[1], Yandi Xie[1], Mei Hao[2], Nan Wu[1], Zilong Wang[1], Huiying Rao[1], Hao Wang[1], Bo Feng[1]

[1]Peking University People's Hospital, Peking University Hepatology Institute, Beijing Key Laboratory for Hepatitis C and Immunotherapy for Liver Disease, Beijing, 100044, China, [2]Medical Information Center, Peking University People's Hospital, Beijing, 100044, China

Introduction: Previous studies demonstrated conflicting results regarding the role of antimitochondrial antibodies (AMA) in addition to the diagnosis of primary biliary cholangitis (PBC).
Objectives: We investigated the basic information of newly-detected AMA-positive patients and explored the clinical significance and correlative factors of AMA levels.
Methods: We collected the demographic data and related clinical information of those newly-detected AMA and/or AMA-M2 positive patients from January 2013 to December 2017 through the Information System of Peking University People's Hospital.
Results: Among 2657 patients with positive AMA and/or AMA-M2, 2408 were found to be AMA positive for the first time, 77% of whom were female with a male to female ratio of 1:3.3. Majority of them were found at Departments of Rheumatology and Immunology, Hematology and Gastroenterology, and involved multiple anatomic organs/systems. Non-PBC group had significantly lower AMA-M2 titers than New-PBC group (159.50 ± 281.78 vs. 465.39 ± 539.01 RU/ml, $p = 0.000$), and PBC Cirrhosis subgroup had significantly higher AMA-M2 titers than PBC non-Cirrhosis subgroup (424.79 ± 525.91 vs. 662.22 ± 563.97 RU/ml, $p = 0.012$). Besides gender and age, AMA-M2 levels were correlated with several biochemical parameters in Non-PBC and New-PBC groups, especially immunoglobulin M ($p < 0.05$).
Conclusion: AMA and/or AMA-M2 can be detected in a variety of conditions in many clinical departments, and its clinical significance remains to be further clarified. AMA levels are likely related to disease severity in patients with PBC, suggesting that the role of AMA not just limited to the diagnostic value of PBC.

Abstract #1106

Type I choledochal cyst diagnosed in second trimester of pregnancy: a case report

Sya'roni AA[1], Suyata[2], Devi SNAR[3], Lestari PM[4], Komar H[5]

[1]Fellows of Gastroenterology and Hepatology, Department of Internal Medicine, Sriwijaya University, Mohammad Hoesin General Hospital, Palembang, Indonesia, [2]Department of Gastroenterology and Hepatology, Sriwijaya University, Mohammad Hoesin General Hospital, Palembang, Indonesia, [3]Department of Radiology, Sriwijaya University, Mohammad Hoesin General Hospital, Palembang, Indonesia, [4]Division of Fetomaternal, Department of Obstetrics and Gynecology, Sriwijaya University, Mohammad Hoesin General Hospital, Palembang, Indonesia, [5] Division of Digestive Surgery, Department of Surgery, Sriwijaya University, Mohammad Hoesin General Hospital, Palembang, Indonesia

Introduction: Choledochal cyst is a rare congenital dilatation of extrahepatic bile ducts. The estimated incidence in Western countries varies between 1/100.000 and 1/150.000, whereas in Asia is higher, around 1/1000 with male to female ratio of 1:3 to 4. Choledochal cyst in pregnancy is extremely rare and represents a diagnostic and therapeutic challenge. Management by considering maternal condition and also maternal–fetal well-being is mandatory.
Case report: A 22-year-old primigravida at 19 weeks' gestation presented with jaundice and epigastric pain. Liver function test shows no hepatitis viral infections, her total bilirubin and alkaline phosphatase were elevated at 10.07 mg/dL and 298 U/L. Ultrasonography revealed dilated maternal biliary tree suggesting choledochal cyst and 19 weeks' gestation fetus with macrocephaly, anteroposterior ventriculomegaly and corpus callosum agenesis. MRCP diagnosed type I choledochal cyst with similar intraoperative findings. The patient underwent cyst resection, cholecystectomy, and roux-en-Y hepaticojejunostomy. The postoperative course was uneventful and tocolysis was used.
Discussion: Pregnancy is a cholestatic state due to effect of estrogen and progesterone causing changes of liver function test. The main expected complications of choledochal cysts in pregnant women are fetal loss or preterm labor. The distortion of normal abdominal anatomy due to gravid uterus may rises difficulties in abdominal ultrasound causing inconclusive expertise in diagnosing. Association between fetal condition and choledochal cyst remains unclear. MRCP is preferred due to non-iodizing modality. The malignancy risk of type I is 28% therefore the patient will need further evaluation.

Abstract #1255

Profile of Portal cavernoma cholangiopathy—a tertiary care centre experience

GN Gireesh[1], A Chezhian[1], R Murali[1], Rajkumar Solomon[1], AR Venketeshwaran[1]

[1]Institute of Medical Gastroenterology, Madras Medical College, Chennai

Introduction: Our aim was to study the imaging features with respect to MRCP and role of endotherapy in the management of PCC (portal cavernoma cholangiopathy).
Methods: Patients with diagnosis of PCC based on clinical features were recruited from 2017 to 2019. Clinical, radiological and treatment outcome were analysed. All cases were evaluated with diagnostic modality (MRCP). Various indications for endotherapy in PCC were studied.

Results: There were a total of 9 patients during the period. Of this 6 (66.6%) was male and 3 (33.3%) was female. The etiology of portal biliopathy was EHPVO in 6 patients, noncirrhotic portal fibrosis in 3 cases. Imaging findings in MRCP included dilated and angulated CBD (21%), upstream CBD dilatation (54%), distal CBD stenosis due to compression by portal cavernoma (33%), choledocolithiasis (62%), ill defined mass in hilum (pseudocholangiocarcinoma sign) (11%). Endotherapy was done for 8 patients. Indications for endotherapy were obstructive jaundice due to choledocolithiais (66%), distal CBD stenosis (34%). All cases underwent stent packing after endoscopic sphincterotomy. One patient has undergone mesocaval shunt with splenectomy and other had an cholecystojejunostomy for cholangitic abscess. No shuntable vein was present for portosystemic shunting for 8 patients. All 8 patients required long term endoscopic management in the form of repeated stent exchanges once in 3 months. For one case we managed with a fully covered self expanding metal stent. There was no cases of pneumobilia or any other complications post ERCP. Two patients had evidence of secondary biliary cirrhosis.
Conclusions: Symptomatic PCC should undergo endotherapy as first line of management for cholestatic jaundice and cholangitis. It is safe and effective in clearing CBD stones. Endotherapy is the definitive long term strategy in patients who are unfit for portosystemic shunting.

Abstract #1503

Markedly elevated Ca 19–9 antigen levels in a patient with choledocholithiasis

Natalia Sisca Wijaya[1], Sidharta Salim[1]

[1]Internal Medicine Department, Mitra Kemayoran Hospital, Jakarta, Indonesia

Introduction: Carbohydrate antigen (CA) 19–9, is a cancer related antigen with high positivity in pancreatico-biliary malignancies. Nevertheless, its high levels is occasionally found in benign disease of the liver, pancreas and biliary tract, especially in gallstone disease.
Case Presentation: A 64 year old female presented with 1 month history of recurrent, sudden and severe abdominal pain; associated with nausea, vomiting; yellowish sclera and darkened urine color. She was jaundice, with epigastric and right upper quadrant abdominal tenderness and positive Murphy's sign. Laboratory test showed a markedly elevated CA 19–9 levels at 1887 U/ml (normal values of 0–37 U/ml); elevated total, direct and indirect bilirubin; as well as ALT, AST and GGT. She was diagnosed with choledocolithiasis without ruling out possibility of a pancreatic neoplasm. Subsequent MRCP showed a stone at distal CBD and gallbladder hydrops. ERCP with sphincterotomy and stone extraction was then performed. Bilirubin levels in line with the CA 19–9 levels gradually declined after the procedure, with normalization 2 weeks after her discharge. This case presents markedly elevated CA 19–9 antigen levels in a patient without pancreatico-biliary malignancies.
Conclusions: A CA 19–9 value of more than 1000 U/ml has been reported to have specificity greater than 99% for pancreatic cancer, nevertheless, false-positive results can be found to benign disease. Giving undue credence to elevated CA 19–9 levels could lead to a misdiagnosis of a pancreatic or biliary malignancy. Therefore, radiological findings and in some cases, surgical and endoscopic interventions should be used in addition to CA 19–9 assessment for an accurate diagnosis.

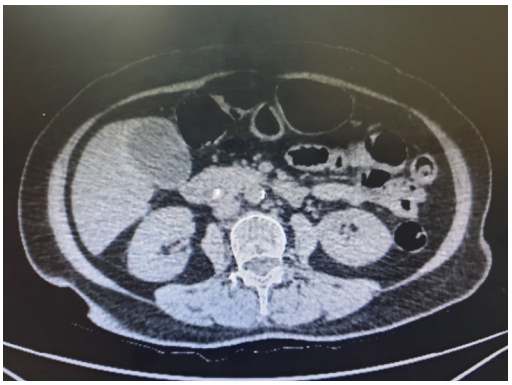


Fig.1. Abdominal CT scan showing a stone at distal common bile duct and hydrops of the gallbladder.

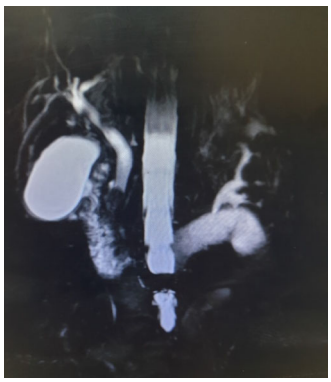


Fig.2. MRCP showed filling defect indicating a stone at distal common bile duct.

Abstract #1504

Efficacy of ursodeoxycholic acid combined with prednisolone and immunosuppressant triple therapy in the treatment of refractory primary biliary cholangitis

Tian–Tian Yao[1], Jian-Dan Qian[1], Yan Wang[1], Gui-Qiang Wang[1,2,3]

[1]Department of Infectious Diseases and the Center for Liver Diseases, Peking University First Hospital, Beijing 100034, China, [2] The Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Zhejiang University, Hangzhou 310003, Zhejiang Province, China, [3]Peking University International Hospital, Beijing 102206, China

Introduction: A significant proportion of UDCA monotherapy patients remains at risk of progression towards cirrhosis.
Objectives: To explore the efficacy of triple therapy including ursodeoxycholic acid, prednisolone and immunosuppressant in refractory PBC patients.
Methods: Triple treatment was prescribed to 47 patients included ursodeoxycholic acid, prednisolone and immunosuppressant. We analyzed the demographic characteristics, biochemistries, immune parameters, noninvasive liver fibrosis assessments for the treatment

efficacy. The primary endpoint was median change from baseline and normalization of biochemical, immune parameters and noninvasive assessments with triple-drug treatment. The secondary outcome was a combined long-term outcome. Independent predict factor were estimated with logistic regression analyses.

Results: The liver pathological stage was centralized in stage II–III (89.4%). After triple therapy, the median change from baseline of ALT, AST, ALP, GGT, TBIL, ALB, IgG, IgM, APRI, FIB-4 and S-INDEX were 59%, 54%, 51%, 52%, 23%, 5%, 23%, 34%, 40%, 57% and 63%, respectively (Figs. 1, 2). The biochemical cumulative normalization rates of ALT, AST, ALP, GGT, TBIL and ALB were higher at the end of 60-month long-term follow-up (96%, 84.6%, 89%, 62%, 80% and 75%) than 18-month short-term follow-up (Fig. 3). ALB at baseline was an independent predict factor of long-term prognosis. Fewer cases were found with side effects under regular supervision.

Conclusions: For refractory PBC patients, triple therapy of UDCA combination with prednisolone and immunosuppressant could result in improvement of parameters and a better long-term chemical normalization rate. Baseline ALB level was associated with long-term outcomes.

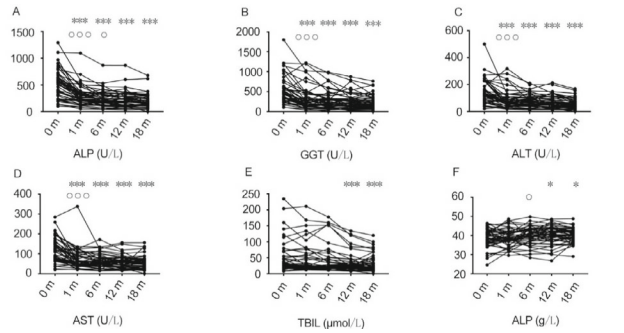


Figure 1. The improvement of chemical parameters after 18-month triple therapy. The dynamic paired data of ALT, AST, ALP, GGT, TBIL and ALB were compared used Friedman test. *P< 0.05, ** P< 0.01, and *** P< 0.001 is shown for comparisons between each follow-up values and baseline values. ° P< 0.05, °° P< 0.01, and °°° P< 0.001 is shown for comparisons between values and the last follow-up values.

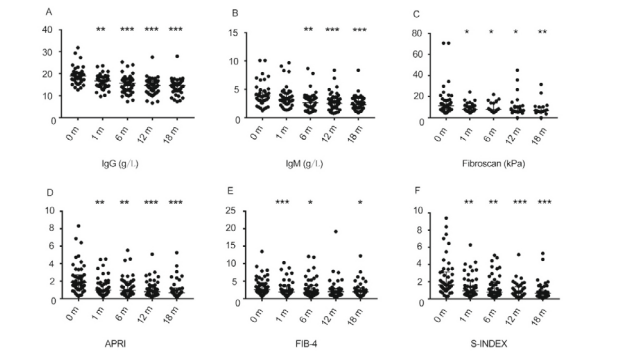


Figure 2. The improvement of IgG, IgM and non-invasive fibrosis assessments after 18-month triple therapy. The dynamic data were compared used Kruskal-Wallis test. *P< 0.05, ** P< 0.01, and *** P< 0.001 is shown for comparisons between each follow-up values and baseline values. ° P< 0.05, °° P< 0.01, and °°° P< 0.001 is shown for comparisons between values and the last follow-up values.

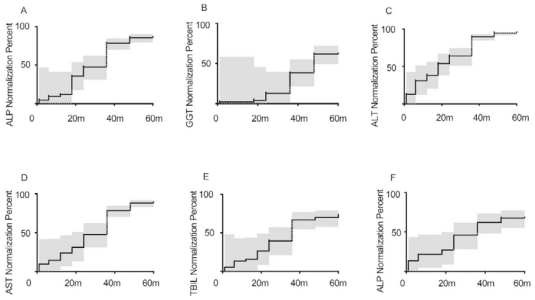


Figure 3. Cumulative incidence of ALP, ALT, AST and GGT normalization. Censored data represent patients who achieved biochemical parameters normalization. Grey area represents 95% confidence interval. The follow time were shown as months.

Abstract #1506

Effective treatment of overlap syndrome between primary sclerosing cholangitis and anti-mitochondrial antibody negative primary biliary cirrhosis: case report

Jian-Dan Qian[1], Wen-Yan Zhu[1], Tian–Tian Yao[1], Yan Wang[1], Gui-Qiang Wang[1,2,3]

[1]Department of Infectious Diseases and the Center for Liver Diseases, Peking University First Hospital, Beijing 100034, China, [2] The Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Zhejiang University, Hangzhou 310003, Zhejiang Province, China, [3]Peking University International Hospital, Beijing 102206, China

The overlap syndrome between primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC) is an extremely rare condition that has been reported in only a few cases. Not to mention the rarity of AMA negative PBC. While there is no effective treatment for PSC, AMA negative PBC is poor reaction with UDCA, there has not effective therapy to the overlap syndrome between them. We report a case of a 57-year-old female, Laboratory tests showed elevated ALP and GGT levels, AMA negative but pANCA was positive. MRCP showed dilatation of the intrahepatic bile duct and thinning of the hilar bile duct. Liver biopsy conformed to primary biliary cirrhosis, stage III. Due to the positive of pANCA, MRCP did not see typical PSC features. ERCP examination was performed in addition to the combined PSC. ERCP was done, which shows common bile duct and intrahepatic bile duct stiffness and multiple stenosis. With imaging results suggestive of PSC, liver biopsy shows PBC, negative for AMA, the diagnosis of an overlap between AMA negative PBC and PSC was proposed. Effectively treated by UDCA (500 mg twice a day), prednisolone (30 mg once daily) combined with azathioprine (100 mg on alternate days), Mycophenolate mofetil (MMF) (0.5 g twice a day) was added at the fourth month of follow up, after 3 years of follow-up, the liver biochemical indicators are normalized and the symptoms disappear.

Abstract #1574

Patients with hyperthyroidism with jaundice: Should be treated with anti-hyperthyroidism?

Zhou Lina[1], Pan Chen[1], Huang Zuxiong[1], Lin Chun[1]

[1]Department of Hepatology, Mengchao Hepatobiliary Hospital of Fujian Medical University, Fuzhou, Fujian Province, China

Introduction: Hyperthyroidism with liver dysfunction is common, mild and usually asymptomatic. But a few patients can cause severe

intrahepatic cholestasis, liver failure or even death due to thyroid hormone overdose, drug-induced liver injury and concomitant liver disease. The common treatment such as anti-hyperthyroidism drugs, ^{131}I may aggravate the liver function damage, so should they be treated with anti-hyperthyroidism is still controversial.

Objective: To investigate the effect of anti-hyperthyroidism therapy on liver function, thyroid function and prognosis in patients with hyperthyroidism complicated with jaundice before and after treatment.

Methods: From January 2008 to February 2019, 218 patients with hyperthyroidism complicated with jaundice in our hospital were retrospectively included in this study. Patients were divided into non-anti-hyperthyroidism group and anti-hyperthyroidism therapy group, 159 patients were matched with sex, age, etiological classification, initial liver function, thyroid function and treatment after propensity score matching. The baseline condition, complication, treatment effect were compared between the two groups before and after propensity score matching, and the clinical outcomes were compared between groups by using Kaplan–Meier survival analysis.

Results: There was no significant difference in age, sex, hospital day, ALT, TSH, FT4, TBIL, DBIL, ALT, AST, GGT, PLT, PTA before treatment between the two groups after propensity score matching ($P > 0.05$), but obvious difference in TBIL, DBIL, TSH, FT3, FT4 after treatment ($P < 0.05$). Kaplan–Meier survival analysis showed that the prognosis of the anti-hyperthyroidism group and the non-anti-hyperthyroidism group was statistically significant after propensity score matching ($P = 0.017$).

Conclusion: The etiology of hyperthyroidism complicated with jaundice is complex, and the diagnosis and treatment were difficult. Anti-hyperthyroidism therapy according to the etiology can control the level of thyroid hormone, improve the patient's liver function and prognosis.

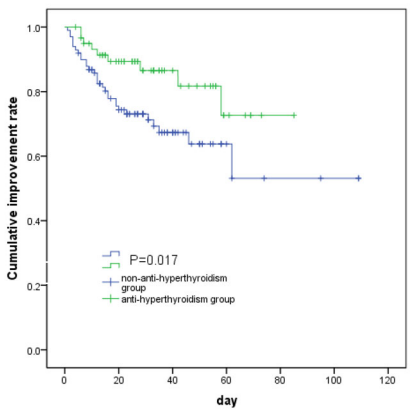


Fig.1 Kaplan-Meier survival curve of non-anti-hyperthyroid group and anti-hyperthyroid group

Abstract #1640

Primary biliary cirrhosis associated with idiopathic thrombocytopenic purpura in adult: a rare case report

Setyani Oky Nur[1], Kalista Kemal Fariz[1,2]

[1]Department of Medical Education, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia, [2]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Introduction: Primary biliary cirrhosis (PBC) is a chronic liver disease characterized by progressive biliary injury as a result of an underlying autoimmune process. Although both primary biliary cirrhosis (PBC) and idiopathic thrombocytopenic purpura (ITP) are autoimmune diseases, the association of the 2 diseases is rare.

Case Presentation: Here, we report a case of ITP that developed during the follow-up of PBC in a 23-year-old man. The patient had been diagnosed with PBC 9 months previously, he was positive of Anti Mitochondrial antibody (AMA) and Ro-52 recombinant. He had received treatment with ursodeoxycholic acid 750 mg/day. He came to Emergency Department due to bleeding from his gums and nose. The platelet count decreased from approximately 80×10^9/L to 2×10^9/L, Total Bilirubin increased from 6.31 mg/dL to 9 mg/dL, Aspartate Aminotransferase (AST) 28 U/L, Alanine Aminotransferase (ALT) 15 U/L and his ANA was positive with titer 1/100, and the association of PBC with ITP was diagnosed. Intravenous steroid therapy were successful in increasing the platelet count. Liver biopsy had not been done because a high risk bleeding procedure due to low platelet and patient had congestive heart failure due to valvular heart disease.

Conclusion: To date, very few PBC cases associated ITP have been reported. Our case might be the first case report in Indonesia. After administration of steroid therapy, his condition was improved afterward and discharged with oral steroid.

Abstract #1730

Primary biliary cholangitis overlapping with autoimmune hepatitis in adult: a rare case report

Cindya Klarisa Simanjuntak[1], Ryan Tresna Putra[1], Juferdy Kurniawan[2], Saut Horas Hatoguan Nababan[2], Marini Stephanie[3]

[1] Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Faculty of Medicine Universitas Indonesia, Jakarta, [2] Hepatobiliary Division, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Faculty of Medicine Universitas Indonesia, Jakarta, [3]Department of Anatomic Pathology, Cipto Mangunkusumo National General Hospital, Faculty of Medicine Universitas Indonesia, Jakarta

Autoimmune hepatitis (AIH) and primary biliary cirrhosis (PBC) are two immune-mediated liver diseases that rarely occur simultaneously. However, early recognition is needed in order to determine the right management. Herein we report a 55-year-old woman diagnosed with PBC since the last 2 years and treated with Ursodeoxycholic 750 mg/day. She came with jaundice since a week before admission. Current laboratory testing showed exacerbation of liver function test with alanine aminotransferase (ALT) reached 1300 IU/L, alkaline phosphatase (ALP) 914 IU/L, and total bilirubin 13.5 mg/dL. No history of any other medication nor alcohol abuse. Serological testing of viral hepatitis was negative. The previous tests showed positive ANA with AMA-M2 +3 and IgG level reached 1950 mg/dL. Her previous liver biopsy revealed bile duct injury with lymphocyte infiltration, diffuse necrosis periportal, and interface hepatitis. We performed re-biopsy of the liver, and found lymphocyte portal infiltration and periportal necrosis. She met Paris criteria which fulfilled at least 2 of 3 accepted criteria of PBC and AIH. She then assessed as PBC-AIH overlap syndrome and treated with Methylprednisolone equal to 50 mg/day Prednisone which tapered gradually, Azathioprine 50 mg/day, and Ursodeoxycholic 750 mg/day. Her condition was improved afterward and no exacerbation episodes found in the past 6 months of treatment.

Abstract #1841

Concurrent autoimmune hepatitis (AIH) in patient with systemic lupus erythematosus (SLE) and grave's disease: a rare case of type 3 multiple autoimmune syndrome (MAS)

Jordan Sardjan[1], Kemal Fariz Kalista[1], Indira Kemalasari[2], Widayat Djoko[2]

[1]Hepatobiliary Division, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia, [2]Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia

Introduction: MAS is defined as the concurrent appearance of at least three autoimmune diseases in the same patient. AIH has been considered as a relatively rare autoimmune disease, especially in Asia–Pacific region, even more as part of MAS manifestation.
Case Report: A 28-year-old female with history of Grave's disease and SLE presented with fever and diarrhea for 3 days. Upon admission, she was diagnosed with thyroid storm, treated with methylprednisolone and propylthiouracil. Later on, she felt epigastric discomfort, nausea and vomiting. Aspartate transaminase, alanine transaminase, amylase and lipase levels increased to 96, 68, 79, and 300 U/L respectively. Abdominal ultrasound revealed chronic hepatitis without pancreatic abnormality. Viral hepatitis were negative. Liver biopsy showed interface hepatitis with steatohepatitis. High serum IgG levels and ANA positivity suggests AIH, which was treated with methylprednisolone. On follow up over 6 months, epigastric discomfort diminished and transaminases were normalized. Amylase and lipase levels were still elevated, suggesting a chronic, possibly autoimmune pancreatitis.
Discussion: As ANA was tested positive, patient belongs to type I AIH. High dose steroid with azathioprine are the staple AIH therapy. Patient was given 62.5 mg intravenous methylprednisolone for 3 days, then tapered down to eventually 1 × 4 mg. The presence of Grave's disease and SLE as chaperones of MAS classify patient as type 3 MAS.
Conclusion: MAS should be considered in patient with autoimmune disease. As such combination of MAS has not been reported, each disease should be closely monitored. Autoimmune pancreatitis could be the fourth findings in index case.

Abstract #1855

Proportion and risk factor of obesity, dyslipidemia, and diabetes mellitus in cholelithiasis patients at Fatmawati General Hospital

Akbar Femmy Nurul[1], Hendarto Hari[1], Mulyana Edi[2], Tjakradidjaja Francisca[3], Muzakki Jewaqa Brako[4], Amri Regi Azistha[4]

[1]Internal Medicine, Faculty of Medicine Syarif Hidayatullah State Islamic University Jakarta, [2]Internal Medicine Fatmawati General Hospital Jakarta Indonesia, [3]Clinical Nutrition Faculty of Medicine Syarif Hidayatullah State Islamic University Jakarta Indonesia, [4]Medical Study Program Faculty of Medicine Syarif Hidayatullah State Islamic University Jakarta

Introduction: Cholelithiasis or gallstone is a disease that hard particles develop in the gallbladder or bile duct. Cholelithiasis has many risk factors, such as age, gender, obesity, dyslipidemia and diabetes mellitus. Prevalence of gallstones in India with dyslipidemia of 76%, and diabetes melitus by 29%.
Objectives: To know the proportion and risk factor of cholelithiasis such as age, gender, obesity, dyslipidemia and diabetes mellitus.
Methods: This study used observational methods with descriptive cross sectional approach. Data was obtained from medical records at Fatmawati Central General Hospital with patients thqt diagnosed cholelitihiasis by abdominal ultrasound examination. Ninety-three samples was taken by consecutive sampling.
Results: Characteristics of cholelithiasis was most frequent in women (65.8%), and with age 56 to 65 years (39.2%). Proportion with age above 40 years was 77.5% and below 40 years was 22.5% Proportion of gallstones patients with obesity was 47.3%. Proportion of Obesity I 31.2% and Obesity II 16.1%. Proportion of cholelithiasis with dyslipidemia was 19%. Proportion of high total cholesterol 54.5%, high LDL cholesterol 90.9%, high triglycerides 27.3%, dan low HDL cholesterol 18.2%. The proportion of cholelithiasis patients with diabetes mellitus was 13.9%.
Conclusions: Proportion of gallstones with obesity 47.3%, dyslipidemia 19% and diabetes mellitus 13.9%.

Abstract #1884

Clinical and immunological characteristics of autoimmune liver diseases in a single center in Kazakhstan

Aisulu Gainutdin[1], Alexander Nersesov[1], Aigul Raissova[2], Lora Kasim[3], Ainur Dosmagul[3], Amir Baikatov[3]

[1]Department of Gastroenterology, Asfendiyarov National Medical University, Almaty, Kazakhstan, [2]Unit of Internal Diseases Nr1, Institute of Cardiology and Internal Diseases, Almaty, Kazakhstan, [3]Autoimmune Disease Diagnostic Laboratory "Medilab Immune", Almaty, Kazakhstan

Introduction: Autoimmune liver diseases (AILD) tend to have increasing prevalence and need to be evaluated in terms of peculiarities characteristic of Kazakhstan population.
Objectives: To characterize clinical and immunological profile of patients with autoimmune hepatitis (AIH), primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC).
Methods: Retrospective single center study (2018–2019) of 50 patients with AILD diagnosed by functional liver tests, autoantibodies (by immunofluorescence, western blotting or ELISA), abdominal ultrasound, MRCP and liver histology.
Results: The majority of patients were Asians (90%), females (90%). AIH was diagnosed in 8 (16%) patients: 7 (87.5%) females and 1 male with mean age 61 and 30 respectively; 2 (25%) were cirrhotic and 100%—ANA positive. PBC was diagnosed in 21 (42%) patients: 19 (90.4%) females and 2 (9.6%) males with mean age 53.3 and 35 respectively; 3 (14.2%) had liver cirrhosis, 6 (28.5%) were AMA, 10 (47.6%) – AMA-M2, 5 (23.8%)—sp100, and 4 (19%) – gp 210 positive. Overlap AIH/PBC was diagnosed in 18 (36%) females with mean age 51; 4 (22.2%) had liver cirrhosis; all were ANA and AMA-M2 positive, and 50% of them—AMA positive. PCS was diagnosed in 3 (6%) patients: 1 (33.3%) female and 2 (66.7%) males with mean 34 and 37 respectively; 1 (33.3%) patient was cirrhotic, all were c- or p-ACA positive.
Conclusion: AILD were characterized by predominance of AMA-positive PBC, prevalence of Asian female patients of older age and more severe disease in AIH, AIH/PBC and PSC.

Abstract #1947

A case report of hepatic cirrhosis in a 38 year-old female with suspicion of primary biliary cirrhosis

Pratama AA[1], Witjaksana RA[2], Christiandari Y[3]

[1]Medical Doctor in Prima Husada Hospital, Sukorejo, East Java, Indonesia, [2]Medical Intern in Prima Husada Hospital, Malang, East Java, Indonesia, [3]Internist in Prima Husada Hospital, Sukorejo, East Java, Indonesia

Introduction: Hepatic cirrhosis is the end stage of progressive pathological condition characterized by hepatic fibrosis, change of liver structure and regenerative nodules. Some contributing factors are the hepatitis viruses, metabolic disorder, malnutrition, autoimmune, obstruction of the biliary duct and veins.
Case Presentation: Patient came with the chief complaints of yellowish eyes and skin since 3 months, dark colored urine, and pale feces. History of herbal potion consumption > 1x per week for over 2 years as well as pain-killers. History of jaundice in the family was found in her father. Physical examination showed blood pressure 160/100 mmHg, icteric sclera, yellowish abdominal skin but unpalpable enlargement of liver and lien. Laboratory examination showed SGOT 233, SGPT 109, total bilirubin 15.34 (8.3 direct bilirubin, 7.04 indirect bilirubin), total protein 5.90, hypoalbuminemia, and ANA Test 1.2 (> 1). The ultrasonography result showed hepatic cirrhosis.
Conclusion: Hypertension in the above case might show the initial sign of cirrhotic cardiomyopathy in which one of the causes is primary biliary cholangitis (PBC). It usually occurs among population with age above 50 years and is diagnosed through antimitochondrial antibody (AMA) examination with the accuracy rate of 95%. In 10% cases, PBC can still be diagnosed even with low AMA level, but accompanied with the increase of alanine aminotransferase serum, IgG and anti-smooth muscle antibodies. Result that has been obtained in this case is the positive ANA test leading to the suspected relationship between autoimmune and PBC as well as the possibility for its early detection.

Abstract #1958

Non-cirrhotic portal hypertension in paroxysmal nocturnal hemoglobinuria: a case report

Fathony Arsyad[1], Wahyu Purnama[1], Monica Raharjo[1], Rebekka Martina[1], Kemal Fariz Kalista[1], Juferdy Kurniawan[1], Saut Horas Nababan[1], Sahat Matondang[2]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Interventional Radiology Division, Department of Radiology, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Backgrounds: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare hematologic disease that manifests with hemolytic anemia, thrombosis, and peripheral blood cytopenias. Portal venous thrombosis were reported in PNH. A rare case of portal hypertension complicating PNH is described.
Case Illustration: A 28-year old man was admitted to the hospital because of haematemesis. The family history was unremarkable. Physical examination revealed splenomegaly. Laboratory findings showed increased serum direct and indirect bilirubin and decreased globulin with pancytopenia. A multiphase abdominal computed tomography scan revealed description of portal hypertension with porta vein and splenic vein thrombosis and splenomegaly. He underwent an investigation with bone marrow puncture that was the histologic correspond with the erythroid hyperplasia. A leukemia phenotyping from bone marrow showed PNH clone.
Discussion: In PNH, deficiency of the glycosyl phosphatidylinositol-anchored complement regulatory proteins CD55 and CD59 induces the intravascular hemolysis that is the main clinical manifestation of the disease. Thrombotic events occur in about 27% of patients with PNH and are the main cause of mortality, accounting for approximately 40% of deaths. It is unclear which of these mechanisms contribute most to thrombosis in PNH; however, complement inhibition with eculizumab is the most effective means to stop thrombosis in PNH.
Conclusion: As a most serious complication, abdominal venous thrombosis critically influences the patient's prognosis. Due to the poor prognosis of advanced cases, appropriate and early diagnosis is important. Complement inhibition through the C5 monoclonal antibody eculizumab has led to dramatic clinical improvement in PNH.

Abstract #2101

Mirizzi's syndrome: a case report

Yohanes Chandra Kurniawan[1], Fiviliani[1], Okkian Wijaya Kotamto[2], Dipdo Petrus Wijaya[3]

[1]Genaral Practitioner at Bethsaida Hospital, Tangerang, Banten, Indonesia, [2]Digestive Surgeon at Bethsaida Hospital, Tangerang, Banten, Indonesia, [3]Internist at Bethsaida Hospital, Tangerang, Banten, Indonesia

Introduction: Mirizzi's syndrome (MS) is a rare condition which gallstone impacted in the cystic duct or neck of the gallbladder causing compression of the common bile duct (CBD) mostly causing cholangitis and obstructive jaundice. It is importat to know MS in order to avoid complication of unrecognized cholecystoenteric fistula or damaged CBD during surgery.
Case Illustration: A 37-year-old man admitted to emergency room due to right hipochondrium colicky pain with acute onset of jaundice, malaise, nausea, vomiting, and dark urine over 4 days.
Blood test shown increased in alanine transaminase (ALT) 359 U/L and aspartate transaminase (AST) 257 U/L; total bilirubin of 4.6 mg/dl, direct bilirubin of 2.1 mg/dl, and indirect bilirubin of 2.5 mg/dl. There was also an increase in LDL cholesterol of 130 mg/dl. Hepatitis markers for type A, B and C were negative. Magnetic resonance cholangiopancreatography (MRCP) with contrast shown multiple cholecystolithiasis, gall bladder neck stone (size 10 mm) and acute cholecystitis.

The next day, patient was undergo laparatomy cholecystectomy and 2 days later, blood test was drawn again; There are decreased of liver function tests, ALT of 199 U/L and AST of 92 U/L, total bilirubin of 1.4 mg/dl, direct bilirubin of 0.5 mg/dl, and indirect bilirubin of 0.9 mg/dL Histology shown acute cholecystitis and necrotizing cholecystitis.
Conclusion: There are several cause of billiary obstruction's sign and symptoms, however the treatment depends of it causes. Laparotomy cholecystectomy preffered for this patient. However, it should be noted that post surgery stricture could happened and biopsy also important to get rid of cholangiocarcinoma.

Abstract #2197

Proportion and risk factor of obesity, dyslipidemia, and diabetes mellitus in cholelithiasis patients at Fatmawati General Hospital

Femmy Nurul Akbar[1], Hari Hendarto[1], Edi Mulyana[1], Francisca Tjakrawerdjaya[1], Jewaqa Brako Muzakki[1], Regi Azistha Amri[1]

[1]UIN Syarif Hidayatullah Jakarta

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Conclusions: Proportion of gallstones with obesity 47.3% dyslipidemia 19% and diabetes mellitus 13.9%.

Abstract #2203

Association of chronic acalculous cholecystitis with infected bile and its management

Chandra Vipin[1], Gupta Jawahar Prasad[2], Kumar P[3]

[1]Department of Urology, Indira Gandhi Institute of Medical Sciences, Patna, India, [2]Department of General Surgery, Patna Medical College, Patna, India, [3]Department of gastroenterology, Institute of Gastrosciences, Apollo Gleaneagles Hospital, Kolkata, India

Introduction: Most patients of cholecystitis have calculi in gall bladder, but a significant proportion of cholecystitis patients do not have gall bladder calculi. This entity is referred to as acalculous cholecystitis. Acute acalculous cholecystis occurs in the setting of serious medical or surgical conditions but chronic acalculous cholecystitis presents with vague symptoms and hence needs high degree of suspicion. Due to absence of calculi in gall bladder the cases go unnoticed. In such cases bile culture can guide medical and/or surgical treatment.
Aim: To study the association of chronic acalculous cholecystitis with infected bile and its effect on outcome.
Methodology: This is a prospective observational study conducted at Patna Medical College and Hospital, Patna, India. All patients with suspected chronic cholecystitis were screened and on the basis of ultrasound findings and 40 acalculous cases of were selected. In all patients bile was aspirated percutaneously and cultured. Data on microbiological profile of bile was obtained and antibiotic given accordingly. For culture positive cases not responding to conservative management for 1 month, open or lap cholecystectomy was performed. Data on microbiological profile and clinical outcomes was analyzed.
Results: Infected bile was found in 16 (40%) cases. E. coli was the commonest organism (75%) followed by Streptococcus and Staphylococcus.11 of 16 (68.75%) culture positive patients responded to conservative management and 5 needed surgical treatment. At 6 months, all patients were symptom free.
Conclusion: Bile culture in chronic acalculous cholecystitis can help in conservative management and surgical treatment can be avoided in some with excellent results.

Abstract #2204

Association of chronic acalculous cholecystitis with infected bile and its management

Chandra Vipin[1], Gupta Jawahar Prasad[2], Kumar P[3]

[1]Department of Urology, Indira Gandhi Institute of Medical Sciences, Patna, India, [2]Department of General Surgery, Patna Medical College, Patna, India. [3]Department of gastroenterology, Institute of Gastrosciences, Apollo Gleaneagles Hospital, Kolkata, India

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Conclusion: Bile culture in chronic acalculous cholecystitis can help in conservative management and surgical treatment can be avoided in some with excellent results.

Abstract #2236

Epidemiological characteristics and survival of obstructive icterus patients in cipto mangunkusumo hospital treated with percutaneous transhepatic biliary drainage (PTBD) intervention

Juferdy Kurniawan[1], Irsan Hasan[1], Rino Alvani Gani[1], Gita Aprilicia[1], Baiq Kirana Dyah Ningrum Mandasari[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Epidemiological characteristics, survival of obstructive icterus, and the effect of Percutaneous Transhepatic Biliary Drainage (PTBD) intervention in Indonesia has not been reported.
Objectives: The aim of this study is to describe characteristics and survival of icterus obstructive patients drained by PTBD intervention and identify factors associated with 1-year mortality in these patients.
Methods: A retrospective cohort was done in Cipto Mangunkusumo Hospital. We performed retrospective icterus obstructive review on patients in the registry (patient drainage using PTBD from 2010 to 2016). Bivariate analysis with Chi Square and multivariate regression analysis were performed.
Results: 287 patients were included in this study. 131 patients (45.6%) were male, mean age was 53 years old, caput pancreas carcinoma is the most common etiology (32.1%), 26 patients (9.1%) diagnosed with stage IV obstructive icterus and 36 patients (12.5%) had ascites. 147 patients (51.2%) treated with PTBD intervention. Bivariate and multivariate analysis found that $\geq$ 60 years, leukocytosis (> 10.000/μL), hypoalbuminemia (< 3 mg/dL), and drainage by PTBD intervention were associated with 1-year survival. Median survival rate of patient drained by PTBD was 4 months. Survival was significantly higher in obstructive icterus patients were drainage by PTBD compare to patient with no intervention. 1-year survival for obstructive icterus patient were drained by PTBD is 28%. Analysis for factor associated with 1-year mortality showed that $\geq$ 60 years, leukocytosis, hypoalbuminemia, and drained by PTBD intervention were associated significantly.
Conclusion: Obstructive icterus patients drained by PTBD intervention have better survival. Age $\geq$ 60 years, leukocytosis, and hypoalbuminemia are associated with poor prognosis.

Inflammation and fibrosis

Oral presentations

Abstract ***#643*** Quantification of hepatic lobular architecture restoration in short-term HBV-induced liver fibrosis and cirrhosis regression

Shuyan Chen[1], Yameng Sun[1], Bingqiong Wang[1], Jialing Zhou[1], Xiaoning Wu[1], Tongtong Meng[1], Shanshan Wu[1], Jinwen Huang[2], Xiaojuan Ou[1], Hong You[1]

Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing Key Laboratory of Translational Medicine in Liver Cirrhosis, National Clinical Research Center of Digestive Diseases, Beijing, China, [2] Beijing Chao-Yang Hospital, Capital Medical University, Beijing, China

Introduction: Liver fibrosis and cirrhosis could develop the distortion of lobular architecture in chronic hepatitis B (CHB) patients. However, whether hepatic lobular architecture could be restored is unclear.
Methods: Approximation of hepatic vein (HV) and portal tract (PT) is the crucial histological feature of abnormal lobular architecture in fibrosis and cirrhosis. Glutamine synthetase (GS) is expressed in hepatocytes surrounding HVs and is used to identify HVs. GSc^+ was defined as HVs not approximating to PT, which means normal or restored lobules. Lobular restoration index (LR-index) was defined as the proportion of GSc^+ among all HVs.
Results: A total of 43 treatment-naive CHB patients with advanced fibrosis (Ishak stage $\geq$ 4) were enrolled. Patients were performed 2nd liver biopsy after 78 weeks of therapy. Based on Ishak score, LR-index increased from 0 at baseline to 0.53 at week 78 in reverse patients ($\geq$ 1 point decrease by Ishak, n = 23). It increased from 0.14 at baseline to 0.31 at week 78 in non-reverse patients (stable or increase $\geq$ 1 point by Ishak, n = 20). Based on P-I-R score at week 78, LR-index in reverse (*predominately regressive*, n = 21) and non-reverse (*predominately progressive* or *indeterminate*, n = 20) patients was increased from 0 and 0.16 at baseline to 0.50 and 0.25 at week 78, respectively. The increasing of LR-index after treatment are more significant in reverse patients than that in non-reverse patients based on both Ishak (P = 0.008) and P-I-R score (P = 0.004).
Conclusion: In the era of antiviral treatment, hepatic lobular architecture could be restored with the improvements of liver fibrosis and cirrhosis.

Abstract #770

Development and validation of a vomogram for predicting hepatic fibrosis in chronic hepatitis B patients: a multicenter retrospective analysis

Xie-Yubao[1], Chi-Xiaoling[1], Xiao-Huanming[1], Shi-Meijie[1], Jiang-Junmin[1], Tian-Guangjun[1], Cai-Gaoshu[1], Li-Qin[2], Mao-Dewen[3], Xue-Jingdong[4], Yang-Hongzhi[5], Lu-Wei[6], Guo-Hui[7], Lei-Chunliang[8], Chen-Liang[9], Liu-Huabao[10], Wang-Jing[11], Gao-Yueqiu[12], Chen-Jiezhen[1], Wu-Shuduo[1], Chen-Huijun[1], Zhao-Pengtao[1], Li-Yingxian[1], Zhang-Chaozhen[1], Liang-Hongcai[1], Xu-Chanyuan[1], Li -Sheng[1]

[1]Hepatology Department, Guangdong Provincial Hospital of Chinese Medicine, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou510120, China, [2]Department of integration of traditional Chinese and Western Medicine, Mengchao Hepatobiliary Hospital of Fujian Medical University, Fuzhou 350025, China, [3]Hepatology Department, First Affiliated Hospital of Guangxi University of Traditional Chinese Medicine, Nanning 530023, China, [4]Liver Diseases Branch, Shaanxi Provincial Hospital of Traditional Chinese Medicine, Xi'an 710003, China, [5]Chinese Medicine Department, Third Affiliated Hospital, Sun Yat-Sen University, Guangzhou 510630, China, [6]Liver Diseases I Branch, Tianjin Second People's Hospital, Tianjin 300192, China, [7]Hepatology Department, First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin 300380, China, [8]Hepatology Department, Guangzhou Eighth People's Hospital, Guangzhou 510060, China, [9]Department of Hepatology, Shanghai Public Health Clinical Center, Shanghai201508, China, [10]Hepatology Department, Chongqing Hospital of Traditional Chinese Medicine, Chongqing 400021, China, [11]Department of Hepatobiliary Disease, Affiliated Traditional Chinese Medicine Hospital of Southwest Medical University, Sichuan 646000, China, [12]Department of Hepatopathy, Shuguang Hospital, Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China

Introduction: Non-invasive methods for diagnosing severe hepatic fibrosis are of clinical value in managing chronic hepatitis B. However, presently adopted models or methods have yielded inconsistent or limited clinical utilities. The present study aimed to develop and validate a nomogram for predicting severe hepatic fibrosis in chronic hepatitis B patients.
Methods: The clinical data of 1370 patients, who underwent liver biopsy between 2011 and 2017 in 12 clinical centers, was reviewed. Patients from nine randomly selected centers were designated as the development cohort, while the remaining three centers as the validation cohort. The risk factors in the development cohort were identified by multivariate analysis. Then, a nomogram for predicting

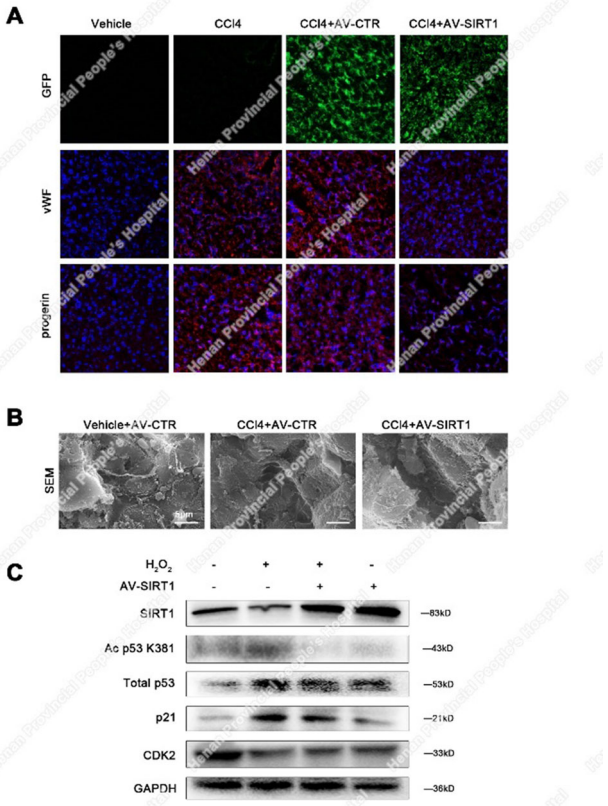
severe hepatic fibrosis was constructed, and this was validated using the validation cohort.
Results: Albumin, globulin, glutamyl transpeptidase, type IV collagen and hyaluronic acid levels, HBeAg positivity and platelet count were significantly associated with severe hepatic fibrosis and incorporated into the nomogram. The area under the receiver operating characteristic curve (AUROC) for severe hepatic fibrosis in the development cohort was 0.802. This was reproduced at 0.781 in the validation cohort, which was significantly higher than AUROC of FIB-4 0.717 and APRI 0.663, resulting in a better net benefit by the nomogram, when threshold probabilities ranged between 15% and 82% in the decision curve analysis. The predicted value of the calibration curve in validation cohort was the actual value when prediction probability fell between 30% and 75%.
Conclusion: A nomogram to predict hepatic fibrosis for chronic hepatitis B patients was developed and validated in the present study. This nomogram performed better than the established FIB-4 and APRI in the present cohorts.

Abstract #1044

Sirtuin 1 attenuates liver sinusoidal endothelial cells defenestration during liver fibrosis via inhibiting stress-induced premature senescence

Xiaoying Luo, Yangqiu Bai, Xiaoke Jiang, Zhiyu Yang, Suofeng Sun, Di Lu, Peiru Wei, Shuangyin Han, Xiuling Li, and Bingyong Zhang

Background: The defenestration of liver sinusoidal endothelial cells (LSECs), which is activation of HSCs, is previous to liver fibrosis. Stress-induced premature senescence, is implicated in the pathogeneses of hepatic fibrogenesis. Progerin, likely leads to premature senescence to influent liver fibrosis. Sirtuin 1 (SIRT1) could enhance cell longevity and attenuate liver fibrosis. However, the mechanism for defenestration and senescence of LSECs, and how SIRT1 regulates LSECs defenestration and premature aging, remain poorly understood.
Methods: We employed the CCl4-induced liver fibrosis rat models and cultured primary LSECs in vitro, administered with the SIRT1-adenovirus vector to overexpressed SIRT1, and knockdown progerin. The fenestrae of LSECs were observed by electron microscopy; meanwhile, progerin, Ac p53 K381, and p53 protein expression were detected by western blot, co-immunoprecipitation, and immunofluorescence.
Results: *In vivo*, we found increase of oxidative stress and premature senescence were triggered during the process of CCl4-induced LSECs defenestration; in contrast, SIRT1-adenovirus vector could decrease LSECs premature senescence and maintain fenestrae to relieve CCl4-induced fibrosis. *In vitro*, during H2O2-induced disappearance of LSECs fenestrae, LSECs premature senescence was triggered via abnormal accumulation of progerin and the activation of nuclear Ac p53 K381-progerin interaction; while SIRT1-adenovirus vector transfected to H2O2-treated LSECs, reversed oxidative stress-induced premature senescence via inhibiting nuclear Ac p53 K381-progerin interaction to maintain LSECs fenestrae.
Conclusions: Our data illuminate a novel role of SIRT1 in regulating stress-induced premature senescence and defenestration of LSECs in liver fibrosis: overexpressed SIRT1 relieves oxidative stress-initiated premature senescence to ameliorate LSECs defenestration via inhibition of Ac p53 K381-progerin interaction.



Abstract #1046

Efficacy of liver stiffness measurement in the left lobe

Abe Satoshi, Suda Takeshi, Sekiguchi Masanori[1], Nakamachi Takashi[1], Imai Rumi[2], Miyashita Hiromi[2], Kanefuji Tsutomu[3], Hoshi Takahiro, Morita Shinichi, Yagi Kazuyoshi, Terai Shuji[4]

Department of Gastroenterology and Hepatology, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Minami-Uonuma, Japan, [1]Department of Radiology, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Minami-Uonuma, Japan, [2]Department of Clinical laboratory, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Minami-Uonuma, Japan,[3]Division of Gastroenterology and Hepatology, Niigata Tokamachi Hospital, Tokamachi, Japan, [4]Division of Gastroenterology and Hepatology, Graduate School of Medical and Dental Sciences, Niigata University, Niigata, Japan

Introduction: Although liver stiffness is recommended to be measured in the right lobe, it is unclear if heterogenous progression of liver fibrosis would be evaluated by measuring the stiffness in both lobes.
Objectives: To clarify the usefulness of liver stiffness measurement in both lobes by comparing the values of 2-dimensional shear wave elastography (2dSWE) and magnetic resonance elastography (MRE).
Methods: MRE and 2dSWE were measured within 6 months in 31 patients. A region-of-interest was placed at 3 sites in each segment for 2dSWE and as much as larger area in each segment for MRE. The values were statistically compared between methodologies, among segments, and with Fibrosis-4 index (FIB4).
Results: The spearman's correlation coefficients between 2dSWE and MRE was 0.733, 0.742, 0.784, 0.455, and 0.513 for entire liver,

posterior, anterior, medial, ant lateral segments, respectively. The correlation coefficients between liver stiffness and FIB4 were 0.677, 0.695, 0.687, 0.626, 0.668 for MRE and 0.782, 0.634, 0.694, 0.594, 0.750 for 2dSWE in the aforementioned order. The ratios of averages in each segment to that of entire liver were 1.0 ± 0.081 and 1.0 ± 0.100 for MRE and 2dSWE.
Conclusion: The correlation coefficients between different methodologies varied among segments and were lower in the left lobes. The deviation in each method was, however, similar among segments, and the correlations between liver stiffness and FIB-4 were not substantially lower in the lateral segment. These results suggest that liver stiffness measurement in the lateral lobe would be valuable to evaluate heterogenous progression of liver fibrosis.

Abstract #1071

The effects of 12-week home-based exercise training on aerobic capacity, muscle mass and quality of life in cirrhotic patients: preliminary results of randomized clinical trial

Pavapol Sirisunhirun[1], Wimolrak Bandidniyamanon[1], Yonworanut Jeerachatakorn[2], Kobkun Muangsomboon[3], Supot Nimanong[1], Watcharasak Chotiyaputta[1], Siwaporn Chainuvati[1]

[1]Division of Gastroenterology, Department of Medicine, Siriraj Hospital, Mahidol University, [2]Department of Health promotion, Siriraj Hospital, Mahidol University, [3]Department of Radiology, Siriraj Hospital, Mahidol University

Background: Physical inactivity and sarcopenia are predictors of mortality in cirrhotic patients. The aim of this study is to prove the benefit of home-based exercise in cirrhotic patients.
Methods: This is a randomized controlled study including cirrhotic patients with Child–Pugh A. Patients were randomized to home-based exercise training (HPET) (N = 11) or control (N = 9) for 12 weeks. HPET includes high intensity interval trainings (keep 60–80% of maximum HR). The primary aim was the changes in 6 min-walk test (6MWT). Secondary aims were the changes in thigh muscle thickness (TMT), liver stiffness (LS), splenic stiffness (SS), and Chronic Liver Disease Questionnaire (CLDQ).
Results: Total 20 patients were enrolled. Mean age was 56 ($\pm$ 8.2) years. Mean 6MWT was 468 ($\pm$ 64.9) m. Mean LS and SS was 17.7 ($\pm$ 10.9), 32 ($\pm$ 24.1) kPa respectively. Mean TMT was 1.7 ($\pm$ 0.4) cm. Thirteen patients (HPET 8 pts, control 5 pts) completed the protocol. The changes in 6MWT were not different between groups. The LS showed significant improved in both groups however, it did not demonstrate the difference when compared between groups. TMT was significantly increased in HPET compared with control. The CLDQ were not significantly changed between groups, but systemic symptoms had a trend to improve in HPET. No adverse events occurred during HPET.
Conclusion: In a preliminary result, 12-week HPET is safe and effective. Although it did not show any differences in the changes in 6MWT of both groups, it demonstrated the increased TMT in exercise patients. Moreover, it showed a trend toward improvement in systemic symptoms score in exercise group.

Abstract #1107

BMS-986263, a novel targeted lipid nanoparticle delivering HSP47 siRNA, for advanced hepatic fibrosis: week 12 results from a phase 2 randomized trial

Lawitz, Eric,[1] Revankar, Ratna,[2] Shevell, Diane,[2] Tirucherai, Giridhar S.,[2] Soule, Benjamin,[2] Duchesne, Dominique,[2] Du, Shuyan,[2] Alkhouri, Naim,[1] Coste, Angie,[1] Poordad, Fred,[1] Charles, Edgar D.[2]

[1]Texas Liver Institute, University of Texas Health San Antonio, San Antonio, TX, USA, [2]Bristol-Myers Squibb, Princeton, NJ, USA

Introduction: BMS-986263, an intravenously administered, hepatic stellate cell-targeted lipid nanoparticle, inhibits heat shock protein 47 (HSP47). Data suggest HSP47 depletion may reverse liver fibrosis.
Objective: Evaluate BMS-986263 efficacy and safety in patients with advanced hepatic fibrosis from HCV with SVR for $\geq$ 1 year (HCV-SVR).
Methods: IM025-006 (NCT03420768) was a randomized, double-blind, placebo-controlled study. Eligible patients had METAVIR F3–F4 (local-read liver biopsy) without decompensation. Patients received 12 weekly BMS-986263 (45 or 90 mg) or placebo infusions and 24 weeks of follow-up. Endpoints included $\geq$ 1 stage METAVIR improvement (week 12; by central-, pair-read liver biopsy), $\geq$ 2 stage Ishak score improvement, and safety.
Results: Of 61 randomized patients, 56% were men, mean age = 60.4 years, and mean platelets = 197×10^9/L. At baseline by central read, 19 patients had F3 and 10 had F4. METAVIR improvements were observed in 2/15 (placebo), 3/18 (45 mg), and 6/28 (90 mg) patients total and in 50% of F4 patients in the 45 mg (1/2) and 90 mg (3/6) groups. Ishak score improvement was observed in the 90 mg group (5/28 total; 3/7 F4). Adverse events (AEs) occurred in 53%–68% of patients. In BMS-986263 groups, most AEs were transient, mild/moderate infusion-related reactions. No treatment discontinuations, treatment-related serious AEs, hepatic decompensation, or drug-induced liver injury occurred.
Conclusions: BMS-986263 QW for 12 weeks was generally well-tolerated in patients with HCV-SVR and hepatic fibrosis, including cirrhosis. Improved METAVIR and Ishak scores were observed in a subset of patients, supporting further evaluation of BMS-986263 in patients with advanced hepatic fibrosis.

Abstract #1358

The gamma-glutamyl transpeptidase to platelet ratio for predicting significant disease activity in untreated HBeAg-negative chronic hepatitis B patients with detectable HBV DNA and normal alanine aminotransferase

Jie Wei[1], Jian Wang[2], Rui Huang[2], Weimao Ding[3], Kefang Yao[1], Xiaomin Yan[2], Zhaoping Zhang[2], Chao Wu[2]

[1]Department of Infectious Diseases, Nanjing Drum Tower Hospital Clinical College of Nanjing Medical University, Nanjing, Jiangsu, China, [2]Department of Infectious Disease, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China, [3]Department of Hepatology, Huai'an No. 4 People's Hospital, Huai'an, Jiangsu, China

Introduction: We aimed to investigate the gamma-glutamyl transpeptidase to platelet ratio (GPR) for predicting the severity of disease activity in untreated HBeAg-negative CHB patients with detectable HBV DNA and normal ALT.

Methods: 137 treatment-naïve HBeAg negative patients with HBV DNA detectable and normal ALT who underwent liver biopsy between 2004 and 2019 were enrolled. The diagnostic values of GPR for liver inflammation and fibrosis were evaluated.
Results: The median HBV DNA level of CHB patients was 3.3 (log10 IU/mL). The liver fibrosis stages of the patients were distributed as follows: S0, 13 (9.5%); S1, 48 (35.0%); S2, 29 (21.2%); S3, 18 (13.1%); and S4, 29 (21.2%). The liver inflammation grades were: G0, 0 (0%); G1, 59 (43.1%); G2, 59 (43.1%); G3, 12 (8.7%); and G4, 7 (5.1%). The AUROCs of GPR in predicting significant liver fibrosis ($\geq$ S2), advanced liver fibrosis ($\geq$ S3) and liver cirrhosis (S4) of the patients were 0.706, 0.783 and 0.781, respectively. The diagnostic performance of GPR was significantly superior to APRI and FIB-4 in identifying advanced liver fibrosis ($P = 0.035$ and $P = 0.023$) and cirrhosis ($P = 0.044$ and $P = 0.016$). For predicting liver inflammation, the AUROCs of GPR in predicting mild inflammation ($\geq$ G2), significant inflammation ($\geq$ G3) and advanced inflammation ($\geq$ G4) were 0.719, 0.878 and 0.935, respectively. GPR was superior to ALT in identifying significant inflammation ($P = 0.003$) and advanced inflammation ($P < 0.001$).
Conclusions: GPR may be a promising predictor for significant disease activity in untreated HBeAg-negative CHB patients with detectable HBV DNA and normal ALT.

Abstract #1374

The value of hepatitis B core antibody levels in predicting significant liver inflammation in chronic hepatitis B patients

Kefang Yao[1], Rui Huang[2], Jian Wang[2], Xiaomin Yan[2], Juan Xia[2], Zhaoping Zhang[2], Chao Wu[1,2]

Department of Infectious Diseases, Nanjing Drum Tower Hospital Clinical College of Nanjing Medical University, Nanjing, Jiangsu, China, [2] Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China

Introduction: The relationship between hepatitis B core antibody (anti-HBc) and liver inflammation remains unclear in chronic hepatitis B patients (CHB) patients.
Objectives: This study aimed to investigate the association between anti-HBc and liver inflammation in CHB patients.
Methods: A total of 440 patients (the training set: 294; the validation set: 146) underwent liver biopsy (LB) were included. Liver histology was evaluated using the Scheuer classification system. The diagnostic accuracy was evaluated by the area under the receiver operating characteristic curve (AUROC).
Results: In the training cohort, patients with significant liver inflammation ($\geq$ G2) showed higher anti-HBc levels ($P < 0.001$) than patients with no or mild liver inflammation ($<$ G2). Anti-HBc levels were positively correlated with liver inflammation grades ($r = 0.318$, $P < 0.001$). Multivariate regression analysis showed that anti-HBc (OR 1.397, 95%CI 1.197–1.630, $P < 0.001$) was an independent predictor of significant inflammation. The AUROCs of Anti-HBc for predicting significant inflammation were 0.675, 0.722 and 0.683 in the entire patients, HBeAg positive and HBeAg negative patients, respectively. The diagnostic accuracy of Anti-HBc for significant inflammation was superior to alanine transaminase (ALT) in HBeAg positive and HBeAg negative patients. In the validation cohort, The AUROCs of Anti-HBc for predicting significant inflammation were 0.730, 0.764 and 0.738 in the entire patients, HBeAg positive and HBeAg negative patients, which was comparable with ALT.
Conclusion: Anti-HBc may be a promising noninvasive clinical biomarker for assessing grades of liver inflammation.

Abstract #1707

Ethanol extract of Garcinia mangostana L pericarp increase blood albumin concentration in rat liver fibrosis model

Triyanta Yuli Pramana[1,2], Bambang Poerwanto[3], Suroto[4], Ambar Mudigdo[5]

[1]Gastroenterology and Hepatology Division, Internal Medicine Department, Faculty of Medicine UNS/Dr, Moewardi Hospital Surakarta, [2]Student of Doctoral Degree of Medical Science Program at Sebelas Maret University, [3]Internal Medicine Department - Faculty of Medicine UNS/Dr, Moewardi hospital Surakarta. [4]Neurology Department - Faculty of Medicine UNS/Dr, Moewardi hospital Surakarta. [5]Pathology Anatomy department - Faculty of Medicine UNS/Dr, Moewardi hospital Surakarta

Introduction: Liver fibrosis is a complex dynamic process, associated with oxidative stress, lipid peroxidation and inflammation and to be a liver cirrhosis. Blood albumin concentration will decrease in liver cirrhosis. *Garcinia mangostana L* pericarp ethanol extract (GME) is rich in polyphenolic compounds that possesses anti-inflammatory and antioxidant activity. This research aimed to study the effect of intake *GME* to malondialdehyde (MDA) as a lipid peroxidation marker and blood albumin in liver fibrosis rat model.
Methods: The laboratory experimental study, with 32 male rats divided into P1 control groups, P2 induction of isoniazid (INH), P3 induction of INH + GME doses of 250 mg $kgBW^{-1}$, P4 induction of INH + GME doses of 500 mg $kgBW^{-1}$; each group consisting of 8 rats. INH doses of 80 mg $kgBW^{-1}$ each rat per day for 5 weeks by intraperitoneally. After getting intervention, the blood was punctured from the periorbital and to be analyzed MDA and albumin.
Results: Giving INH significantly increased MDA (1.45 ± 0.35 vs 9.88 ± 0.45 nmol/mL; $p < 0001$) and decreased albumin (4.84 ± 0.37 vs 1.33 ± 0.22 g/dL; $p < 0.001$) compared to control group. Giving GME dose 250 mg/kgBW significantly ($p < 0.001$) decreased MDA (5.12 ± 0.62 nmol/mL) and increased albumin (2.75 ± 0.07 g/dL). Giving GME dose 500 mg/kgBW significantly ($p < 0.001$) decreased MDA (3.23 ± 0.44 nmol/mL) and increased albumin (4.09 ± 0.14 g/dL), which were better than 250 mg/kgBW dose.
Conclusion: Giving GME significantly reppressed lipid peroxidation and hepatocellular injury, and increased blood albumin concentration, it's meaned suppressed liver injury and increased liver function. Effect of GME increased with increasing dose.

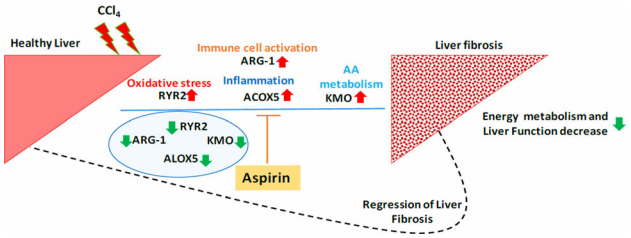
Abstract #1737

Aspirin induces autophagy and alleviates liver fibrosis by modulating liver microbiome and reducing inflammation in mice model of chronic liver injury

Adil Bhat[1], Sudrishti Chaudhary[1], Gaurav Yadav[1], Anupama Kumari[1], Chaggan Bihari[2], Jaswinder Singh Maras[1], Shiv K Sarin[1,3]

[1]Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi, India, [2]Department of Histopathology, Institute of Liver and Biliary Sciences, New Delhi, India, [3]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Aspirin has potent anti-platelet activities and possibly helps regression of fibrosis. We investigated the putative antifibrotic mechanisms of aspirin in liver using an integrated omics approach. C57/B6 mice were treated with CCl_4 for 8 weeks, followed by aspirin treatment.
Methods: Integrated proteomic, metabolomic and metaproteomics analysis followed by global cross-correlation network analysis predicted network regulated by aspirin, and identified targets which were validated in mouse model as well as in patients with liver fibrosis.
Results: Biochemical, histopathological changes and hepatic fibrosis were greater in the CCl_4-treated group compared to CCl_4 + Aspirin (CCl_4 + ASA) or controls ($p < 0.05$). The proteome (> 450 up- and > 340 downregulated proteins) and metabolome (> 70 up- and > 60 downregulated metabolites) in CCl_4 group were distinctly different compared to CCl_4 + ASA group or controls ($p < 0.05$). Aspirin treatment significantly induced proteins and metabolites linked to autophagy, drug and/fatty acid metabolism ($p < 0.05$) and reduced proteins/metabolites linked to inflammatory pathways, arachidonic acid and butanoate metabolism ($p < 0.05$). Protein-metabolite network identified a significant increase in the urea-cycle (Arginase-1; ARG-1), leukotriene-metabolism (Arachidonate-5-lipoxygenase; ALOX-5), oxidative-stress (Ryanodine-receptor-2; RYR2) and tryptophan metabolism (kynurenine 3-monooxygenase; KMO) in mouse model which were attenuated with aspirin. Expression of ARG1, ALOX5, and RYR2 correlated with α-SMA, PDGFR-β and degree of liver fibrosis ($r^2 > 0.75$; $p < 0.05$); both in the mouse model and in the patients with liver fibrosis. Moreover, aspirin was able to modulate liver microbiota particularly, increasing abundance of Firmicutes; Enterococcaceae, Staphylococcaceae and Proteobacteria; Enterobacteriaceae.
Conclusion: Aspirin is effective in regression of hepatic fibrosis, possibly by altering liver microbiota and improves liver functions by enhancing autophagy. Further, aspirin reduces key pro-fibrotic proteins and/or targeting these may provide new therapeutics for hepatic fibrosis.



Aspirin treatment was able to reduce bacterial species associated with liver disease progression. Furthermore, aspirin mediated decrease in key fibrotic proteins (RYR2, ALOX-5, ARG-1, and KMO) correlates with reduction of liver fibrosis and diseases severity.

Abstract #1796

Salidroside alleviates bile duct ligation induced liver fibrosis via regulating SphK/S1P/S1PRs signaling pathway

Qiannan Ye[1,2], Hui Zhu[1,2], Jian Ping[1,2,3], Lieming Xu [1,2,3]

[1]Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, China, [2]Institute of Liver Diseases, Shanghai University of Traditional Chinese Medicine, Shanghai, China, [3]Shanghai Key Laboratory of Traditional Chinese Medicine, Shanghai, China

Introduction: SphK/S1P/S1PRs pathway is an important signaling pathway involved in the regulation of liver fibrosis. Our previous study has show that salidroside(Sal)inhibit activation and migration of haptic stellate cell.
Objectives: To explore the effect of salidroside (Sal) on liver fibrosis induced by Bile Duct Ligation (BDL), and changes of SphK/S1P/S1PRs signaling pathway.
Methods: Liver fibrosis model was established by bile duct ligation (BDL) in SD rats. The rats were divided into three groups: sham group, BDL group and Sal group. Sal group was intragastric administration with Sal (436 mg/kg)) once a day for 4 weeks. HE staining and sirius red staining were used to observe liver pathological changes. Genes or proteins associated with liver fibrosis and SphK/S1P/S1PRs pathway expression levels were determined by realtime-PCR and Western-blot.
Results: Compared to sham group, BDL exhibited significant increases the mRNA levels of Col.I, α-SMA, TGF-β1, TNFα and PDGF in the liver. Sal alleviated liver fibrosis, effectively inhibited these genes expressions in comparison with BDL group. The protein levels of SphK1 and SphK2 were decreased in the BDL liver, and Sal reversed these effects. BDL reduced the protein level of Sphingosine-1-phosphate (S1P), a bioactive lipid mediator of sphingosine catalyzed by Sphingosine kinase (SphK). However, Sal didn't affect its expression. Additionally, BDL also regulated receptors of S1P. Interestingly, it inhibited the levels of S1PR1 and S1PR2, but increased the expression of S1PR3. Spectacularly, Sal significantly eliminated the effects of S1PRs induced by BDL.
Conclusion: The effect of Sal in alleviating rats hepatic fibrosis induced by BDL may be related to the regulation of SphK/S1P/S1PRs signaling pathways.

Abstract #1894

Evaluation of ^{13}C-aminopyrine breath test (^{13}C-ABT) in various stages of chronic liver disease in hepatitis C virus (HCV) patients

Khairy Ahmed[1], Gaber Yasmine[1], Zayed Naglaa[1], Yosry Ayman[1]

[1]Endemic Medicine and Hepatology Department, Faculty of Medicine, Cairo University, Egypt

Introduction: ^{13}C-ABT is a non-invasive, dynamic test for measuring hepatic functional reserve, thus can identify patients with advanced chronic liver disease (CLD) and hepatic decompensation.
Objective: Evaluate the role of ^{13}C-ABT as a non-invasive tool of hepatic fibrosis and decompensation among HCV patients.
Method: Patients with HCV-related CLD (30 chronic hepatitis, 25 compensated and 25 decompensated liver cirrhosis) in addition to 25 healthy control, were prospectively enrolled from Cairo University Center of Hepatic Fibrosis (Center of excellence, funded by Science and Technology Development Fund, project ID: 5274), Faculty of medicine, Cairo university. All participants underwent clinical, laboratory assessment and liver stiffness measurements using transient elastography and acoustic radiation force impulse.^{13}C-ABT values were expressed as percentage dose per hour and cumulative dose. Receiver operating characteristic curves were constructed to determine the optimal cut-off values of ^{13}C-ABT which were correlated with non-invasive tools.
Results: ^{13}C-ABT values showed significant decrease with increase liver disease severity among study groups. Optimal cut-off values using ^{13}C-ABT percentage dose per hour at 40 min; 7.45%, 5.6% and 2.9%, area under curve (AUC) 0.75, 0.9 and 0.99 and cumulative dose at 120 min; 12.05%, 10.3% and 5.55%, AUC 0.75, 0.89 and 0.99 could differentiate patients with chronic hepatitis, compensated and decompensated liver cirrhosis, respectively. ^{13}C-ABT values at 40

and 120 min were significantly correlated with liver stiffness, FIB4 and aspartate aminotransferase to platelet ratio index.
Conclusion: ^{13}C-ABT could be an effective, non-invasive tool for assessment of hepatic fibrosis and decompensation in HCV-related CLD.

Abstract #1906

The impact of the liver volume change on share wave velocity (SWE)

Kanefuji Tsutomu[1], Yu Saito[1], Hoshi Takahiro[2], Abe Satoshi[2], Morita Shinichi[2], Suda Takeshi[2], Yagi Kazuyoshi[2], Shuji Terai[3]

[1]Department of Internal Medicine, Niigata Prefectural Tokamachi Hospital, Tokamachi, Japan, Tokamachi, Japan, [2]Department of Gastroenterology and Hepatology, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Minami-Uonuma, Japan, [3]Division of Gastroenterology and Hepatology, Graduate School of Medical and Dental Sciences, Niigata University, Niigata, Japan

Introduction: SWE provides non-invasive approaches to evaluate the liver fibrosis, however, other factors sometimes affect a result.
Objectives: To elucidate the impact of liver volume change on SWE.
Methods: We measured share wave velocity (SWV) and liver volume before and after treatments in two cases of choledocholitiasis and a Kwashiorkor-type malnutrition caused by a protein intake deficiency. SWV was measured three times in each segment and a median value was calculated as a representative of a case. The liver volume was calculated based on CT volume data that was taken within a day before or after a measurement of SWV.
Results: As a treatment, an endoscopic stone extraction was performed to two cases with choledocholitiasis, and a nutrition therapy was given to a Kwashiorkor case. The mean level of AST, ALT, and T-Bil before treatments were 178.7 (63.8) U/L, 222.3 (165.1) U/L, and 4.2 (3.2) mg/dl, and decreased after treatments into 29.3 (9.5) U/L, 44.7 (30.8) U/L, and 1.0 (0.4) mg/dl. The level of AST was significantly lower after treatments ($p = 0.04$), and ALT and T-Bil were tended to be lower ($p = 0.17$ and 0.19) after treatments. SWVs and liver volumes were 1.67, 1.95, and 1.67 m/s, and 1680, 1535, and 765 ml before treatments, whereas 1.53, 1.53 and 1.43 ml, and 1400, 1210, and 659 ml after treatments. Both SWV and liver volume were tended to be lower after the treatment.
Conclusion: The liver volume gain may lead higher SWV, and may be a key determinant of SWE.

Abstract #1916

Stem cells therapy as an initial treatment prior to liver transplantation for liver cirrhosis case

Lionardi Samuel[1], Stella[1], Tendean Marshell[2], Indradjaja Patrick[3]

[1]Faculty of Medicine Krida Wacana Christian University, Jakarta, Indonesia, [2]Department of Internal Medicine; Faculty of Medicine Krida Wacana Christian University, Jakarta, Indonesia, [3]Docquity Global Indonesia

Introduction: Liver transplantation is by far the best treatment option for patients with advanced *liver cirrhosis* (LC). However, severe limitation restricted the availability of transplantation worldwide. In 1999, hematopoietic stem cells (HSC) in both peripheral blood and bone marrow (BM) showed some evidence of liver regeneration by differentiating into hepatocytes, cholangiocytes and other epithelial cells.
Method: We searched in 5 databases (Cochrane, Proquest, Pubmed, EBSCO, Manual Search). Seven articles were found using the keywords "stem cell (s) (SC)", paired with "Liver Cirrhosis". The search was limited to cohort study, clinical trial study, patient with LC/alcoholic LC/decompensated LC published in English, and full text availability.
Results: Many studies indicate an initial therapeutic for treating LC with cellular therapy (BM, peripheral blood, and umbilical cord SC) by inducing hepatocyte proliferations and releasing proliferative cytokines, or might reduce liver fibrosis through facilitating breakdown of scar tissues. The administration of BM SC and Umbilical Cord-MSC in LC patients might reduce the Model of End-Stage Liver Disease (MELD) score after 6 weeks and 48 weeks of post transfusion ($P = 0.0001$). However this evidence is controversial for decompensated LC case. Contrary to SC therapy, the administration of CD133 + cells or MNC, and autologous CD34 + infusions only change MELD over the first 3 months, shown the idea of additional window to *delay transplantation*.
Conclusion: SC infusion through peripheral or portal vein appears to be a safe and effective modality for a potential initial treatment in reducing MELD Score that could *extend the need of transplantation* or while waiting for a donor.

Abstract #2024

Second harmonic generation (SHG) microscopy and Hepatic venous pressure gradient based validation of a novel histological staging system for alcoholic hepatitis

Patil N[1], Rastogi A[1], Maiwall R[2], Soshi A[3], Bihari C[1], Choudhury A[2], Sarin SK[2]

[1]Department of Pathology, Institute of Liver and Biliary Sciences, New Delhi 110070, India, [2]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi 110070, India, [3]2-Photon/SHG Tissue Imaging Centre of Excellence, Institute of Liver and Biliary Sciences, New Delhi-110070, India

Introduction: Alcoholic hepatitis (AH) lacks specific histological staging; centrilobular distribution with presence of advanced fibrosis precludes application of other aetiology based staging systems. Hepatic venous pressure gradient (HVPG) and automated fibrosis quantification by Second Harmonic Generation microscopy (SHG) could correctly assess nature and distribution of fibrous tissue in AH.
Objective: To correlate histological stages of AH with SHG based q-fibrosis, HVPG and activated stellate cells (HSCs).
Methods: AH with liver biopsy (n = 175) were segregated into stages by two pathologists. Semiquantitative score developed: 0 = no fibrosis, 1 = minimal zone 3, 2 = mild, 3A = prominent expansive perisinusoidal fibrosis, 3B- occasional fibrous septa in 3A, Laennec stages 4A, 4B, 4C. Histological stages were correlated with the dual photon/SHG q-fibrosis parameters, along with HVPG and α-SMA positive HSCs.
Results: Consecutive AH patients, [mean age 41.2 ± 9.4, 96.6% Males, bilirubin 20.58 ± 8.0 mg/dl, MDF 78.9 ± 36.7]; displayed advanced fibrosis in 98.6%. With increasing histological stages, q-fibrosis indices and mean HVPG, showed significant increase ($p < 0.000$). Stage 4C showed most significant difference from other stages ($p < 0.000$) (Table) Stages 3A-4A and 3B-4B were comparable, for q-fibrosis ($p = 1$) and HVPG ($p = 1$). HSCs (> 30%) were significantly higher in stage 3 (75%) compared to 4 (49%) and 2 (59%); $p = 0.018$. Overall agreement was excellent for all stages (0.82) but lowest for stage 3 (0.55).

Conclusion: SHG quantified fibrosis provides histological staging more authentically in AH which correlates well with HVPG. Extensive perisinusoidal fibrosis illustrates collagen content and clinical severity equivalent to early substages of cirrhosis, highlighting need for accurate quantification and staging by SHG microscopy.

Table: Correlation of novel histological stages of AH with SHG based q-fibrosis parameters and HVPG

Fibrosis stage (N=175)	Collagen proportionate area Mean ±SD	Collagen fibre mean thickness	Collagen fibre mean length	Collagen fibre no. per sq mt	Collagen reticulation index	HVPG mean
2 (n=20)	26.15±12.34	2.83±0.62	9.74±1.88	3492.50±1386.61	2.50±0.27	12.38±2.79
3A (n=35)	37.28±10.35	3.21±0.58	10.50±1.21	4192.76±1515.38	2.59±0.25	16.13±3.40
3B (n=24)	43.93±11.29	3.49±0.73	11.26±1.89	4724.99±844.20	2.58±0.24	18.86±5.17
4A (n=13)	37.90±7.13	3.22±0.39	10.59±0.89	4519.62±1834.05	2.62±0.28	16.92±3.75
4B (n=40)	44.00±11.51	3.51±0.50	11.25±1.19	4696.41±1476.75	2.58±0.24	19.31±4.41
4C (n=43)	61.24±12.32	4.42±0.76	13.17±1.69	4180.93±1494.60	2.36±0.30	21.03±5.7
Overall significance ANOVA	P<0.000	P<0.000	P<0.000	P=0.037	P<0.000	P<0.000
Bonferroni Multiple paired comparisons	2vs3A (p=0.009) 2vs3B, 4B, 4C (p<0.000) 3A, 3B, 3C, 4B vs 4C (p<0.001)	2vs3B (p=0.01) 2vs 4B (p<0.002) 2vs4C (p<0.000) 3A, 3B, 3C, 4B vs 4C (p<0.001)	2vs3B (p=0.01) 2vs 4B (p<0.005) 2vs4C (p<0.000) 3A, 3B, 3C, 4B vs 4C (p<0.001)	2vs4B (0.039)	3Avs4C (p=0.003) 3Bvs4C (0.014) 4Avs4C (0.028) 4Bvs4C (0.002)	2vs3B (p=0.002) 2vs 4B (p<0.000) 2vs4C (p<0.000) 3A vs 4C (p=0.001)

Abstract #2033

HDV viral load related liver fibrosis patients clinical evaluation based on M2BPGi level in serum

LKHAGVA-OCHIR Tovuu

Introduction: HBV-HDV coinfection which significantly increases the risk of developing liver cirrhosis and hepatocellular carcinoma (HCC), in Mongolia. HDV-related HCC is understudied, the underlying biological mechanisms associated with liver cancer remains unclear. Mac-2 Binding Protein Glycosylation isomer (M2BPGi) is a novel serological glyco-biomarker for staging liver fibrosis and cirrhosis. We investigate to evaluate the efficiency of serum M2BPGi with chronic hepatitis D infection.
Methods: Serum M2BPGi levels were evaluated in 50 patients with chronic hepatitis D and 25 healthy controls who underwent the hepatologist control in our institution were enrolled in this study. HDV viral load and M2BPGi, PIVKA II level in serum both groups were examined using real time reverse transcription-polymerase chain reaction and ELISA immunoassay. The patients were divided into two groups: high and low groups, based on the HDV viral load. We compared the clinicopathological factors between the high expression.
Results: M2BPGi serum level was in between healthy controls (0.8 ± 0.49) and hepatitis D patients (6.04 ± 5.8). M2BPGi concentrations also was between in HDV high viral load group 10.8 ± 7.1 (> 200 IU/mL, $n = 40$), HDV low viral load group 1.3 ± 1.4 (< 200 IU/mL, $n = 10$). In the univariate analysis, serum alanine aminotranferase, aspartate aminotranferase, PIVKA II and M2BPGi were determined as the significant risk factors of HDV viral load. Compared with other non-invasive markers, M2BPGi had the greatest specificity for diagnosing cirrhosis and cirrhosis in hepatitis D patients.
Conclusion: Serum M2BPGi could be a non-invasive, predictive new biomarkers for liver fibrosis, cirrhosis and progression of HCC among HDV infected patients.

Abstract #2141

Hepatic proteomic analysis reveals distinct molecular signatures in double hit model of thioacetamide and ethanol induced liver fibrosis in mice

Chaudhary Sudrishti [1], Bhat Adil[1], Kumari Anupama[1], Rastogi Archana[2], Sharma Shvetank[1], Maras Jaswinder[1], Shiv K Sarin[1,3]

[1]Department of Molecular and Cellular Medicine, [2]Department of Histopathology, [3]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Liver fibrosis is an impaired wound-healing mechanism that results in the accumulation of extracellular matrix and impairment of hepatic functions. Two hit hypothesis i.e., thioacetamide (TAA) in combination with ethanol induce liver fibrosis, which leads to alterations in hepatic proteome during fibrosis progression. Our aim was to investigate the differential expression of proteins and create a proteomic profile of the effects of ethanol administration in mice with TAA-induced liver fibrosis.
Methods: C57/B6J male mice (n = 15) were pair-fed isocaloric Lieber-DeCarli liquid diet containing 5% ethanol plus TAA twice for 12 weeks. Liver was harvested at 12 weeks and studied for histology, injury markers, and biochemical parameters. Label free quantitative proteomic analysis was performed by using high-resolution mass spectrometry.
Results: When compared with the TAA group, mice in the TAA/EtOH group displayed higher inflammation and increased intrahepatic fibrosis. A total of 4292 proteins were identified, of them 429 differentially expressed proteins (DEPs) were in TAA group ($>$ 218up, $>$ 211downregulated) and 1447 DEPs in TAA/EtOH group ($>$ 353up, $>$ 1094 downregulated; fold change $\pm$ 1.5p > 0.05). The proteomic analysis revealed the levels of distinct proteins modulated by TAA/EtOH, namely Kif5c, Nod2, Hnf4a, Fxr1 (FC > 1.5; $p < 0.05$). Whereas proteins upregulated and unique to TAA group were Tmsb4x, Cd14, Anxa6, Acot9 (FC > 1.5; $p < 0.05$). The dysregulated pathways associated with TAA/EtOH were associated with ABC transporters, fatty acid metabolism, drug metabolism, inflammation and glutathione metabolism.
Conclusion: In context to pathogenesis of alcoholic liver fibrosis, our results revealed key marker proteins that can be used as therapeutic target in alcoholic liver injury and/or liver fibrosis accelerated by thioacetamide.

Poster Presentations

Abstract #23

Changes in amino acid composition (Fisher ratio and BTR) with the progress of liver cirrhosis

Masahiro Kikuchi

Introduction: As amino acid metabolic indicator for liver damage, there are Fisher ratio (branched-chain amino acids (BCAA)/aromatic amino acids (AAA)) and BTR (branched-chain amino acids/tyrosine (Tyr) molar ratio). It is known that they decrease related with hepatic cirrhosis because BCAA reduces and AAA, such as Tyr, increases due to inhibition of metabolism in liver.
Objectives: In this study, we examined the change in amino acid composition with the progress of liver cirrhosis. Method-1:374 cases who received a medical checkup were enrolled. Leucine (Leu), Isoleucine (Iso), Varine (Var), Tyr, Phenylalanine (Phe), Methionine (Met), Arginine (Arg), Lysine (Lys), Histidine (His), Fisher ratio and

BTR were investigated. These markers were compared with FIB-4 index (FIB-4) and Aminotransferase to Platelet Ratio Index (APRI).
Result-1: FIB-4 and APRI were correlated with Phe, Thr, Fisher ratio and BTR, not with Leu, Iso and Var. Method-2: 270 patients who received a department of gastroenterology in a hospital as outpatient and investigated Liver stiffness measurement (LSM) with Fibroscan were enrolled. We examined the relationship between cirrhotic markers (LSM, Hyaluronic acid, Type IV collagen 7s, FIB-4, M2BPGi, Autotaxin) and amino acids (BCAA, Tyr).
Result-2: All cirrhotic markers were correlated with Tyr, not with BCAA.
Conclusion: Increased AAA specifically metabolized in the liver showed a higher correlation with hepatic cirrhotic markers. It was important in picking up liver stiffness from the initial stage.

Abstract #107

Non-invasive probing of liver disease using novel mac 2 binding protein glycosylation isomer comparing with FibroTest and FIB-4

Swee Jin Tan[1], Nghiep Trinh Hoang[2]

[1]Sysmex Asia Pacific Pte Ltd, [2]Medic Ca Mau hospital

Introduction: Liver disease among Vietnamese population is a leading cause of hepatocellular carcinoma (HCC) that leads to high healthcare burden and mortality. The current challenges are effective probing of the disease and routine monitoring of patients under treatment.
Objectives: In the current study, we aimed to evaluate the accuracy of a novel serum biomarker, mac 2 binding protein glycosylation isomer (M2BPGi) against commonly used FibroTest and FIB-4.
Methods: 66 randomly selected patients that received treatment at Medic Camau were tested. As part of routine clinical practice, complete blood count and associated liver function tests were performed. Patients with positive viral hepatitis had viral load measured. Fibrotest and FIB-4 measurements for each subject was collected and compared with the results of M2BPGi.
Results: The maximum and minimum cutoff index (COI) of M2BPGi were 12.4 and 0.22 respectively. Using a median split among the sample cohort, we observed close correlations for M2BPGi measurements with Fibrotest (p value < 0.0001) and FIB-4 (p value = 0.0008) scores. The results demonstrated the suitability of M2BPGi as a single marker to address liver fibrosis. Closer investigation for patients with high fibrotest scores (> 0.9) showed a distinct separation using M2BPGi ranging from 4 to 12.4 COI. The ability to separate the patient cohort allows better stratification and grouping of advanced disease.
Conclusion: Serum biomarkers offers the advantage of non-invasive sample collection and fast turnaround time. M2BPGi offers clear advantages in routine clinical investigation of liver disease and allowing better distinction of advanced fibrosis.

Abstract #285

Correlation between interleukin-6 serum level and liver fibrosis level according to fibroscan in chronic liver disease patients at RSMH Palembang

Suyata[1], Nunki[1], Sya'roni AA[1], Rahmayani F[1], Antoridi D[1], Santoso MJ[1], Bardiman S[1], Bakry F[1], Bahar E[2]

[1]Division of Gastroenterohepatology, Internal Medicine Department, Faculty of Medicine, Sriwijaya University, Mohammad Hoesin Hospital, Palembang, Indonesia, [2]Faculty of Medicine, Sriwijaya University, Mohammad Hoesin Hospital, Palembang, Indonesia

Background: Liver fibrosis occurs in response to chronic liver damage. The inflammatory process can be determined by measuring IL-6 serum levels, whereas IL-6 serum is one of the most important cytokines in the fibrogenesis process. No publication has yet examined the correlation between IL-6 serum and liver fibrosis level in Indonesia. The purpose of this study was to analyze the correlation between IL-6 serum and liver fibrosis level according to fibroscan in chronic liver disease patients at RSMH Palembang.
Method: This analytical observational research with cross sectional design was conducted from August 2017 to December 2017 in 33 subjects. The subjects were chronic hepatitis B and C outpatients in Gastroenterology and hepatology clinic at RSMH Palembang who undergone the fibroscan. Interleukin-6 serum levels were measured by the enzyme-linked immunosorbent assay (ELISA) quantitative method. Spearman analysis was used to assess the correlation between IL-6 serum and liver fibrosis level according to fibroscan.
Results: Of the 33 subjects, the median of IL-6 serum was 2.16 (0.62–29.13) pg/mL and the median of fibroscan was 12.6 (6.3–28.4) kPa. There was a moderate positive correlation between IL-6 serum and fibroscan levels ($r = 0.522$; $p = 0.002$).
Conclusion: There was a moderate positive correlation between IL-6 serum levels and liver fibrosis according to fibroscan in chronic liver disease patients at RSMH Palembang.

Abstract #286

Correlaton TGF-β1 serum with fibrosis degrees based on fibroscan on chronic liver disease in RSMH Palembang

Suyata[1], Rozalena S[1], Sya'roni AA[1], Rahmayani F[1], Antoridi D[1], Santoso MJ[1], Bardiman S[1], Bakry F[1], Legiran[2]

[1]Division of Gastroenterohepatology, Internal Medicine Department, Faculty of Medicine, Sriwijaya University, Mohammad Hoesin Hospital, Palembang, Indonesia, [2]Faculty of Medicine, Sriwijaya University, Mohammad Hoesin Hospital, Palembang, Indonesia

Background: Liver fibrosis is a mechanism of response to liver damage characterized by excessive deposits of extracellular protein matrix especially collagen. Fibrosis and liver cirrhosis are mediated by various cytokines. TGF-β is a pro-fibrotic fibrogenic cytokine master, which represents the mass of extracellular matrix (ECM) and liver fibrogenic activity. TGF-β not only activates hepatic stellate cells but also stimulates ECM synthesis by hepatic stellate cells, matrix-synthesizing myofibroblasts (MFB), and fibrosites. TGF-β may be used as a non-invasive marker to assess progression of disease in chronic HCV patients.
Method: Analytical observational research with cross sectional design. Conducted in gastroenterohepatology division RSMH Palembang from August to December 2017. Patients with chronic hepatitis disease caused by hepatitis virus treated in RSMH and performed *fibroscan* examination to see the degree of fibrosis and TGF-β1 serum. Measurement of liver stiffness by means of a *fibroscan* device (echosens) and expressed in kilopascals (KPa). Serum TGF-β1 measured by quantikine ELISA human TGF-β1 immunoassay method is quantitative sandwich enzyme immunoassay. Data treated with *SPSS* 24.0, *Pearson* analysis was used to assess the correlation of serum TGF-β1 levels with fibrosis-based fibrosis degree.
Results: Of the 33 subjects, there were 23 males (69.7%). The median *fibroscan* was 12.6 (6.3–28.40) kPa and the mean serum TGF-β1 was 37,422 ± 16,545 pg/ml. Serum beta TGF levels are negatively

correlated with fibrosis degree based on *fibroscans* ($p = 0.003$, $r = -0.497$).
Conclusion: There was a negative correlation with moderate strength between serum TGF-β1 levels and fibrosis based on fibroscans in chronic liver disease at RSMH Palembang.

Abstract #289

Machine learning assisted liver cirrhosis detection in ultrasonographic images

Su Tung-Hung[1,2], Chang Hao-Chun[3], Tsai Ming-Tse[3], Kao Jia-Horng[1,2,4,5], Yang Kai-Chieh[3], Wu Chih-Horng[6]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, [2]Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan, [3]Kura Care LLC, San Diego, California, USA, [4]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, [5]Department of Medical Research, National Taiwan University Hospital, Taipei, Taiwan, [6]Department of Radiology, National Taiwan University Hospital, Taipei, Taiwan

Introduction: Abdominal ultrasonography is frequently used to detect liver cirrhosis; however, it's operator-dependent and subject to inter-operator variability. Additional efforts such as fibroscan or acoustic radiation force impulse (ARFI) imaging were required for fibrosis evaluation.
Objectives: To investigate whether machine learning can help in cirrhosis recognition from ultrasonographic images.
Methods: We conducted a retrospective study to collect ultrasonographic liver images from routine exams. Fibrosis stages were defined by shear wave velocity measured during ARFI examination. Images labeled with either normal (F0) or cirrhosis (F4) were selected, and then randomly split into the training set and the test set in a ratio of 4:1. The training set was used for model establishment. The texture features like properties of grey-level co-occurrence matrix derived from training images were used to train non-neural-network models while raw pixels were used to train Convolutional Neural Network (CNN). The accuracy, sensitivity, and specificity of models on the test set were measured.
Results: 220 normal and 362 cirrhosis images were used for training. Meanwhile, 55 normal and 92 cirrhosis images were in the test set. In the test set, XGBboost classifier and calibrated Random Forest both scored the highest accuracy of 75.5%. The former achieved 65.4% specificity and 81.5% sensitivity, while the latter demonstrated 78.2% specificity and 73.9% sensitivity. Vanilla CNN achieved accuracy of 72.8% with 67.3% specificity and 76.1% sensitivity.
Conclusion: We trained various models for classifying liver cirrhosis and obtained acceptable performance. This study demonstrated image recognition could be applied in liver ultrasound to detect cirrhosis.

Abstract #305

Phenomenon of independence of fibrosis and steatosis indicators

Zykin B.I.[1], Kuhareva E.I. [1], Krasnitskaya S.K. [1], Tarasova O.I. [1], Mazurchik N.V. [1], Ngameni M.Ya. [1], Malinina N.A. [1], Ogurtsov P.P. [1]

[1]Peoples' Friendship University of Russia (RUDN University), Hospital Therapy Department of Medical Institute, Moscow, Russian Federation

Introduction: Detection of fibrosis and steatosis of the liver in the early stages is a difficult task for clinical practice, due to the lack of early signs in the routine radiation diagnosis.
Methods: 38 patients with chronic liver diseases (32 men and 6 women (40.6 ± 9.1 years) after liver biopsy were included in study. Depending on the degree of fibrosis (due to Metavir score), patients were divided into 4 subgroups: 1st (N = 17) with F0–1; 2nd (N = 10) with F2; 3rd (N = 7) with F3 and 4th (N = 4) with F4. Depending on the severity of degenerative fatty changes in the liver, the group was divided into 4 additional subgroups: S0 (N = 5) with S0; S1 (N = 11)—with S1; S2 (N = 12)—with S2 and S3 (N = 10)—with S3. In all three groups, liver stiffness (kPa) was determined using ultrasound diagnostic systems Angiodin and Fibroscan502. Ultrasonic steatometry by measuring the attenuation coefficient (dB/cm) was performed on an Angiodin ultrasonic system.
Results: The study revealed a difference between subgroup of patients with a low stage of fibrosis and patients with progressive fibrosis (between F01 subgroups and F2, F3, F4) ($p < 0.05$). Within the F2, F3 and F4 subgroups (stages F2–F4 according to biopsy), there was no significant correlation between the severity of fibrosis and the attenuation coefficient ($p > 0.05$). Correlation of liver' stiffness indicators and the attenuation coefficient of the ultrasound waves in the liver was not found.
Conclusion: The attenuation coefficient of ultrasound waves in the liver are independent of the liver stiffness index.

Abstract #352

Case report: serious liver disease caused by sea-blue histiocytosis

Wen T. Luo[1], Chong J. Gan[1], Ruo M. Ke[1], Peng Y. He[1], Ming X. Huang[1], Jin Y. Xia[1]

[1]The Department of Infectious Diseases, in the Fifth Affiliated Hospital, Sun Yat-Sen University, Zhuhai, Guangdong, China

Introduction: Sea-blue histiocytosis (SBH) is considered as a disease of abnormal lipid metabolism, which is rare around the world. As for liver, the most important organ of lipid metabolism, is easily suffer from damaged.
Case presentation: A 14-year-old girl was admitted to the hospital with fatigue, jaundice and fever for 1 week. The blood test revealed liver damage: ALT 53U/L, AST 83U/L, DBIL 37 μmol/L, IBIL 65.3 μmol/L, and coagulation disfunction: PT 21.30 s, APTT 52.00 s. Confusingly, the blood system was inhibited: WBC $3.87 \times 10\text{^}9$/L, HGB 107 g/L, PLT 90x10^9/L. We also found that Ig G was up to 23.78 g/L, but Ig G4 was normal (0.874 g/L). The ceruloplasmin was 11.2 mg/dl, and no KF ring was found in slit lamp inspection. The G-6-PD was within the normal range and hemolysis testes (like the Coomb's test) were negative. Except the ANA was positive (titer, 1:100), other antibodies, such as AMA, ASMA were negative. Markers of viral hepatitis were all negative. Magnetic resonance cholangiopancreatography (MRCP) only suggestive spleen enlargement obviously (Figure 1). We highly suspected the patient had autoimmune liver disease, but her parents did not agree with liver biopsy. We finally figured out the diagnose by bone marrow biopsy. In surprise, we found the sea-blue histiocytes (Figure 2). Though the diagnosis was clear, but there is no specific way to treat it.
Conclusion: Liver is often damaged by various reasons, when facing unexplained liver damage, we must should consider the possibility of rare diseases.

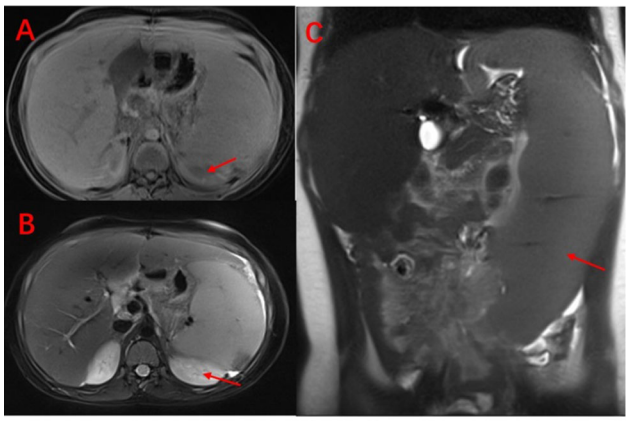


Figure1. MRCP shows that the spleen is obviously enlarged with partial infarction. (Figure 1A is T1stir phase, figure 1B is T2stir phase, figure 1C is T2 fast phase.)

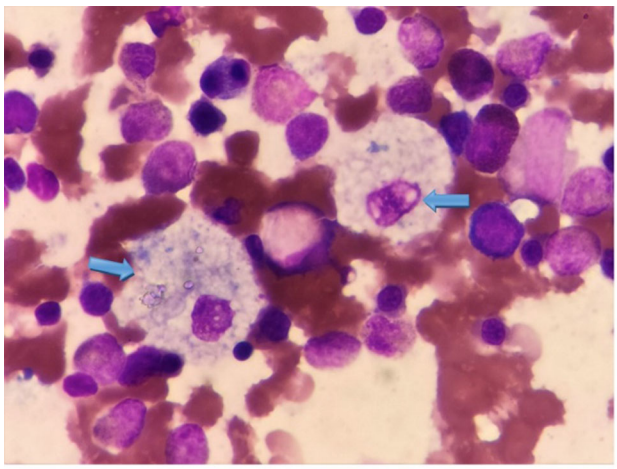


Figure 2. Bone marrow aspirate. Typical sea-blue histiocytes, containing with coarse blue staining pigment granules and foam. (May-Grünwald-Giemsa. ×100).

Abstract #475

Role of liver biopsy in the management of liver diseases following the end of the interferon Era: experience of a tertiary referral centre

Nermine Ehsan[1], Dina Sweed[1], Esraa Karman[1], Eman Abdelsameea[2], Anwar Mohamed[2], Maha Elsabaawy[2]

[1]Department of Pathology, National Liver Institute, Menoufia University, Egypt, [2]Department of Hepatology, National Liver Institute, Menoufia University

Introduction: Liver biopsy is the cornerstone for the management of patients with liver diseases. During the interferon era for the treatment of chronic hepatitis C patients, liver biopsy was mandatory for evaluating the degree of necroinflammation activity and the stage of fibrosis. The development of direct acting antiviral agents for hepatitis C virus made liver biopsy less required.
Objective: The purpose of this study was to explore the role of liver biopsy related to adult liver disease following the end of the interferon era.
Methods: Pathology and medical records of patients who had underwent needle liver biopsy from January 2015 through December 2018 were collected. Liver biopsy taken for evaluation of donor liver histology, post liver transplant or focal lesion was excluded from the study.
Results: A total of 275 liver biopsies were collected, 191 males and 84 females with mean age 41.22 ± 13.36. The pathological diagnosis was as follows 48 drug induced liver injury, 38 Non alcoholic fatty liver disease, 34 chronic hepatitis B or hepatitis C with cholestasis, 29 autoimmune hepatitis, 26 primary sclerosing cholangitis, 8 primary biliary cholangitis, 7 autoimmune overlap syndrome, 13 ascending cholangitis, 13 active bilharziasis, 10 Wilson's disease, 11 sarcoidosis, 10 cytomegalovirus/Epstein-Barr virus infection, 7 Dubin Johnson syndrome, 6 liver abscess, 4 resolving acute hepatitis. Solitary cases of latent congenital hepatic fibrosis, amyloidosis, hemochromatosis, hepatic amoebiasis, malaria, polyarteritis nodosa, myeloproliferative disease were noticed. Four cases of non specific hepatitis were also seen. Initial diagnosis was made by liver biopsy and confirmed by laboratory investigations.
Conclusions: Liver biopsy remains to be an integral component for the hepatologist's diagnostic decision.

Abstract #479

Etiological factors of vascular liver diseases in adults outside cirrhosis in a Moroccan population

F. Lamarti[1], I. Benelbarhdadi, S[1]. Zertiti, C[1]. Berhili, N[1]. Lagdali, M[1]. Borahma, FZ[1]. Ajana[1]

[1]Department of medicine C, Hospital IBN SINA, Mohammed V university, Rabat-Morocco

Introduction: Risk factors for vascular liver disease (VLD) are local and systemic. There is a thrombosis site specificity depending on the prothrombotic factor and this specificity is still poorly explained. Our objective is to describe the characteristics of our study population as well as the prevalence of the main etiological factors identified.
Methods: A retrospective, descriptive and single-center study over a 28-year period including 325 patients followed for VLD. Statistical analysis was done using SPSS22.0.
Results: All patients were in the stage of portal hypertension:192 on portal thrombosis (PT), 114 with porto sinusoidal vascular disease (PSVD) and 19 with Budd-Chiari syndrome (BCS). The mean age was 37.5 ± 14.81 years old. The sex ratio F/H was 2.9. An abdominal ultrasound examination: PT in 42.6%, a portal cavernoma in 54.3% and small hepatic veins in 78.4% of patients followed for BCS, only 1patient had a secondary BCS.2patients had PT and thrombosis of hepatic veins. The prevalence of myeloproliferative syndromes (MPS) was 7% for PT, 5.3% PSVD and 2% BCS. The constitutional deficit in coagulation inhibitors in 32.6% PT, 15.7% BCS and 9.6% PSVD. Paroxysmal nocturnal hemoglobinuria (PNH) positive in 3.5% PSVD, but none of patients followed for PT or BCS had this condition. Antiphospholipid syndrome in 0.8% PT, 1.9% BCS and no PSVD patient. Behçet's disease was found only during BCS in 2.1%. Celiac disease in 3% PT, 2.6% PSVD and 0.7% BCS. Hyperhomocysteinemia in 3% PT, 2.1% BCS and 5.2% PSVD. Local risk factors were associated with PT in 4.7%, 0.5% BCS and not studied in PSVD. Recent oral contraception in 0.8% PT, 0.5% BCS and not studied during PSVD. A recent pregnancy in1.6% PT, in no patient BCS and not studied during PSVD.
Conclusion: The etiological factors of VLD were multiple dominated by thrombophilia then MPS. Their prevalence was different depending on the site of the hepatic vascular involvement.

Abstract #607

Real world efficacy of M2BPGi on diagnosing liver fibrosis in chronic hepatitis patients

Young Youn Cho[1], Hansol Lhim[1], Hyun Woong Lee[2], Hyung Jun Kim[1]

[1]Department of Internal Medicine, Chung-Ang University Hospital, [2]Department of Internal Medicine, Yonsei University College of Medicine

Background: Mac-2 binding protein glycosylation isomer (M2BPGi) is a novel non-invasive marker for liver fibrosis, but still needs more validation.
Aims: We aimed to compare the diagnostic efficacy of M2BPGi with transient elastography (TE), FIB-4, and APRI.
Methods: This retrospective study included chronic hepatitis patients who underwent M2BPGi and TE for evaluation of liver fibrosis.
Results: A total of 302 patients were included: non alcoholic fatty liver disease 135 (44.7%), fatty liver 76 (25.2%), alcoholic hepatitis 61 (20.2%). M2BPGi levels were well correlated with TE levels (r = 0.715). Clinically significant liver cirrhosis (LC) was observed in 37 (12.3%) patients. Using cut-off 1.0 and 3.0 the AUROC of M2BPGi for predicting clinical liver cirrhosis was 0.839, which was comparable with TE, FIB-4 and APRI, 0.921, 0.918 and 0.818, respectively. The sensitivity and specificity for predicting clinical LC were 97.3% and 86.8% for TE alone, however positive predictive value (PPV) was only 50.7%. Adding TE with M2BPGi increased the PPV to 80.8%.
Conclusions: A novel fibrosis marker M2BPGi well correlates with TE and other non-invasive markers, and M2BPGi can improve the diagnostic probability of TE.

Abstract #768

A Hairy tail has something to tell you: rapunzel syndrome associated with gastric outlet obstruction, recurrent pancreatitis, malabsorption, and gastric lesion

Butt N[1], Rai L[1], Khemani H [1], Channa RH[1], Soomro SA[1]

Gastroenterology Department, Jinnah Postgraduate Medical Centre, Karachi, Pakistan

Introduction: Bezoar is a mass of undigestible material in the gastrointestinal (GI) tract. Trichobezoar is more common in females with psychiatric disorders and learning disabilities having trichotillomania and Trichophagia. The usual site is the stomach, but any part of the tract can be involved including large intestine: a condition called Rapunzel syndrome. Here we report two cases of Rapunzel syndrome with unusual presentations.
Case presentation: The first patient was a 17-year-old male, with a history of recurrent pancreatitis. Abdominal examination revealed tenderness in epigastric area. Blood tests showed elevated serum lipase and amylase, and low serum albumin. Computed tomography (CT) scan revealed large gastric bezoar and acute pancreatitis with moderate ascites. Magnetic resonance cholangiopancreatography showed separate openings of the common bile duct and the pancreatic duct in duodenum superiorly and inferiorly. Esophagogastroduodenoscopy revealed large trichobezoar in the stomach extending beyond pylorus reaching up to duodenum causing obstruction. The second patient was a 16-year-old female presented with complaints of epigastric pain and non-projectile foul-smelling vomiting associated with low-grade fever. There was history of depression and compulsive hair pulling and eating. There was a mass in the epigastric region extending in the right hypochondriac region. X-ray and ultrasound abdomen reveled findings of pyloric stenosis. CT scan abdomen showed findings suggestive of gastric bezoar. Endoscopy showed large trichobezoar extending up to duodenum and a sessile gastric mass. Biopsy revealed Helicobacter Pylori gastritis. Both patients were eventually referred for surgery.
Conclusion: Physicians should think of the trichobezoar as a differential diagnosis in young adults presenting with abdominal pain/mass or gastric outlet obstruction having a history of psychiatric disorders. Surgical or endoscopic removal is the treatment of choice. However, psychiatric evaluation and behavioral therapy are mandatory to prevent a recurrence.

Abstract #817

Identifying the tipping point and driving molecules during liver fibrosis progression by dynamic network biomarker analysis

Jinsheng Guo[1], Weixin Liu[2], Zhiping Zeng[1], Jie Lin[2], Xinxin Zhang[1], Luonan Chen[2]

Division of Digestive Diseases, Zhongshan Hospital, Fudan University, Shanghai Institute of Liver Diseases, Shanghai 200032, China, [2]Key Laboratory of Systems Biology, Innovation Center for Cell Signaling Network, Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences, Shanghai 200032, China

Introduction: Liver fibrosis is the scar-forming phenomenon of liver in response to a variety of chronic injuries ultimately leading to advanced cirrhosis. Hepatic stellate cells (HSC) are the major scar-forming cells in the liver. The aim of the present study was to identify the tipping point and key molecules driving liver fibrosis progression.
Methods: Mice model of liver fibrosis was induced by intraperitoneally injection of thioacetamide (TAA) for 17 weeks. Liver tissues were collected at different time points post TAA administration.
Results: By principle component analysis (PCA) and unsupervised hierarchical analysis (HCA) on the differentially expressed genes (DEGs), and Dynamic Network Biomarker (DNB) analysis to the time-series of liver transcriptomes, week 9 post TAA treatment (pathologically relevant to bridging fibrosis) was identified as a critical time point just before the significant fibrosis transition. In addition, 153 DNB genes were candidates as the key factors for the critical transition, most of them were functionally enriched in fibrosis-associated pathways. By functional analysis with high-confident interaction network (IPA) database and KEGG database, TGFB3 was ranked as the top DNB gene, which had a negative regulation to MMP13 in the interaction path. The promoting activity of TGFB3 on fibrogenic (e.g., CTGF and collagen type 1) genes, whereas down-regulating MMP13 gene transcription were confirmed by in vitro study with an immortalized mouse HSC line JS1.
Conclusion: The results indicated that there was a tipping point during liver fibrogenesis driven by key factors, which marks not only the initiation of the significant fibrogenesis but also the repression of the resolving of scar.

Abstract #849

The use of transient elastography (fibroscan) in correlation with APRI score and Fib-4 in monitoring NAFLD and chronic hepatitis B: a single center retrospective study

Lao, Bryan Christopher C. MD[1]; Tan, Jose A. MD[1]

[1]Section of Gastroenterology, Chinese General Hospital and Medical Center, Manila Philippines

Introduction: Fibroscan has been used for the detection of liver stiffness however there were few studies on how liver stiffness changes overtime and what happens to the liver stiffness as patients undergo treatment which can be used for monitoring treatment response.
Objectives: The aim of this study was to compare liver stiffness measurement (LSM) of Fibroscan with APRI and Fib-4 in monitoring treatment response of NAFLD and Chronic Hepatitis B patients at our institution.
Methods: Adult patients' records in an outpatient clinic at Chinese General Hospital from May, 2015 to July, 2019 were reviewed. Baseline characteristics and two determinations of LSM, APRI, Fib-4 over 6 months of treatment were collected and analyzed.
Results: A total of 101 subjects were included whose mean age was 57 years old and mostly male. Majority were diagnosed with NAFLD (56%). There was a significant positive correlation between the changes in LSM and changes in APRI (r = 0.2064 p = 0.0384) and Fib-4 (r = 0.3045 p = 0.0020) among all patients over a period of 6 months. Subgroup analysis showed same significant correlation in the NAFLD group where changes in LSM is significantly correlated to changes in APRI (R = 0.2881, p = 0.0298), and Fib-4 (R = 0.3317, p = 0.0117). However, chronic hepatitis B group did not show significant correlation.
Conclusion: Fibroscan is a good non-invasive monitoring tool for treatment response of patients with chronic liver disease especially for patients with NAFLD which can be well correlated with APRI and FIB-4.

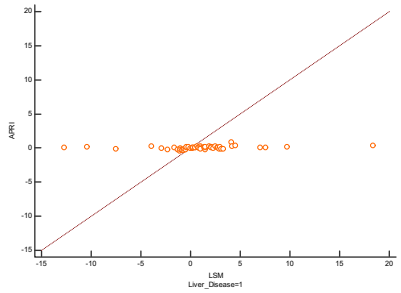


Figure 1. Correlation between changes in LSM and APRI (NAFLD). *R=0.2881, p=0.0298*

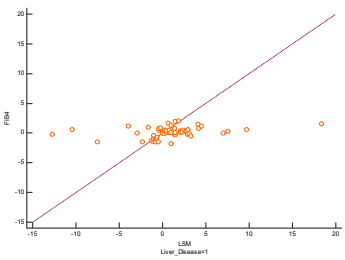


Figure 2. Correlation between changes in LSM and FIB4 (NAFLD). *R=0.3317, p=0.0117*

Abstract #906

Non invasive elastographies: echosens and livertouch

Abdullah Mübin Özercan[1], Özgün Ömer Asiller[2], Zeynep Melekoğlu Ellik[1], Mesut Gümüşsoy[1], Necati Örmeci[1]

[1]Ankara University School of Medicine Gastroenterology Department, [2]Ankara University School of Medicine

Background: Non invasive methods are under evaluation for detecting liver fibrosis because of invasiveness of biopsy. Transient elastography is one of the most common non invasive methods. There are many calculations like APRI and FIB-4 for measure the degree of liver fibrosis. We aimed to compare of two different elastographs that echosens and livertouch according to FIB-4 and APRI scores.
Methods: We have evaluated patients admitted for elastography by two transient elastographic equipments between March and October 2019. Their APRI and FIB4 scores was measured from laboratory surveys in 1 mounths to the procedures.
Results: 60 (%50.4) male and 59 (%49.6) female were included the study (total 119 patients). Their mean age was 54.62 ± 14.4. Etiologies of liver diseases were 41 (%34.5) hepatitis B, 34 (%28.6) non alcoholic hepatosteatosis, 13 (%10.9) primary biliary cholangitis, 13 (%10.9) criptogenic cirrhosis, 8 (%6.7) autoimmune hepatitis and 10 others. We measured 10–12 valid scores for the equipments and the invalid numbers of measurements to reach the validity were 7.29 ± 9.8 for echosense and 2.48 ± 4.2 for livertouch. Stiffness was 10.1 (1.8–75) kPa in echosense and 11.9 (1.6–75) kPa in livertouch (p = 0.82). And there are significant correlations between echosense and liver touch stiffness, CAP and fibrosis score measurements (p = 0.001). Correlation between ecosense stifness and FIB4 score was statistically significant (p = 0.027) but correlation of livertouch was not significant (p = 0.074).
Conclusion: Ecosense and livertouch are not different for asssesing liver fibrosis noninvasively. We revealed sensation of livertouch probe is higher than echosense even measure by large size probe.

Abstract #964

The influence of colonic stem cells on vegf and histopathology of colorectal adenocarsinoma patients: in vitro

Muhammad Ade Satia Putra, M.D[1], Paulus Kusnanto, MD[1]

[1]Residen of Internal Medicine, Gastroenterologist-Hepatologist, Moewardi General Hospital/Faculty of Medicine UNS, Surakarta, Central Java, Indonesia

Background: Colorectal cancer (CRC) accounts for 9% of all cancers globally, making it the number 2 most common cancer in women and the third most common in men. Adenocarcinomas that arise from the colonic and rectal epithelium account for 90% of cases of CRC. While surgery may have the potential to cure, less than 25% of cases can be operated with a recurrence rate of up to 70%. In cases that are inoperable, recurrence or CRC metastases are generally treated with palliative chemotherapy. Recent research shows that, Colonic Stem Cells (CSC) can lead to the recovery of CRC.
Objective: The aim of this study was to determine the effect of CSC administration on VEGF and histopathological changes in patients with colorectal adenocarcinoma.
Methods: This study used an experimental research design with the Pretest Posttest Control Group Design method with the object of research using a WIDR line which was divided into 6 treatment groups including control groups that did not receive treatment, before and after treatment, which were divided based on the amount of stem cell dose given. The results were carried out an analysis of VEGF and histopathology. Statistical test using Kruskal–Wallis and the Mann–Whitney test with P is significant if $p < 0.05$.
Results: In VEGF examination was found were tightly daubed in the control. With 5000 stem cell doses, there was a change in the VEGF outward appearance, which was moderate, although after the 20,000 dose there was no difference in control. Whereas in histopathology,

there were no significant differences before and after the administration of stem cells with the dose range given to the control.
Conclusion: Giving stem cells can affect angiogenesis in CRC but not significantly decrease the severity of CRC.

Abstract #1023

A comparative study of non-invasive methods for fibrosis assessment in chronic HCV infection

Abd EI-Atti E[1], Elshayeb E[1], Belal M[1]

[1]Internal Medicine Department, Faculty of Medicine - Menoufia University, Egypt

Introduction: Liver biopsy remains the gold standard in diagnosis and staging of liver fibrosis. It is costly and carries risk of complication, in addition there could be sampling error, inter- and intra-observer discrepancies in assessing hepatic fibrosis.
Objective: This study aimed to assess the diagnostic accuracies of four laboratory scores (FIB-4 score, APRI score, LOK score and platelets count) in comparison to each other and to liver biopsy for assessment of hepatic fibrosis.
Methods: The study was conducted on 500 patients suffering from chronic HCV infection with or without cirrhosis (as proved by biopsy). They were randomly selected from outpatient clinic of Menoufia University Hospitals (Egypt). They underwent full history taking, physical examination and laboratory investigations (CBC, liver profile {ALT, AST, alkaline phosphatase, serum albumin, bilirubin, prothrombin time (PT)}, renal profile {urea, creatinine}, viral markers {HCV Ab, HCV PCR, HBsAg}, AFP and ANA). Child–Pugh and MELD scores were calculated for all patients. Abdominal ultrasound and upper endoscopy were done for all patients. AST/Platelet ratio index (APRI score), Lok score [exp (log odds)]/[1 + exp (log odds)] and FIB-4 score were calculated for all patients. Log odds = $(1.26 \times (AST/ALT)) + (5.27 \times INR) - (0.0089 \times \text{platelet count } (10^3/mm3)) - 5.56$.
Results: There were 356 male (71.2%) and 144 female (28.8%) and their ages ranged from18 to 59 years (mean 40.5 ± 9). Liver biopsy of studied population revealed that 3.2% (n = 16) F0, 32.2% (n = 161) F1, 46% (n = 234) F2, 16.4% (n = 83) F3 and 1.4% (n = 70) F4. Diagnostic accuracy of noninvasive scores for assessment of hepatic fibrosis was calculated. Lok score at cutoff > 0.25 has 68.8% sensitivity, 55.1% specificity and 64.9% accuracy. FIB-4 score at cutoff > 1.26 has 55.9% sensitivity, 68.5% specificity and 65.9% accuracy. APRI score at cutoff > 0.66 has 50% sensitivity, 74.2% specificity and 65% accuracy. Platelet count at cutoff < 208 (10^3) has 67.7% sensitivity, 59.6.2% specificity and 67.6% accuracy.
Conclusion: Non-invasive tests as Fib-4 score, platelet count, APRI and LOK scores can identify the clinical stages of chronic hepatitis C by using their specific cut-offs in identify degree of liver fibrosis. Therefore, the number of unnecessary liver biopsies will be reduced.

Abstract #1026

High risk of liver fibrosis among the south Asian students

Das Shommya[1], Tarasova O.I.[1], Ogurtsov P.P.[1]

[1]Peoples' Friendship University of Russia (RUDN University). Hospital Therapy Department of Medical Institute, Moscow, Russian Federation

Introduction: In a recent medical research, it has been shown that the prevalence of liver fibrosis in a general population about 10–30%, especially among the Asian population, the risk of liver fibrosis is higher.
Objective: To identify the prevalence of liver fibrosis among the south Asian population without any history of chronic liver disease.
Materials and methods: 50 (14 female and 36 male) young students from Bangladesh, India, and Nepal participated. The subjects' parameters were: age: 21 to 35 years (m = 25.8), height: 1.61–1.77 m (m = 1.678), weight: 50–89 kg (m = 64.92) and waist circumference − 0.64–1.07 m (m = 0.775). Body mass index was 17.1–32.7 kg/m^2 (m = 23). To asses fibrosis and steatosis Fibroscan (502 Touch) was used.
Result: 66% (69.5% of male and 57.2% female) of students had liver stiffness more than normal range. 16% (19.4% male, 7.1% female) had signs of liver steatosis. Seventeen subjects from the thirty-three, who have liver fibrosis inform that they often eat fast food or drink regularly sweet soda water, two of them often consume alcohol and both of them have fibrosis and steatosis. Five subjects among the remaining seventeen were professional sportsmen and none of them has signs of liver fibrosis or steatosis.
Conclusion: The South Asian population has higher risk of liver fibrosis. The reason behind this not only the obesity, several dietary patterns, consumption of alcohol, sedentary lifestyle but also a traditional using of spices in a large number may lead to liver fibrosis. Cannot be excluded the genetic predisposition.

Abstract #1143

Correlation between TNF-α serum and degree of liver fibrosis by fibroscan in chronic liver disease patients at RSMH Palembang

Suyata[1], Meiliana[1], Rahmayani F[1], Bakry F[1], Saleh I[2]

[1]Division of Gastroenterohepatology, Internal Medicine Department, Faculty of Medicine, Sriwijaya University, Mohammad Hoesin Hospital, Palembang, Indonesia, [2]Faculty of Medicine, Sriwijaya University, Mohammad Hoesin Hospital, Palembang, Indonesia

Background: Liver fibrosis results from dysregulation of normal wound healing, inflammation, activation of myofibroblasts, deposition, and degradation of extracellular matrix (ECM). TNF-α is one of the fibrogenic cytokines which is secreted by both inflammatory cells and injured hepatocytes and play role in the pathogenesis of hepatocyte apoptosis. No publication has yet observed the correlation between TNF-α and liver fibrosis level in Indonesia. The aim of this study was to measure serum level of TNF-α, the degree of liver fibrosis and to correlate between TNF-α and degree of liver fibrosis by fibroscan.
Method: This analytical observational research with cross sectional design was conducted from August to December 2017 in 33 subjects. The subjects were hepatitis B and C outpatients in Gastroenterology and hepatology clinic at RSMH Palembang who undergone the fibroscan. Liver stiffness was measured by fibroscan device and stated in kilopascal (kPa). TNF-α serum levels were measured by ELISA quantitative method. The data were processed using the SPSS statistical package, with an analysis of the correlation based on the Spearman statistic.
Results: Of the 33 subjects, there were males 24 males (72.7%). The median of TNF-α serum was 2.06 (1.01–19.4) pg/mL and the median of fibroscan was 12.6 (6.3–28.4) kPa. There was a moderate positive correlation between TNF-α serum and liver fibrosis (r = 0.535; p = 0.001).
Conclusion: There was a moderate positive correlation between TNF-α serum levels and liver fibrosis by fibroscan in chronic liver disease patients at RSMH Palembang.

Abstract #1192

Hepatitis B viral load (HBV DNA) is a significant risk factor of liver fibrosis in HbeAg positive and negative chronic hepatitis B (CHB)

Windradi C[1], Maimunah U[2], Kholili U[2], Widodo B[2], Thamrin H[2], Miftahussurur M[2], Vidyani A[2]

[1]Resident of Internal Medicine Department, Universitas Airlangga, Surabaya Indonesia, [2]Division of Gastroenterology and Hepatology, Internal Medicine Department, Universitas Airlangga, Dr. Soetomo General Academic, Surabaya Indonesia

Introduction: The development of advanced fibrosis is one of the most significant sequelae of chronic hepatitis B. In recent clinical practice, levels of serum on HBV DNA levels as the initiation and evaluation for antiviral therapy. The association between serum HBV DNA levels and liver fibrosis has not been fully evaluated.
Objective: To evaluate the interaction between HBeAg status, HBV DNA, and significant fibrosis based on transient elastography in the Gastroenterohepatology Outpatient Installation at Dr. RSUD. Soetomo Surabaya.
Methods: We perfomed a retrospective study of patient presenting with CHB who underwent laboratory and fibroscan test between January to June 2018. Patient were divided into 3 groups consist of HBeAg positive/DNA detected (EP); HBeAg negative/DNA < 25 000 IU/ml (ENLR); HBeAg negative/DNA > 25 000 IU/ml (ENHR).
Results: 119 patients new analyzed, 78 (65.5%) were in the EP group, 24 (20.2%) in the ENHR and 17 (14.3%) in the ENLR group. The highest prevalence of F2/3/4 fibrosis was found in the EP group at 21.8%. The prevalence of F2/3/4 fibrosis in the EP, ENLR and ENHR groups were significantly different ($P < 0.05$). The prevalence of F2/3/4 fibrosis increased in HBeAg-negative and HbeAg-positive patients with HBV DNA of $< 10^5$ IU/ml and those with HBV DNA of $> 10^7$ IU/ml from 11.76% to 21% and 10% to 54.6% respectively. Using logistic regression, a significant interaction was found between the HBeAg status (p 0.015) and HBV DNA level (p 0.037), with F2/3/4 fibrosis as the outcome.
Conclusion: Levels of HBV DNA are associated with increasing prevalence of significant fibrosis in patients with HBeAg- negative and positive CHB.

Abstract #1226

Hepatoprotective activity of White turple Curcuma zedoaria extract

Eva Pravitasari Nefertiti[1], Troef Soemarno[1], Iswan A Nusi[2], Poernomo Boedi Setiawan[2], Herry Purbayu[2], Titong Sugihartono[2], Ummi Maimunah[2], Ulfa Kholili[2], Budi Widodo[2], Husin Thamrin[2], Amie Vidyani[2], IGM Sanies Ermawan[3]

[1]Faculty of Medicine, Hang Tuah University, Surabaya, East Java, Indonesia, [2]Division of Gastroentero-Hepatology, Department on Internal Medicine, Faculty of Medicine, Airlangga University, Soetomo Hospital, Surabaya, East Java, Indonesia, [3]Mataram Hospital, Mataram, West Nusa Tenggara, Indonesia

Background: *Curcuma zedoaria* rhizomes were collected from West Nusa Tenggara, Indonesia. *White turmeric rhizome (Curcuma zedoaria)* has the main substance, which is curcumin contains diferuloylmethan as a natural antioxidant, can capture free radicals and receptive oxygen species that can cause an inflammatory reaction. Acetaminophen is a nonsteroidal antiinflammatory drug (NSAID) used largely for acute treatment of pain.
Aims: The study was designed to the hepatoprotective activity of Curcuma zedoaria extract in acute experimental liver injury induced by acetaminophen.
Methods: Wistar albino rats weighing 175–250 g of male sex were used. The animals were divided into 4 groups of 10 each. The animals were then subjected to either one of the folowing treatment for 14 days. This is an experimental study with *a post-test only controlled group design*. The research used were 20 male mice (*Rattus norvegicus)*, Strain Wistar, aged + 2 months old, weighed 175 grams. They were divided into 4 groups, and each group consisted of 10 mice. Group 1 was control group. Group 2 was exposed to one-time administration of acetaminophen with the toxic dosage of 1.35 g over each kilogram of body weight. Groups 3 and 4 were each given turmeric extract with the dosage of 5 milligrams and 10 milligrams over each kilogram of body weight respectively; after 2 h, they were subject to one-time acetaminophen administration with the dosage of 1.35 grams over each kilogram of body weight. The animals were sacrificed 24 h after the administration of acetaminophen. The liver was immediately isolated and washed with normal saline, was then subjected to histopathological examination. The effects observed were compared. In the acute liver damaged induced by acetaminophen.
Results: Turmeric extract significantly reduced the inflammation, degenerative changes and steatosis.
Conclusions: That the turmeric extract possesses good hepatoprotective activity.

Abstract #1258

Comparison of MAC-2 binding protein glycosylation isomer as a non-invasive biomarker for probing liver disease

T. Kawin[1], S. Tanita[1], S. Prakasit[1], K. Churairat[1], S. Wattana[2]

[1]Division of Gastroenterology, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, [2]Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Introduction: Liver disease remains a major critical challenge in Thailand as a result of viral hepatitis and other etiologies. Clinical management requires monitoring the extend of liver fibrosis. Non-invasive testing presents an attractive mode for probing of disease progression.
Objectives: MAC-2 Binding Protein Glycosylation Isomer (M2BPGi) is a novel serum marker for fibrosis staging. The current study evaluates the marker among healthy donors, hepatitis B and C patients as well as NASH patients.
Methods: A total of 256 subjects were hepatitis B, C and NASH patients with mixed fibrosis stages by Metavir scores. Healthy donors were confirmed with normal liver functions tests, serology and ultrasound. Comparisons of M2BPGi levels among different study groups were performed using one way analysis of variance (ANOVA) and the effectiveness using receiver operating characteristics (ROC) curves.
Results: The median M2BPGi levels for healthy donors was 0.12 cut off index (COI). ANOVA showed statistical significance of M2BPGi levels were different among hepatitis B, C, NASH and healthy subjects. Hepatitis C demonstrated the largest range of values and the highest mean levels. ROC curves demonstrated superior results for M2BPGi levels among diseased populations and healthy controls. AUROC were 0.983, 0.937 and 0.951 in hepatitis C, hepatitis B and NASH patients, respectively. Comparing with Fibroscan, APRI, FIB-4 and Fibrotest, M2BPGi levels showed a positive linear trend.

Conclusion: M2BPGi addresses a critical need for management of liver disease and fibrosis. In the study, we demonstrated significant differences among different etiologies and established the background levels among healthy donors.

Abstract #1269

Liver stiffness (elastography) success rate in Hasan Sadikin General Hospital Bandung during January 2014–December 2018

Mario Budi Purwanegara Tambunan[1], Muhammad Begawan Bestari[1], Dolvy Girawan[1], Nenny Agustanti[1], Yudi Wahyudi[1], Siti Aminah Abdurahman[1]

[1]Division of Gastroenterohepatology, Department of Internal Medicine, Faculty of Medicine, Universitas Padjadjaran, Hasan Sadikin General Hospital Bandung, Indonesia

Background: Chronic liver diseases caused by chronic Hepatitis B and C, non alcoholic fatty liver disease (NAFLD) and alcoholic liver diseases are the leading cause of morbidity and mortality globally. Transient elastography (TEG) is now widely used as a non invasive method to evaluate liver fibrosis. Based on recommendation, TEG is reliable if there are 10 valid reading with IQR $\leq$ 30% and success rate $\geq$ 60%. This study was done to evaluate the TEG validity and success rate during 5-year period.
Methods: This was a cross-sectional descriptive-analytic study, samples were patients who had undergone TEG examination in Hasan Sadikin General Hospital from January 2014 to December 2018 and data was collected from medical record database.
Results: In our hospital, TEG was performed by Hepatologists or trainee doctors in Hepatology. Of 1840 subjects, 1642 subjects (89.2%) were included and 198 subjects (10.8%) were excluded. Of 1642 subjects, there were 62.4% males and 37.6% females. Median liver stiffness was 8.0 kPa (3.5–75.0 kPa). There were 54.3% subjects with 100% success rate, followed by 19.9% with 90–99%, 10.3% with 80–89%, 10% with 70–79% and 5.5% with 60–69% success rate.
Conclusion: TEG is an effective method to evaluate liver stiffness. It is a non invasive method and easy to use with 89.2% validity and 100% success rate as high as 54.3%.

Abstract #1352

APRI and FIB-4 for predicting liver fibrosis in patients with chronic hepatitis B concurrent with nonalcoholic fatty liver disease

Weimao Ding[1], Rui Huang[2], Jian Wang[2], Juan Xia[2], Weihua Wu[2], Xiaomin Yan[2], Chao Wu[2]

[1] Department of Hepatology, Huai'an No. 4 People's Hospital, Huai'an, Jiangsu, China, [2] Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China

Introduction: Non-invasive tools for predicting liver fibrosis stages in chronic hepatitis B (CHB) patients concurrent with nonalcoholic fatty liver disease (NAFLD) are lacking.
Objectives: We aimed to investigate the diagnostic values of aspartate aminotransferase-to-platelet ratio index (APRI) and fibrosis-4 (FIB-4) in assessing liver fibrosis in CHB patients with NAFLD.
Methods: One hundred forty-five liver biopsy-proven treatment-naïve CHB patients concurrent with NAFLD were enrolled. Liver fibrosis was staged using the Scheuer classification system. Steatosis was assessed according to Brunt classification. Diagnostic performance was evaluated by receiver operating characteristic (ROC) curve.
Results: The distribution of liver fibrosis stages was as follows: S0, 16 (11.0%), S1, 54 (37.2%), S2, 27 (18.6%), S3, 26 (17.9%), and S4, 22 (15.2%) patients. The distribution of hepatic steatosis grade was as follows: F1, 97 (66.9%), F2, 32 (22.1%), F3, 16 (11.0%) patients. APRI ($r = 0.376$, $p < 0.001$) and FIB-4 ($r = 0.393$, $p < 0.001$) were positively associated with the stages of liver fibrosis. The area under the receiver operating characteristic curves (AUROCs) of APRI and FIB-4 for predicting significant fibrosis ($\geq$ S2), advanced fibrosis ($\geq$ S3) and cirrhosis (S4) were 0.697 and 0.708, 0.730 and 0.689, 0.719 and 0.725, respectively. The diagnostic accuracy was not significant difference between APRI and FIB-4 in predicting significant fibrosis ($p = 0.765$), advanced fibrosis ($p = 0.284$) and cirrhosis ($p = 0.9$).
Conclusion: APRI and FIB-4 could predict liver fibrosis stages in CHB patients concurrent with NAFLD with moderate diagnostic accuracy. Novel non-invasive tools in predicting liver fibrosis stages with high diagnostic accuracy are needed in CHB patients concurrent with NAFLD.

Abstract #1377

Plateletcrit as a novel index for predicting significant liver fibrosis in patients with chronic hepatitis B

Rui Huang[1], Jian Wang[1], Yong Liu[2], Yuxin Chen[2], Xiaomin Yan[1], Zhaoping Zhang[1], Weimao Ding[3], Chao Wu[1]

[1]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China, [2]Department of Laboratory Medicine, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China, [3]Department of Hepatology, Huai'an No. 4 People's Hospital, Huai'an, Jiangsu, China

Introduction: Assessing liver fibrosis is important for chronic hepatitis B (CHB) patients.
Objectives: We aimed to investigate the association between the plateletcrit (PCT) and liver fibrosis stage in CHB patients.
Methods: Five hundred and sixty-seven treatment-naïve CHB patients who underwent liver biopsy were enrolled. Liver fibrosis stage was scored based on the Scheuer scoring system. Patients were randomly (2:1) divided into a derivation cohort ($n = 378$) and a validation cohort ($n = 189$). The diagnostic accuracy was evaluated by the area under the receiver operating characteristic curve (AUROC).
Results: In the derivation cohort, the median PCT levels in patients with S2–S4, S3–S4 and S4 were 0.14%, 0.13% and 0.12%, which were significantly lower than patients with S0–S1 (0.17%), S0-S2 (0.17%) and S0–S3 (0.16%). PCT levels were negatively associated with fibrosis stages ($r = -0.354$, $p < 0.001$). Multivariate regression analysis showed that PCT (OR 0.849, 95% CI 0.801–0.900, $p < 0.001$) was an independent predictor of significant fibrosis. The AUROCs of PCT in predicting significant fibrosis, advanced fibrosis and liver cirrhosis were 0.645 (95%CI 0.587 to 0.703), 0.709 (95%CI 0.657 to 0.761) and 0.714 (95%CI 0.651 to 0.777), respectively. The AUROCs of PCT were significantly higher than aspartate transaminase to PLT ratio index (APRI) in identifying advanced fibrosis ($p = 0.004$) and cirrhosis ($p = 0.003$). However, the diagnostic performance of PCT were comparable with fibrosis-4 score (FIB-4) in predicting significant fibrosis ($p = 0.729$), advanced fibrosis ($p = 0.996$) and cirrhosis ($p = 0.963$). In the validation cohort, PCT

could also predict significant fibrosis, advanced fibrosis and cirrhosis with similar diagnostic accuracy.
Conclusion: PCT was positively associated with severity of liver fibrosis and can be as a novel potential indictor for predicting liver fibrosis in CHB patients.

Abstract #1385

The role of somatostatin as treatment for post endoscopic retrograde cholangio-pancreatography pancreatitis

Banjuradja I, MD[1]; Indriani RN, MD[2], Suryamin M, MD[2]

[1]Internal Medicine Resident, Indonesia University, Jakarta, [2]Internal Medicine Department, Persahabatan General Hospital, Jakarta

Introduction: Pancreatitis is the most common complication in patients undergoing endoscopic retrograde cholangio-pancreatography (ERCP). Prompt evaluation and treatment are important to improve its outcome. Somatostatin is one of pharmacological modalities known to have some benefits in management of pancreatitis, but so far it has not been routinely recommended by guidelines.
Case presentation: We herein report a case of a 54-year old female who suffered post ERCP pancreatitis (PEP) which only significantly improve after administration of somatostatin.
Conclusion: In spite of wide range of therapeutic options for the management of PEP, somatostatin is believed to still have benefits as management of this condition.

Abstract #1429

A rare case of Banti's syndrome and its 1 year survival

Ihsanul Rajasa[1], Anastasia Putri[1], Saut. H. Nababan[2]

[1]Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, [2]Hepatology Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia

Introduction: Banti's syndrome, also known as idiopathic congestive splenomegaly or idiopathic non-cirrhotic portal hypertension, it is marked by portal hypertension in the absence of liver cirrhosis. Due to its rarity, diagnosis can be quite challenging.
Case Illustration: A 38-year-old male with a repeated haematemesis. Upon physical examination, we found pale conjunctiva and massive splenomegaly extending to Schuffner IV point. Esophagogastroduodenoscopy examination revealed oesophageal- fundal varices and severe portal hypertension. Abdominal CT scan results showed idiopathic, non-cirrhotic portal hypertension, and multiple vein enlargements. Portal vein has no obstruction. Fibroscan result was normal. Patient denied history of hepatitis or alcohol consumption. The diagnosis made after the HPVG performed and showed normal result.
Discussion: Classic sign of Banti's Syndrome is found, portal hypertension along with splenomegaly, and variceal bleeding that manifested as hematemesis. The most prevalent in Asian male and has been associated with infections, immune-based diseases, such as HIV. Diagnosis is made by exclusion. Treatment involves medication such as beta blocker, also endoscopic variceal ligation. Trans-jugular intrahepatic portosystemic shunting (TIPSS) is the next choice. Prognosis of Banti's disease is excellent. Even in acute variceal bleeding, the mortality is significantly lower than cirrhotic patients. Several studies reported that the 5-year survival could be as high as 100% in patient with definitive treatment. Unfortunately, in this case, the patient has died only 1 year after the diagnosis was made.
Conclusion: Banti's syndrome is a rare condition that is challenging, but has a good survival rate if it treated rightly through definitive treatment like TIPSS.

Abstract #1434

Broad and densely compacted septa present frequently in patients with HBV-related compensated cirrhosis after long-term anti-viral therapy

Yameng Sun[1], Shuyan Chen[1], Jialing Zhou[1], Xiaoning Wu[1], Bingqiong Wang[1], Tongtong Meng[1], Xiaojuan Ou[1], Jidong Jia[1], Hong You[1]

Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing Key Laboratory of Translational Medicine in Liver Cirrhosis, National Clinical Research Center of Digestive Diseases, Beijing, China

Introduction: HBV-related compensated cirrhosis is reversible after long-term suppression of viral replication. However, whether those patients still have broad and densely compacted septa after long term anti-viral therapy remains unclear.
Methods: Treatment-naive patients with HBV-related compensated liver cirrhosis were enrolled. Cirrhosis was diagnosed if 2 of the following 4 criteria were met: liver surface nodularity and echogenicity on imaging, platelets $< 100 \times 10^9$/L, albumin < 35.0 g/L or INR > 1.3, liver stiffness > 12.4 kPa. Patients were performed liver biopsy after 5 years of entecavir-based therapy. Fibrosis was assessed by Ishak modified histology activity index (HAI) grading and staging system.
Results: A total of 26 compensated cirrhotic patients with qualified liver biopsy at year 5 were included in this analysis. Patients were predominantly male (88%), with the median age of 47. After 5 years of treatment, 22 (85%) patients have no or mild necroinflammation (modified HAI ≤ 3). For liver fibrosis, 2 (8%) patients were significant fibrosis (Ishak = 3), 9 (35%) patients were advanced fibrosis (Ishak = 4), and the remaining 15 (58%) patients were still liver cirrhosis (Ishak stage 5 and 6). According to the width of septa, 8 (31%) patients had very thin/delicate septa, whereas 14 (54%) patients still have broad and densely compacted fibrous septa on biopsy. Clinical characteristics are comparable at baseline between patients with and without broad septa. Patients with broad septa had a higher liver stiffness value at year 5 ($P = 0.013$).
Conclusion: Although HBV-related compensated cirrhosis could be reversed, broad fibrous septa and cirrhosis present frequently after 5 years of treatment.

Abstract #1446

Differences in clinical profile of Budd-Chiari syndrome and chronic parenchymal liver disease with ascites which caused by hepatitis B or C infection

Gunady, Hirlan[1], Agung P[1], Didik I[1], Hery DP[1]

[1]Division of Gastroentero Hepatology, Department of Internal Medicine, Diponegoro University, Dr. Kariadi Hospital, Semarang, Indonesia

Introduction: Liver cell damage can directly caused by hepatitis viruses and indirectly due to liver vascular disorders. Budd-Chiari Syndrome causes non-cirrhosis portal hypertension and ascites. Cirrhosis due to hepatitis B or C virus is the most common cause of chronic liver damage that will cause portal hypertension and eventually ascites.
Objectives: To find the differences in the clinical profile of Budd-Chiari Syndrome and chronic parenchymal liver disease with ascites caused by hepatitis or C virus.
Methods: A Cross-sectional study between January 2017 and April 2019, included 453 patients who met the inclusion and exclusion criteria. The diagnosis of Budd-Chiari Syndrome is based on radiological features (USG and MSCT Contrast).
Results: Based on gender ($p = 0.304$), the median age of the BCS group was 40.5 years, the parenchymal liver disease group was 51 years ($p < 0.001$). Based on the main complaint ($0 < 0.05$), we found abdominal pain in right upper quadrant, hematemesis, and/or melena. On radiological examination ($p < 0.001$) we found hepatomegaly, splenomegaly, liver nodules, intrahepatic collateral, and enlargement of caudate lobe. Laboratory results showed higher liver function test ($p < 0.05$) on total bilirubin, direct bilirubin, AST, ALT, ALP, Gamma GT, albumin, and Prothrombin time. SAAG calculation results in both groups ($p = 0.877$).
Conclusion: This study found significant differences between BCS groups and parenchymal liver disease group in age, chief complaints, radiological findings, and some of the liver function tests.

Abstract #1566

The clinical significance of serum amyloid A levels in patients with liver diseases

Zi-Ying Yuan[1,2], Xing-Xin Zhang[1], Yu-Jing Wu[1], Zhi-Ping Zeng[1,3], Wei-Min She[1], Shi-Yao Chen[1], Yuan-Qing Zhang[1,4], Jin-Sheng Guo[1]

[1]Department of Gastroenterology and Hepatology, Zhong Shan Hospital, Fudan University, Shanghai Institute of Liver Diseases, Shanghai 200032, China, [2]Department of Gastroenterology, Peking University Third Hospital, Beijing 100191, China, [3]Department of Gastroenterology, The Third Affiliated Hospital of Nanchang University, Nanchang, Jiangxi 330008, P.R.China, [4]The First Affiliated Hospital, Yunnan Institute of Digestive Disease, Kunming Medical University, Kunming 650000, Yunnan Province, China

Introduction: Serum amyloid A (SAA) is an acute phase protein mainly synthesized by the liver. The aim of the present study was to investigate the serum levels of SAA in patients with different liver diseases and association factors.
Methods: Two hundred and seventy-eight patients with different liver diseases and 117 healthy controls were included in this study, including 205 with chronic hepatitis B (CHB), 22 with active autoimmune liver disease (AILD), 21 with nonalcoholic steatohepatitis (NASH), 14 with drug-induced liver injury (DILI), and 16 with pyogenic liver abscess (PLA). Serum levels of SAA and other clinical parameters were collected for the analysis of the factors associated with SAA level.
Results: All patients with active liver diseases had higher serum SAA levels than healthy controls and the inactive CHB patients, with the highest SAA level found in patients with PLA (398.4 ± 246.8 mg/L). Patients with active AILD (19.73 ± 24.81 mg/L) or DILI (8.036 ± 5.685 mg/L) showed higher SAA levels than those with active CHB (6.621 ± 6.776 mg/L) and NASH (6.624 ± 4.891 mg/L). Single and multivariate logistic regression analyses for the CHB patients suggested that patients with active CHB were associated with SAA level higher than 6.4 mg/L. Serum levels of SAA and CRP (C-reactive protein) were positively correlated in patients with CHB, PLA, and active AILD.
Conclusion: Serum level of SAA is a sensitive biomarker for inflammatory activity of PLA. It may also be a weak marker reflecting milder inflammatory status in the liver of patients with other active liver diseases.

Abstract #1589

Salvia Miltiorrhiza ameliorates chronic liver injury via inhibiting NLRP3/IL-1β axis

Yuan Peng[1], Yuanyuan Ma[1], Yanyan Tao[1], Chenghai Liu[1]

[1]Institute of Liver Diseases, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China

Introduction: Pro-inflammatory macrophages aggravated progress of chronic liver injury is confirmed both in patients and animal models. High expression of nucleotide binding oligonucleotide domain like receptor protein 3 (NLRP3) on pro-inflammatory macrophages contributes to liver injury. Salvia miltiorrhiza (SM), a Chinese herbal medicine, is effective in treating liver injury in our previous study, but the immunological mechanism remains unclearly.
Objectives: We aimed to test the hypothesis that the anti-inflammatory effect of SM was associated with inhibiting activation of pro-inflammatory macrophages via modulating NLRP3/IL-1β axis.
Methods: Liver injury was induced with 0.1% DDC diet in vivo. Primary bone marrow cells were isolated and induced to BMDMs. BMDMs were stimulated with LPS plus ATP to induce NLRP3 inflammasomes in vitro. Effects of SM on NLRP3 and IL-1β were investigated in vivo and in vitro.
Results: After treatment for 3 weeks, SM could decrease the serum levels of ALT, AST and TBIL and the liver index in model mice, alleviate the pathological changes of liver tissue, improve the inflammatory cells infiltration, decrease the content of IL-1β and reduce the positive expression of NLRP3 in vivo. NLRP3 inflammasomes in primary BMDMs induced by LPS + ATP were significantly downregulated after incubation of SM in vitro. mRNA expressions of NLRP3, IL-1β and TNF-α of the BMDMs were also decreased synchronously.
Conclusion: Salvia Miltiorrhiza can effectively alleviate chronic liver injury, which is associated with inhibition on NLRP3/IL-1βactivation in vivo and in vitro.

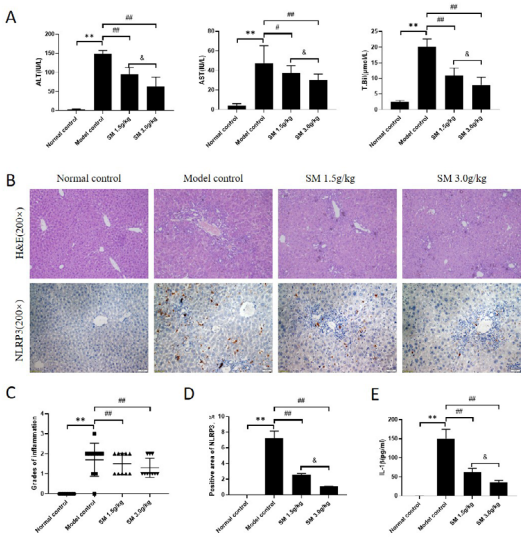


Fig 1 SM attenuated DDC-induced liver injury in mice. Male mice were orally administrated with 0.1% DDC for 3 weeks, starting at 8 weeks of age. Synchronously, once-daily treatment with SM extractum were begun. Three weeks later, mice were sacrificed 48 h after the last SM treatment. (A) Serum levels of serum ALT and AST were assayed by using commercial kits. (B) Liver inflammation was examined by H&E staining and expression of NLRP3 was investigated by immunohistochemical staining in the liver sections. The data were examined under bright field microscope (magnification 200×). (C) Grades of hepatic inflammation were analyzed according to the Knodell histological activity index. (D) Semi-quantification data for NLRP3 expression were expressed as the % of total liver area, and the data were assessed by analyzing five fields of positive stained liver sections per animal. Each field was acquired at 200× magnification. (E) Levels of IL-1β in liver tissues. Data were acquired using Image-Pro Plus software. Values represent means ± SD (n = 10). $^{*}P < 0.05$, $^{**}P < 0.01$, versus normal control group; $^{\#}P < 0.05$, $^{\#\#}P < 0.01$, versus model control group.

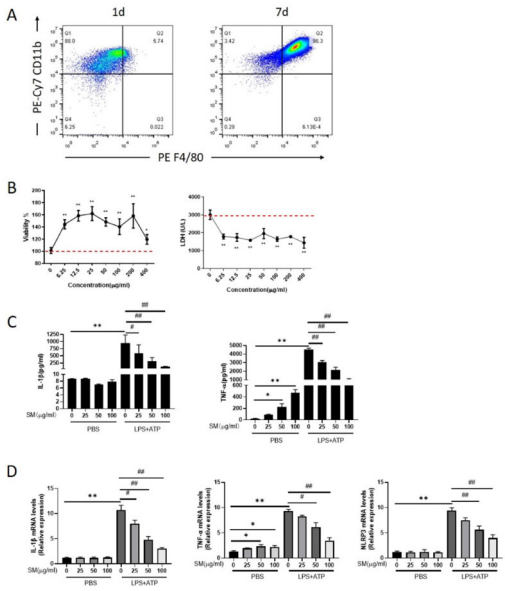


Fig 2 SM inhibited pro-inflammatory macrophages via regulating NLRP3/IL-1β in vitro. (A) BMs were isolated from normal C57BL/6 mice shankbone and thighbone, and then were cultured with supernatant of L929 cell lines to induce BMDMs. Seven days after the cell culture, the phenotype and purity of the BMDMs were analyzed by flow cytometry. (A) The purity of primary BMDMs were higher than 95% after culturing for 7 days. (B) Cells were cultured in a 96-well plate at the appropriate density and incubated with 6.25-400 μg/ml of SM. Cell viability was detected by CCK8 and LDH content in the supernatant was assayed after incubation with SM for 24h. (C) For inducing NLRP3 activation in vitro, BMDMs were incubated with 10ng/ml LPS for 16 h and then were co-incubated with 5mM ATP for another 5 h, following cells were cultured with 25-100μg/ml of SM. The levels of TNF-α and IL-1β in the cell supernatant were evaluated by Elisa kits. (D) mRNA levels of NLRP3, TNF-α and IL-1β were quantified by RT-qPCR. $^{*}P < 0.05$, $^{**}P < 0.01$; $^{\#}P < 0.05$, $^{\#\#}P < 0.01$.

Abstract #1684

Safety and effectiveness of statin in patients with chronic liver disease: an evidence based case report

Kemal Fariz Kalista[1], Patriotika Ismail[2]

Division of Hepatobiliary, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Background: Statin is a cholesterol-lowering drug to treat hypercholesterolemia. Its has been limited because one of its potential and most feared side effects is hepatotoxicity. Recent studies showed controversial results regarding safety and effectiveness of statin in patient with chronic liver disease. In this evidence based case report (EBCR) our PICO was P: chronic liver disease, I: statin, C: no comparison, O: fibrosis, cirrhosis and death.
Methods: Two selected articles are made through Pubmed, EBSCO Host according to clinical questions. The selection of articles is based on inclusion and exclusion criteria.
Results : Kim RG, et al. revealed that statin use significantly with 46% lower risk of hepatic decompensation (RR 0.54; 95% CI 0.46–0.62; $I^2 = 0\%$) and 46% lower mortality (RR 0.54; 95% CI 0.47–0.61; $I^2 = 10\%$) and was associated with 27% lower risk of variceal bleeding or progression of portal hypertension (hazard ratio 0.73; 95% CI 0.59–0.91; $I^2 = 0\%$) while Yaqin Wang, et al. revealed that statins decrease the risk of cirrhosis by 11% (OR 0.89; 95% CI 0.86–0.93, $P = 0.001$).
Conclusion: Statins have several benefits in preventing cirrhosis fibrosis, decompensated cirrhosis, reduced risk of portal hypertension, death and even evidence of prevention in the direction of liver cancer. Further research is needed to conduct prospective observational studies and randomized controlled trials.

Abstract #1718

Fuzheng Huayu recipe prevented and treated CCl4-induced mice liver fibrosis through regulating polarization and chemotaxis of intrahepatic macrophages via CCL2-CX3CL1 axis

Man Zhang[1], Hongliang Liu[1], Kai Huang[1], Yuan Peng[1], Yanyan Tao[1], Xudong Hu[2*†], Chenghai Liu[1,3,4]

[1]Institute of Liver Diseases, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China, [2]Department of Biology, School of Basic Medical Sciences, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China, [3]Shanghai Key Laboratory of Traditional Chinese Clinical Medicine, Shanghai 201203, China, [4]Shanghai Innovation Center of TCM Health Service, shanghai 201203, China

Introduction: Fuzheng Huayu recipe (FZHY) has been used in the treatment of liver fibrosis for nearly 20 years and achieved a good clinical effect.
Objectives: This study aimed to elucidate the prevention and treatment mechanism of Fuzheng Huayu recipe (FZHY) on carbon tetrachloride (CCl4)-induced mice liver fibrosis by regulating the recruitment and polarization of intrahepatic macrophages.
Methods: FZHY was administered to prevent and treat CCl4-induced liver fibrosis. The anti-liver fibrosis effects of FZHY were evaluated by pathological staining, biochemical test, RNA-Seq transcriptome analysis, western blot assay, qRT-PCR, immunofluorescence assay and flow cytometry.
Results: FZHY significantly decreased serum ALT and AST levels, improved liver inflammation and reduced the degree of liver fibrosis. KEGG pathway enrichment analysis of RNA-seq data showed that the TNF signaling pathway was the most important signaling pathway related to macrophage polarization and recruitment. The expression of various chemotaxis-related and inflammation-related genes such as chemokine CCL2 in the TNF signaling pathway were significantly

increased by CCl4 and significantly decreased by FZHY. Experimental results also showed that the CCL2 gene expression in primary intrahepatic macrophages was significantly down-regulated and the CX3CL1 gene expression was significantly up-regulated by FZHY. FZHY significantly down-regulated the ratio of pro-inflammatory Kupffer cell and significantly up-regulated the ratio of anti-inflammatory Kupffer macrophage. Meanwhile, FZHY significantly reduced the ratio of pro-inflammatory Ly6C^{high} macrophage recruited from blood circulation by CCL2 and significantly increased the ratio of restorative Ly6C^{low} macrophage recruited from blood circulation by CX3CL1.

Conclusion: FZHY could regulate the recruitment and polarization of intrahepatic macrophages via CCL2/CX3CL1 axis, so as to play its anti-inflammation and anti-fibrosis pharmacological effects in the liver.

Abstract #1924

FuZheng HuaYu tablet promotes entecavir effect on pathological regression of HBV cirrhosis: a randomized, placebo control, double-blind and multicenter clinical trial

Chenghai Liu, Zhimin Zhao, Jian Liang, Biao Zhang, Xiaodong Li, Huanwei Zheng, Chuanwu Zhu, Kewei Sun, Yunhai Lv, Xizhong Shen, Huichun Xing, Jiaquan Huang, Kejun Zhang, Yong Zhang, Xiangao Jiang, Yali Zong, Yuxi Zhang, Cheng Xu, Qing Xie, Xiuhui Li, Anlin Ma, Ping Liu

Background: Entecavir (ETV) can regress HBV fibrosis with limitations. FuZheng HuaYu (FZHY), a patent Chinese herbal product, can modulate early or intermediate liver fibrosis alone in chronic hepatitis B (CHB). We aim to observe the efficacy and safety of FZHY tablet plus ETV in patients with HBV cirrhosis.

Method: We performed a randomized, double-blind, placebo control and multicenter clinical trial. HBV compensatory cirrhosis, Ishak fibrosis greater than or equal to 5, were enrolled and randomly assigned to ETV (0.5 mg qd) plus FZHY tablets (1.6 g tid) or ETV plus FZHY placebo for 48 weeks, at which time a liver biopsy was repeated. The primary efficacy end point was histological improvement at week 48. Safety was also assessed.

Results: 322 compensatory cirrhosis patients completed 48 weeks treatment and secondary biopsy, 164 patients in the ETV plus FZHY tablets group (experimental group), and 158 in the ETV plus FZHY placebo group (control). 64.6% (106/164) showed fibrosis regression (at least a 1-point decrease in Ishak scores) in the experimental group, as compared with 50.0% (79/158) in the control group (P = 0.01). Adverse events (AE) occurred in 16.8% (54/322) patients, 16.5% were reported in the experimental group and 17.1% in the control group (P = 0.881).

Conclusion: For naïve patients with HBV induced compensate cirrhosis, FZHY could promote ETV effect on pathological regression for 48 weeks treatment, and no more significant AEs.

Table 1. Demographic and Baseline Characteristics of the Patients

Characteristics	Patients with HBV Cirrhosis (n=322)		
	ETV + FZHY (n=164)	ETV + Placebo (n=158)	*P* value
Demographics			
Age (yrs)	42.6±9.2	43.1±8.6	0.667
Male, n (%)	130(79.3)	128(81.0)	0.695
BMI	23.7±3.1	24.0±2.8	0.354
Han Nationality n (%)	159(97.0)	152(96.2)	0.712
Disease Course			
Duration CHB (mos)	123.5 (51.4～205.8)	124.9 (31.4～197.7)	0.851
Duration Ishak 5/6 (mos)	1.3 (0.4～6.7)	1.3 (0.4～8.4)	0.818
Biological data			
Child-Turcotte Pugh score (CTP)	5.2±0.5	5.1±0.6	0.301
AFP (μg/L)	37.0±83.5	29.6±80.2	0.425

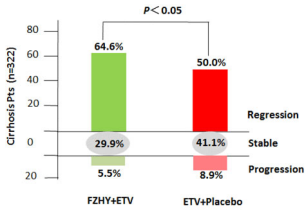


Figure 1. Effects of FZHY plus ETV and ETV plus placebo on the changes of fibrotic stages pre and post treatments

Abstract #1944

Liver stiffness measurement by FibroScan in patients with cirrhosis at risk of having large oesophageal varices

Maung ST[1], Bwa AH[1], Win STS[1], Aye HY[1], Naing TK[1], May TT[1,2], Win KM[1,3]

[1]Department of Hepatology, Yangon GI and Liver Centre, Yangon, Myanmar, [2]Honorary Professor, Department of Gastroenterology, University of Medicine 1, Yangon, Myanmar,[3]Honorary Professor, Department of Hepatology, University of Medicine 1, Yangon, Myanmar

Introduction: Endoscopic surveillance for oesophageal varices (OV) is recommended in patients with cirrhosis, but might be limited due to invasiveness and availability of endoscopic facilities only in tertiary centres. Therefore, the development of non-invasive methods of assessing the risk of having Large OV is requiring.

Objectives: The aim of this prospective study was to evaluate the accuracy of Liver Stiffness Measurement (LSM) by FibroScan® for assessing the risk of having large OV in patients with cirrhosis.

Methods: We retrospectively examined the correlation of LSM with the incidence of large OV among 158 patients who underwent FibroScan® and Oesophago-Gastro-Duodeno Scopy (OGDS) in Yangon GI and Liver Centre from May to December 2019.

Results: Liver stiffness measurement was correlated to the grade of OV. Total 158 patients with Metavir Score F4 were undergone OGDS for the detection of OV: 38 with no OV (mean LSM 15.8 kPa), 33 with small OV (mean LSM 31.7 kPa), 42 with moderate OV (mean LSM 24.3 kPa) and 45 with large OV (mean LSM 29.8 kPa). Patients with previous bleeding episodes had significantly higher LSM (37.3 kPa) than those without a history of bleeding (LSM of 15.4 kPa). Liver stiffness measurement value < 28.5 kPa was highly predictive of the absence of large OV (PPV: 52%, NPV: 94%).

Conclusion: LSM determined by FibroScan is positively correlated with having OV in patients with cirrhosis of liver. Its use for the follow up of cirrhotic patients should be evaluated further.

Abstract #1951

Evaluation of Albumin–Bilirubin (ALBI) Grade, Platelet–Albumin–Bilirubin (PALBI) grade and FIB-4 with mortality risk in patients with liver cirrhosis

Dwijo Anargha Sindhughosa[1], I Dewa Nyoman Wibawa[2], I Gusti Agung Suryadarma[2], I Ketut Mariadi[2], Gde Somayana[2], Cok Istri Yuliandari[2]

[1]Internal Medicine Resident, Faculty of Medicine of Udayana University/Sanglah Hospital, Denpasar, Bali, Indonesia, [2]Gastroenterohepatology Division, Faculty of Medicine of Udayana University/Sanglah Hospital, Denpasar, Bali, Indonesia

Introduction: The model for end stage liver disease (MELD) score was validated subsequently as an accurate predictor of survival among different populations of patients with advanced liver disease. Albumin, bilirubin and platelet were variables that contributed to liver function.
Objective: This study aimed to evaluate the correlation of albumin-bilirubin (ALBI), platelet-albumin-bilirubin (PALBI) and FIB-4 scores with risk of mortality according to MELD score, also evaluate its value to predict higher mortality rate in patients with liver cirrhosis.
Methods: A total of 62 liver cirrhosis patients were included in this study. Patient with infection, various chronic disease, malignancy, steroid use, thrombocyte transfusion and massive bleeding were excluded. The ALBI grade was calculated with the following formula: $[(\log_{10}$ bilirubin $\times$ 0.66) + (albumin $\times$ [$-$ 0.085]), while PALBI: $2.02 \times \log_{10}$ bilirubin $- 0.37 \times (\log_{10}$ bilirubin$)^2 - 0.04 \times$ albumin $- 3.48 \times \log_{10}$ platelets + 1.01 $\times (\log_{10}$ platelets$)^{2.}$
Results: The mean age of the patients involved in this study was 52.95 $\pm$ 12.05. Either ALBI, PALBI, or FIB-4 significantly correlated with MELD score. Either ALBI, PALBI or FIB-4 may predict higher risk of mortality in patients with liver cirrhosis (cut off for ALBI: -1.26, sensitivity 47.8, specificity 52.2. Cut off for PALBI: -2.05, sensitivity 78.3, specificity 79.5. Cut off for FIB-4: 5.84, sensitivity 73.9, specificity 74.4).
Conclusion: Either ALBI, PALBI or FIB-4 positively correlated with MELD score. ALBI of $\geq$ 1.26, PALBI of $\geq$ 2.05 and FIB-4 of $\geq$ 5.84 predict higher risk of mortality with high sensitivity and specificity.

Abstract #1952

Modified Fibrosis-4 (mFib-4) score can predict the severity of decompensated liver cirrhosis based on child-turcotte pugh (CTP) score

I Putu Fajar Sukma Jaya P[1], I Dewa Nyoman Wibawa[2], I Gusti Agung Suryadarma[2], I Ketut Mariadi[2], Gde Somayana[2], Cok Istri Yuliandari[2]

[1]Internal Medicine Resident, Faculty of Medicine of Udayana University/Sanglah Hospital, Denpasar, Bali, Indonesia, [2]Gastroenterohepatology Division, Faculty of Medicine of Udayana University/Sanglah Hospital, Denpasar, Bali, Indonesia

Introduction: Liver cirrhosis is a disorder characterized by fibrosis and nodules in the liver which cause structural changes in the liver. Child-Turcotte-Pugh (CTP) score is used to determine the severity and survival rate for the patient with liver cirrhosis. Modified fibrosis-4 scores have recently been developed to predict the presence of fibrosis in the liver.
Objective: In this study we aimed to and determine whether the mFib-4 score could be used to predict the severity of liver cirrhosis based on the CTP score.
Methods: Total of 62 patients with liver cirrhosis were included in this study. Patient with infection, malignancy, chronic disease, steroid use, thrombocyte transfusion and massive bleeding were excluded from this study. mFib-4 score was calculated with formula of 10 $\times$ Age (years) $\times$ AST (U/L)/Platelet count (10^9/L) x ALT (U/L).
Results: The mean age of patients was 52.95 $\pm$ 12.054. mFib-4 score in high risk group was higher compared with lower risk group (16.59 $\pm$ 10.48, $p < 0.001$ and 7.43 $\pm$ 5.01, $p < 0.001$). mFib-4 has moderate positive correlation with severity of liver cirrhosis based on CTP score ($r = 0.516$, $p = <0.001$). mFib-4 score can predict severity of patients with liver cirrhosis (cutoff for mFib-4 score 10.58, sensitivity 72.2%, spesificity 72.7%, AUC 0.826, $p < 0.001$).
Conclusions: Score of mFib-4 $>$ 10.58 can predict severity of liver cirrhosis with high sensitivity and specificity.

Abstract #1956

A case report: a 71-year-old female patient with idiopathic portal hypertension

Buanantri AC[2], Prasetyo D[2], Darmayani A[2], Kusnanto. P[2], Pramana TY[2]

[1]Resident of Internal Medicine, Department of Internal Medicine, Faculty of Medicine, Sebelas Maret University/Dr. Moewardi Hospital, Surakarta, Indonesia, [2]Division of GastroEnteroHepatology, Department of Internal Medicine, Faculty of Medicine, Sebelas Maret University/Dr. Moewardi Hospital, Surakarta, Indonesia

Introduction: Idiopathic Portal Hypertension (IPH) is a sort of liver disorder in the absence of cirrhosis and its main clinical-pathological findings are in the portal venous system. Typically, patients come to the hospital with esophageal varices and upper gastrointestinal bleeding.
Case Illustration: A 71- year- old female came to the emergency unit of Moewardi Hospital with hematemesis melena. From physical examination, there were a splenomegaly but no stigmata of liver cirrhosis.
The liver function test was within normal limits with the level of albumin slightly decreased. There was no evidence of hepatitis B, hepatitis C, and any infection history. The abdominal CT Scan showed no thrombus in portal vein and bilateral hepatica vein and multiple limphadenophaty in paraaorta and inguinal. The result of liver biopsy showed mild periportal fibrosis supports the diagnosis of idiopathic portal hypertension. The result of esophagogastroduodenoscopy (EGD) showed esophageal varices grade III with gastropathy portal hypertension.
Discussion: The final diagnosis was hematemesis melena caused by rupture of esophageal varices, idiopathic portal hypertension. Multiple lymphadenopathy can't be evaluated because patient refused further examination. Ligation and endoscopy were performed. Other treatments covered somatostatin, propranolol, and spironolactone.
Conclusion: Based on this case, we conclude that the patient has idiopathic portal hypertension with varied clinical pictures including splenomegaly and variceal bleeding. Further studies are essential in order to clarify the etiology and possible genetic background.

Abstract #1966

A case of hepatic involvement of IgG4-related disease that was initially suspicious of multiple liver metastasis of prostate cancer

Kanayama Yuki[1], Sato Ken[1], Nagashima Tamon[2], Arai Yosuke[2], Furuya Kensuke[2], Suzuki Tsukasa,[3] Tamura Yoshimi[4], Kato Haruo[4,] Koyama Yoshinori[5], Moriya Shingo[5], Kurabayashi Takemi[5], Kakizaki Satoru[1], Uraoka Toshio[1]

[1]Department of Gastroenterology and Hepatology, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi, Gunma 371-8511, Japan, [2]Department of Gastroenterology, National Hospital Organization Shibukawa Medical Center, 383 Shirai, Shibukawa, Gunma 377-0280, Japan, [3]Department of Diagnostic Pathology, National Hospital Organization Shibukawa Medical Center, 383 Shirai, Shibukawa, Gunma 377-0280, Japan, [4]Department of Urology, National Hospital Organization Shibukawa Medical

Center, 383 Shirai, Shibukawa, Gunma 377-0280, Japan, [5]Department of Diagnostic Radiology, National Hospital Organization Shibukawa Medical Center, 383 Shirai, Shibukawa, Gunma 377-0280, Japan

Case presentation: A 58-year-old male had diabetes mellitus, hypertension, hyperlipidemia, hyperuricemia, and prostate hypertrophy was referred to another hospital because of his laboratory data that showed γGTP 365 IU/L and CA19–9 170 IU/ml. Abdominal contrasted CT showed multiple hepatic mass. Esophagogastroduodenoscopy and complete colonoscopy showed no remarkable findings. Gallium-67 scintigraphy showed soft tissue masses surrounding the spine. A mass in the prostate was detected by a rectal examination and thus the multiple liver metastasis of prostate cancer was suspected and referred to our hospital. We performed liver and prostate biopsies. However, there were no tumorous lesion but a marked lymphocyte infiltration in the prostate tissue. On the other hand, there were an atypical tubular proliferation as well as fibrosis, lymphocyte and eosinophil infiltrations in the liver tissue. The liver tissue was negative for prostate-specific antigen, partially positive for p53, and slightly positive for MIB1 as the proliferative activity in immunostaing. Thus, the liver tissue was considered as adenocarcinoma or ductal proliferation. Notably, liver and prostate tissues were significantly positive for IgG4 and the laboratory data showed serum IgG 4254 mg/dL and IgG4 1800 mg/dL. Whole-body CT scanning depicted the submaxillary, parotid gland and retroperitoneal lesions and resultantly, our case was diagnosed as IgG4-related disease. Steroid administration decreased serum IgG and IgG4 levels and reduced the size of multiple liver lesions that were considered as an inflammatory pseudotumor due to IgG4-related disease.
Conclusion: Suspecting IgG4-related disease based on the pathology and laboratory data was critical for a correct diagnosis in our case.

Abstract #1967

The relationship between expression of Ed-EOB-DTPA transporter OATPs and stage of hepatic fibrosis in different mice models and patients with hepatitis C

Li XH[1], Rao HY[1]

Peking University People's Hospital, Peking University Hepatology Institute, Beijing Key Laboratory of Hepatitis C and Immunotherapy for Liver Diseases, Beijing International Cooperation Base for Science and Technology on NAFLD Diagnosis,Beijing 100044, China

Introduction: Ed-EOB-DTPA is as a liver cell specific MRI contrast agent, used to distinguish benign and malignant tumors. The transportation of Ed-EOB-DTPA into hepatocytes is mainly depend on organic anion-transporting polypeptides (OATPs), specially OATP1B1 and 1B3 in human and oatp1a1 in mice.
Objective: We aim to clarify the relationship between the expression of OATPs and stage of liver fibrosis and steatosis, including in human and mice.
Methods: Immunochemistry of oatp1a1 and OATP 1B1/3 were tested in the paraffin embedded liver biopsy specimens from model of MCD mouse, TAA mouse, CCL4 mouse and chronic hepatitis C patients respectively. Western blot was tested for the oatp1a1 in different model of mice. Mean IOD for immunochemistry (iIOD) and Western Blot (wbIOD) was used to semi-quantitate the OATPs.
Outcome: In advanced fibrosis chronic hepatitis C patients (Ishark grade ≥ 4), iIOD is significantly decreased (0.0129 vs 0.0394, $p < 0.01$). In Pearson correlation analysis, the expression of OATP1B1/3 is negatively correlated with Ishark score ($r = -0.616$, $p < 0.01$). The results (wbIOD) are similar in CCL4 and TAA mouse model with advanced fibrosis group (0.938 vs 1.55, $p = 0.019$ in CCL4 mice; 1.076 vs 1.410, $p = 0.019$ in TAA mice). Negative correlation also exists ($r = -0.678$, $p < 0.01$ in CCL4 mouse; $r = -0.444$, $p = -0.003$ in TAA mouse).
Conclusion: We find the decreased expression of Ed-EOB-DTPA transporter oatp 1a1 in mice and OATP 1B1/3 in HCV patients were related with the progression of liver fibrosis, which may prompt us Ed-EOB-DTPA MRI could be used to distinguish different stage of liver fibrosis.

Abstract #1994

Carabin deficiency promotes liver fibrosis via regulating ras and calcineurin pathway in macrophage

Rong Xue

Background and aims: Liver fibrosis a typical wound-healing response to chronic injury of variety etiologies, which can develop to cirrhosis and carcinoma. Carabin, an endogenous inhibitor of calcineurin (CaN) and Ras, its role in adaptive immune response has been documented, however, much less is known about its role in cells of the innate immune system such as macrophage.
Method: We induced experimental liver fibrosis in mice by intraperitoneal injection of 10% carbon tetrachloride (CCL4) twice a week for 8 weeks. To investigate the role of Carabin in the progression of liver fibrosis, we generated Carabinfl/fl LysMcre mice. Following the establishment of the fibrotic mouse model, hepatic macrophages were isolated.
Results: Carabinfl/fl LysMcre mice exposed to CCl4 were more susceptible to inflammation and fibrosis compared to wild-type counterparts. Carabin invalidation in myeloid cells is enhance inflammation and fibrosis progression. Cultured macrophages from Carabinfl/fl LysMcre mice displayed increased cytokine secretion and polarized toward to M1 or $Ly6^{hi}$ macrophage. Further studied demonstrated that Carabin regulatory macrophage polarization via inhibiting Ras and Calcineurin pathways.
Conclusion: Our findings suggest that Carabin plays a crucial proinflammatory role in liver fibrosis by regulating the Ras and Calcineurin pathways in macrophages and therefore may be a potential therapeutic target for immune-mediated liver fibrosis.

Abstract #2021

Case report: a 32-year-old man with non-cirrhotic portal hypertension and myelodysplastic syndrome

Gerald Abraham Harianja[1], Juferdy Kurniawan[2], Saut Horas Hatoguan Nababan[2], Sahat Basana Romanti Ezer Matondang[2]

[1]Department of Internal Medicine, Medical Faculty University of Indonesia-Cipto Mangunkusumo General Hospital, [2]Division of Hepatobiliary, Department of Internal Medicine, Medical Faculty University of Indonesia-Cipto Mangunkusumo General Hospital, [3]Department of Radiology, Medical Faculty University of Indonesia-Cipto Mangunkusumo General Hospital

Introduction: Non-cirrhotic portal hypertension (NCPH) encompasses primarily diverse vascular disorders that lead to portal hypertension with normal synthetic liver function and normal or mild elevation in hepatic venous pressure gradient. The most common causes of NCPH are extrahepatic portal vein obstruction (EHPVO) and non-cirrhotic portal fibrosis (NCPF). The key approach to management in NCPF and EHPVO is to control acute variceal bleeding and prevent rebleeding.

Case descriptions: In this paper, we report the case of Mr. V, a 32-year-old man with recurrent hematemesis. Patient had the first hematemesis episode when he was 27 years old. He also complained of abdominal distention. Esophagogastroduodenoscopy (EGD) revealed grade III esophageal varices with stigmata, mild to moderate cardiac and fundic varices, moderate to severe portal hypertensive gastropathy, bile reflux gastritis, and duodenopathy. Patient then underwent endoscopic variceal ligation (EVL) and were given propranolol for preventing rebleed episodes.
Discussion: Abdominal ultrasound revealed splenomegaly, portal hypertension, and intrahepatic biliary system dilatation. There was no JAK2-V617F mutation. Whole abdominal with Gadoxetic acid contrast MRI revealed proximal CBD stricture with abrupt proximal CBD that cause common hepatic duct and left–right intrahepatic duct dilatation, portal vein stenosis at hilar level with prominent dilatation of posterior branch of right intrahepatic portal vein. The MRI also revealed splenomegaly with tortuous dilatation of lienalis vein. Bone marrow biopsy revealed hypocellular bone marrow, maybe myelodysplastic syndrome (MDS) with fibrosis. After underwent EVL procedure and were given propranolol, patient has never experienced hematemesis until now. Chronic inflammatory condition may be the factor that can explain NCPH in MDS.

Abstract #2099

Relation of serum uric acid concentrations with etiology and severity in patients with cirrhosis of liver

Rashedul Hasan

Background: Hyperuricemia is now an established factor to cause oxidative stress, insulin resistance and systemic inflammation. So it is likely that hyperuricemia might be involved in hepatic necroinflammation and destruction which are the common underlying pathophysiology of cirrhosis. On the other hand, as uric acid is the end product of cellular degradation, increased hepatocyte destruction due to any etiology increases the level of serum uric acid which might further aggravate hepatic necroinflammation, cirrhosis and complications.
Objectives: To assess serum uric acid concentrations in patients of cirrhosis of liver and its relation with cirrhosis of different etiology, disease severity and liver enzymes.
Materials and methods: This cross sectional observational study was carried out in the Department of Gastroenterology, BSMMU, Bangladesh during the period of September 2015 to October 2016. A total of 220 diagnosed cases of cirrhosis of liver due to any cause from inpatient and outpatient Department of Gastroenterology of Banghabandhu Sheikh Mujib Medical University were enrolled as the study population. Serum uric acid level was measured in each patient and its relationship with different etiology of cirrhosis, severity of cirrhosis and liver enzymes were assessed.
Results: The mean age was found to be 47.8 ± 14.6 years and male: female ratio was 1.9:1. Majority patients (52.3%) belonged to CTP Class C. The mean (± SD) value of serum uric acid was 6.19 (± 3.25 mg/dl) and hyperuricemia (> 7 mg/dl) was detected in 27.73% patients. Among all etiologies of CLD, the higher mean (± SD) level of serum uric acid was found in NAFLD (19.54 ± 2.20 mg/dl). There was positive correlation of serum uric acid with liver enzymes.
Conclusion: Mean serum uric acid level increased gradually as the cirrhotic patients progressed to higher CTP classes and there was positive correlation of serum uric acid with liver enzymes. It requires further large scale multicenter studies with increased sample size and prolong follow-up to establish serum uric acid as a risk factor of CLD.

Abstract #2122

Elevated alanine aminotransferase (ALT) as an early marker of severe thrombocytopenia in dengue patients

Ryan Herardi[1,2], Ayudya Tarita Alda[2], Al Adip Indra Mustafa[2]

[1]Faculty of Medicine, Universitas Pembangunan Nasional "Veteran" Jakarta, Indonesia, [2]Hermina Mekarsari Hospital, Bogor, Indonesia

Introduction: Hepatic inflammation is a recognized feature in dengue infection, characterized by hepatomegaly and increased transaminase levels, including alanine aminotransferase (ALT). This process may result from dengue viral effect on hepatocytes or dysregulated host immune response against infection. Thrombocytopenia is one of the important criteria to indicate severity of the dengue infection caused by high viral activity.
Objectives: The objectives of this study was to evaluate early elevated ALT as a predictive marker of thrombocytopenia in dengue patients.
Methods: Dengue patients being treated in Hermina Mekarsari Hospital, Bogor, Indonesia since January to June 2019 were consecutively included in this cross-sectional study. Data of early ALT levels and the platelet counts during critical periods were collected from medical records.
Results: From a total of 69 dengue patients, 47 patients (68.1%) had elevated ALT levels > 40 IU/L and 44 patients (63.8%) got severe thrombocytopenia < 50,000/L during critical periods. There was a significant association between elevated ALT and severe thrombocytopenia ($p = 0.03$; OR = 3.14 [95% CI 1.09–9.01]; Chi Square Test).
Conclusion: Early elevated ALT could be used as a predictive marker of thrombocytopenia during critical periods in dengue patients.

Abstract #2136

Acalculous cholecystitis, its etiological relation with infected bile and management

Vipin Chandra

Introduction: One of the most common cause of pain abdomen in middle aged people is cholecystitis. The main cause of cholecystitis in majority of patients is calculi in gall bladder, but in significant percentage of cholecystitis patients' calculi are not found, cases of this group are called acalculous cholecystitis. Acalculous cholecystis is a severe illness that is a complication of various other medical or surgical conditions. This disease may often go unrecognized due to the complexity of the patient's medical and surgical problems. The diagnosis often is difficult and is delayed because of comorbidities that decrease sensitivity and specificity of clinical and imaging evaluation. A high degree of suspicion is required on the part of the surgeon and physician.
Objective: This disease may often go unrecognized due to the complexity of the patient's medical and surgical problems. The diagnosis often is difficult and is delayed because of comorbidities that decrease sensitivity and specificity of clinical and imaging evaluation. A high degree of suspicion is required on the part of the surgeon and physician.
Methods: This study will be conducted mainly in the department of surgery, Patna Medical College and Hospital, Patna with the help of other departments like Medicine, Pathology, Microbiology and Radiology etc.
Results: Incidence of acalculous cholecystitis was 5%. The commonest age-group affected was 31–40 years (60%). The youngest patient was 13 years old and the eldest was 59 years. Female

predominates over male in the ratio of 3:1. 75% females are multiparous, 12% belonged to uniparous and 1 case in nulliparous. The incidence of acalculous cholecystitis was more in vegetarians (60%) than non-vegetarian (40%). Pain and tenderness in the right hypochondrium was found to be the commonest presenting feature, there was no significant difference in the presentation of acalculous and calculous cholecystitis. Thickening of the gall bladder wall was present in all the cases (100%). Pericholecystic collection (70%) with subserosal oedema i.e. 'halo sign' was detected on ultrasonography Biliary sludge was dected in one case by ultrasonography. Culture of the bile revealed presence of infection in 40% cases, *E. coli* being the commonest (75%) offending organism followed by *Streptococcus* and *Staphyllococcus*. Salmonella was not found in any of the case in this dtudy. Other than infective etiology ischaemia and/or biliary stasis are the probable factors for the causation of acalculous cholecystitis. Bile from strawberry gall bladder was found non-infective. Correlation of clinical features HIDA scan, ultrasonographic findings and operative findings have been done with an idea to correlate the post-operative results. OCG had shown poor contraction of gall bladder after fatty meal in two cases (20%) only. These were the cases of chronic dyspepsia and turned out to be a strawberry gall bladder. HIDA scan had shown poor ejection fraction after CCK induction in all cases. After surgical treatment result was excellent.

Conclusion: Acalculous cholecystitis is a known pathological identity. All cases of chronic dyspepsia with history of failure of prolonged medical treatment must be viewed and investigated for bladder pathology. Mostly these are the cases of acalculous cholecystitis. Such patients should be subjected to surgery for complete relief. The result is always gratifying. Acute acalculous cholecystitis is an uncommon but very serious illness. The condition causes approximately 5–10% of all cases of acute cholecystitis. The disease may often go unrecognized due to the complexity of the patients medical and surgical problems. Early diagnosis is essential to avoid the high rates of associated morbidity and mortality.

Liver surgery and transplantation

Oral presentations

Abstract #122

Improved outcomes of laparoscopic liver resection for hepatocellular carcinoma located in posterosuperior segments of the liver

Jai Young Cho

Background: LLR is widely adapted for HCC, while LLR in PS segments is still challenging. However, with recent improvement of techniques and accumulation of experiences, LLR in PS segments is feasible. This study was performed to compare outcomes of laparoscopic liver resection (LLR) for hepatocellular carcinoma (HCC) located in posterosuperior (PS) segments before and after the adaptation of technological improvements.

Methods: We retrospectively analyzed 149 patients who underwent LLR for HCC located in PS segments from September 2003 to December 2016. The patients were divided into Group 1 (n = 43) and Group 2 (n = 106) who underwent LLR before and after 2012 respectively, when advanced techniques including use of intercostal trocars, Pringle maneuver, and semi-lateral position of patient were introduced. We also compared these patients with those who underwent open liver resection (OLR; n = 124) for HCC in PS segments during the same period.

Results: Mean operative time (394.7 min vs 331.2 min; $P = 0.013$), intraoperative blood loss (1545.8 ml vs 1208.2 ml; $P = 0.020$), and hospital stay (11.6 days vs 9.2, $P < 0.001$) were significantly less in Group 2. Postoperative complication rate (18.6% vs 18.9%; $P = 0.970$), open conversion rate (23% vs 17%; $P = 0.374$), 5-year overall (79% vs 89%; $P = 0.607$) and 5-year disease-free (52% vs 53%; $P = 0.657$) survival rates were not significantly different between the groups. Compared to the OLR group, complication rate (40.3% vs 18.8%; $P < 0.001$) and hospital stay (17.6 days vs 9.7 days; $P < 0.001$) were significantly lower in the LLR group.

Conclusion: The complexity of LLR for HCC in PS segments is being gradually overcome by the introduction of advanced techniques.

Abstract #704

Quantitative magnetic resonance imaging predicts individual future liver performance after liver resection for cancer

Mole Damian J[1,2], Fallowfield Jonathan A[2], Welsh Fenella[3], Sherif Ahmed E[4,5], Kendall Timothy[2,6], Semple Scott[7], Kelly Matthew[8], Ridgway Gerard[8], Connell John J[8], Wilman Henry[8], McGonigle John[8], Bachtiar Velicia[8], Banerjee Rajarshi[8], Brady Michael[8], Zheng Xiaozhong[2], Neyton Lucile P[2], Adair Anya[4], Harrison Ewen M[1], Healey Andrew J[4], Parks Rowan W[1], Ravindran Rajan[4], Thomasset Sarah[4], Wigmore Stephen J[1], Garden O James[1], Hughes Michael J[1], McClintock Joanna[3], Tucker Garry[9], Nailon Hilary[9], Patel Dilip[10], Gordon-Smith Jim[10], Ireland Hamish[10], Masson Neil[10], Wackett Anthony[11], Steven Michelle[11], Watson Angela[5], Cresswell Ben[3], John Tim[3], Mustajab Asmat[3], Peppercorn Delia[3], Scott Karen[3], Thrower Andrew[3], Rees Myrddin[3]

[1]Clinical Surgery, University of Edinburgh, Royal Infirmary of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4TJ, UK, [2]Centre for Inflammation Research, University of Edinburgh, Queen's Medical Research Institute, 47 Little France Crescent, Edinburgh, EH16 4TJ, UK, [3]Hampshire Hospitals Foundation Trust, Basingstoke, UK, [4]Department of Surgery, NHS Lothian, Edinburgh, EH16 4SA, UK, [5]Department of HPB Surgery, National Liver Institute, Menoufia University, Shibin Elkom, Egypt, [6]Edinburgh Pathology, University of Edinburgh. Edinburgh, UK, [7]Centre for Cardiovascular Science, University of Edinburgh, Queen's Medical Research Institute, 47 Little France Crescent, Edinburgh, EH16 4TJ, UK, [8]Perspectum Diagnostics, 23-38 Hythe Bridge Street, Oxford, UK, [9]Clinical Research Facility, NHS Lothian, Edinburgh, EH16 4TJ, UK, [10]Clinical Radiology, NHS Lothian, 51 Little France Crescent, Edinburgh, EH16 4TJ, UK, [11]Edinburgh Clinical Trials Unit, No. 9 Bioquarter, Edinburgh EH16 4TJ, UK

Introduction/objectives: Future liver performance (FLP) of an individual undergoing surgical liver resection to remove cancer is critical for their survival and recovery. We report development and clinical testing of a novel MRI post-processing tool for predicting post-operative liver performance.

Method: This software combines quantitative iron-corrected T1 (cT1) mapping, previously demonstrated to correlate with fibro-inflammation and predict clinical outcomes in chronic liver disease, with a 3D U-net pipeline to automatically delineate liver volume prior to defining Couinaud segments based on anatomical landmarks. Interactive removal of these segments or interactively-defined virtual wedge resections enables accurate estimation of future liver remnant volume, which when combined with cT1, provides a prediction of FLP, termed "HepaT1ca score". The ability of this score to predict

post-operative morbidity, length of stay and regenerative capacity was evaluated in a prospective trial (NCT03213314).
Results: 135 patients underwent liver resection. 84% had liver metastases from colorectal cancer. 21% had cT1 values above the upper limit of normal (795 ms) indicating increased risk of background liver disease. HepaT1ca score showed a significant linear correlation with the modified Hyder-Pawlik score, an indicator of post-operative morbidity (adjusted $R^2 = 0.26$, $P < 0.001$), and liver regenerative performance (adjusted $R^2 = 0.46$, $P < 0.001$). In patients with an FLR below 90%, high mean cT1 (> 795 ms) was associated with longer duration of hospital stay [median (IQR) 6.5 (5.3–12) vs 5 (4–7.1); P = 0.0053].
Conclusion: We demonstrate the utility of a non-invasive quantitative MRI approach for predicting post-operative liver performance with potential to transform surgical decision-making and augment individualised risk assessment for patients undergoing liver resection for cancer.

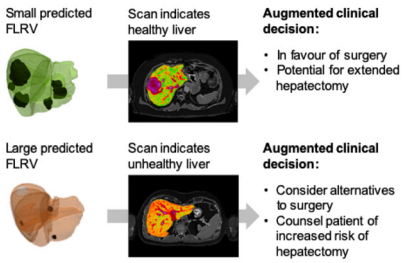


Figure: Concept diagram showing use of quantitative MRI in a clinical workflow highlighting exemplar case from the HepaT1ca study.

Abstract #1191

Relationship between pre-transplantation C-reactive protein levels and bacterial infection post-liver transplantation: a cohort study

Hongcui Cao

Background and Aims: The relationship of systemic inflammation and postoperative bacterial infection is unclear. We aimed to investigate the correlation of the serum C-reactive protein (CRP) as a surrogate marker of systemic inflammatory with bacterial infection after liver transplantation (LT).
Methods: This retrospective cohort study enrolled 989 patients who received LT and followed 6 months. The primary end point was 6-month infection events. Cox regression models were fitted to study the relation between CRP and bacterial infection after LT.
Results: A total of 424 bacterial infectious events in 306 recipients were observed within 6 months. C-reactive protein concentration was related to total infection (hazard ratio (HR) 5.38; 95% confidence interval (CI) 3.44–8.43) comparing last quartile to first quartile of CRP. It was also found that, the relationship between plasma CRP concentration and postoperative infection is stable, regardless of the site of infection include pneumonia, abdominal infection, and skin and soft tissue infection. Sensitivity analyses after excluding patients with a history of infection before transplant in 30 days or with an infection diagnosis within 1, 2, and 5 days of follow-up showed similar results. No effect modification was observed by recipient, donor, and transplant and postoperative factors ((P-values for interaction > 0.05).
Conclusions: Our study demonstrates that CRP value is a factor for infection post LT regardless of the site of infection.

Abstract #1197

Evaluation of peri-operative antibiotics prophylaxis in live liver donors: a randomized control trial

Sahil Gupta

Introduction: Donor safety is the cornerstone of a successful live donor liver transplant (LDLT) program. Infective complications (9.5%) are most common morbidity among the donors. Judicious use of antibiotics is the need of the hour. As per available literature, there is no standard protocol for antibiotic duration in donor hepatectomy. Thus we aim to compare efficacy of 3 doses with 9 doses of peri-operative antibiotics.
Methodology: This study is a double blind, prospective randomized controlled trial done at a single tertiary care transplant center. All consecutive live donor hepatectomies performed from August 2018 till August 2019, were randomly divided into two groups, Group A received 3 doses and Group B received 9 doses of peri-operative antibiotics (piperacillin + tazobactam − 4.5 g intravenous, 8 hourly). Infective complications during hospital course were noted.
Results: Total of 70 patients were included with 35 patients in each arm. Median age of patients was 31 years (18–52 years). 45 patients (64.2%) underwent right lobe donation. 16 patients (22.8%) experienced post-operative morbidity and only 1 patient (1.4%) had major complication (Clavien–dindo ≥ grade 3). Infective complications were the most common morbidity, seen in 8 patients (11.4%) with 4 patients in each group. Both groups had comparable hospital stay (9 days in group A versus 8 days in group B (p value − 0.91). No donor mortality was seen in our series.
Conclusion: 3 doses regimen of antibiotics are equivalent to 9 doses regimen of antibiotics in preventing infective complications among donor hepatectomy patients.

Abstract #1520

Parietal peritoneum as a novel substitute for middle hepatic vein reconstruction during living-donor liver transplantation

Kyung-Suk Suh, Suk Kyun Hong, Nam-Joon Yi, Jae-Hyung Cho, Jeong-Moo Lee, Kwangpyo Hong, Eui Soo Han, Kwang-Woong Lee

Background: Although autologous, cryopreserved, or artificial vascular grafts can be used as interpositional vascular substitutes for MHV reconstruction during LDLT, they are not always available, are limited in size and length, and are associated with risks of infection. The aim of this study is to evaluate parietal peritoneum as a novel substitute for middle hepatic vein (MHV) reconstruction during living donor liver transplantation (LDLT).
Methods: Prospectively collected data of 15 patients who underwent LDLT using the right liver with reconstruction of MHV using the patients' own parietal peritoneum graft were retrospectively reviewed. The patency of the graft was defined as having intact flow without definite thrombus on routine liver Doppler or computed tomography (CT).
Results: Fifteen LDLT patients underwent MHV reconstruction using the parietal peritoneum. The 1-, 2-, 3-, and 5-month patency rates were 57.1%, 57.1%, 57.1%, and 28.6%, respectively. Among the total 15 cases assessed, the most recent 6 cases showed patent graft flow until discharge with 1-, 2-, 3-, and 5-month patency rates of 80.0%, 80.0%, 80.0%, and 20.0%, respectively. All patients survived with tolerable liver function tests. There were no significant congestion-related problems, except for one patient who experienced MHV thrombosis requiring aspiration thrombectomy and stent insertion.

The median duration of hospital stay was 14 days (interquartile range, 12–19 days). There were no infection-related complications. All patients survived to the final follow-up, with a minimum follow-up duration of 8 months.
Conclusion: Parietal peritoneum may be a novel autologous substitute for MHV reconstruction during LDLT.

Abstract #1628

Preoperative risk assessment for delirium after hepatic resection in the elderly: a prospective multicenter study

Atsushi Ishihara

Background: Hepatic resection often results in delirium in preoperatively self-sufficient elderly people. The association of frailty with postoperative delirium remains unclear, and preoperative risk assessment, including frailty, of postoperative delirium has not been established.
Methods: This prospective multicenter study included 295 independently living patients aged ≥ 65 years scheduled for initial hepatic resection. All patients answered the phenotypic frailty index Kihon Checklist, which is a self-reporting list of 25 questions, within a week before surgery. The risk factors for postoperative delirium were investigated. Patients who scored ≥ 4 in the Intensive Care Delirium Screening Checklist were designated as having postoperative delirium.
Results: Delirium developed after liver resection in 22 of 295 patients (7.5%). Total Kihon Checklist score (≥ 6 points), age (≥ 75 years), and serum albumin concentration (≤ 3.7 g/dL) were the independent risk factors for postoperative delirium. The proportion of patients with postoperative delirium was 0% in those with no applicable risk factors, 3.2% in those with one applicable risk factor, 12.0% in those with two applicable risk factors, and 40.9% in those with all three factors ($p < 0.001$). The area under the receiver operating characteristic curve for this risk assessment for predicting postoperative delirium was 0.842.
Conclusion: The use of these three factors for preoperative risk assessment may be effective in predicting and preparing for delirium after hepatic resection in elderly patients.

Abstract #1663

Association of postoperative morbidity with survival and recurrence following hepatectomy for hepatocellular carcinoma: a large-scale multicenter study

Lei Liang[1], Chao Li[1], Hao Xing[1], Yao-Ming Zhang[2,3], Wan-Guang Zhang[4], Hong Wang[5], Ya-Hao Zhou[6], Wei-Min Gu[7], Ting-Hao Chen[8], Jie Li[9], Hong-Xing Xu[10], Yong-Yi Zeng[11], Tian Yang[3]

[1]Department of Hepatobiliary Surgery, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, China, [2]The Second Department of Hepatobiliary Surgery, Meizhou People's Hospital, Meizhou, China, [3]Guangdong Provincial Key Laboratory of Precision Medicine and Clinical Translational Research of Hakka Population, Meizhou, China, [4]Department of Hepatic Surgery, Tongji Hospital, Huazhong University of Science and Technology, Wuhan, China, [5]Department of General Surgery, Liuyang People's Hospital, Hunan, China, [6]Department of Hepatobiliary Surgery, Pu'er People's Hospital, Yunnan, China, [7]The First Department of General Surgery, the Fourth Hospital of Harbin, Heilongjiang, China, [8]Department of General Surgery, Ziyang First People's Hospital, Sichuan, China, [9]Department of Hepatobiliary Surgery, Fuyang People's Hospital, Anhui, China, [10]Department of Hepatobiliary Surgery, Taicang People's Hospital, Soochow, China, [11]Department of Hepatobiliary Surgery, Mengchao Hepatobiliary Hospital, Fujian Medical University, Fujian, China

Background and aims: Postoperative morbidity following hepatectomy for hepatocellular carcinoma (HCC) is common and its impact on oncological outcome remains unclear. To investigate if postoperative morbidity impacts long-term survival and recurrence after HCC resection.
Methods: A multicenter database of curative-intent hepatectomy for HCC collected data from 10 Chinese hospitals (2002–2014). Independent risk factors of postoperative 30-day morbidity were identified. After excluding patients with postoperative early deaths (≤ 90 days), early (≤ 2 years) and late (> 2 years) recurrence rates, overall survival (OS), and time-to-recurrence (TTR) were compared between patients with and without postoperative morbidity.
Results: Among 2161 patients eligible for the study, 758 (35.1%), 29 (1.3%) and 67 (3.1%) had postoperative 30-day morbidity, 30-day mortality and 90-day mortality, respectively. Multivariable logistic regression analysis showed that diabetes mellitus, obesity, Child–Pugh grade B, cirrhosis, and intraoperative blood transfusion were independent risks of postoperative morbidity. The rates of early and late recurrence among patients with postoperative morbidity were greater than those without (50.7% vs. 38.8%, $P < 0.001$; and 41.7% vs. 34.1%, $P = 0.017$). Postoperative morbidity was associated with a significant reduction in median OS (48.1 vs 91.6 months; $P < 0.001$) and median TTR (19.8 vs 46.1 months; $P < 0.001$). After adjustment of confounding factors, multivariable Cox-regression analyses showed that postoperative morbidity was associated with a 27.8% and 18.7% greater likelihood of mortality (hazard ratio 1.278; 95% confidence interval: 1.126–1.451; $P < 0.001$) and recurrence (1.187; 1.058–1.331; $P = 0.004$).
Conclusion: This large multicenter study provides strong evidence that postoperative morbidity adversely impacts long-term oncologic outcomes after hepatectomy for HCC. The prevention and management of postoperative adverse events may be oncologically important.

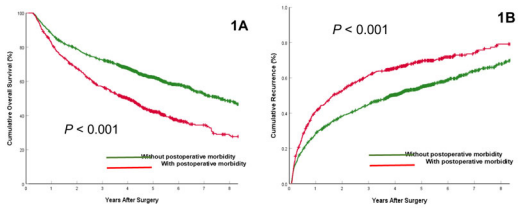


Figure 1. Cumulative incidence of overall survival (1A) and recurrence (1B) curves comparisons between patients with and without postoperative 30-day morbidity.

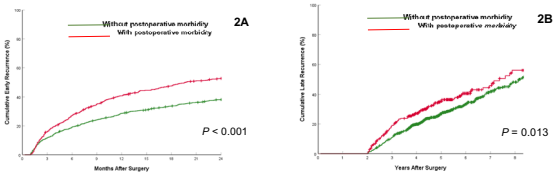


Figure 2. Cumulative incidence of early recurrence (≤ 2 years after surgery, **2A**) and late recurrence (> 2 years after surgery, **2B**) curves comparisons between patients with and without postoperative 30-day morbidity.

Abstract #1667

Repeat hepatectomy for early and late recurrence of hepatocellular carcinoma: a multicenter study with propensity score matching analysis

Lei Liang[1], Chao Li[1], Hao Xing[1], Zhi-Yu Chen[2], Ya-Hao Zhou[3], Hong Wang[4], Jian-Hong Zhong[5], Wei-Min Gu[6], Ting-Hao Chen[7], Timothy M. Pawlik[8], Wan Yee Lau[2,9], Tian Yang[1]

[1]Department of Hepatobiliary Surgery, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University (Navy Medical University), Shanghai, China, [2]Department of Hepatobiliary Surgery, Southwest Hospital, Third Military Medical University (Army Medical University), Chongqing, China, [3]Department of Hepatobiliary Surgery, Pu'er People's Hospital, Yunnan, China, [4]Department of General Surgery, Liuyang People's Hospital, Hunan, China, [5]Department of Hepatobiliary Surgery, Affiliated Tumor Hospital of Guangxi Medical University, Nanning, China, [6]The First Department of General Surgery, the Fourth Hospital of Harbin, Heilongjiang, China, [7]Department of General Surgery, Ziyang First People's Hospital, Sichuan, China, [8]Department of Surgery, Ohio State University, Wexner Medical Center, Columbus, OH, United States, [9]Faculty of Medicine, the Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China

Background: Repeat hepatectomy is a feasible treatment modality for intrahepatic recurrence after hepatectomy of hepatocellular carcinoma (HCC), yet the survival benefit remains ill-defined. The objective of the current study was to define long-term oncologic outcomes after repeat hepatectomy among patients with early recurrence ($\leq$ 1 year after initial hepatectomy) and late recurrence ($>$ 1 year).
Methods: Patients undergoing curative-intent repeat hepatectomy for recurrent HCC were identified using a multi-intuitional database. Patient clinical characteristics, overall survival (OS) and disease-free survival (DFS) were compared among patients with early and late recurrence before and after propensity score matching (PSM).
Results: Among all the patients, 81 and 129 had early and late recurrence from which 74 matched pairs were included in the PSM analytic cohort. Before PSM, 5-year OS and DFS following resection of an early recurrence were 41.7% and 17.9%, respectively, which were worse compared with patients who had resection of a late recurrence (57.0% and 39.4%, both $P < 0.01$). After PSM, 5-year OS and DFS among patients with early recurrence were worse compared with patients with late recurrence (41.0% and 19.2% vs. 64.3% and 43.2%, both $P < 0.01$). After adjustment for other confounding factors on multivariable Cox-regression analysis, early recurrence remained independently associated with decreased OS and DFS (HR 2.22, 95% CI 1.35–3.34, $P = 0.001$, and HR 1.86, 95% CI 1.26–2.74, $P = 0.002$).
Conclusion: Repeat hepatectomy for early recurrence was associated with worse OS and DFS compared with late recurrence. These data may help inform patient and selection of patients being considered for repeat hepatectomy of recurrent HCC.

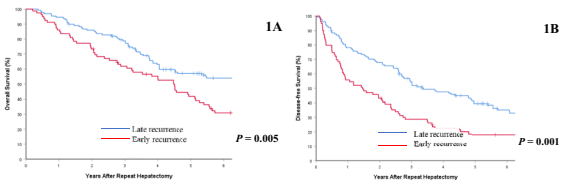


FIGURE 1. Cumulative incidence of overall survival (1A) and disease-free survival (1B) curves comparisons between patients with early recurrence and late recurrence after repeat hepatectomy in the entire cohort.

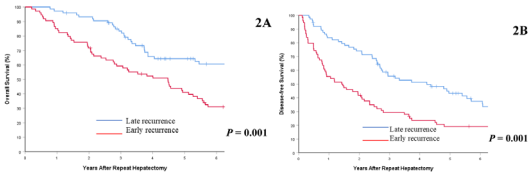


FIGURE 2. Cumulative incidence of overall survival (2A) and disease-free survival (2B) curves comparisons between patients with early recurrence and late recurrence after repeat hepatectomy in the propensity score matching (PSM) cohort.

Abstract #2011

Pancreatic endosonographic changes in portal cavenorma cholangiopathy and effect of portosystemic shunt surgery in children

Sen Sarma M,[1] Ravindranath A,[1] Rai P,[2] Yachha SK[1]

[1]Department of Pediatric Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, 226014, India, [2]Department of Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, 226014, India

Aims: Portal cavernoma cholangiopathy (PCC) is a serious complication affecting the hepatobiliary outcome in extrahepatic portal venous obstruction (EHPVO). We aimed to address the concomitant changes in the pancreas in this condition.
Methods: Children with EHPVO (unfit for Meso-Rex bypass) with PCC prospectively underwent endosonography and magnetic resonance cholangiography-portovenography (MRC-MRPV) before and after (at least 6 months of) proximal splenorenal shunt surgery. PCC was graded as per modified Llop classification on MRC.
Results: Of 72 screened EHPVO children, 66 (asymptomatic, n = 61; symptomatic cholangiopathy, n = 5) had PCC changes [grades 1 (18%), II (11%), III (63%)] on MRC. On endosonography (table 1), intrapancreatic collaterals (n = 30) were statistically significant with pancreatic parenchyma changes (n = 33; $p < 0.001$), intracholedochal varices (n = 41; p = 0.02) and choledochal perforators (n = 39; p = 0.03). All had normal pancreatic duct diameter, serum lipase and fasting blood sugar. Twenty-eight patients with baseline PCC underwent shunt surgery and were reevaluated after 18 (6–54) months with documented shunt patency on MRPV. Pancreatic vascular and parenchymal changes [resolution (n = 11), persistence (n = 17)] correlated with biliary changes [resolution (n = 9), persistence (n = 18)] on endosonography. MRC showed progression (n = 6) and persistence (n = 22) of PCC after surgery. Superior mesenteric vein non-patency [p = 0.003; OR 4.3 (1.8–12.9)] and baseline grade III cholangiopathy [p = 0.01; OR 2.6 (2.0–5.1)] were predictors of persistent pancreatic changes. No progression to chronic pancreatitis was seen in any patient at follow-up.
Conclusions: Portal cavernoma pancreatic vasculopathy may mimic changes of chronic pancreatitis on endosonography in PCC. The pancreatic changes may persist despite shunt surgery due to concomitant superior mesenteric vein block and correlates with advanced cholangiopathy.

Abstract #2143

Circulating platelets and plasma proteomic profiling during liver regeneration in living liver donors

Bhat Adil [1], Chaudhary Sudrishti [1], P Kumaraswamy [2], Yadav Gaurav [1], Pamecha Viniyendra [2], Maras Jaswinder [1*], Sarin Shiv K [1,3]

[1]Department of Molecular and Cellular Medicine, [2]Department of HPB surgery and [3]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: The speedy regeneration capacity of human liver after resection has allowed successful outcomes for living-donor-liver-transplantation (LDLT) procedures. However, the proteomic profile of circulating platelets and plasma occurring during liver regeneration after resection and throughout the repair process is still unknown.
Methods: Purified platelets were taken from liver donors at defined time points preoperatively (POD-0) and postoperatively (POD 1, 3, 7). We performed a comprehensive global-proteome analysis of plasma and circulating platelets from 10 healthy LDLT donors to define key target signatures during liver regeneration at defined time points.
Results: Out of total 1236 identified proteins, 842 were differentially expressed proteins (DEPs). The common proteins which showed the similar trend across the time point were identified (DEPs > 62up- and > 42downregulated proteins). The differential pathways like platelet activation, ATP synthesis, and oxidative phosphorylation were distinctly present. Family analysis highlights increase in the energy pathways (ATP-synthase, NADH-dehydrogenase, guanine nucleotide-binding proteins), liver functions (coagulation), in donors this increase in key energetic pathways could be direct implication of healthy liver regeneration process in donors. In addition, blood transcription module (BTM) analysis indicate that platelet carry immune derived proteins which could be helpful for the normal process of liver regeneration. Moreover, proteins such as Lumican (LUM), Alpha-1B-glycoprotein (A1BG), Fibulin-5 (FBLN5), Annexin-A5 (ANXA5) and Peroxiredoxin-2 (PRDX-2) are directly linked to TGF-β protein, which showed downregulation in platelets after liver resection (FC < 1.5; $p < 0.05$).
Conclusion: The results establish temporal and dynamic platelet protein profile following surgical liver resection that can be detected in the plasma and potentially need validation as biomarker signatures for monitoring stages of liver regeneration.

Abstract #2181

Long-term outcomes of liver transplantation for hepatocellular carcinoma-a single center experience using beyond Milan criteria

Dali Zhang,[1] George Lau,[1,2] Liu Hongling,[1] Liu Zhenwen[1]

[1]Liver Transplantation Center, the Fifth Medical Center of Chinese PLA General Hospital, Beijing, China, [2]Humanity and Health Clinical Trial Center, Humanity and Health Medical Group, Hong Kong SAR, China

Background: Orthotopic liver transplantation (OLTx) remains an important life-saving options for those patients with liver cirrhosis complicated with the development of hepatocellular carcinoma (HCC). In Chinese, as differed from the western world, the majority of liver cirrhosis is related to chronic hepatitis B (CHB) infection with possible different pathobiology. It remains uncertain whether the same pre-transplant criteria can be applied to Chinese cirrhotic patients with HCC.
Objective: To compare three different OLTx criteria-Milan, "Up-to-seven" and Hangzhou criteria in a single cohort of Chinese cirrhotic patients with HCC and had OLTx.
Methods: From Jan 2005 to September 2018, a consecutive 391 chronic hepatitis B infected Chinese with HCC and had orthotopic liver transplantation at the Fifth Clinical Medical Center of General Hospital of Chinese People's Liberation Army with follow-up at a 3–6 monthly interval with alpha-fetoprotein and imaging with either USS or MRI, were recruited. Mann–Whitney or t-test and Cox proportional hazard regression analysis were performed. Kaplan analysis was used to analyze survival, and log-rank test was used to compare survivals of patients under various transplantation criteria. A p value < 0.05 was considered significant.
Results: Among 391 patients who underwent liver transplantation for HCC, 348 were male with a mean age of 51.84 ± 9.90 years. Up to 12 years follow-up, 78 (19.94%) patients had post-transplant HCC recurrence. Preoperative alpha-fetoprotein (AFP) ($p < 0.001$), tumor size ($p = 0.008$), vascular invasion ($p = 0.007$) and pathological Edmondson rating ($p = 0.001$) were risk factors for HCC recurrence after OLTx. The 1, 5, and 12 years overall survival (OS) rates were 95%, 86%, and 86% and the 1, 5, and 12 years disease-free survival (DFS) rates were 84%, 75%, and 75%. Compared to Milan criteria, patients who exceeded Milan criteria but satisfy "Up- to- seven" criteria ($n = 55$) had similar HCC recurrence ($p = 0.13$), TNM stage ($p = 0.061$), AFP level ($p = 0.198$), OS ($p = 0.727$) and DFS ($p = 0.879$). Patients who exceeded "Up- to- seven" criteria but met Hangzhou criteria ($n = 74$) had significant difference in tumor recurrence ($p < 0.001$), vascular invasion ($p < 0.001$), TNM stage ($p < 0.001$), AFP ($p < 0.001$), and DFS ($P = 0.02$). AFP combined with Milan criteria have predictive value for survival status of recurrent HCC patients.
Conclusion: Pre-transplant high AFP level, large tumors, and vascular invasion were high risk factors for recurrent HCC patients. The OS and DFS after OLTx in Chinese cirrhotic CHB patients with HCC who exceed Milan but within "Up-to-seven" criteria were excellent and should offered the option of OLTx.

Poster Presentations

Abstract #94

Impact of ethnicity on the conversion of immediate-release tacrolimus to prolonged-release tacrolimus in stable liver transplant patients

Gary Peh, Mark Dhinesh Muthiah, Koh Tsing Yi, Lee Guan Huei

Background: Tacrolimus is the backbone of immunosuppression in liver transplantation; prolonged-release tacrolimus (Tac-PR) is recommended by some guidelines as it preserves renal function. Although the conversion of immediate-release tacrolimus (Tac-IR) to Tac-PR is affected by CYP3A5 genetic polymorphism, the impact on Asian liver transplant patients is unknown. This study examined the impact of inter-ethnicity variability on tacrolimus metabolism in the local population.
Methods: A retrospective study was conducted on 77 stable liver transplant patients. We compared the patients according to their ethnicity. As the Singaporean Malays and Indians have similar CYP3A5 polymorphism frequency, we compared them against the Chinese. Clinical parameters at baseline and at 12-month post-conversion to Tac-PR were analysed. The primary outcome was change in tacrolimus concentration/dose ratio from baseline on conversion.
Results: There was no significant difference in tacrolimus concentration/dose ratio between recipients of Chinese and non-Chinese ethnicity ($-$ 0.33 μg L^{-1} mg^{-1} versus $-$ 0.28 μg L^{-1} mg^{-1}) ($p = 0.86$). Compared to recipients of Chinese liver grafts, recipients of non-Chinese liver grafts demonstrated a trend towards reduction in tacrolimus bioavailability ($-$ 0.30 μg L^{-1} mg^{-1} versus $-$ 0.56 μg L^{-1} mg^{-1}) ($p = 0.48$).
Conclusion: There was no significant difference in tacrolimus bioavailability between Chinese and non-Chinese recipients. The reduction in tacrolimus bioavailability seen in recipients of non-

Chinese liver graft may be due to the longer GIT transit time that amplifies the effects of CYP3A5 genetic polymorphism.

Abstract #96

Differences of bile microbiology and antibiotic susceptibilities in liver transplant recipients from non-transplant population with acute biliary infection

Suk-Won Suh[1], Seung Eun Lee, Yoo Shin Choi

Department of Surgery, Chung-Ang University, Korea

Background: Because of immunosuppression, signs and symptoms of biliary infection in liver transplantation (LT) recipients are frequently subtler than those of non-transplant population that infection progresses easily to bacteremia, therefore the usage of effective antibiotics is important.
Methods: We performed a comparative analysis of 376 positive bile cultures between LT recipients with biliary complication (n = 127, LT group) and non-LT population who underwent cholecystectomy for acute cholecystitis (n = 249, non-LT group) from January 2009 to December 2018 at multiple centers.
Results: There were significant differences of incidences of commonly isolated microorganisms between LT and non-LT group ($P < 0.001$); *Enterococcus* (31.5% vs. 26.5%), *Klebsiella* (18.1% vs. 12.4%), *Pseudomonas* (14.2% vs. 4.0%), *Escherichia* (11.0% vs. 29.3%), and *Enterobacter (*3.9% vs. 8.4%). Extended-spectrum beta-lactamase (ESBL) producing Gram-negative bacteria was significantly more common in LT group than non-LT group (62.9% vs. 13.0%, $P < 0.001$). Frequently isolated microorganisms were significantly changed over time after LT; *Enterococcus* (35.8%)*, Klebsiella* (26.4%), and *Pseudomonas* (13.2%) within 6 months of LT and *Enterococcus* (28.4%), *Escherichia* (17.6%), and *Pseudomonas* (14.2%) after 6 months of LT ($P = 0.029$). Many of the commonly used antibiotics with a good effectiveness in non-LT group provided inadequate coverage for frequently encountered microorganisms in LT group, except amikacin and imipenem against commonly isolated Gram-negative microorganisms and linezolid, streptomycin, and teicoplanin against *Enterococcus* including vancomycin-resistant *Enterococcus* sp. (VRE).
Conclusion: Differences of bile microbiology and antibiotic susceptibilities in LT recipients should be considered before selection of antibiotics in biliary infection.

Abstract #125

Preoperative assessment of frailty predicts age-related events after hepatic resection: a prospective multicenter study

Shogo Tanaka[1], Masaki Ueno[2], Hiroya Iida[3], Masaki Kaibori[4], Takeo Nomi[5], Fumitoshi Hirokawa[6], Hisashi Ikoma[7], Takuya Nakai[8], Hidetoshi Eguchi[9], Hiroji Shinkawa[1], Shoji Kubo[1]

[1]Department of Hepato-Biliary-Pancreatic Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan, [2]Second Department of Surgery, Wakayama Medical University, Wakayama, Japan, [3]Division of Gastrointestinal, Breast, and General Surgery, Department of Surgery, Shiga University of Medical Science, Otsu, Japan, [4]Department of Surgery, Hirakata Hospital, Kansai Medical University, Hirakata, Osaka, Japan, [5]Department of Surgery, Nara Medical University, Kashihara, Nara, [6] Department of General and Gastroenterological Surgery, Osaka Medical College, Takatsuki, Osaka, Japan, [7]Division of Digestive Surgery, Department of Surgery, Kyoto Prefectural University of Medicine, Kyoto, Japan, [8]Department of Surgery, Faculty of Medicine, Kindai University, Osaka-Sayama, Osaka, Japan, and [9]Department of Gastroenterological Surgery, Graduate School of Medicine, Osaka University, Suita, Osaka, Japan

Backgrounds: Age-related events, such as cardiopulmonary complications, delirium, transfer to rehabilitation facility, and dependency are a major problem after hepatic resection in elderly. This prospective multicenter study aimed to preoperatively evaluate frailty in the elderly according to a phenotypic frail index, named the "Kihon Checklist (KCL)," to predict "age-related events" after hepatic resection.
Methods: Between May 2016 and September 2017, 217 independently living patients who consented among all patients aged $\geq$ 65 years who planned to undergo hepatic resection were included in the study. Preoperative frailty was defined as a total KCL score $\geq$ 8. We analyzed clinical characteristics and outcomes, including age-related events (major respiratory and cardiac complications, delirium medication needed, transfer to rehabilitation facility, and dependency) between patients with and without frailty.
Results: Of the 217 patients, 63 and 154 were classified into the frail and non-frail groups, respectively. The incidences of age-related events (31.7% vs.7.8%, $P < 0.001$) were higher in the frail group. Multivariate analysis indicated that frailty ($P < 0.001$, hazard ratio 5.16) and resection of $\geq$ 2 sectors ($P = 0.014$, hazard ratio 2.98) were independent risk factors for age-related events.
Conclusions: Frailty evaluated by KCL in the elderly can predict postoperative age-related events after hepatic resection.

Abstract #250

Compliance in liver transplant recipients: single center experience

Kosmacheva H[1], Babich A[2]

[1]State-budgetary healthcare institution "Scientific and Research Institute – S.V. Ochapovsky Regional Clinical Hospital №1", Ministry of Health, Cardiology Department, Krasnodar, Russia, [2]State-budgetary healthcare institution "Scientific and Research Institute – S.V. Ochapovsky Regional Clinical Hospital №1", Ministry of Health, Gastroenterology Department, Krasnodar, Russia

Objectives: The aim was to evaluate the compliance in patients who underwent orthotopic liver transplantation (OLT) in the "Scientific and Research Institute – S.V. Ochapovsky Regional Clinical Hospital №1".
Methods: A voluntary anonymous survey was conducted among 86 patients who underwent OLT (main group 1) and 56 patients with chronic diseases requiring persistent treatment (control group 2). The questionnaire "The Level of Compliance" designed by R.V. Kadyrov was used in the research (Kadyrov et al. 2014). Three types of compliance behavior—social, behavioral and emotional—were assessed. Statistical processing of the results was carried out using Statistica 10 software package.
Results: The main causes of liver failure that required transplantation were viral hepatitis (60.5%), primary biliary cirrhosis (16.3%), autoimmune (9.3%) and toxic hepatitis (9.3%). The mean age of the recipients was 50.3 ± 8.6 years, with the proportion of men being 54.7%. The following compliance levels were identified in liver transplant recipients: the general level—95.8 ± 9.4; the social level—30.4 ± 4.2; the emotional level—33.3 ± 3.7; the behavioral level—32.0 ± 3.8. The compliance levels of the control group were significantly lower compared to the values of group 1, respectively: the general level—by 9%, the social level—by 5.6%, the emotional level—by 10.3% and the behavioral level—by 11.9%.

Conclusion: Liver transplant patients have higher levels of general, behavioral and emotional compliance compared to patients with chronic diseases. Neither gender nor age differences were identified in any types of compliance.

Abstract #359

Predictors of positive blood culture and the outcome of culture positive sepsis in Indian liver transplant recipients

Rajesh Dey[1], Subhash Gupta[1]

Max Super Speciality Hospital, Delhi, India

Introduction: Sepsis is a leading cause of mortality after living donor liver transplantation (LDLT). The pre-operative factors that predispose a liver transplant (LT) recipient to sepsis are still not well defined.
Objective: (1) To find out the predictors of positive blood culture in Indian liver transplant recipients. (2) Analyse the outcome of culture positive sepsis in LDLT recipients.
Methods: Indian adult liver transplant recipients are subjects of this study. Recipients in whom blood culture became positive are compared to culture negative group. Statistical analysis of predictive factors are performed including univariate and multivariate analysis. Outcomes are described according to descriptive epidemiology norms.
Results: 114 Indians underwent LT in our center in one calendar year. Paired blood culture was sent using standardized protocol in 84 (73%). Culture positive in 15 patients. On univariate analysis number of cultures sent, ICU admission before LT, duration of hospital stay before LT, Child–Pugh (CP) score, pre-operative Hb level, hepatic encephalopathy, extubation after LT, were found to be significant ($p < 0.05$). On multivariate analysis Hb of < 8gm/dl, CP score, day of extubation of recipient were significant factors. Mortality was not significantly different in the two groups ($p > 0.05$). Most of the positive cultures were due to *E. coli* or Klebsiella.
Conclusion: Pre transplant Hb level, day of extubation after transplant, CP score were related to a positive blood culture after transplant. However, a positive did not imply increased mortality in this group when compared to recipients with negative blood culture. None in whom a culture was not sent had mortality after LT.

Abstract #426

Epidemiological characteristics of De novo Hepatitis B infection in liver transplant recipients: an experience from a tertiary care centre in Qatar

Nair, Arun Prabhakaran[1], Sasi, Sreethish[2], Al-Maslamani, Muna[1], Hashim, Samar[1], Abu Jarir, Sulieman[1], Chandra, Prem[3], Sheikh, Zeeshan[3], Derbala, Moutaz[4]

[1]Department of Infectious Diseases, Communicable Disease Center, Hamad Medical Corporation, Doha, Qatar, [2]Department of Internal Medicine, Hamad Medical Corporation, Doha, Qatar, [3]Medical Research Center, Hamad Medical Corporation, Doha, Qatar, [4]Department of Medical Gastroenterology, Hamad Medical Corporation, Doha, Qatar

Introduction: Emergence of HbsAg in a patient with previously negative Hepatitis B Virus (HBV) serology post Orthotropic Liver Transplant (OTLX) is known as De novo Hepatitis B (DNHB). Risk of DNHB post OTLX was reported as 16–88% internationally and 5–7% from the Mid-east.
Objectives: To study the clinical profile and epidemiology of patients with DNHB in Qatar.
Methods: Descriptive epidemiological study done by retrospectively reviewing records of 159 post OTLX patients followed in Liver transplantation clinic from 2011 to 2018. Seventeen DNHB cases were identified. Baseline epidemiological characteristics of DNHB cases were defined and compared with remaining. Patients with DNHB were analyzed statistically using Chi square test and Kaplan–Meier Curve.
Results: Incidence of DNHB was 10.7% with transplants in China having significantly higher incidence of 22.6% vs 1.12% in transplants from all other countries [Relative Risk (RR) = 20.34; 95%CI 2.7, 149.7]. Epidemiological characteristics are summarized in the table. Mortality rate was 23.5% in DNHB cases compared to 2.8% in non-DNHB (RR 8.4, 95%CI 2.3, 30.4, p = 0.0002). 67% of patients survived at least 64 months after diagnosis of DNHB (Figure). 5-year survival did not vary significantly between those with DNHB and those without (93.8% vs 96.4%; p = 0.605).
Conclusions: OTLX in centers selecting donors liberally without screening for HBV pose risk of DNHB. However, 5-year survival of those with DNHB is comparable to those without. It is recommended to have protective levels of HBs antibodies prior to OTLX. Prophylactic antiviral treatment should be considered until peri-operative HBV transmission has been excluded by screening hepatic tissue for HBV DNA.

Epidemiological Characteristics of DNHB (Table)

Age	56±10 years
Sex	Males (67%), Females (33%)
Country of Transplant	China (94%), Qatar (6%)
Mean onset of infection after OTLX	43±26 months
LFT at detection of DNHB	Mean total Bilirubin= 21 µmol/L, ALT= 79 U/L and AST =77 U/L
HBs Ab titre	> 10 IU/L = 29.4%
	> 100 IU/L = 11.7%
Liver biopsy (Scheuer score)	Hepatitis grade: 33% (Grade I), 45% (Grade II), 22 % (Grade III)
	Fibrosis stage: 33% (Stage I), 45% (Stage II), 11% each (Stage III & IV)
Mean elastography score	6.7±1.9
Antiviral treatment	Entecavir (50%), Tenofovir (25%), Lamivudine (6%), Combination (19%)
Hbe Ag Seroconversion with treatment	Converted (59%), Not converted (29%), Negative from start (12%)
Hbs Ag seroconversion with treatment	Converted (35%), Not converted (65%)
Outcome	Survived (76%), Died (24%)

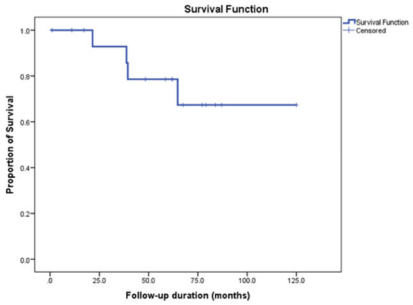


Figure: Kaplan-Meier Survival Curve of DNHB

Abstract #593

Predicting complications in liver transplant recipients using neural networks

Kosmacheva H[1], Babich A[2], Kompaniets O[3]

[1]State-Budgetary Healthcare Institution "Scientific and Research Institute – S.V. Ochapovsky Regional Clinical Hospital №1", Ministry of Health, Cardiology Department, Krasnodar, Russia, [2] State-budgetary healthcare institution "Scientific and Research Institute – S.V. Ochapovsky Regional Clinical Hospital №1",

Ministry of Health, Gastroenterology Department, Krasnodar, Russia, [3] Kuban State Medical University, Krasnodar, Russia

Objective: To analyze cardiovascular disorders, lipid metabolism disorders, compliance level and quality of life in liver transplant recipients and to develop individualized approach to prediction of complications development with the use of artificial neural networks.
Methods: In the retrospective part of the study a database of 135 patients who underwent orthotopic liver transplantation in "Scientific and Research Institute –Regional Clinical Hospital №1"was developed. The present article analyses recipients cardiovascular status before and 4 years after liver transplantation as well as lipid and carbohydrate metabolism disorders at 6, 12, 24, 36, and 48 months. Compliance and quality of life was also analyzed. The database was used for development of neural networks models for prognosis of complications in liver transplant recipients according to combined endpoint—transplant hepatitis, thrombosis, tumors and episodes of transplant rejection.
Results: Low density lipoprotein level before operation was 2.3 ± 1.4 mmol/l and in 2 years increased by 8.7%, in 3 and 4 years by 21.7 and 26.1%, respectively. Before transplantation arterial hypertension was diagnosed in 21.5% of patients, the number increased to 29.6%. Diabetes mellitus was diagnosed in 14.4% of patients before transplantation and in 22.7% of patients 4 years after it.
Low compliance was observed according to Morisky–Green questionnaire.
Conclusion: Study of compliance, quality of life and formed database of clinical, laboratory and instrumental data with the use of neural networks allowed to create a program "Complication prognosis in liver recipients" with total predictive capability of the network accounted for 98.49%.

Abstract #717

Successful journey of 100 living donor of liver transplant from stumbling to incline in remote area of Pakistan; beginning of New Era

Baig M.A, Dogar AW, Zehri Shams, Abbas Hasnain Ali

Pir Abdul Qadir Shah Jeelani institute of Medical Sciences, Gambat

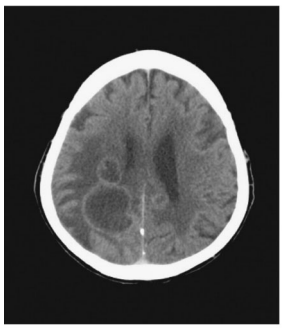
Background: End stage liver disease (ESLD) is an important cause of morbidity and mortality, Living donor liver transplant (LDLT) is matchless choice for ESLD where cadaveric program is a dream.
Aims: Aim of this study was to comprehend single center outcome of 100 LDLT recipients in GAMBAT small town in remote area of Pakistan and to focus challenges in public sector living donor liver program in a developing country.
Methods and Results: This is a Single center study in which we retrospectively reviewed patients who underwent living donor liver transplant (LDLT) from April 2016 till November 2019, Patients Demographics, Causes of liver disease, Graft, Operative variables, complications were assessed, Liver transplant outcome was assessed on the basis of number of days survived and mortality. Median age was 40.2 (9–60) years, whereas median BMI22.5 (15.5–4.26). The male to female ratio was 9:1. ESLD secondary to hepatitis B and D was the most common indication (56% patients) followed by hepatitis C (28%), other indications HCC within Milan criteria (10%), Primary sclerosing cholangitis 2%, Wilson (2%), PFIC (1%) and Bud Chari (1%), Most of the patients belong from Sindh (64%), Balochistant (17%), Punjab (18%), KPK (1%). Right lobe graft without MHV in 90% of recipient (8 patients with MHV), Average cold ischemia time was 20–25 min, while warm ischemia time 35–45 min, Mean Duration of transplant surgery 10 h (8–22 h), average ICU stay 8 days (4–70 days) with minimum ICU related complications (10–15% plural tap, drain placements, 08–10% Psychosis, 3 seizure episode, 4 cardiac events)., Overall biliary complications were 15.62%, (leak 8%, Stricture 7%), Survival 8 days to 1160 days, most of our patients are in between 150 to 300 days survival phase and still alive, Estimated 6 months and 1 year survival 85–88%, overall 16 patients died (most of them in between 1 and 22 number liver transplant).
Conclusion: Overall success, outcome improve as experience grows, public sector LDLT program can achieve results comparable to any other international center and start new era in Living donor liver transplant world which will be beneficial for End stage liver disease.

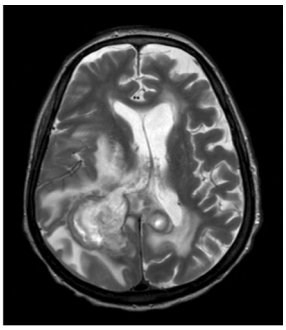
Abstract #760

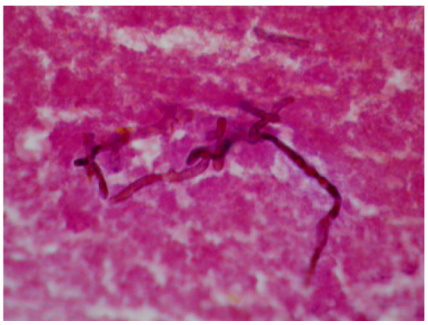
Cerebral Phaeohyphomycosis due to Rhinocladiella in living donor liver transplant recipient: case report

Baig M.A, Dogar AW, Zehri Shams, Abbas Hasnain Ali

Rhinocladiella Mackenziei, a melanized neurotropic fungus, is one of the causative agent for Cerebral Phaeohyphomycosis, resulting in grave with a high mortality rate. Only few cases are reported in Living Donor Liver Transplant (LDLT) Recipient, Our patient underwent LDLT seven months back, indication for liver transplant was HBV with HCC within Milan criteria, (alfa fetoprotein 27), His postoperative and ICU course was unremarkable, he was regular and compliant in follow up, Presented 3 months back with short history of persistent fever, Headache, vomiting, features of raised intracranial pressure with no focal deficit or seizures, CT scan brain showed ring enhancing lesion at parietal occipital area, followed by MRI which showed similar findings, underwent first Craniotomy and evacuation, fungal smear showed moderate septate hypae, Culture grew Rhiocladiella Mackenziei, started on oral Voriconazole and immunosuppression adjusted, His fever, headache partially improved, repeat MRI after 1 month showed persistent non resolution of brain findings, Second Craniotomy and evacuation performed, repeat culture showed similar organism, Voriconazol continued, His liver function test remained stable for last 3 months, After 2 months of voriconazole and 2 surgeries he is doing much better, Last MRI showed resolution of brain lesions and marked symptomatic improvement. Rhinocladiella Mackenziei is a highly virulent agent and should be considered in differential diagnosis of central nervous system disease in Living Donor Liver Transplant Recipients.







Abstract #764

Validation of the Metroticket 2.0 model for 5-year HCC specific survival in an Australian liver transplant cohort

Stoklosa Ted

Objectives: Predicting the prognosis of patients with hepatocellular carcinoma (HCC) who undergo liver transplant (LT) is complex. The Metroticket 2.0 model (1) has recently been described to predict HCC-specific survival. We aimed to evaluate this model in an Australian context.
Methods: All adult patients who underwent LT for HCC between 01/01/1998 and 15/03/2014 at our centre were included (N = 182). Milan and Metroticket 2.0 criteria were compared to predict post LT 5-year HCC-specific survival (5Y-HSS). Data were collected at waitlisting and at the time of last imaging prior to LT.
Results: Hepatitis C was the most common aetiology (55%) and 128 (70%) had prior locoregional therapy. Median post LT follow-up was 7.2 [IQR 5.0- 11.1] years. 59 (32%) patients died with 14 due to HCC recurrence. At waitlisting, 180/182 (99%) were within Milan, 179/182 (98%) within Metroticket 2.0. 5-year overall survival was 68%. At waitlisting, Metroticket 2.0 predicted median 5YHSS was 95% (IQR 93%-98%), similar to the observed 5Y-HSS of 93% (Figure 1a). Prior to LT (median time last imaging and LT was 1 month [1–2]), there was a difference in 5Y-HSS for patients outside Metroticket 2.0, unlike Milan criteria (Figure 1b, c). The sensitivity and specificity for 5Y-HSS were respectively: Metroticket 2.0; 98% and 17%, Milan; 96% and 17%. The positive and negative predictive values LT were respectively: Metroticket 2.0; 94% and 33%, Milan; 94% and 22%.
Conclusion: Metroticket 2.0 predicted 5Y-HSS is similar to observed outcomes. The Metroticket 2.0 model has better discriminatory value for 5Y-HSS prior to LT compared with Milan.

Abstract #886 Effectiveness of lifestyle modification in weight loss and improvement of steatosis in potential liver donors

Tan E Y[1,3], C S H Melissa[1,3], D Q Y Huang[1,3], Pang N Q[2,3], I G Shridhar[2,3], K W C Alfred[2,3], G K Bonney[2,3], Lee G H[1,3], Lee Y M[1,3], M D Muthiah[1,3]

Department of Gastroenterology, National University Health System, Singapore, [2]University Surgical Cluster, National University Health System, Singapore, [3]National University Centre for Organ Transplantation, National University Health System, Singapore

Introduction: Liver transplantation (LT) is the only curative treatment for end-stage liver disease. Due to scarcity of deceased donor organs in Asia, living donors make up a significant proportion of donors. NAFLD is highly prevalent worldwide, with the highest worldwide prevalence in Southeast Asia. Consequently, many potential donors are ineligible for donation due to significant steatosis in the liver, leading to unacceptable risks to both donor and recipient.
Aim: This study aimed to evaluate effectiveness of rigorous lifestyle modification in achieving weight loss and improvement in steatosis in potential living liver donors.
Methods: Analysis of retrospective records of all individuals evaluated as potential living donors in our centre from January 2013 to March 2019 was carried out. Significant steatosis was defined as more than 20% steatosis on MRI, or significant steatosis on CT or US.
Results: 320 healthy potential donors were evaluated. 49 (15.3%) had significant steatosis. 19 (38.8%) were referred for lifestyle modification, of which 2 were lost to follow-up. Median follow-up time was 2.93 months. Mean and median weight reduction (WR) were 5.18% and 4.12% body weight (BW) respectively. 5 (26.3%) achieved WR of 5–10% BW and 3 (15.8%) achieved WR of at least 10% BW. Mean and median velocity of WR were 2.04% and 1.51% BW/month respectively. Of the 19, 5 patients (26.3%) were able to achieve enough weight loss to qualify as living liver donors.
Conclusion: In potential liver donors with significant steatosis, rigorous lifestyle modification is effective in reducing steatosis and increasing donor eligibility.

Abstract #910

Pre-transplant sarcopenia prolongs duration of stay in ICU & HD in liver transplant patients

Chua SH Melissa[1,3], En Ying Tan[1,3], Daniel Q Huang[1,3,4], Ning Qi Pang[2,3], Glenn K. Bonney[2,3,4], Alfred WC Kow[2,3,4], Shridhar G. Iyer[2,3,4], Wai Mun Loo[1,3,4], Alex YS Soh[1,3,4], Kristie HR Fan[1,3,4], Guan-Huei Lee[1,3,4], Mark D. Muthiah[1,3,4]

Division of Gastroenterology and Hepatology, National University Health System, Singapore, [2]Department of Hepatobiliary and Pancreatic Surgery, National University Health System, Singapore, [3]National University Centre for Organ Transplantation, National University Health System, Singapore, [4]Yong Loo Lin School of Medicine, National University of Singapore

Introduction: Sarcopenia, the loss of muscle tissue, is a common complication of end stage liver disease. It is increasingly recognized as a factor affecting both pre- and post- liver transplant (LT) outcomes.
Objective: Our aim was to evaluate prevalence of sarcopenia in LT patients in a multi-ethnic Asian cohort and determine the impact of sarcopenia on length of intensive care and high dependency (ICU & HD) stay, total length of stay and other outcomes including short-term mortality.

Methods: Retrospective analysis included patients who underwent LT from 2010 to 2014 in the National University Centre for Organ Transplantation and had cross-sectional imaging (CT or MRI) involving the L3 vertebral level within 90 days of transplant. An independent radiologist performed cross-sectional analysis of the L3 level and normalised it for height to determine the skeletal muscle index (L3SMI). Sarcopenia was defined as L3SMI $\leq$ 50 cm^2/m^2 in males and $\leq$ 42 cm^2/m^2 in females.
Results: Of the 60 patients analysed, 46 (76.7%) were male. Mean age was 52.4 years. Underlying disease included Hepatitis B (41.7%), Hepatitis C (33.3%), NASH (18.3%) and autoimmune causes (6.7%). 25 patients (41.7%) had hepatocellular carcinoma. Of the 60 patients, 53 (88.3%) had sarcopenia. Univariate analysis revealed that median length of ICU & HD stay was significantly longer in sarcopenic patients compared to non-sarcopenic patients (9 days vs 6 days) ($p < 0.05$). There was no significant difference in all other outcomes measured including overall length of stay, short-term mortality and infections within 90 days.
Conclusion: Presence of sarcopenia pre-transplantation correlates with longer ICU & HD stay.

Abstract #986

Splanchnic vein thrombosis after splenectomy or splenic artery embolization: a systematic review and meta-analysis

Yanyan Wu[1,2], Hongyu Li[1], Tiansong Zhang[3], Zhaohui Bai[1,4], Xiangbo Xu[1,4], Giovanni Battista Levi Sandri[5], Le Wang[1,6], Xingshun Qi[1]

[1]Liver Cirrhosis Study Group, Department of Gastroenterology, General Hospital of Northern Theater Command (formerly called General Hospital of Shenyang Military Area), Shenyang, P.R. China, [2]Postgraduate College, Jinzhou Medical University, Jinzhou, P.R. China, [3]Department of Traditional Chinese Medicine, Jing'an District Central Hospital, Shanghai, China, [4]Postgraduate College, Shenyang Pharmaceutical University, Shenyang, P.R. China, [5]Division of General Surgery and Liver Transplantation, S. Camillo Hospital, Rome, Italy, [6]Postgraduate College, Dalian Medical University, Dalian, P.R. China

Background and aims: Splenectomy and splenic artery embolization are treatment options for cirrhosis and portal hypertension, but may lead to splanchnic vein thrombosis (SVT). We conducted a systematic review and meta-analysis to explore the incidence of SVT after splenectomy or splenic artery embolization and the risk factors of SVT.
Methods: All studies were searched through the PubMed, EMBASE, and Cochrane Library databases. The incidence of SVT after splenectomy or splenic artery embolization in cirrhosis was pooled. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.
Result: Sixty-six studies with 5632 cirrhotic patients were included. The pooled incidence of SVT after splenectomy and splenic artery embolization was 24.6% (95%CI: 0.20–0.29) and 11.7% (95%CI: 0.07–0.17), respectively. But a meta-analysis of 3 comparative studies demonstrated that the risk of SVT after splenectomy was similar with that after splenic artery embolization (OR = 3.15, 95%CI: 0.38–25.91; P = 0.290). Age, platelet count, mean platelet volume, preoperative splenic or portal vein diameter, preoperative or postoperative portal blood velocity, splenic volume and weight, and periesophagogastric devascularization were significant risk factors of SVT after splenectomy. Postoperative use of preventive antithrombotic therapy was a significant protective factor of SVT after splenectomy.
Conclusions: SVT is common after splenectomy and splenic artery embolization. Coagulation and hemostasis factors, anatomical factors, and surgery related factors have been widely identified for the assessment of high risk of SVT after splenectomy. Prophylactic strategy after splenectomy, such as antithrombotic therapy, might be considered in such high-risk patients.

Abstract #1533

Liver transplantation for bongkrekic acid poisoning

Jun Chen

A 41-year-old woman developed symptoms of severe diarrhea, nausea, vomiting and weakness after eating soaked black fungus for over 2 days. When admitted to the hospital, she was sane and responsible, and all vital signs were normal. The physical examination was only for skin and jaundice sclera. Serum alanine aminotransferase was 8188 U/L, aspartate aminotransferase was 7500 U/L, total bilirubin was 4.8 mg/dL, the international normalized ratio was 6.42 and brain natriuretic peptide was 1920 pg/ml. High concentration of bongkrekic acid was detected in her serum. The preliminary diagnosis was bongkrekic acid caused severe multiple organ failure. A series of rescue measures were taken immediately, but the patient's condition deteriorated further and he fell into a deep coma the next day. A liver transplantation was performed at the fifth day of the disease onset. Three days later after liver transplantation, her consciousness returned to normal. However, during the next few days, celiac hemorrhage, septicemia, shock, DIC, pleural and pericardial haemorrhagic effusion occurred. 52 days after liver transplantation, the patient died of intracranial hemorrhage and hernia. Liver failure often presented as first and most severe injury. Whether liver transplantation may successful cure these patients is unknown. As we know, this is the first report about liver transplantation for bongkrekic acid poisoning. We presented her biopsy of liver (replaced and postmortem), heart (postmortem) and kidney (postmortem) in our figures, which showed the bongkrekic acid is quite toxic and liver transplantation may not release its toxicity.

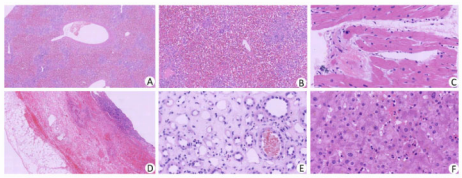


Figure A & B : The histopathology of the replaced liver showed large area necrosis of hepatocytes, extensive bleeding, infiltration of inflammatory cells, and completely collapsed liver stent. Figure C : Myocardial edema and denaturation with focal celluloid necrosis and intramuscular hemorrhage and lymph cell distinct infiltration(postmortem biopsy). Figure D: Pericardial diffuse extensive hemorrhage with hemorrhagic necrosis and lymph cell distinct infiltration(postmortem biopsy). Figure E:Scattered red blood cells casts in the renal tubules, with partial necrotic epithelial cells and inflammatory cells infiltration(postmortem biopsy). Figure F:Liver plate structure disorder, hepatocytes turbid and swollen degeneration, mild infiltration of inflammatory cells (postmortem biopsy).

Abstract #1747

The clinical impact of irreversible electroporation ablation for inoperable hilar cholangiocarcinoma

Kai-Wen Huang

Background: Irreversible electroporation (IRE) is a non-thermal ablation modality and appears to be safe and effective when applied closed to biliary tracts. The study aimed to assess the safety and efficacy of IRE for inoperable hilar cholangiocarcinoma.
Methods: 9 patients with inoperable hilar cholangiocarcinoma received IRE treatment from June 2015 to July 2017 in two hospitals

of EAST. PTCD was inserted for biliary decompression in 8 patients and internal stenting was performed in one patient before IRE treatment. All IRE ablation was performed under ultrasound guidance. 5 patients were treated during laparotomy and 4 patients was treated percutaneously. The median follow-up period is 36 months.
Results: The operations of all patients were tolerated well. The tumor size is not enlarged or stationary without contrast enhancement in 8 patients. The level of CA19-9 decreased significantly after IRE in all patients; PTCD was replaced by the expandable stent in one patient, no drainage was needed in 2 patients and the other 6 patents kept PTCD after IRE till the end of the follow-up period. The morbidity including 1 febrile and 1 transient elevation of hepatic enzyme and the overall survival is 24.8 ± 6.84 months, progression-free survival is 18.5 ± 8.41 months.
Conclusion: IRE ablation of unresectable hilar cholangiocarcinoma involving vital structures is a safe and feasible primary treatment for local control and will be more effective to prolong survival.

Abstract #1836

Hemobilia caused by pseudoaneurysm after laparoscopic cholecystectomy

Agung Putra IGN[1], Didik I[1], Hery DP[1], Gunawan S[2], Agung P[1], Hirlan[1]

[1]Division of Gastroentero Hepatology, Department of Internal Medicine, Diponegoro University, Dr. Kariadi Hospital, Semarang, Indonesia, [2]Department of Radiology, Diponegoro University, Dr. Kariadi Hospital, Semarang, Indonesia

Introduction: Hemobilia, the occurrence of blood in biliary tract is an uncommon causes (6%) of upper gastrointestinal bleeding. The main etiology are iatrogenic injury, trauma, tumors, inflammatory conditions and vascular abnormalities.
Case report: A woman 60-year-old was brought to Kariadi Hospital because of frequent hematemesis, melena, jaundice and weakness. Symptoms appeared after underwent cholecystectomy 6 months before. Ultrasonography showed hepatomegaly and dilatation of extra and intra hepatic duct. During admission she had hematemesis, melena, anemia and septic shock. No significant upper gastrointestinal bleeding on esophagogastroduodenoscopy and gastrointestinal scintigraphy with Tc-99 m. On MRCP, there was dilation of common and intra hepatic biliary duct with stricture on distal CBD. Arteriography found big pseudoaneurysm of right hepatic artery. Embolization was done with 4 coil and foam gel. Then 10 F 13 cm stent placed with ERCP. Patient went home with normal hemoglobin and no hematemesis and melena.
Discussion: Classic presentation of hemobilia known as Quincke's triad consist of jaundice, right upper abdominal pain, and upper gastrointestinal hemorrhage. Cholecystectomy, liver transplantation, and pancreaticoduodenectomy could be the cause of hemobilia, through formation of hepatic artery pseudoaneurysms.
Endoscopically, active bleeding can be seen from the duodenal papilla. Angiography is the choice for diagnosis. Hemobilia from hepatic artery source requires transcatheter embolization or hepatic artery ligation, stent placement, and resection with or without reconstruction.

ERCP with plastic stent placement used to maintain biliary drainage and prevent recurrent obstruction.
Conclusion: In upper gastrointestinal hemorrhage following cholecystectomy, hemobilia may be one of differential diagnosis.

Abstract #1982

Clinical analysis of the patients undergoing renal replacement therapy following living donor liver transplantation

Choi Ho Joong, Park Sung Eun, Ahn Joseph, and You Young Kyoung

Department of Surgery, Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Korea

Introduction: Renal dysfunction is a common complication in patients undergoing liver transplantation (LT) for end stage liver disease (ESLD), and renal replacement therapy (RRT) is required in many cases. This study was performed to identify risk factors for failure to stop RRT after living donor liver transplantation (LDLT).
Methods: From January 2010 to December 2018, LDLT was performed in 464 adult patients in our center. We reviewed 38 cases of preoperative RRT patients among 464 consecutive cases of LDLT. Patients who had not been able to terminate RRT were who remain on RRT during the post-transplant period, or who undergo subsequent kidney transplantation.
Results: The mean age of 38 patients who underwent RRT before LDLT was 49.9 years old and 32 (84.2%) patients were male. HBV was the most common cause of liver transplantation in 20 (52.6%) patients, followed by alcohol in 9 (23.7%) patients. Mean Child score was 11.5 and mean model for end-stage liver disease (MELD) score was 31.3. Among 38 patients, 16 patients failed to terminate RRT after LDLT. The preoperative duration (day) of RRT was longer in the patients who did not terminate RRT compared to the patients who could stop RRT but, it was not statistically significant. In the patients who did not terminate RRT, total bilirubin was elevated higher and mortality was higher after LDLT.
Conclusion: Isolated liver transplant recipients who remain on RRT during the post-transplant period have poor outcome. If these patients can be identified, early or simultaneous kidney transplantation may be considered.

Abstract #2046

Challenges to adult living donor liver transplantation program: early experience from A single centre in Malaysia

T Jayaraman[1], RB Rajaram[2], BK Yoong[3], PS Ko[3], JK Koong[3], S Mahadeva[2]

[1]Gastroenterology Unit, Faculty of Medicine, Universiti Teknologi MARA (UiTM), Malaysia, [2]Department of Medicine, University of Malaya Medical Centre, Malaysia, [3]Department of Surgery, University of Malaya Medical Center, Malaysia

Introduction: Living donor liver transplantation (LDLT) is a life-saving treatment for end-stage liver disease. We aimed to review the current status of adult-to-adult LDLT in University of Malaya Medical Centre (UMMC).
Method: All patients who were referred to the Adult Liver Transplant team at UMMC since its inception in July 2015 for consideration of LDLT were identified. Baseline demography, indication for LT, concomitant complication and co-morbidities, MELD score at evaluation, potential donor workup, transplant status and outcome at 12 months were analyzed.
Results: A total of 28 patients were evaluated for LDLT with the following demographics: mean age—46.7 (SD ± 14.99) years, 60.7% male and ethnicity—42.9% Chinese, 35.7% Indian and 21.4% Malay patients. The mean MELD score was 22.85 (SD ± 8.45). Most patients (24/28) had advanced liver cirrhosis with complications,

followed by acute liver failure (3/28), and biliary disease (1/28). Non-alcoholic steatohepatitis (29%) and autoimmune liver diseases (14%) were the most common aetiologies. Four patients underwent LDLT in UMMC (3 alive and 1 dead) and two patients were referred to other centres. LDLT wasn't performed on 22 patients, the reasons being: unsuitable donor (54.5%), recipient refusal (22.8%), unsuitable recipient (18.2%) and improvement in recipient's condition (4.5%). Common reasons for donors to be deemed unsuitable are significant hepatic steatosis (6/12), overweight with fatty liver (4/12), donor refusal (2/12), and other medical conditions (2/12).
Conclusion: Scarcity of suitable donors and poor acceptance of LDLT among recipients are the main barriers for LDLT in UMMC.

Abstract #2142

Portal venous thrombosis in transplanted cirrhotic patients at the "Hospital Clinico Universidad de Chile"

Urzúa, Alvaro, Henriquez-Auba, Victor, Vera, Daniela, Diaz, Juan Carlos, Castillo, Jaime, Lembach, hans, Saure, Alex, Cattaneo, Maximo, Poniachik, Jaime, Urzua, Alvaro

Sección Gastroenterologia, Hospital Clinico Universidad de Chile, Santiago, Chile, Unidad de Trasplantes, Hospital Clinico Universidad de Chile, Santiago, Chile

Background: Portal vein thrombosis (PVT) is a frequent complication in cirrhotic patients on the waiting list for liver transplantation (LT); this is associated with increased post-LT mortality. There is limited information in our country regarding PVT in LT.
Objective: Characterize the presence of PVT in patients with LT in our center.
Methods: Retrospective observational study between January 1, 2014 and February 28, 2018. Clinical records, laboratory and images were reviewed. Survival was recorded.
Results: 82 patients were included; Age 58 (21–71) years; Etiology of cirrhosis: non-alcoholic fatty liver 40.2%, alcoholic liver disease 20.7%, autoimmunity 13.4% and hepatitis C 8.5%; Child–Pugh: 7.3% A, 30.4% B and 62.2% C; MELD-Na 22 (8–40). PVT was diagnosed before or during LT in 26.8%: Child A 16.6%, B 16.0%, and C 33.3%; MELD-Na 25 (12–40) in those with PVT vs 21 (8–40) in those without PVT (non significant, NS); 34% had hepatocarcinoma (32.1% with PVT vs. 24.4% without PVT; NS). The diagnosis of PVT was 77.2% pre LT and almost 1/4 during transplant surgery. The extension of the PVT was complete occlusion in 11.7%, partial in 70.5% (29.4% only of the portal vein, 11.7% with extension to intrahepatic branches and 29.4% with extension to the mesenteric vein or porto-spleno-mesenteric confluence); 11.7% had only intrahepatic branches compromised; 1 case with incomplete data. In 76% of the patients anticoagulation (AC) was started during waiting list; none had complications associated to AC. Complete re-canalization was achieved in 53.8%. The 5-year survival was 70%; 71.7% in those without PVT and 63.6% in those with PVT (NS).
Conclusion: PVT is a frequent complication in cirrhotic patients in the waiting list who received LT. Most receive AC without complications. The 5-year survival in this series was similar despite the presence of PVT.

Hepatocellular carcinoma

Oral presentations

Abstract #26

Assessments of frailty as a predictor of mortality in hepatocellular carcinoma patients with transarterial chemoembolization

Kim Hong Joo[1], Kim Nam Hee[1]

[1]Division of Gastroenterology, Department of Internal Medicine, Sungkyunkwan University Kangbuk Samsung Hospital, Seoul, Korea

Introduction: Currently available prognostic indices for functional status of patients with hepatocellular carcinoma (HCC) who underwent transarterial chemoembolization (TACE) such as Child–Pugh–Turcotte (CTP) class, or Model for End Stage Liver Disease (MELD) provide an incomplete picture of a given patient's prognosis. We explored whether frailty indices can be added to conventional prognostic indices to improve the predictive capability for prognosis in HCC patients with TACE.
Methods: Four hundred fifty-five HCC patients who received TACE treatment in our institution from January 2006 to March 2016 were enrolled in this retrospective cohort study. The admitting nurse performed three functional assessments: (1) activities of daily living (ADL), (2) Braden scale, and (3) Morse fall risk score.
Results: The 1-year liver-related mortality for all enrolled patients was 25.7% (117/455). Univariate analysis reveals 1-year mortality was significantly associated with younger age, male gender, lower number of TACE, higher World Health Organization (WHO) performance grade, modified Response Evaluation Criteria in Solid Tumors (mRECIST) criteria, New Japanese TNM Staging criteria, low ADL score, low Braden scale, high Morse fall risk score, higher CTP class, and higher MELD score. Cox regression analyses reveals that number of TACE > 2, ADL class score, Braden scale score, mRECIST, New Japanese TNM Staging criteria, CTP class C, and MELD score ≥ 20 were independent and significant prognosticators for overall survival in HCC patients with TACE treatment.
Conclusions: Simple assessment of frailty indices at admission has a powerful impact on the prediction of prognosis for patients with HCC who subsequently underwent TACE treatment.

Abstract #200

High-risk of early postoperative recurrence in multinodular HCC with multiple common oncogenic mutations

Iimuro Yuji[1], Takano Atsushi[1], Hirotsu Yosuke[2], Amemiya Kenji[2,3], Mochizuki Hitoshi[2,4], Oyama Toshio[3], Omata Masao[4,5]

[1]Department of Surgery, [2]Genome Analysis Center, [3]Department of Pathology, and [4]Department of Medicine, Yamanashi Central Hospital, Yamanashi 400-8506; [5]The University of Tokyo, Tokyo 113-8655, Japan

Introduction: After resection of multinodular HCC, recurrence pattern is believed to differ between patients with intrahepatic metastasis (IM) and those with multicentric occurrence (MC). We investigated postoperative recurrence patterns in multinodular HCC in reference to genetic mutational differentiation.
Methods: We genetically analyzed 134 microdissected tumor samples from 55 HCC patients (43 solitary, 12 multinodular) employing a next generation sequencer. We performed in-house targeted

sequencing covering 72 significantly mutated genes (SMGs) associated with HCC, spanning 285,470 nucleotides.
Results: Genomic analysis in all HCCs revealed frequent genetic mutations in TERT promoter, TP53, CTNNB1, ALB, ARID1A. In multinodular HCC, MC was identified in 3 cases without common genetic alterations, while IM was diagnosed in 9 cases with at least one common mutation. In IM cases, 5 cases possessed only TERT promotor as a sole common mutation regardless of tumor size, while multiple common alterations were detected in others. In one IM case, all 3 nodules harbored 3 common oncogenic mutations including TP53 and NFE2L2. As for postoperative recurrence, MC cases had longer recurrence-free survival (RFS). IM cases harboring TERT promotor as a sole common mutation had better RFS compared to other IM cases. Meanwhile, very early multiple intrahepatic recurrence was detected in an IM case with multiple common oncogenic mutations.
Conclusion: Genomic analysis in multinodular HCCs can possibly stratify patients at risk for early postoperative recurrence. Patients with multiple common oncogenic mutations in all HCC nodules are at high risk of aggressive recurrence, implying requirement of intensive additional treatment such as with TKIs.

Abstract #316

Serum miRNA-320 as a potent diagnostic biomarker for human hepatocellular carcinoma irrespective of etiology

George Joseph[1*], Saito Takashi[1], Toshikuni Nobuyuki[1], Tsuchishima Mutsumi[1], and Tsutsumi Mikihiro[1]

[1]Department of Hepatology, Kanazawa Medical University, Uchinada, Ishikawa 920-0293, Japan

Introduction: Hepatocellular carcinoma (HCC) is one of the leading causes of cancer death worldwide. MicroRNAs (miRNAs) play a pivotal role in the pathogenesis and progression of HCC.
Objectives: The present study was designed to identify a markedly downregulated circulating miRNA to diagnosis HCC irrespective of etiology.
Methods: Over 20 miRNAs with expected aberrant expression were screened in around 100 serum samples from HCC patients with different etiology along with healthy controls. The total miRNAs were isolated using Qiagen miRNeasy kit. About 200 nanogram of isolated total miRNA was hybridized with respective oligo for a particular miRNA in 96-well plates and the hybridized product with a biotinylated tag is detected using chemiluminescence technique as counts, which is a very sensitive and specific method to quantify miRNAs.
Results: The microarray data demonstrated that miRNA-320 is dramatically downregulated in all the serum samples from HCC patients irrespective of etiology. About 8–10 fold reduction ($P < 0.0001$) was observed in the serum levels of miRNA-320 compared to healthy controls. There was no significant difference in the mean miRNA-320 levels in serum samples between HCC patients with different etiology such as alcoholic liver cirrhosis, liver cirrhosis due to other reasons, chronic hepatitis due to hepatitis C virus (HCV) and HCC developed from other unknown causes.
Conclusion: The results of the present study demonstrated that there is a remarkable reduction in the serum levels of miRNA-320 in all HCC patients irrespective of etiology. Therefore, the circulating miRNA-320 could be used as a diagnostic biomarker for HCC along with other clinical parameters.

Abstract #345

Impact of laparoscopic liver resection for hepatocellular carcinoma on the development of postoperative complication

Shirai Daisuke[1], Shinkawa Hiroji[1], Takemura Shigekazu[1], Tanaka Shogo[1], Amano Ryosuke[1], Kimura Kenjiro[1], Yamazoe Sadaaki[1], Ohira Go[1], Nishioka Takayoshi[1], Tauchi Jun[1], Miyazaki Toru[1], Ishihara Atsushi[1], Eguchi Shinpei[1], Kubo Shoji[1]

[1]Department of Hepato-Biliary-Pancreatic Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan

Aim: This study was aimed to compare the postoperative complication rate between laparoscopic and open liver resection.
Methods: From January 2008 to June 2018, 384 patients underwent curative liver resection for hepatocellular carcinoma (HCC) within 5 cm in size without macroscopic vascular invasion. The subjects were 321 patients who underwent limited resection or segmentectomy. Of these, laparoscopic liver resection was adopted in 191 patients (Lap group) and open liver resection was done in 130 patients (Open group). Propensity score matching (PSM) was conducted to adjust potentially confounding factors. Postoperative complication rate (Clavien-Dindo classification ≥ 2) were compared between Lap and Open groups after PSM. In addition, subgroup analysis was performed between subphrenic HCC (segment 7, 8) and non-subphrenic HCC subgroups.
Results: After PSM, the study group of 206 patients were well matched. Postoperative complications (27.2% vs. 7.8%, $p < 0.001$), abdominal abscess (7.8% vs. 1%, $p = 0.035$), bile leakage (5.8% vs. 0%, $p = 0.029$) were more frequently observed in Open group than Lap group. The blood loss volume was significantly lower in Lap group than Open group (100 ml vs. 355 ml, $p < 0.001$), and the length of hospital stay was significantly shorter in Lap group (9 days vs. 13 days, $p < 0.001$). In the subgroup analysis, among subphrenic HCC patients, abdominal abscess (14.6% vs. 0%, $p = 0.012$) were more frequently observed in Open group than Lap group, whereas among non-subphrenic HCC patients, no statistical significance was confirmed between the both group.
Conclusions: Compared to open liver resection, laparoscopic liver resection might reduce the development of postoperative abdominal abscess, especially for subphrenic HCC.

Abstract #528

Post-treatments of lenvatinib in patients with advanced hepatocellular carcinoma

Susumu Maruta

Introduction: Lenvatinib has been the second frontline systemic therapy for patients with advanced hepatocellular carcinoma (HCC) in Japan. However, post-treatments of lenvatinib have not been standardized yet.

Objectives: We investigated the clinical outcomes of lenvatinib post-treatments in patients with advanced HCC in the Japanese field of practice.
Methods: Clinical data were retrospectively analyzed in patients with advanced HCC who received lenvatinib in 7 institutions since March 2018. Radiological assessments were evaluated using mRECIST. CTCAE version 4.0 was used for assessment of adverse events (AEs).
Results: A total of 42 patients (28%) received post-treatment after being unresponsive to or unable to tolerate lenvatinib. There were 25 patients receiving sorafenib, 7 receiving regorafenib, and 6 receiving HAIC. In sorafenib, the best overall response (BOR) was SD, disease control rate (DCR) was 16.0%, and progression-free survival (PFS) was 1.8 months. In regorafenib, BOR was PR, DCR was 57.1%, AE withdrawal was observed in 2 patients, and PFS was not achieved. For both the drugs, dose modification was required in 13 patients (39%) because of anorexia and fatigue.
Conclusion: DCR and PFS of sorafenib after lenvatinib treatment were worse than those after general frontline therapy in patients with advanced HCC. However, regorafenib might be a potential post-treatment of lenvatinib. Further study is required for establishing the most appropriate treatment option after lenvatinib in patients with advanced HCC.

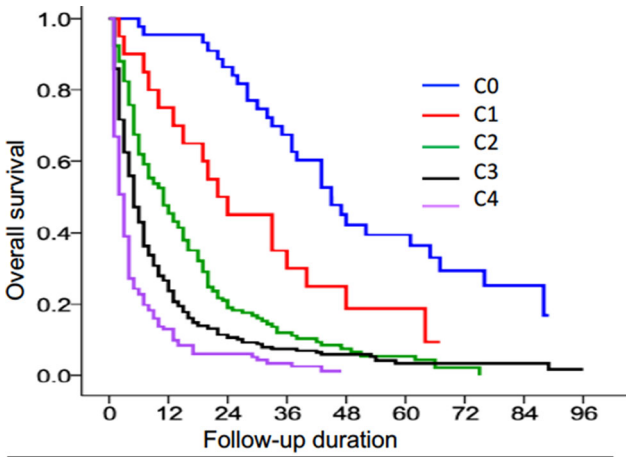
Abstract #574

Prognostic evaluations using a new subclassification for advanced-stage hepatocellular carcinoma

Chih-Wen Lin[1,2,4], Gin-Ho Lo[1], Tsung-Chin Wu[1], Jen-Hao Yeh[1], Chao-Ming Hung[3,4], Hung-Yu Lin[3,4], Chih-Wen Shu[4], Yu-Chan Li[4], Pei-Min Hsieh[3], Yaw-Sen Chen[3,4]

[1]Division of Gastroenterology and Hepatology, E-Da Dachang Hospital, I-Shou University, Kaohsiung, [3]Health Examination Center, E-Da Hospital, I-Shou University, Kaohsiung, [4]Department of Surgery, E-Da Hospital, I-Shou University, Kaohsiung, [4]School of Medicine, College of Medicine, I-Shou University, Kaohsiung, Taiwan

Background and aims: Hepatocellular carcinoma (HCC) comprises heterogeneous populations classified as Barcelona Clinic Liver Cancer stage C (BCLC C). Advanced HCC needs subclassification to more precisely predict overall survival (OS). This aims of this study investigate to set a new subclassifiction of BCLC stage C HCC for precise prognosis.
Methods: We collected 622 BCLC C HCC patients between 2011 and 2017 at E-DA Hospital, Kaohsiung, Taiwan. Variables affecting OS were analyzed and patients were subclassified based on the number of prognostic factors.
Results: The mean age was 62 years; the patients were predominantly male. About 50% patients were hepatitis B virus infection and 30% patients were hepatitis C virus infection. Tumor factors such as tumor load $\geq$ 10 cm, macrovesicular invasion and lymph nodule or/and distal metastasis, as well as underlying liver function were significantly associated with OS. BCLC stage C was classified into five substages (C0–4) based on Performance status and the number of prognostic factors. Substages C0, C1, C2, C3 and C4 is no risk factor with PS1, no risk factor with PS2, one risk, two risk factors, and three or four risk factor, respectively. Substages C0, C1, C2, C3 and C4 showed a median OS of 45.5 months (95% confidence interval [CI], 36.6–53.5), 10.13 months (95% CI, 13.2–30.8), 22.8 months (95% CI, 8.02–14.1), 11.2 months (95% CI, 8.02–14.1), and, 5.9 months (95% CI, 4.02–6.00) and 3.2 months (95% CI, 2.41–3.59) respectively ($P < 0.05$) in Figure 1. This substaging system also had good discriminative ability in predicting survival.
Conclusion: Our substaging for BCLC stage C might have a better predictive prognosis.



Substage	n	Median OS (95% CI)	HR (95% CI)	*P*-value
C0	58	45.5 (36.6-53.5)	Ref	Ref
C1	89	22.8 (13.2-30.8)	1.88 (1.03-3.42)	0.038
C2	245	11.2 (8.02-14.1)	3.31 (2.22-4.94)	<0.0001
C3	185	5.9 (4.02-6.00)	4.78 (3.23-7.07)	<0.0001
C4	45	3.2 (2.41-3.59)	8.03 (5.31-12.1)	<0.0001
Total	622	6.5 (5.08-6.92)		

Abstract #615

SMG9 play a role in tumor proliferation and invasion in hepatocellular carcinoma

Zhi-shuo Mo[1], Pei–Pei Wang[1], Ze-qian Wu[1]

[1]Department of Infectious Disease, The Third Affiliated Hospital, Sun Yat-Sen University, Guangzhou, China

Introduction: SMG9 is a nuclear export receptor for tRNA. It has been shown that decreased expression of SMG9 is related to inhibition of cell proliferation. However, whether SMG9 plays a role in tumor progression in hepatocellular carcinoma (HCC) has not been studied.
Objectives: This study is aimed to study the role of SMG9 in the proliferation and invasion of HCC.
Methods: To investigate the function of SMG9 in HCC, HepG2 and SMMC-7721 cell lines were transfected 3 siRNA (si-1, si-2, and si-3) targeting SMG9, and control siRNA. Western blotting was used to detected the expression of SMG9. The Cell Counting Kit-8 (CCK8) assay was used to measure cell proliferation. Cell invasion was assessed by the Transwell assay.
Results: The expression of SMG9 was significantly decreased in SMG9-siRNA-transfected cells compared with control groups. The CCK8 assay results indicated that down-regulation of SMG9 in both

hepG2 and 7721 cell lines inhibited cell proliferation at 24 h after transfection, as compared with the control groups ($P < 0.05$). In the Transwell invasion assay, downregulation of SMG9 significantly decreased the invasive ability of both SMMC-7721 and HepG2 cells ($P < 0.05$).
Conclusion: These data suggest that SMG9 plays a critical role in the cell proliferation and motility of HCC cells. SMG9 maybe a target for new treatment.

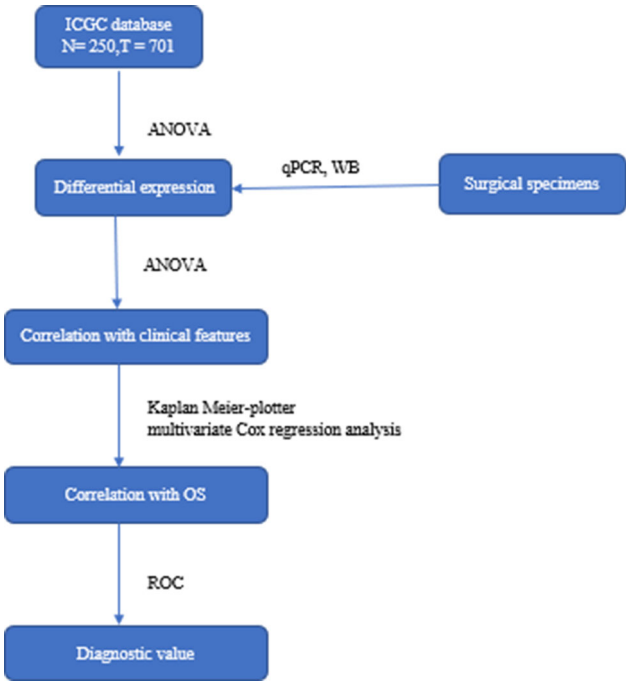
Abstract #631

Prognostic and diagnostic value of acetyl-coa acetyltransferase-1 in hepatocellular carcinoma

Zhou Hui[1], Li Wenchao[1], Xiong Zhiyong[1], Yao Zhicheng[1], Huang Shaozhuo[1], Liu Bo[1], Hu Kunpeng[1]

[1]Department of General Surgery, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

Introduction: Despite of rapid progress of diagnosis and treatment, hepatocellular carcinoma (HCC) is still a global challenge due to high mortality and recurrence. The underlying molecular mechanisms of HCC are poorly understood.
Objectives: Acyl-coenzyme A acyltransferase-1 (ACAT1) catalyses reversible formation of acetoacetyl-CoA from two molecules of acetyl-CoA during ketogenesis and ketolysis. It has been studied in various cancers. We aim to investigate the diagnostic and prognostic values of ACAT1 in HCC.
Methods: RNA sequencing and clinical information of HCC patients (N = 250, T = 701) were gathered from International Cancer Genome Consortium (ICGC) database, ANOVA were used to reveal relevance of ACAT1 and clinical features, Kaplan–Meier-plotter and multivariate Cox regression analysis were performed to explore correlation with overall survival (OS), receiver operating characteristic (ROC) curves was used to evaluate ACAT1's diagnostic values. In the end, Western Blots and qRT-PCR was applied to verify expression pattern of ACAT1.
Results: Based on TCGA information, ACAT1 was found to be overexpressed in normal liver tissues, higher ACAT1 expression was related to favorable clinical features including smaller tumor size, earlier tumor grade and earlier tumor stage. Kaplan–Meier-plotter showed that patients with higher ACAT1 expression have better OS. ROC curves and multivariate Cox regression analysis indicate that ACAT1 have excellent diagnostic and prognostic values for HCC. Western blots and qRT-PCR confirmed the same expression pattern of ACAT1 with the result of ICGC database.
Conclusion: This study suggests that ACAT1 could be a potential diagnostic and prognostic biomarker for HCC.



Abstract #635

Comparison of the therapeutic effects between hepatic arterial infusion chemotherapy "New FP" and sorafenib for advanced hepatocellular carcinoma with major macrovascular invasion—multicenter retrospective analysis

Hideki Iwamoto

Background: Macrovascular invasion (MVI) is one of the factors which carry poor prognosis for the patients with advanced hepatocellular carcinoma (HCC). Among them, MVI into 1st branch or trunk of portal vein is called major MVI, which results in extremely poor prognosis. Overall survival (OS) of the major MVI-HCC patients treated with sorafenib is only 6 months. Therefore, alternative treatment is needed to improve prognosis of major MVI-HCC patients. We retrospectively compared the effects between New FP, a novel regimen of hepatic arterial infusion chemotherapy (HAIC), and sorafenib for major MVI-HCC.
Methods: New FP is one of the regimens of HAIC, which use cisplatin in lipiodol suspension combined with 5-fluorouracil. From 2005 to 2018, we treated 289 patients with New FP and 448 patients with sorafenib, respectively. Among them, major MVI-HCC were 92 cases (New FP: 78 cases, sorafenib: 14 cases). We assessed OS and the factors associated with better prognosis of major MVI-HCC patients.
Results: Patients' characteristics are described below. Child–Pugh score: 5/6/7; 42/30/20, Location of portal invasion: 1st branch/trunk;

52/40. MST of New FP and sorafenib was 14 and 6.7 months, respectively ($p < 0.0001$). Multivariate analysis showed that better therapeutic response was an only independent factor in better prognosis of major MVI-HCC [p = 0.0001, HR 0.27 (0.14–0.52)]. To achieve better therapeutic response, smaller tumor diameter (p = 0.0046) and choosing New FP ($p < 0.0001$) were independent factors in multivariate analysis.
Conclusion: New FP dramatically prolonged survival of the patients with major MVI-HCC, compared with sorafenib.

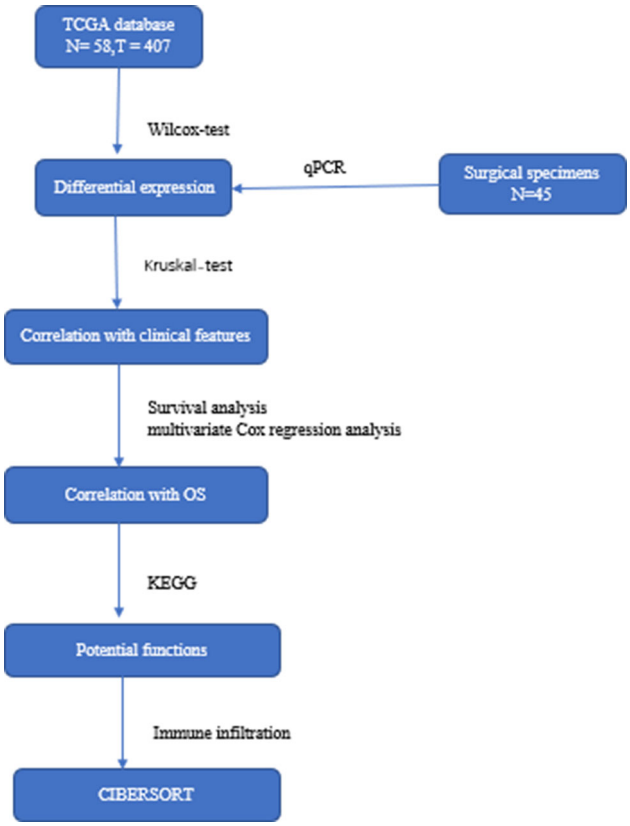
Abstract #641

Prognostic value of Golgi-localized, γ-ear containing, Arf-binding family of proteins in hepatocellular carcinoma

Xiong Zhiyong[1], Hu Kunpeng[1], Zhou Hui[1], Li Wenchao[1], Yao Zhicheng[1], Huang Shaozhuo[1], Liu Bo[1]

[1]Department of General Surgery, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

Introduction: Hepatocellular carcinoma (HCC) is the sixth most commonly diagnosed cancer worldwide. However, the molecular mechanisms of HCC development are poorly understood.
Objectives: Golgi-localized, γ-ear containing, Arf-binding family of proteins (GGAs) are a group of newly found proteins, compound of GGA1, GGA2 and GGA3. They play important roles in vesicle transport between trans Golgi network (TGN) and endosomes. We intend to reveal GGAs' performance in HCC which has never been studied before.
Methods: A total 407 HCC tissues and 58 normal liver tissues' information were obtained from the cancer genome atlas (TCGA) database, Wilcox-test and Kruskal-test were used to reveal correlations between GGAs' mRNA expression pattern and clinical features. Survival analysis and forest map analysis were applied to evaluate their impact on overall survival (OS). Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis and CIBERSORT were used to explore GGAs' potential functions and their correlations of immune infiltration. Quantitative Real-time PCR (qRT-PCR) was applied to verify expression pattern of GGA1 and GGA3.
Results: All GGAs were overexpressed in HCC tissues and associated with tumors size and tumor stage. Survival and forest map analysis showed that GGA1 and GGA3 were related with preferable OS and were independent risk factors of HCC. KEGG analysis showed that GGAs were associated with cancer- related signaling pathway and immune-related signaling pathways. CIBERSORT showed that GGAs were associated with various types of immune cells. qRT-PCR verified GGA1's and GGA3′s expression patterns.
Conclusion: GGA1 and GGA3 could be potential prognostic biomarkers of HCC.



Abstract #666

Atezolizumab + bevacizumab versus sorafenib in patients with unresectable hepatocellular carcinoma (HCC): results from the global and China enrolment phases of IMbrave150

Toh HC[1], Kim T-Y[2], Cheng AL[3], Ryoo B-Y[4], Kudo M[5], Ikeda M[6], Ren Z[7], Feng YH[8], Lim HY[9], Verret W[10], Xu D-Z[11], Li L[11], Hernandez S[10], Huang C[11], Ding B[10], Qin S[12]

[1]National Cancer Centre Singapore, Singapore, [2]Seoul National University College of Medicine, Seoul, Korea, [3]National Taiwan University Cancer Center and National Taiwan University Hospital, Taipei, Taiwan, [4]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea, [5]Kindai University Faculty of Medicine, Osaka, Japan, [6]National Cancer Center Hospital East, Kashiwa, Japan, [7]Zhongshan Hospital, Fudan University, Shanghai, People's Republic of China, [8]Chi Mei Medical Center, Tainan, Taiwan, [9]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, [10]Genentech, Inc., South San Fransisco, CA, [11]Roche Product Development, Shanghai, People's Republic of China, [12]People's Liberation Army Cancer Center, Jingling Hospital, Nanjing, People's Republic of China

Introduction: IMbrave150 demonstrated a statistically significant and clinically meaningful improvement with atezolizumab + bevacizumab versus sorafenib for co-primary endpoints overall survival (OS) and independent review facility (IRF)-assessed progression-free survival (PFS) per RECIST 1.1 in patients with unresectable HCC without prior systemic therapy (Cheng ESMO Asia 2019; Qin EASL 2020).
Objectives: Efficacy and safety in IMbrave150 Global enrolment and China enrolment phases.
Methods: Patients with systemic treatment-naive unresectable HCC were randomized 2:1 to receive atezolizumab 1200 mg IV

q3w + bevacizumab 15 mg/kg IV q3w or sorafenib 400 mg bid until unacceptable toxicity or clinical benefit loss.

Results: IMbrave150's global population (n = 501) included 137 Chinese patients; during the China enrolment phase another 57 patients enrolled for a total of 194 patients from China. The China subpopulation had greater proportions of BCLC Stage C, macrovascular invasion and/or extrahepatic spread, and α-fetoprotein ≥ 400 ng/mL than the global population.

The global population (atezolizumab + bevacizumab, n = 336; sorafenib, n = 165), stratified HR for OS was 0.58 (95%CI, 0.42–0.79; $P < 0.001$) and for IRF-PFS per RECIST 1.1 was 0.59 (95%CI, 0.47–0.76; $P < 0.001$). The China subpopulation (atezolizumab + bevacizumab, n = 133; sorafenib, n = 61) stratified HR for OS was 0.44 (95%CI, 0.25–0.76) and for IRF-PFS per RECIST 1.1 was 0.60 (95%CI, 0.40–0.90). Grade 3–4 AEs occurred in 57% of the atezolizumab + bevacizumab-treated and 55% of the sorafenib-treated global population, and 59% of the atezolizumab + bevacizumab-treated and 47% of sorafenib-treated China subpopulation.

Conclusion: Efficacy and safety results were consistent between the two populations. Overall, atezolizumab + bevacizumab was well-tolerated. Atezolizumab + bevacizumab should be considered a practice-changing treatment for patients with unresectable HCC.

Abstract #682

Hepatocellular carcinoma recurrence after liver transplantation: a single centre experience over 19-years of follow-up

Than-Nwe Ni[1], Stoklosa-Ted[1], Tsoutsman-Tatiana[1,2], Liu-Ken[1,2,3], McCaughan-Geoffrey W[1,2,3], Strasser- Simone I[1,2], Majumdar-Avik[1,2]

[1]Australian National Liver Transplant Unit, Royal Prince Alfred Hospital, University of Sydney, Australia, [2]Sydney Medical School, University of Sydney, Sydney, Australia, [3]Liver Injury and Cancer Program, The Centenary Institute, Sydney, Australia

Introduction: Hepatocellular carcinoma (HCC) is an increasing indication for liver transplantation (LT) in selected patients. Despite validated eligibility criteria, HCC recurrence post-LT is reported to occur in 15–20% and is associated with poor outcomes.

Objectives: Our main aim was to characterize post-LT HCC recurrence and outcomes in our centre.

Methods: We retrospectively reviewed all adult patients who underwent deceased donor LT for HCC at our centre between 1990 and 2019 and developed post-LT HCC recurrence. Patients with non-HCC malignancies or incidental HCCs on explant or were excluded. Data were extracted from the liver transplant and HCC databases and medical records. The outcome of interest was patient survival post-HCC recurrence.

Results: A total of 322 patients underwent LT for HCC over the study period and 30 (9.3%) developed HCC recurrence. Median time from LT to recurrence was 2.7 years (IQR 1.6–6.6), Table 1A. All patients with HCC recurrence received organs from donation after brain death donors. Recurrent HCC patients were mostly male (93%) and the most common underlying disease was HCV (30%), followed by HCV and alcohol (20%). At LT, 26 (87%) were within Milan criteria and 27 (90%) were within UCSF criteria. On explant, 20 (67%) had moderate tumour differentiation and 10 (33%) had microvascular invasion. The site of recurrence was bone in 12 (40%), liver in 11 (37%) and lungs in 10 (33%). Amongst treatment modalities, 14 (47%) received Sorafenib, 6 (20%) received external beam radiotherapy and 6 (20%) underwent surgical excision. At the time of HCC recurrence, 29 (97%) were on Tacrolimus and 6 (20%) were on Sirolimus immunosuppression. HCC recurrence related death occurred in 24 (80%), Table 1B. Median survival after HCC recurrence was 0.8 years (IQR 0.5–2.2). Among non-survivors, 70% had microvascular invasion on explant and all had serum alpha-fetoprotein (AFP) over 300kIU/L at time of LT. Time from HCC diagnosis to LT was 11 months in non-survivors (IQR 6–18) compared to 22 months in survivors (IQR 16–25), p = 0.05. Time from LT to HCC recurrence was 14 months (IQR 7–24) in non-survivors versus 37 months (IQR 25–42) in survivors, p = 0.05.

Conclusion: In this single Australian centre study, recurrent HCC post LT occurred in 9.3%. Recurrent HCC generally occurred within 3 years of LT. Prognosis was poor after recurrence, with median patient survival under 1 year.

Table 1: Number of patients who developed recurrence of hepatocellular carcinoma (HCC) post liver transplantation (LT) over the period of 10 years (Table A), Number of patients who died after recurrence of HCC post LT over the period of 5 years (Table B).

A: Time from LT to HCC recurrence	Total n=30	Alive n=6	Died n=24
<1 year	9	0	9
1-3 years	16	3	13
3-5 years	2	2	0
>5 years	2	0	2
>10 years	1	1	0
B: Time from HCC recurrence to death	Died n=24		
<1 year	14		
1-3 years	7		
3- 5 years	3		

Abstract #739

Use of a novel thyroid-stimulating hormone model for predicting the progression of hepatocellular carcinoma

Yu Lihua[1,2], Liu Xiaoli[1], Jiang Yuyong[1], Wang Xinhui[1], Wang Xianbo[1], Yang Zhiyun[1]

[1]Center of Integrative Medicine, Beijing Ditan Hospital, Capital Medical University, Beijing 100015, P.R. China, [2]First Clinical Medical College, Beijing University of Chinese Medicine, Chaoyang District, Beijing 100029, P.R. China

Background and aims: Individuals with hepatocellular carcinoma (HCC) are at risk of tumor recurrence after surgical resection, which affects their survival. The present study aimed to establish a model for predicting tumor progression in patients with HCC.

Method: To develop and validate the efficacy of a novel prognostic model, a retrospective cohort with HCC (n = 1005) at Beijing Ditan Hospital was enrolled from January 2008 and June 2017. Furthermore, a prospective cohort (n = 77) was recruited to validate the association between thyroid-stimulating hormone (TSH) levels and tumor progression in patients with HCC.

Results: The model used in predicting the progression of HCC included four variables (namely, Barcelona Clinic Liver Cancer [BCLC] stage, presence of portal vein tumor thrombus, alpha-fetoprotein level, and TSH level). The AUROC of the 1-year progression-free survival (PFS) model were 0.755 and 0.753 in the deriving cohort and validation cohort, respectively, and these values were significantly higher than those of the Child–Pugh score, Model for End-stage Liver Disease (MELD), tumor–lymph node–metastasis (TNM) staging system, Okuda classification, and CLIP score. A simple assessment using a nomogram showed the 1-year PFS rate of patients with HCC. In the prospective cohort, the KM curve showed that the high TSH level group had a shorter PFS than the low TSH level (p = 0.001).

Conclusion: The prognostic model of HCC progression was superior to other well-known classical tumor scoring systems. A high TSH level was correlated to poor outcome, particularly those with advanced HCC.

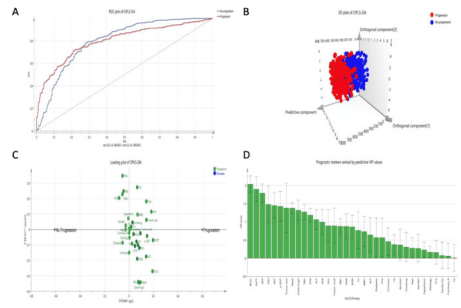


Fig.1A,B,C,D

Fig.1. Orthogonal partial least squares discriminant analysis (OPLS-DA) of the prognosis of HCC. (A) Receiver operating characteristic (ROC) curve of OPLS-DA. (B) The OPLS-DA 3D plot of progression and no progression was distinguished using the predictive component: blue dots representing no progression and red dots indicating rogression. (C) Loading plot from the OPLS-DA of the progression and no progression groups. (D) When the predictive VIP (VIP-pred) value is higher, the ability to predict the progression of HCC is stronger.

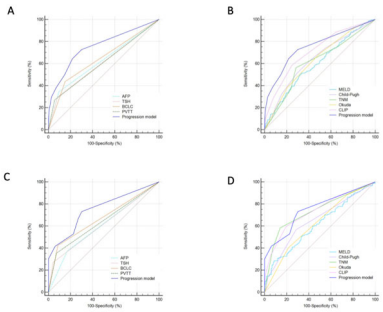


Fig.2A,B,C,D

Fig.2. Receiver operating characteristic curves of the different models in predicting the 1-year PFS of patients with hepatocellular carcinoma. (A-B) Separate prognostic variables and other models in the deriving cohort. (C-D) Separate prognostic variables and other models in the validation cohort.

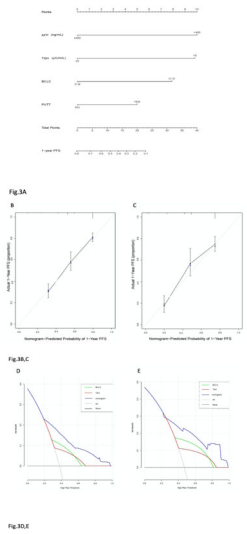


Fig.3A

Fig.3B,C

Fig.3D,E

Fig.3. Prognostic nomogram and calibration curves and decision curve analysis. Nomogram predicted progression-free survival (PFS) (A) for HCC patients. The calibration curves for 1-year PFS (B, C) in the deriving and validation cohorts were identified. The nomogram-predicted probabilities of 1-year PFS (D, E) in the deriving and validation cohorts are compared with BCLC stage and TSH level.

Abstract #793

A new role of cancer stem cell marker CD90/THY-1 in cell autophagy upon chemotherapy

Huy Do[1,2], An Luong[1,2], Deborah Bonazza[3], Cristina Bottin[3], Long Tran[2], Thao Doan[2], Gianluca Tell[4], Hoa Pham[2], Claudio Tiribelli[1], Caecilia Sukowati[1,4]

[1]Fondazione Italiana Fegato - ONLUS, AREA Science Park, Basovizza, Trieste, Italy, [2]University of Medicine and Pharmacy, Ho Chi Minh City, Vietnam, [3]Azienda Sanitaria Universitaria Integrata di Trieste, Trieste, Italy, [4]Laboratory of Molecular Biology and DNA repair, Department of Medicine, University of Udine, Udine, Italy

Introduction: Analysis of cancer biomarkers is an important tool in developing targeted-therapy. Here, we analyze the relevance of CD90, a marker of cancer stem cells (CSC) in hepatocellular carcinoma (HCC). Further, we correlate CD90 with autophagy that is closely-related to drug resistance.
Methods: For in vivo study, 156 specimens were collected from 52 patients undergoing liver resections. In each patient, HCC nodule, peri-HCC, and surrounding-liver-cirrhosis (SLC) were collected. For in vitro study, human HCC cells JHH6 subpopulations expressing CD90 + and CD90- were isolated using magnetic and flow-activated-cell-sorting. Upon doxorubicin treatment, autophagy turn-over was analyzed by RTqPCR for mRNA expression, Western blot for protein expression, and autophagosome staining for autophagy flux. Cytotoxicity test of autophagy inducers was performed by MTT assay. mRNA and protein analysis was also performed in clinical samples.
Results: Progressive increase of CD90 was noticed in HCC compared to SLC and peri-HCC (ANOVA $p < 0.0001$). Linear regression analysis showed positive correlation between CD90 and autophagy gene ATG8F mRNA ($p < 0.001$), confirmed in LC3-II blotting. In vitro model showed that CD90 + and CD90- cells had diverse expressions of autophagy-related genes ATG8F, ATG18, REDD1. Upon doxorubicin treatment, autophagy was activated in both cells by increasing LC3-II protein expression, autophagy-related mRNAs, and autophagic vacuoles. A differential autophagic capacity was noticed between two subpopulations and correlated with cellular toxicity assay.
Conclusion: We confirmed the relevance of autophagy in HCC, probably related with CSC CD90. It involved in cancer-defence mechanism against doxorubicin. Cancer promoting function of autophagy in CD90 + cells was related with cancer environment.

Abstract #796

Distribution of cancer stem cells mRNA markers in HCC clinical samples: Eastern vs. Western populations

An Luong bac[1,2], Do Huy quang[1,2], Tarchi Paola[3], Bonazza Deborah[3], Bottin Cristina[3], Long Tran cong duy[2], Thao Doan phuong[2], Crocè Lory[3], Tell Gianluca[4], Hoa Pham le[2], Tiribelli Claudio[1], Sukowati Caecilia[1,4]

[1]Fondazione Italiana Fegato - ONLUS, AREA Science Park, Basovizza, Trieste, Italy, [2]University of Medicine and Pharmacy, Ho Chi Minh City, Vietnam, [3]Azienda Sanitaria Universitaria Integrata di Trieste, Trieste, Italy, [4]Laboratory of Molecular Biology and DNA repair, Department of Medicine, University of Udine, Udine, Italy

Introduction and objective: Epidemiology of hepatocellular carcinoma (HCC) showed a correlation between incidence and geographical-relevant risk factors. Additionally, the search of common biomarkers is crucial for early diagnosis and effective treatment. This preliminary study aims to compare the distributions of HCC

cancer stem cells (CSC), a population regarded as cancer origin, in two distant populations.
Methods: We collected 52 and 40 selected HCC patients undergoing hepatotectomy in Ho Chi Minh City (Vietnam) and Trieste (Italy). Each collection consisted of HCC, peri-HCC, and non-tumoral tissue. Demographic data was recorded together with clinical findings including histology, laboratory measurements, tumor parameters, and outcome. Protocol of samples and RNA collection was standardized in both laboratories. RNA integrity was measured by BioAnalyzer. Analysis of CD90/THY-1, CD133/PROM-1, and CD326/EpCAM by RT-qPCR was performed in a single laboratory with similar PCR condition. Statistical analysis of continuous variables of mRNA distribution was calculated.
Results: Baseline analysis showed comparable laboratory finding between groups. Vietnamese group was dominated with HBV-related while metabolic/exotoxic in Italian. Morphological analysis showed high percentage of poorly-differentiated HCC in Vietnamese cases. mRNA data showed a similar pattern of CSC between two groups. The mRNA expression of both CD133 was found higher in the distal portion of HCC ($p < 0.0001$). Conversely, the mRNA expression of CD90 was progressively increased from distal to be highest in HCC ($p < 0.0001$), with highest expression in HBV-related HCC.
Conclusion: This pilot study showed that mRNA expressions of CSC markers are comparable between Eastern and Western HCC cases, suggesting a common indicator of hepatocarcinogenesis

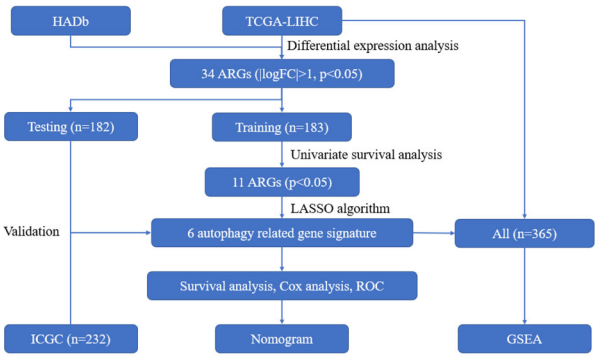
Abstract #858

Construction of autophagy-related risk signature predicting survival in hepatocellular carcinoma

Huang Shaozhuo[1], Liu Bo[1], Li Wenchao[1], Zhou Hui[1], Liao Weixin[2], Hu Kunpeng[1]

[1]Department of General Surgery, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China, [2]Department of Infectious Diseases, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Introduction: Hepatocellular carcinoma (HCC) is a heterogeneous disease with poor prognosis. A robust signature is needed to assess the prognosis of HCC patients for therapeutic customization.
Objectives: While considerable evidence suggests that altered autophagic genes play a crucial role in HCC, the prognostic role of them remains to be further clarified. The aim of this study was to identify a robust autophagy-related prognostic signature for HCC.
Methods: mRNA expression and clinical data were obtained from The Cancer Genome Atlas and the International Cancer Genome Consortium (ICGC) database. Autophagy-related genes (ARGs) were screened by Human Autophagy Database (HADb). Univariate and Lasso Cox regression analyses were performed in the training cohort (n = 183) to identify overall survival-related ARGs and construct an autophagic signature for HCC prognosis prediction. The validation for that was performed in an internal validation cohort (n = 182) and an external validation cohort (n = 232). Bioinformatics functions were investigated by gene set enrichment analysis (GSEA).
Results: A six-gene signature comprising HDAC1, RHEB, PRKCD, RAC1, SQSTM1 and ATIC was established to predict overall survival of HCC. Survival analysis illustrated that patients in high-risk group had poorer survival than patients in low-risk group. A nomogram and forest plot constructed by multivariate Cox regression suggested that the six-gene autophagy-related signature can be an independent prognostic factor for HCC survival.
Conclusion: Our study identified a novel six-gene autophagic signature and established a prognostic nomogram that predict overall survival in HCC. The findings may serve as an independent prognostic indicator of HCC.



Abstract #928

A comparitive study between radiofreguency, microwave and ithanol injection in treatment of hepatocellular carcinoma: a single center experience

Mohamed Abdel-Samiee[1], Reham Reda Elkazaz[1], Mohamed Akl Rady[1], Hazem Omer Metwaly[2], Asmaa Ibrahim Elsayed Gomaa [1]

[1]Department of Hepatology and Gastroenterology, National Liver Institute, Menoufia University, Menoufia, Egypt, [2]Department of Interventional Radiology, National Liver Institute, Menoufia University, Menoufia, Egypt

Introduction: Hepatocellular carcinoma (HCC) is the third most common malignancy worldwide. It results in the second highest cancer-related mortality. The increased incidence of HCC is related to many risk factors.
Objectives: The aim of this work was to compare between microwave ablation (MWA), Radiofrequency ablation (RFA) and percutaneous ethanol injection (PEI) (alone or in combination with RFA, MWA) for treatment of HCC according to outcome, survival, complications, cost and recurrence of the tumor in as single HCC up to 5 cm.
Methods: The current retrospective prospective study was conducted on 250 patients who recruited from National Liver Institute, Menoufia University were divided into 5 groups (50 patient of each group) according to the line of therapy into: group 1: patients treated with RFA, group 2: patients treated with MWA, group3: patients treated with PEI, group 4: patients treated with combined RFA and PEI and group 5: patients treated with combined MWA and PEI. The inclusion and exclusion criteria for ablation therapy were in accordance to the Barcelona-Clinic Liver Cancer (BCLC) criteria for the indications and contraindications for ablation therapy of HCC.
Results: Three patients received antiviral therapy after HCC ablation by 1–2 years, 2 patients after PEI and one patient after MWA and PEI. The mean of intervention cost was 17340 ± 700; 1200 ± 900; 1140 ± 300; 17500 ± 0.0; 1500 ± 0.0 respectively. HCC progression beyond any intervention in short term was 12%; 8%; 18%; 4%; 2% respectively. After a follow up period of 36 months: 250 patients were alive within 6 months after ablation. The mean survival time for each group was: 2.44 ± 1.17, 2.59 ± 1.02, 2.69 ± 0.99, 2.91 ± 1.04, 2.91 ± 1.04 respectively. The complications were minor and almost occurred in majority (95%) of cases included: pain, nausea and low grade fever. Abscess was in 1 patient and biloma in another patient post MWA, minimal pleural effusion in 1 patient, abdominal wall hematoma in 2 patients post combined intervention.

Conclusion: RFA, MWA and PEI alone or in combination are considered curative therapy for patients with very early or early HCC with a very good outcome regarding overall survival, recurrence free survival and progression free survival. Combination MWA and PEI is the best therapy compared with other lines of local ablation therapy according to outcome, recurrence and progression free survival then combination MWA and PEI then MWA then RFA then PEI.

Table 1: Comparison between the studied groups according to mortality

	RFA (n = 50)		MW (n = 50)		PEI (n = 50)		RFA&PEI (n = 50)		MW& PEI (n = 50)		Test of sig. (p)
	No.	%	No.	%	No.	%	No.	%	No.	%	
Mortality (in 6 months)											
Die	0	0.0	0	0.0	1	2.0	0	0.0	0	0.0	χ^2=3.923 (^{MC}p= 1.000)
Alive	50	100.0	50	100.0	49	98.0	50	100.0	50	100.0	
Alive or dead at end of research											
Unknown	0	0.0	0	0.0	1	2.0	0	0.0	0	0.0	χ^2=6.958 (^{MC}p= 0.558)
Die	10	20.0	6	12.0	5	10.0	5	10.0	6	12.0	
Alive	40	80.0	44	88.0	44	88.0	45	90.0	44	88.0	

Abstract #965

Characteristics of portal vein thrombosis basing on histopathology and immunohistochemistry in patients with hepatocellular carcinoma

Le Thi Thu Hien[1], Le Quoc Tuan[2], Dong Duc Hoang[1]

[1]Thai Nguyen University of Medicine and Pharmacy, [2]Thanh Ba Hospital

Introduction: Detection of portal vein thrombosis (PVT), especially benign or neoplastic PVT in new diagnosed hepatocellular carcinoma (HCC) has key meaning for prognosis as well as making choice of treatment methods.
Objectives: to analysis of histopathology and immunohistochemistry of PVT in patiens with HCC.
Methods: 50 patients with HCC have PVT at Clinic 103 Cam Khe from June 2017 to August 2019. The PVT specimens was collected by biopsy through the skin according to ultrasound guidance. Immunohistochemistry test: the dyeing was performed by BondMax automatic dyeing machine (Leica Biosystems—Australia).
Results: As regard to histopathological characteristic of PVT: all of the PVT in patients with HCC were malignant thromboses with moderate differentiation of 57.3%, poor differentiation of 4.6%, high differentiation of 9.8%. Neoangiogenesis in the thromboses was observed by using immunohistochemistry: low level of 6%, moderate level of 45.6% and a high level of 48.4%. The neoangiogenesis in the thromboses significantly related with cancer cell differentiation ($p < 0.001$).
Conclusion: The more angiogenesis was, the lower the grate of cell differentiation.

Abstract #968

Study of toll-like receptor 3 gene polymorphism as a novel risk factor for HCV-related hepatocellular carcinoma in Egypt

Sherief Abd-Elsalam[1], Shimaa EL-Sharawy[1], Osama El- Sayed Negm[1], Hesham Ahmed EL-Sorogy[2], Mona Ahmed Helmy Shehata[1]

[1]Department of Tropical Medicine and Infectious Diseases, Faculty of Medicine, Tanta University, Tanta, Egypt, [2]Department of Clinical pathology, Faculty of Medicine, Tanta University, Tanta, Egypt

Background and aims: Hepatocellular carcinoma (HCC) is a highly aggressive cancer with few treatment options. Toll-like receptor 3 (TLR3) plays a key role in innate immunity and may affect the development of cancers. This study aimed to investigate the association between Toll-like receptor 3 gene polymorphism and HCV-related hepatocellular carcinoma in Egypt.
Methods: This work was conducted on 70 individuals; fifty HCV cirrhotic patients were included in two groups; with HCC (30 patients) and without HCC (20 patients) in compared with a group of 20 apparently healthy controls. All of the studied individuals underwent clinico-laboratory evaluation. TLR3 gene single-nucleotide polymorphism (SNP) (+1234C/T) was tested by polymerase chain reaction–restriction fragment length polymorphism.
Results: This study reported that the prevalence of TLR3 +1234TT genotype was significantly increased in cirrhotic patients with HCC than without HCC, while it was not detected at all among the controls. When analyzing the TLR3 SNP +1234C/T with different clinical parameters in HCC patients, there were a significant association between + 1234C/T SNP; namely TT genotype and each of the hepatic focal lesions' number, size and the patients' higher Okuda and BCLC stages. No association could be detected between TLR3 SNP and each of the age, sex, Child–Pugh grades, MELD score or AFP of the studied HCC cases.
Conclusion: These data indicate that TLR3 gene SNP +1234C/T could be a novel risk factor for HCC, especially the HCV-related HCC among the Egyptian population.

Abstract #983

The effect of stem cell hepatocyte on VEGF and cytology patient of hepatocellular carcinoma (HepG2)

Asih Sasamijati Lestari Suprapto Putri[1], Paulus Kusnanto[1]

[1]Internist, Gastroenterologist-Hepatologist, Moewardi General Hospital/Faculty of Medicine UNS, Surakarta, Central Java, Indonesia

Introduction: Hepatocellular Carcinoma is the most common liver malignancy, with survival rates ranging from 6 to 20 months. Of all the malignant liver tumors that has been diagnosed, 85% are HCC, 10% CC and 5% are other types. Hepatocellular Carcinoma (HCC) ranks second as the most common cause of death from cancer worldwide and is the fifth most common cancer in the world in men. In Indonesia, HCC ranks fourth as the most common cancer in men after lung, colorectal and prostate cancer, with an age-standardized rate of 13.4 per 100,000 population. Stem cells, especially stem cell hepatocyte, are cell products that work as anti-fibrosis, anti-inflammatory (immunomodulation), apoptotic activation, proliferation and anti angiogenesis.
Objective: The aim at this study is to prove whether there is an influence of stem cell hepatocyte in the impairment of VGEF as a marker in the process of angiogenesis and cytology of patients with hepatocellular carcinoma (HepG2).
Methods: This research is an experimental study with the object of HepG2 cell line culture research which is divided into 6 groups, namely the control group, and several treatment groups, then analyzed for VEGF and cytology. With each treatment group differentiated between dosing of stem cells. We do the post-test only with control design method. Each group will then be analyzed statistically using the Shapiro–Wilk parametric test of normality tests and in the VEGF group an abnormal data is obtained so for statistical testing using Kruskal–Wallis which is then continued with the Mann–Whitney test. Likewise in the cytology group of a significance limit: the P value was significant if $p < 0.05$.
Results: The results showed that the administration of stem cells with different doses—in patients with hepatocellular carcinoma had a significant effect on cell cytology, but for VEGF gave a decrease but

not significant. In the control group it was found in grade IV, whereas in the treatment groups it was found to be decrease in grading from the sample after stem cell administration by 15 thousand. The effective dose in this study to reduce grading from HCC was found in the administration of 20 thousand stem cells, and in the 25 thousand dose group the results were not as good as in the administration of 20 thousand stem cell doses. In the VEGF treatment group, the results were not different from the control group and the treatment groups and the results from the VEGF smear were + 3.

Conclusion: From the results of the study it can be concluded that there is an effect of stem cell hepatocyte administration on changes in cytology of patients with hepatocellular carcinoma, but in VEGF administration of stem cell hepatocyte does not have a significant effect.

Abstract #1091

The incidence of acute kidney injury after platinum-based transcatheher arterial chemoembolization and transarterial infusion chemotherapy using anthracycline in patients with hepatocellular carcinoma

Wahyu Purnama[1], Lucky Nosih[1], Nurhidayati[2]

[1]General Practitioner in Massenrempulu Hospital, Enrekang, South Sulawesi, [2]Internal medicine in Massenrempulu Hospital, Enrekang, South Sulawesi

Backgrounds: The incidence of acute kidney injury have been reported about transcatheher arterial chemoembolization using antracycline but still remains unclear.

Objective: The aim of this study was to investigate association between acute kidney injury after platinum-based transcatheter arterial chemoembolization/transarterial infusion chemotherapy and prognosis in patients with hepatocellular carcinoma.

Methods: We retrospectively analyzed 300 sessions in 130 patients who underwent platinum-based transcatheher arterial chemoembolization/transarterial infusion chemotherapy. Acute kidney injury was diagnosed according to the criteria established by the International Club of Ascites. The incidence of acute kidney injury, risk factors for serum creatinin elevation and association between acute kidney injury and prognosis were assessed.

Results: Fifteen cases of acute kidney injury (5.3%, 16/300) developed in 20 patients (6.7%, 20/300). Ascites (coefficient: 0.059, P = 0.004), low estimated glomerular filtration rate (coefficient: − 0.007, P = 0.03), diabetes (coefficient: 0.06, P < 0.001) and high albumin-bilirubin grade (albumin-bilirubin grade 2: coefficient: 0.051, P = 0.003; and albumin-bilirubin grade 3: coefficient: 0.1, P < 0.0001) were significantly associated with an elevation in serum creatinin levels after transcatheher arterial chemoembolization/transarterial infusion chemotherapy. The development of acute kidney injury was associated with poor prognosis (hazard ratio: 3.2, 95% CI 1.5–2.4, P = 0.005). Patients with acute kidney injury had a significantly lower survival rate than patients without acute kidney injury (P = 0.04).

Conclusion: The incidence of acute kidney injury after platinum-based trancatheher arterial chemoembolization/transarterial infusion chemotherapy was associated with poor prognosis.

Abstract #1165

Liver stiffness measurement (LSM) predicts development of hepatocellular carcinoma (HCC) in patients with chronic hepatitis C treated with direct acting antiviral agents (DAAs)

Mahmoud Helmy Allam[1], Maha Mohammad Elsabaawy[1], Mohamed Akl Rady[1], Mohamed Ahmed Samy Kohla[1]

[1]Department of Hepatology and Gastroenterology, National Liver Institute, Menoufia University, Shebin El-Kom, Egypt

Background: Development of hepatocellular carcinoma after treatment of HCV infection by direct acting antiviral agents (DAAs) remains debatable. Predicting tumor development remains an important challenge.

Patients and methods: One hundred twenty-six patients with HCV infection were enrolled in this study between January 2015 and December 2018. Initial assessment of patients was done by requesting liver and kidney function tests, CBC, alpha-fetoprotein, HCV viremia level by polymerase chain reaction (PCR), ultrasonography of the abdomen (U/S) and assessment of liver fibrosis by transient elastography (FibroScan®) before starting treatment with DAAs. Patients with hepatic or other extra-hepatic malignancies and those with co-infection with hepatitis B or alcoholics were excluded from this study. Patients were treated by different DAA regimens according to standard protocol for HCV treatment. Follow up of patients was done every 3 months for 24 months after end of DAAs therapy. Diagnosis of HCC was confirmed by dynamic imaging technique on detecting any suspicious liver lesion on routine U/S.

Results: Thirty-two patients (25.3%) developed HCC during their follow up after DAA therapy. Baseline mean serum AST was higher (68.3 ± 38.2 U/L vs. 48.7 ± 32.4 U/L) and mean platelets' count was lower (129.5 ± 55.6 vs. 179.5 ± 69.8 × 10^3/μL) in those who developed HCC when compared to other patients, (p < 0.05). Also, baseline liver stiffness measurement (LSM) was higher for those patients, (33.1 ± 10.7 vs. 15.5 ± 11.5 kPa, p < 0.05). At a cutoff value of 18.8 kPa, LSM was significant in predicting HCC after DAAs, (90.0% sensitivity, 80.0% specificity, 55.0% PPV, 97.3% NPV, 80.0% accuracy)

Conclusion: Baseline LSM may be valuable in predicting HCC after DAA therapy.

Abstract #1279

Serum cytokeratin as a biomarker in assessing the severity of patients with liver cirrhosis with hepatocellular carcinoma

G. N. Gireesh[1], A. R. Venketeshwaran[1], K. Premkumar[1], K. Muthukumar[1], R. Murali[1], A. Chezhian[1]

[1]Institute of Medical Gastroenterology, Madras Medical College, Chennai

Aim: To study the significance of CK 18 in patients with liver cirrhosis with hepatocellular carcinoma and evaluate the diagnostic role and severity for HCC

Methods: Patients with a diagnosis of cirrhosis with hepatocellular carcinoma (HCC) were included from the time period of January 2019 to august 2019. Total number of patients were 35. The etiology for HCC were hepatitis B in 17; hepatitis C in 12 and alcoholic liver disease in 6 patients.

Pheripheral blood was taken and Serum CK 18 was measured using specific enzyme-linked immunosorbent assays in patients with liver cirrhosis and HCC on admission and compared with non cirrhotic patients

Results: Serum CK 18 levels were markedly elevated in patients with cirrhosis due to various etiology than compared with non cirrhotic patients (total CK18: 234 ± 122.0 U/L, control 142.7 ± 32.6 U/L, P = 0.042).5 patients with HCC with BCLC stage 1 undergone radiofrequency ablation. In these patients total CK 18 reduced to 182 ± 111.0 U/L on post procedure day5.
There was a significant correlation between serum AFP and serum CK 18 with a sensitivity of 96% with combined use. The correlation coeffecients between serum CK18 released by and ALT levels were 0.545 in the HCC group and 0.922 in the control group
Conclusion: Serum levels of total CK18 were higher in HCC patients with liver cirrhosis due to various etiology compared with levels in patients with non cirrhotic liver. Serum CK 18 has greater diagnostic and therapeutic value in HCC which decreases after treatment. The combination of AFP and CK18 increased the sensitivity of detection for HCC.

Abstract #1287

Development of a urine test for liver cancer screening

Ying-Hsiu Su[5], James P. Hamilton[2], Amy K. Kim[2], Ting-Tsung Chang[3], Hie-Won Hann[4], Chi-Tan Hu[5], Selena Lin[1], Harry Luu[2], Wei Song[1]

[1]JBS Science, [2]Gastroenterology and Hepatology, Johns Hopkins University, [3]National Cheng Kung University Medical College and Hospital, [4]Thomas Jefferson University, [5]Division of Gastroenterology, Hualien Tzu-Chi Hospital, [5]Baruch Blumberg Research Institute, Doylestown, PA

Introduction: Hepatocellular carcinoma (HCC) is the third-most common cause of cancer-related death worldwide.
Objectives: The purpose of this study was to develop urine DNA biomarkers for the early detection of HCC.
Methods: Two frequent HCC-associated hotspot mutations, *TP53* codon 249 (*TP53* 249) and *CTNNB1* codons 32–37 (*CTNNB1* 32–37*)*, and six genes (*RASSF1A, GSTP1, CDKN2A, SFRP1, TFPI* and *MGMT*) commonly aberrantly methylated (*m*) in HCC were selected as candidates. We measured these abnormalities in urine from HCC and non-HCC controls (cirrhosis and hepatitis), developed using Logistic Regression (LR) and Two-Step (TS) machine learning algorithms in a training set of 73 HCC and 162 non-HCC patients, then tested in a blinded, validation set of 150 HCC and 476 non-HCC patients.
Results: Mutations in *TP53* 249, and methylated *RASSF1A, GSTP1* were significantly higher in the urine of HCC versus non-HCC patients (Kruskall-Wallis test: $p < 0.001$) and were selected for further development. In the training set, these 3 urine DNA markers, by LR, distinguished HCC from non-HCC with an AUROC of 0.874 (95% CI 0.815–0.933). Using the TS model, the panel markers classified HCC vs. Non-HCC with an AUROC of 0.962 (95% CI 0.938–0.986), with 93.2% sensitivity at 90.1% specificity. In the blinded validation set, using the TS model generated from training set, we detected HCC with 82.0% sensitivity at 80.0% specificity.
Conclusion: A urine DNA biomarker panel, consisting of mutations in *TP53* 249, and methylated *RASSF1A,* and *GSTP1*, in addition to serum AFP, exhibits substantial potential as a non-invasive, diagnostic modality for HCC.
Abstract #1556

PAGE-B score in predicting hepatocellular carcinoma (HCC) in Chinese with chronic hepatitis B (CHB)-related cirrhosis

Dong Ji[1], Song-Hai Chen[1], Yudong Wang[2], Guofeng Chen[1], Gregory Cheng[2], George Lau[1,2]

[1]Second Liver Cirrhosis Diagnosis and Treatment Center, The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China. [2]Humanity and Health Clinical Trial Center, Humanity and Health Medical Group, Hong Kong SAR, China

Background and aim: PAGE-B score was reported to be a simple and reliable score for prediction of the 5-year hepatocellular carcinoma (HCC) risk in Caucasian chronic hepatitis B patients (CHB) receiving entecavir/tenofovir treatment. We performed a retrospective analysis of Chinese CHB patients on entecavir/tenofovir to assess the predictive value of PAGE-B score.
Method: 2571 Chinese CHB patients who had received entecavir/tenofovir treatment for 5 or more years from Jan 2010 were included in analysis. These patients had followed-up to Dec 31 2019. Diagnosis of HCC was based on APSAL HCC 2017 updated guidelines. Clinical and laboratory parameters at the time of entecavir/tenofovir treatment and up to 5 years before the diagnosis of HCC were collected. PAGE-B score calculated and the cumulative incidence of HCC among the low (< 10), immediate (10–17) and high (> 18) score groups were compared.
Results: Totally, 2571 patients with HBV-related cirrhosis were included, 304 patients developed HCC during follow-up, and 2267 patients did not develop HCC. Total PAGE-B scores were similar in both groups. Patients with PAGE-B < 10 (low risk), 10–17 (intermediate risk), ≥ 18 scores (high risk) were 9 (3.0%), 143 (47.0%), 152 (50.0%) and 141 (6.2%), 1030 (45.4%), 1096 (48.3%), in HCC and non-HCC groups respectively ($p > 0.05$ by Chi square) Furthermore, 9/150 (6%) of the subjects in the low risk group developed HCC during the follow-up period as compared with 143/1173 (12%) and 152/1248 (12%) of the subjects in the intermediate and high score groups respectively ($p = 0.03$). ROC analysis showed that the AUC of PAGE-B scores for 5-year HCC incidence was 0.515 with 95% CI of 0.496–0.535 (P = 0.342).
Conclusion: Chinese CHB patients on entecavir/tenofovir in the low PAGE-B score group had a lower risk of developing HCC than those in the intermediate and high score groups. However, the annual HCC incidence of > 0.5% in the low risk group is still quite significant and these patients should not be exempted from HCC surveillance

Abstract #1569

Overall survival of patients with unresectable hepatocellular carcinoma under real-life clinical practice in Asia–Pacific region

Dong Ji[1], Guo-feng Chen[1], Yinjie Gao[2], Zhenwen Liu[2], Ritsuko Yokouchi[3], Naho Sato[3], Hitoshi Mochizuki[3], Yudong Wang[4], Rick Chong[4], Gregory Chung[4], George Lau[1,2,4], Masao Omata[3,5]

[1]Second Liver Cirrhosis Diagnosis and Treatment Center, The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China, [2]Hepatobiliary Department And Liver Transplant Center, The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China, [3]Yamanashi Prefectural Central Hospital, Yamanashi, Japan. [4]Humanity and Health Clinical Trial Center, Humanity and Health Medical Group, Hong Kong SAR, China. [5]University of Tokyo, Tokyo, Japan.

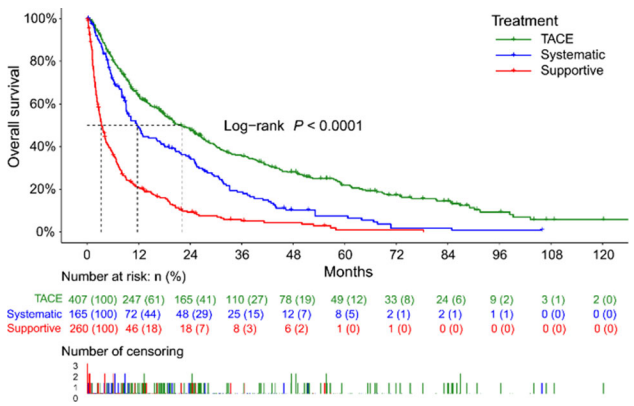
Background: Hepatocellular carcinoma (HCC) represents about 90% of primary liver cancers and constitutes a major global health problem. The pattern of HCC occurrence shows a significant geographical imbalance, with the highest incidence rates in East Asia (more than 50% of the cases occurring in China). The aim of this study is to investigate the overall survival (OS) of patients diagnosed with

unresectable hepatocellular carcinoma under real-world practice conditions in Asia-Pacific region.

Methods: Patients with unresectable HCC diagnosed according APASL guideline from December 2008 to March 2019 in different hospitals in Asia-Pacific region were included. Patient demographics, treatment modalities and survival status were retrospectively collected. Overall survival (OS) is defined as the time (days) from the date of unresectable HCC diagnosis to the date of death, due to any reason. Systematic therapy included chemotherapy, target therapy, and traditional Chinese medicine. Patients alive or lost to follow-up at the time of analysis will be censored at their last date of follow-up. Survival outcomes were assessed with Kaplan–Meier curves and compared with the log-rank test. A Cox- proportional hazard model was constructed with treatment modalities to assess their impact on survival.

Results: Altogether, 832 patients with unresectable HCC were enrolled, 695 (83.5%) were male, median age (IQR) was 59.0 (51.1–66.7) years, 670 (80.5%) patients had hepatitis B infection. Patients receiving TACE, systematic therapy, and supportive therapy only were 407 (48.9%), 165 (19.8%), and 260 (31.3%), respectively. Overall 677 (81.4%) patients died during follow-up, median follow-up time was 67.4 (95% CI 55.8–84.2) months. Median survival time was 11.1 (95% CI 9.7–12.6) months and the median survival time of patients receiving TACE, systematic, supportive therapy only were 22.0 (18.1–26.6), 11.7 (9.1–17.2), and 3.3 (2.9–4.3) months respectively. Kaplan–Meier curves were showed in figure below. The median OS of TACE treated patients was comparable to that reported in literature (22.0 months vs 19.4 months).[1] Multivariate COX proportional hazard model showed that the treatment modality was independent high-risk factors for death in unresectable HCC patients. Compared with supportive therapy only, the HR (95% CI) of TACE and systemic therapy were 0.275 (0.230–0.329) and 0.444 (0.359–0.548), respectively.

Conclusions: In a diverse cohort of hepatitis B infected patients with unresectable HCC in Asia-Pacific region, systemic therapy prolonged OS as compared with supportive therapy only. TACE treatment was effective in HCC patients with chronic hepatitis B infection



Abstract #1571

Fibrosis-4 Index predicts the risk of hepatocellular carcinoma in patients with untreated chronic hepatitis C

Chang Shan-Han[1], Su Tung-Hung[1,2], Lee Mei-Hsuan[3], Liu Chun-Jen[1,2], Chen Pei-Jer[1,2,4,5], Yang Hung-Chih[1,2], Liu Chen-Hua[1,2], Chen Chi-Ling[4], Tseng Tai-Chung[1,2], Chen Chien-Hung[6], Lee Hsuan-Shu[1], Chen Ding-Shinn[1,2,7], Chen Chien-Jen[7], Kao Jia-Horng[1,2,4,5]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, [2]Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan, [3]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [4]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, [5]Department of Medical Research, National Taiwan University Hospital, Taipei, Taiwan, [6]Department of Internal Medicine, National Taiwan University Hospital Yunlin Branch, Yunlin County, Taiwan, [7]Genomics Research Center, Academia Sinica, Taipei, Taiwan

Introduction: The fibrosis-4 index (Fib-4) is a useful noninvasive marker for severity of liver fibrosis in patients with chronic hepatitis C.

Objectives: To investigate the predictive role of baseline Fib-4 index in the development of hepatocellular carcinoma (HCC) among untreated chronic hepatitis C patients.

Methods: We conducted a retrospective study to include untreated chronic hepatitis C patients who received longitudinal follow-up at the liver clinic of National Taiwan University Hospital during 1986–2014. Patients were screened if they had positive anti-HCV, HCV RNA or had a diagnosis of chronic hepatitis C. We excluded patients with incomplete medical records, coinfection of HBV or HIV, HCC development in the first year of follow-up, or a follow-up duration less than 3 years.

Results: A total of 1155 patients were included in the ERADICATE-C cohort. After excluding patients without complete data for Fib-4 index calculation, 772 patients were enrolled. The mean age was 55 years, 63% were females and 74 patients had baseline clinical cirrhosis. After 12 years of follow-up, 163 patients developed HCC. The median baseline Fib-4 level was 2.1. The Fib-4 index < 1.45 (n = 225), 1.45–3.25 (n = 289) and > 3.25 (n = 258) stratified the risk of HCC (log rank $P < 0.0001$) over time. Multivariable cox regression analysis showed that male (hazard ratio [HR]: 1.943, 95% confidence interval [CI]: 1.378–2.740), AFP $\geq$ 20 ng/mL vs. $<$ 20 ng/mL (HR: 3.396, 95% CI 2.287–5.045) and higher Fib-4 index had a greater risk of HCC. Compared with patients with Fib-4 < 1.45, patients with Fib-4 between 1.45 and 3.25 had HR: 6.860, 95% CI 3.032–15.522), and those with Fib-4 > 3.25 had the highest risk (HR: 8.627, 95% CI 3.530–21.083).

Conclusion: Baseline Fib-4 index can stratify the risk of HCC in patients of chronic hepatitis C without antiviral therapy and thus prioritize the usage of anti-viral therapy in resource-constrained countries.

Abstract #1576

Sarcopenia is a poor prognostic marker following curative resection for hepatocellular carcinoma: a single centre experience

Santhakumar, Cositha[1], Bartlett, Adam[2,3], Plank, Lindsay[3], Cameron Wells[3], Lily Wu[2], Edward Gane[1], John McCall[1,2]

[1]New Zealand Liver Transplant Unit, Auckland City Hospital, Auckland, New Zealand, [2]Hepatopancreaticobiliary Unit, Department of General Surgery, Auckland City Hospital, Auckland, New Zealand, [3]Department of Surgery, University of Auckland, Auckland, New Zealand

Introduction: Sarcopenia is a surrogate marker of frailty and is common in cirrhosis. Although sarcopenia is associated with poor outcomes following liver transplantation, its prognostic significance following hepatectomy for hepatocellular carcinoma (HCC) is less clear.

Objectives: We evaluated the prevalence and prognostic impact of sarcopenia in a large cohort of patients undergoing resection for HCC.
Methods: Data were collected retrospectively on consecutive patients undergoing hepatectomy for HCC between June 1998 until December 2014 at Auckland City Hospital. The skeletal muscle index was calculated using the total skeletal muscle area at the third lumbar vertebrae on preoperative computed tomography or magnetic resonance imaging. The clinicopathological and surgical characteristics of sarcopenic and non-sarcopenic groups were compared and outcomes including overall survival and recurrence-free survival were assessed.
Results: Of the 147 patients, 40 were sarcopenic (27%). Sarcopenia correlated significantly ($p < 0.01$) with older age and larger tumour size. At a median follow up of 5.9 years, sarcopenia was a predictor of worse overall survival ($p < 0.01$) (Figure 1), liver cancer-specific survival ($p = 0.02$) and recurrence-free survival ($p < 0.01$). Median survival times after resection for sarcopenic and non-sarcopenic patients were 5.4 and 10.5 years, respectively. Recurrence-free survival rates at 5 years were 25.6% and 43.8% respectively. Sarcopenia was an independent predictor of survival on multivariate analysis.
Conclusion: Sarcopenia predicted worse overall and recurrence-free survival in patients undergoing hepatectomy for HCC. In the preoperative assessment, sarcopenia may provide an objective marker of the patient's general health, facilitating the implementation of strategies to optimise muscle mass, thereby improving patient outcomes.

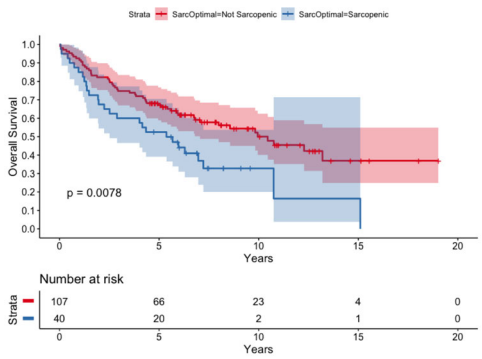


Figure 1. Overall survival following hepatectomy for HCC in patients with and without sarcopenia

Abstract #1608

Kinesin family member 15 promotes cancer stem cell phenotype and malignancy via reactive oxygen species imbalance in hepatocellular carcinoma

Qing Li[1,2], Xuehao Wang[1,2]

[1]School of Medicine, Southeast University, Nanjing, China, [2]Hepatobiliary Center, The First Affiliated Hospital of Nanjing Medical University, Key Laboratory of Liver Transplantation, Chinese Academy of Medical Sciences, NHC Key Laboratory of Living Donor Liver Transplantation, Nanjing, China

Introduction and objectives: Accumulating evidence demonstrates that the development and progression of hepatocellular carcinoma (HCC) is associated with the presence of cancer stem cells (CSCs). However, it is unclear how the stem cell features of HCC cells are maintained.
Method: KIF15 expression was determined by real-time PCR and western blot analyses. Functional assays were performed in HCC cells, HCC organoids and mice. Immunoprecipitation (IP)/mass spectrum (MS), co-immunoprecipitation (co-IP), immunofluorescence (IF) and immunohistochemistry (IHC) analyses were conducted to evaluate the interaction between KIF15 and Phosphoglycerate dehydrogenase (PHGDH). Intracellular reactive oxygen species (ROS) levels were determined using 2′,7′-dichlorofluorescin diacetate (H2DCFDA).
Results: In the present study, kinesin family member 15 (KIF15) expression was shown to be overexpressed in HCC tissues, cell lines, and CSCs. Patients with HCC with high KIF15 expression had shortened overall survival (OS) and high recurrence probability. Downregulation of KIF15 in vitro as well as in HCC organoids resulted in a significant reduction in sphere formation and expression of stemness-related genes. KIF15 downregulation in human HCC xenograft models delayed tumor initiation, growth, and metastasis. KIF15 was also demonstrated to interact with phosphoglycerate dehydrogenase (PHGDH) and inhibit proteasomal degradation of PHGDH, thus promoting CSC phenotype and malignancy via PHGDH-mediated intracellular reactive oxygen species (ROS) imbalance in HCC. Moreover, AAA nuclear coregulator cancer-associated protein (ANCCA) upregulation acts as a key mediator in KIF15 expression upregulation in HCC.
Conclusion: We found that KIF15 promotes the CSC phenotype and malignancy via PHGDH-mediated ROS imbalance in HCC. These findings highlight potential therapeutic targets for HCC.

Abstract #1635

Serum Mac-2-binding protein glycosylation isomer (M2bpgi) as a predictor of hepatocellular carcinoma development in chronic hepatitis B patients: a systematic review

Sartika KD[1], Setiawan SI[1], Leonard EN[2], Saputra IY[3], Tendean M[4], Kurniawan J[5]

[1]General Practitioner, Bhakti Asih Hospital, Tangerang, Indonesia, [2]General Practitioner, Ende General Hospital, Ende, Indonesia, [3]General Practitioner, Panti Wilasa Dr. Cipto Hospital, Semarang, Indonesia, [4]Department of Internal Medicine, UKRIDA Faculty of Medicine, Jakarta, Indonesia, [5]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia/Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Hepatocellular carcinoma (HCC) is the fourth leading cause of cancer-related deaths. Moreover, chronic hepatitis B (CHB) infection is a major risk of HCC development. Previously, studies revealed M2BPGi as reliable marker for diagnosing liver fibrosis including HCC. However, no clear recommendation on elevated serum M2BPGi cut-off index (COI) for prediction of HCC development.
Objectives: To evaluate the role of M2BPGi and optimal serum COI for prediction of HCC development in CHB patients.
Methods: Several research databases (PubMed, Science Direct, Lancet, SpringerLink, Cochrane, and ProQuest) were utilised in this review with keywords "hepatitis B[MESH]" AND "M2BPGi[MESH]" AND "hepatocellular carcinoma[MESH]". The inclusion criteria were patient CHB in nucleos (t)ide analogues (NA) therapy with minimal 1 year followed-up and study design including meta-analysis or cohort study. Studies were appraised using evidence-based toolkit by the Centre for Evidence-Based Medicine (CEBM).
Results: Six eligible cohort studies were reviewed. The studies revealed that baseline M2BPGi before NA administration is a useful short-term predictor of HCC in CHB. Baseline M2BPGi level $>$ 0.685 COI could predict 15 years risk of HCC development with 91.7% sensitivity and 80.8% specificity, AUC 0.883 (95% CI 0.771–0.995, p = 0001). In patients with virological remission, serum M2BPGi $\geq$ 3 COI also predict the 4 years risk of HCC with 58% sensitivity and 90% specificity, AUC 0.79 (95% CI 0.67–0.91,

p = 0.001). However long term NA therapy would affect M2BPGi level especially after 3 years of treatment.
Conclusion: The evidence supports M2BPGi as a short-term predictor of HCC development in CHB patient, but further studies are needed to complete this recommendation.

Abstract #1662

Risk factors, patterns and long-term prognosis of early and late recurrence in patients with hepatitis B virus-associated hepatocellular carcinoma

Ming-Da Wang[1*], Chao Li[1*], Lei Liang[1*], Hao Xing[1*], Li-Yang Sun[1,2*], Bing Quan[1,2*], Han Wu[1], Xin-Fei Xu[1], Meng-Chao Wu[1], Timothy M. Pawlik[3], Wan Yee Lau[1,4], Feng Shen[1#], Tian Yang[1#]

[1]Department of Hepatobiliary Surgery, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University (Navy Medical University), Shanghai, China, [2]Department of Clinical Medicine, Second Military Medical University (Navy Medical University), Shanghai, China, [3]Department of Surgery, Ohio State University, Wexner Medical Center, Columbus, OH, United States, [4]Faculty of Medicine, the Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, N.T., Hong Kong SAR, China

Background: Survival after liver resection of hepatocellular carcinoma (HCC) remains poor due to a high incidence of recurrence. We sought to investigate risk factors, patterns, and long-term prognosis among patients with early and late recurrence after liver resection for hepatitis B virus (HBV)-associated HCC.
Methods: Data of consecutive patients undergoing curative resection for HBV-associated HCC were analyzed. According to the time to recurrence after surgery, recurrence was divided into early ($\leq$ 2 years) and late recurrence ($>$ 2 years). Characteristics, patterns of initial recurrence and post-recurrence survival (PRS) were compared between patients with early and late recurrence. Risk factors of early and late recurrence, and predictors of PRS were identified by univariable and multivariable Cox-regression analyses.
Results: Among 894 patients, 322 (36.0%) and 282 (31.5%) developed early and late recurrence, respectively. On multivariable analyses preoperative HBV-DNA $> 10^4$ copies/ml was associated with both early and late recurrence, while postoperative no/irregular antiviral therapy was associated with late recurrence. Compared with patients with late recurrence, patients with early recurrence had a lower proportion of intrahepatic only recurrence (72.0% vs. 91.1%, $P < 0.001$), as well as a lower chance of receiving potentially-curative treatments for recurrence (33.9% vs. 50.7%, $P < 0.001$) and a worse median PRS (19.1 vs. 37.5 months, $P < 0.001$). Multivariable analysis demonstrated that early recurrence was independently associated with worse PRS (HR 1.361, 95% CI 1.094–1.692, P = 0.006).
Conclusions: Although risk factors associated with early recurrence and late recurrence were different, a high preoperative HBV-DNA load was an independent hepatitis-related risk for both early and late recurrence. Early recurrence was associated with worse post-recurrence survival among patients with recurrence.

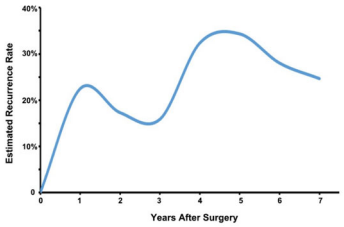


Figure 1. The estimated rate of recurrence (per year) over time after curative liver resection of hepatitis B-associated hepatocellular carcinoma.

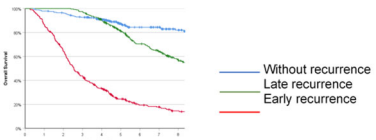


Figure 2. Kaplan-Meier analysis of overall survival in patients without recurrence, patients with early recurrence and with late recurrence after curative liver resection of hepatitis B virus-associated hepatocellular carcinoma. $P < 0.001$ (without recurrence vs. early recurrence), $P < 0.001$ (without recurrence vs. late recurrence) , and $P < 0.001$ (early recurrence vs. late recurrence) (log rank test).

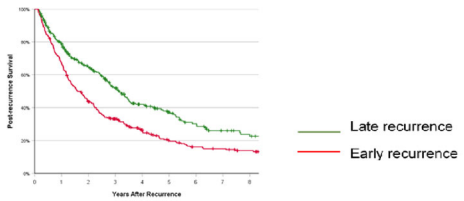


Figure 3. Kaplan-Meier analysis of post-recurrence survival in patients with early and late recurrence after curative liver resection of hepatitis B virus-associated hepatocellular carcinoma. $P < 0.001$ (log rank test).

Abstract #1672

Yttrium-90 radioembolization might have better efficacy in overall survival in patients with hepatocellular carcinoma compared with conventional chemoembolization: a propensity score-matched study

Minseok Albert Kim[1], Heejoon Jang[1], Hyunwoo Oh[1], Sun Woong Kim[1], Yun Bin Lee[1], Eun Ju Cho[1], Jeong-Hoon Lee[1], Su Jong Yu[1], Jung-Hwan Yoon[1], Hyo-Cheol Kim[2], Jin Wook Chung[2], Yoon Jun Kim[1]

[1]Department of Internal Medicine and Liver Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea, [2]Department of Radiology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

Background/aims: Locoregional therapies, such as yttrium-90 (Y-90) radioembolization (RE) and conventional chemoembolization (CE) can effectively control localized hepatocellular carcinoma (HCC) in patients who are not amenable to curative resection. However, it has not yet been fully established which modality is more effective. The aim of this study was to compare effectiveness of RE and CE as the first treatment of HCC.
Methods: We retrospectively reviewed data of patients who received RE or CE as the first treatment of HCC at Seoul National University Hospital from March 2012 to December 2017. A propensity score matching was performed to reduce selection bias. Overall survival (OS), progression-free survival (PFS), and intrahepatic PFS were compared.

Results: A total of 138 patients who were initially treated with RE (n = 54) or CE (n = 84) was included in this study and baseline characteristics was well-balanced between the two groups. Of 138 patients, median age was 59 and median follow-up period was 22.5 months. RE showed better overall survival than CE (hazard ratio [HR] = 0.30, 95% confidence interval [CI] = 0.10–0.90, log-rank $P = 0.02$) and tended toward better intrahepatic PFS than CE (HR = 0.52, 95% CI = 0.25–1.09, log-rank $P = 0.08$). However, progression-free survival was not significantly different between the two groups (HR = 0.67, 95% CI = 0.39–1.16, log-rank $P = 0.15$). In multivariable analysis, RE was an independent prognositc factor for overall survival (adjusted HR = 0.31, 95% CI = 0.11–0.92, $P = 0.04$).
Conclusion: RE might be more effective as the initial treatment than CE in patients with HCC.

Table 1. Univariable and multivariable analyses for overall survival

	Univariable			Multivariable*		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Age ≥60	1.14	0.50–2.64	0.75			
Male	0.98	0.28–3.30	0.97			
Cirrhosis	3.21	0.75–13.73	0.12			
PVTT	2.93	1.235–6.86	0.01	2.83	1.21–6.62	0.02
RE	0.30	0.10–0.90	0.03	0.31	0.11–0.92	0.04

*Adjusted for PVTT
Abbreviations: PVTT, portal vein tumor thrombus; RE, radioembolization

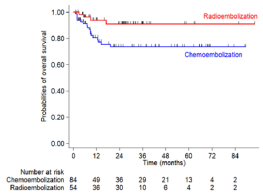


Figure 1. Kaplan-Meier estimates of overall survival between the two groups in the entire population (n = 138)

Abstract #1698

KIAA1522 promotes cell proliferation, migration, and invasion through the activation of Mtorc1 signalling pathway in hepatocellular carcinoma

Longfeng Jiang[1], Jingjing Dai[1], Ping Shi[1], Yuyun Shao[1], Jun Li[1]

[1]Department of Infectious Diseases, the First Affiliated Hospital, Nanjing Medical University, Nanjing, China

Introduction and objectives: KIAA1522 has been demonstrated to play critical roles in regulating cancer development and progression. Nevertheless, its biological functions and molecular mechanisms in hepatocellular carcinoma (HCC) remain currently unclear.
Method: The expression of KIAA1522 was screened from The Cancer Genome Atlas (TCGA) and validated in HCC tissues and cell lines using RT-qPCR, Western blot and immunohistochemistry (IHC). The functions of KIAA1522 on HCC progression were determined using loss-of-function and gain-of-function experiments both in vitro and in vivo. The interaction of KIAA1522 with prolyl 4-hydroxylase subunit beta (P4HB) was determined using Immunoprecipitation/mass spectrum, co-immunoprecipitation, immunofluorescence and IHC. Pathway enrichment was performed using gene set enrichment analysis (GSEA).
Results: The present study demonstrated that the KIAA1522 expression level was significantly overexpressed in HCC tissues and cell lines. KIAA1522 expression level was closely correlated with unfavorable clinicopathological characteristics. Stepwise survival analyses revealed that upregulated KIAA1522 expression level predicted poor overall survival and higher recurrence probability in HCC patients. Functional studies revealed that KIAA1522 significantly promoted HCC proliferation, migration and invasion both in vitro and in vivo. Mechanistically, KIAA1522 could interact with P4HB to stabilize P4HB by inhibiting its ubiquitin-mediated degradation and subsequently activated mTOR1 signaling which was verified by the subsequent experiments.
Conclusion: In this study, we determined the oncogenic role of KIAA1522 on HCC by interacting with P4HB to activate mTOR1 signaling, and provided a promising therapeutic target for HCC.

Abstract #1712

Efficacy of combined electric-field and C-Plane imaging for ultrasound-ultrasound fusion imaging for monopolar radiofrequency ablation

Masashi Hirooka[1], Yohei Koizumi[1], Takaaki Tanaka[1], Yoshiko Nakamura[1], Atsushi Yukimoto[1], Kotarou Sunago[1], Takao Watanabe[1], Yoshio Tokumoto[1], Masanori Abe[1], Yoichi Hiasa[1]

[1]Department of Gastroenterology and Metabology, Ehime University Graduate School of Medicine, Touon, Japan

Objectives: Ablation area in the head cannot be envisaged preoperatively, even by experts. This study aimed to assess the clinical feasibility of combined electric-field (E-field) and coronary (C)-plane simulations for ultrasound-ultrasound (US-US) fusion imaging for radiofrequency ablation.
Subjects and methods: The study protocols were approved by the institutional ethics committee. Between October 2017 and July 2019, 151 patients with 151 hepatocellular carcinoma (HCC) nodules were enrolled retrospectively (80 patients were treated by monopolar ablation with navigation images and 71 by monopolar ablation without navigation images). The E-field applied to acquire the US–US fusion images was determined from heat source distribution. C-plane was defined as a sagittal plane in relation to the original two-dimensional multiplanar reconstruction images, which was synchronized to B-mode images acquired by virtual US. Positions of each E-field area in the maximum cross-sectional area of the tumor were identified from the C-plane results. Shape of the ablation volume and width of the safety margin were assessed.
Results: Clinical characteristics showed no significant differences between the two groups. The median sphericity was 0.55 with navigation images and 0.42 without navigation images ($P < 0.001$). The rate of achieving a sufficient safety margin (> 5 mm) was significantly higher in the group treated with navigation images (71/80) than the group treated without navigation images (31/71; $p < 0.001$).
Conclusions: Combined use of E-field and C-plane for US-US fusion imaging can be a feasible method to ensure sufficient safety margin during radiofrequency ablation.

Abstract #1743

Role of aryl hydrocarbon receptor nuclear translocator and aryl hydrocarbon receptor pathway in hepatoma cell metabolism genes

Fun-Yu Su[1], Ching-Hui Lin[1], Ren-In You[1]

[1]Department of Laboratory Medicine and Biotechnology, Tzu Chi University, College of Medicine, Hualien, Taiwan

Introduction and aims: The Aryl hydrocarbon Receptor Nuclear Translocator (ARNT) triggers signal via binding with partner

members, which are HLH (helix–loop–helix)–PER–ARNT–SIM (bHLH/PAS) family of transcription factors. Hypoxia-Inducible Factor-1-α (HIF-1α), Hypoxia-Inducible Factor-2-α (HIF-2α) and Aryl hydrocarbon Receptor (AhR) are the basic members of bHLH/PAS family. When ARNT interacting with different partners, this allows formation of active transcription complexes, which regulates gene expression for cell proliferation, metabolism and invasion/metastasis pathways. Some reports have proved that AhR involved in regulating liver functions.

Methods: To investigate the relationship of ARNT with AhR mediated pathways in liver, we firstly accessed the AhR and ARNT nucleus location by fluorescence microscopy. We found that AhR co-localize with ARNT in HepG2 hepatoma cell line and heat shock protein 90 inhibitor (Geldanamycin) can block AhR translocation. We further evaluated the AhR-associated mRNA expression, and found the induction of Cyp1a1, SULT1a1 and UGT1a8 expression under AhR ligand stimulation. In addition, we performed liver immunohistochemistry by staining the tissue sections with anti-AhR and anti-ARNT antibodies.

Results and conclusion: We found that the expression pattern of AhR and ARNT in the tissue sections are co-localized. These hints suggest that AhR and ARNT play roles in the regulation of liver function and could be a valuable tool in evaluating hepatoma drug response

Abstract #1790

HIF-1α and HDAC1 mediated down-regulation of LncRNA FAM99A contributes to hypoxia induced hepatocellular carcinoma cell metastasis

Bixing Zhao[1], Kun Ke[1], Yingchao Wang[1], Fei Wang[1], Xiaolong Liu[1], Jingfeng Liu[1]

[1]The United Innovation of Mengchao Hepatobiliary Technology Key Laboratory of Fujian Province, Mengchao Hepatobiliary Hospital of Fujian Medical University, Fuzhou 350025, Peoples' Republic of China

Introduction and objectives: Hypoxic microenvironment is clinically associated with metastasis and poor prognosis of numerous cancers. Previous studies have shown that many protein-coding genes and microRNAs are regulated upon hypoxia and involved in the progression of cancer. However, the roles of lncRNAs in the hypoxia-responsive gene networks and how lncRNA-related signaling network regulates hypoxia-induced tumor metastasis is still not clear.

Methods: The expression of lncRNA FAM99A was analyzed in 103 paired HCC tissues by RT-qPCR and the correlation between FAM99A expression and clinical pathology features was analyzed. The function of FAM99A on HCC cell metastasis was analyzed by transwell, wound healing assay and tail vein injection metastasis model in mice. Downstream microRNA targets of FAM99A was studied by bioinformatics analysis and luciferase reporter assays. The binding of HIF-1α, HDAC1 to the promoter region of FAM99A and the histone acetylation of FAM99A promoter were analyzed by ChIP assays and luciferase reporter assays.

Results: LncRNA FAM99A is down-regulated in HCC and correlates with poor prognosis. Moreover, FAM99A inhibits HCC metastasis by acting as a miR-92a sponge both in vitro and in vivo. More importantly, HIF-1α induces the down-regulation of FAM99A via hypoxic-environment. Mechanism wise, HIF-1α binds to the hypoxia response elements on the FAM99A promoter and recruits HDAC1 to repress FAM99A expression by reducing the histone acetylation of FAM99A promoter region.

Conclusion: Hypoxic microenvironment down-regulates FAM99A expression via HIF-1α–HDAC1 mediated histone acetylation modification, resulting in the upregulation of miR-92a and downregulation of E-cadherin mediated signaling pathways to facilitate HCC metastasis.

Abstract #1845

Tissue transglutaminase promotes metastatic potential and cancer stemness of hepatocellular carcinoma

Wenyue Tian

Introduction: Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related deaths. Tissue transglutaminase (TG2) has shown to play a critical role in cancer progression, invasion, migration, and stemness of many cancer types.

Objectives: The role of TG2 in stemness and molecule mechanism of invasion and migration in HCC progression remains unclear.

Methods: Two cell line with stable knockdown and overexpression of TG2 were established (shRNA-TG2, OE-TG2). Cell migration and invasion ware analyzed by wound healing and transwell assay. The expression levels of TG2, integrinβ1, phosphorylation of PI3K and Akt in the cells were examined via western blot. Cancer stemness was analyzed by self-renewal ability, expression of stemness-related genes and CSC marker-positive cell populations. We also investigated TG2 expression level in different HCC patients by Immunohistochemistry.

Results: Our data showed overexpression of TG2 contributes to migratory and invasive phenotypes while knockdown TG2 exhibited the opposite results. The integrinβ1, phosphorylation of PI3K and AKT were associated with the quantity of TG2. Besides the effects on metastatic phenotypes, we also observed that TG2 contributes to HCC stem-like properties. Knockdown of TG2 impair the Spheroid formation ability. The expression of stemness-related genes (CD44\SOX2\EpCAM\OCT4)and $CD133^+$ cells were increased in the overexpression group. Immunohistochemistry revealed higher TG2 expression level in Poorly differentiated carcinoma than Highly differentiated carcinoma.

Conclusion: TG2 expression is critical for cancer cell migration, invasiveness and cancer cell-stemness during HCC progression.

Abstract #1850

Quantitative magnetic resonance imaging shows improved parenchymal health following contralateral lobar hypertrophy after selective internal radiation therapy (SIRT) with Yttrium-90 for hepatocellular carcinoma

Seah, Stephanie[1], Ng, David CE[2], Gogna, Apoorva[3], Goh, Brian KP[4], Tai, David W-M[5], Toh, Han Chong[5], Chan, Wan Ying[6], Hennedige, Tiffany[6], Tan, Iain BH[5], Lo, Richard HG[3], Yan, Sean XX[2], Chua, Clarinda[5], Koo, Si Lin[5], Lim, Tony KH[7], AL, Julianah[8], Chua, Siew Huang[8], Connell, John[9], Jenkins, Lewis[9], Thng, Choon Hua[6], Kelly, Matt[9], Banerjee, Rajarshi[9], Brady, Michael[9], Chow, Pierce K-H[10]

[1]Perspectum Diagnostics, Singapore, [2]Department of Nuclear Medicine and Molecular Imaging, Singapore General Hospital, Singapore, [3]Department of Vascular and Interventional Radiology, Singapore General Hospital, Singapore, [4]Department of Hepatopancreatobiliary and Transplant Surgery, Singapore General Hospital, Singapore, [5]Division of Medical Oncology, National Cancer Centre, Singapore, [6]Division of Oncologic Imaging, National Cancer Centre, Singapore, [7]Department of Anatomic Pathology, Singapore General Hospital, Singapore, [8]Speciality Nursing, Singapore General Hospital, Singapore, [9]Perspectum Diagnostics, Oxford, United

Kingdom, [10]Division of Surgery and Surgical Oncology, National Cancer Centre, Singapore

Introduction: Selective internal radiation therapy (SIRT) with Yttrium-90 (Y90) (or radio-embolization) is loco-regional therapy for locally advanced hepatocellular carcinoma (HCC) minimising collateral injury to the adjacent liver parenchyma. 20% of patients still develop grade 3/4 bilirubin toxicity. Liver*MultiScan* is a multiparametric MRI-based tool quantifying iron-corrected T1 (cT1) and proton density fat fraction (PDFF) which correlate with hepatic fibro-inflammation and steatosis respectively.
Objectives: To determine progressive cT1 and PDFF changes in the adjacent liver parenchyma with Liver*MultiScan* pre/post Y90 SIRT for HCC.
Methods: In this prospective clinical study, inclusion criteria were patients with locally advanced HCC (BCLC B or BCLC C without extra-hepatic metastases), Child-Pugh ≤ 7, ECOG 0–1 who underwent single delivery of SIRT as mono- therapy. Liver*MultiScan* was carried out before and at 1 and 3 months after SIRT.
Results: 7 patients were recruited. At baseline, mean $\pm$ SD liver parenchymal cT1 was 790 $\pm$ 72 ms. At 1 and 3 months post-treatment, mean cT1 values were 761 $\pm$ 48 ms and 716 $\pm$ 46 ms, respectively. Significant reduction in cT1 was observed ($p < 0.001$) between baseline and 3 months post-treatment. No significant change in mean PDFF values were observed across the three timepoints.
Conclusion: Reduction in liver parenchymal cT1 with hypertrophy of the contralateral lobe possibly represents an improvement in hepatic health or new liver tissue growth. Confirming the mechanism behind this may allow selection of patients post-SIRT for curative resection consequently. Liver*MultiScan* potentially offers a unique, quantitative MRI process by which the effect of therapeutic interventions on adjacent parenchyma can be quantified and modelled.

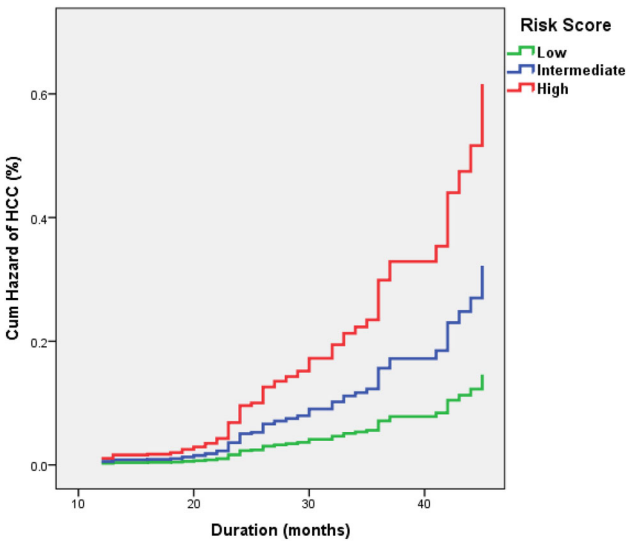
Abstract #1885

A simple score for hepatocellular carcinoma risk stratification in CHC patients with cirrhosis who achieved SVR following direct acting antivirals

Gamal Shiha[1,2], Reham Soliman[1,3], Nabiel NH Mikhail[1,4], Talal Amer[1], Mohammed Eslam[5] Imam Waked[6]

[1]Egyptian Liver Research Institute and Hospital (ELRIAH), Sherbin, El Mansoura, Egypt, [2]Hepatology and Gastroenterology Unit, Internal Medicine Department, Faculty of Medicine, Mansoura University, Egypt, [3]Tropical Medicine Department, Faculty of Medicine, Port Said University, Egypt, [4]Biostatistics and Cancer Epidemiology Department, South Egypt Cancer Institute, Assiut University, Egypt, [5]Storr Liver Centre, Westmead Institute for Medical Research, Westmead Hospital and University of Sydney, NSW, Australia. [6]Hepatology Department, National Liver Institute, Menoufia University, Shebeen Elkom, Egypt

Background and aims: Patients with advanced fibrosis (F3) or cirrhosis (F4) who achieved sustained virologic response (SVR) following direct-acting antivirals (DAAs) continue to have risk for hepatocellular carcinoma (HCC) for several years. Our aim to develop a model that offer individualized patient HCC risk prediction.
Methods: This is a prospective study including CHC F3 or F4 patients who achieved SVR following DAAs. Factors associated with HCC were identified through multivariable Cox regression and used to develop a scoring model for prediction of HCC risk and the performance of the model was assessed by Receiver operating characteristic (ROC) curve. Internal and external validation was done.
Results: 2326 CHC consecutive F3 and F4 patients who achieved SVR were included as training set. Follow up period was 23.51 $\pm$ 8.21 months. 109 patients (4.7%) developed HCC during the follow up. Age, sex, serum albumin, α-feto-protein (AFP) and pre-treatment fibrosis stage were identified as risk factors for HCC. A simple predictive model was constructed by assigning points for each covariate in proportion to the hazard ratios in the multivariable model. Using ROC analysis, patients were then stratified into three groups (low, intermediate and high risk). The 2-year cumulative HCC incidence using Kaplan–Meier method was 2%, 4.5% and 10.3% in the low-risk, medium-risk and high-risk groups respectively. Internal and external validation showed highly significant difference between the three risk groups ($p < 0.001$) as regards cumulative hazard of HCC.
Conclusion: The GES score, using readily available parameters, has good predictive ability for development of HCC after eradication of HCV. It may be useful for HCC risk stratification in CHC patients with cirrhosis who achieved SVR following direct acting antivirals.



Abstract #2090

Effectiveness of transarterial radioembolization (TARE) compared to transarterial chemoembolization (TACE) for patients with hepatocellular carcinoma

Irsan Hasan[1], Abigail Prasetyaningtyas[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Patients with hepatocellular carcinoma (HCC) are often diagnosed in the intermediate stage for whom liver resection is no longer an option. Transarterial chemoembolization (TACE) is a recommended locoregional therapy for intermediate stage HCC patients; however, it is associated with complications such as postembolization syndrome, liver failure, and metastasis. Transarterial radioembolization (TARE) can be considered as an alternative to TACE for unresectable HCC patients.
Objectives: This study serves to compare the survival rate of HCC patients receiving TARE compared to TACE.
Methods: Online search of PubMed, Cochrane Library, and Google Scholar led to two meta-analyses. Only relevant clinical studies or meta analyses with human subjects and written in English were included. Critical appraisal was performed with the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) Guideline.

Results: Zhang et al reported that survival rate up to 4 years were not statistically different between patients receiving TARE compared to TACE (HR 1.06, 95% CI 0.81–1.46, p = 0.56). Facciourusso et al also reported that one-year survival rate was not different between the two groups (OR 1.01, 95% CI 0.78–1.31, p = 0.93).
Conclusion: There was no difference in effectiveness of TARE compared to TACE in terms of increasing survival rate of HCC patients.

Abstract #2113

Transarterial chemoembolization response and polarization of Th17/Th1-like cells in hepatocellular carcinoma patients

Irsan Hasan[1], Rino Alvani Gani[1], Laurentius A Lesmana[1], Siti Boedina Kresno[2], Jacub Pandelaki[3], Suhendro Suwarto[1]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Department of Clinical Pathology, Dharmais Cancer Hospital, Jakarta, Indonesia, [3]Department of Radiology, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Background: The immune system played an essential role in malignancy, including hepatocellular carcinoma (HCC). Th17 cells, an IL-17 producing-cells, has controversial effect, both pro-tumor and anti-tumor, in HCC. Meanwhile, Th1, IFN-γ producing-cells, are the most effective in eliminating tumor cells. Most of the newly-diagnosed HCC patients in Indonesia had unresectable tumor. Transarterial chemoembolization (TACE) is the palliative treatment of choice for these patients.
Objective: To determine the role of Th1, Th17, IL-17, and IFN-γ towards the response to TACE treatment.
Method: A prospective cohort study was conducted in Cipto Mangunkusumo National General Hospital and several affiliated hospitals in Jakarta from June 2015 to January 2019. HCC and cirrhosis patients that fulfilled the inclusion and exclusion criteria were enrolled in this study. Blood samples were obtained immediately before and 30 days after TACE. Th1 and Th17 were analyzed using flow cytometry. IL-17 and IFN-γ were examined using ELISA technique. TACE response was evaluated with the mRECIST criteria.
Results: 41 HCC and 40 cirrhosis patients were enrolled in this study. mRECIST response group (complete and partial response) and non-response group (stable disease and progressive disease) were reported in 12 and 29 patients, respectively. The levels of Th1, Th17, and CD4 +/IFN-γ +/IL-17 + T cells levels were significantly increased after TACE in the response group. On the other hand, IL-17 and IFN-γ were found decreased after TACE in both response and nonresponse group but not statistically significant.
Conclusions: Increased circulating Th17 and CD4 +/IFN-γ +/IL-17 + T cells were observed in HCC patients with excellent response to TACE.

Abstract #2240

Perioperative management for portal hypertension in patients with hepatocellular carcinoma

Takemura Nobuyuki[1], Hasegawa Kiyoshi[2], Aoki Taku[3], Arita Junichi[2], Kaneko Junichi[2], Akamatsu Nobuhisa[2], Kokudo Norihiro[4]

[1]Department of Surgery, Hepato-Biliary Pancreatic Surgery Division, National Center for Global Health and Medicine, Tokyo, Japan, [2]Department of Surgery, Hepato-Biliary-Pancreatic Surgery Division, Artificial Organ and Transplantation Division, Graduate School of Medicine, University of Tokyo, Tokyo, Japan, [3]Second Department of Surgery, Dokkyo Medical University, Tochigi, Japan, [4]President, National Center for Global Health and Medicine, Tokyo, Japan

Introduction: Patients with hepatocellular carcinoma (HCC) frequently have concomitant portal hypertension (PH) and complications associated with PH present obstacles for liver resection. Some studies have concluded that PH is a contraindication for hepatectomy, while others present perioperative prophylactic management (PPM) to overcome post-hepatectomy complications associated with PH.
Objectives: To assess the short- and long-term outcomes after hepatectomy for HCC in patients with PH with or without PPM.
Methods: Patients who underwent hepatectomy and/or preoperative management of PH for HCC in this single institution from 1994 to 2015 were reviewed retrospectively. Patients were divided into three groups according to the status of PH: PPM, non-PPM (who had PH but did not receive PPM), and non-PH.
Results: A total of 1259 patients were enrolled, including 123 in the PPM group, 181 in the non-PPM group, and 955 in the non-PH group. Three and 5-year overall survivals were 74.3% and 53.1% in the PPM group, 69.2% and 54.9% in the non-PPM group, and 78.1% and 64.2% in the non-PH group, respectively. Postoperative morbidity and mortality rates were 26.0% and 0.8% in the PPM group, 29.8% and 1.1% in the non-PPM group and 20.3% and 0% in the non-PH group, respectively.
Conclusion: Enhancement of the safety of hepatic resection through use of PPM may provide an acceptable prognosis for patients with HCC and PH.

Poster Presentations

Abstract #17

Relative dose intensity is very important to maximize the effect of lenvatinib among advance hepatocellular carcinoma patients

Takamasa Ohki[1], Hideo Yoshida[2], Shuntaro Obi[3]

[1]Mitsui Memorial Hospital, Department of Gastroenterology, [2]Japan red-cross medical center, Department of Gastroenterology, [3]Teikyo Chiba medical center, Department of Gastroenterology

Backgrounds and aims: Lenvatinib (LEN) is a newly developed tyrosine kinase inhibitor (TKI) in Japan and approved as a first-line treatment for advanced hepatocellular carcinoma (HCC) in March 2018. Thus, the experience of LEN in real clinical settings is still limited. We conducted this study to elucidate the importance of relative dose intensity (RDI) on its effect and progression free-survival (PFS).
Methods: In this retrospective study, we enrolled 77 advanced HCC patients treated with LEN from 8 hospitals in Japan between 2018 March and 2019 May. We divided these patients into 2 groups according to RDI until the first month; RDI over or equal to 70% (group 1, N = 42), RDI under 70% (group 2, N = 35). We evaluated each patient's background, response rate based on mRECIST and PFS. We also performed multivariate analysis to clarify the significant factors contributed to response rate and PFS.
Results: The proportion of Child-Pugh 5A had a tendency to be higher in group 1 (P = 0.06). On the other hands, the number of patients who needs cessation due to adverse events were significantly higher in group 2 (22.9% vs. 4.8%, P = 0.04). The response rate

(CR + PR) was significantly higher in group 1 (45.2% vs. 11.4%, $P < 0.01$). Multivariate analysis showed RDI over or equal to 70% (OR 5.61, P = 0.015), Child-Pugh 5A (OR 4.77, P = 0.018), and reduction of AFP level (OR 10.3, $P < 0.01$) as independent factors contributed to response rate. COX proportional multivariate analysis revealed Child-Pugh 5A (HR 0.41, P = 0.027), grade over 2 thyroid dysfunction (HR 4.57, $P < 0.01$), grade over 1 appetite loss (HR 3.58, $P < 0.01$), maximum tumor size over 4 cm (HR 2.27, P = 0.015), and responder (HR 0.40, P = 0.039) as independent factors related to PFS.
Conclusions: It is very important to achieve RDI over or equal to 70% until the first month to maximize the effect of LEN. If the RDI does not reach to 70%, we should consider to change the treatment because the effect of LEN is limited when RDI is under 70%.

Abstract #20

Adrenal metastasis as a poor prognostic indicator in hepatocellular carcinoma after complete response from serial transarterial chemoembolization: a case report

Lutfie[1], Nababan S[2], Gani RA[2], Hasan I[2], Sanityoso A[2], Lesmana CR[2], Kurniawan J[2], Jasirwan CO[2], Kalista KF[2]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Dr. Cipto Mangunkusumo General Hospital, Jakarta, [2]Division of Hepatobiliary, Faculty of Medicine Universitas Indonesia, Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia

Introduction: Adrenal metastasis from primary hepatocellular carcinoma (HCC) is quite rare, with the incidence of only 1–3.9%. Hereby, we report a case of adrenal metastasis from HCC after complete response from serial transarterial chemoembolization (TACE).
Case illustration: A male patient, 71 years old with chronic hepatitis B infection, came to our clinic for radiological evaluation after serial TACE. The patient was diagnosed with HCC BCLC stage B for two years, had undergone TACE three times in segment 7–8, with complete response according to modified response evaluation criteria in solid tumor (mRECIST) criteria. Three months later, we found a left suprarenal mass and a new viable nodule in segment 6. The patient underwent left adrenalectomy, and it was histopathologically confirmed to be a metastatic lesion from HCC. We planned sorafenib treatment for the patient. During follow up, we found the patient had a declining performance status, with a new right adrenal mass, a new lung metastasis, and increasing size of liver nodule in segment 6. The patient died six months after the adrenal metastasis.
Discussion: Adrenal metastasis in HCC is rarely seen in clinical practice because of its lower metastatic potential compared to the other malignancies. The metastasis in this patient may occur due to either virological breakthrough or tumoral angiogenesis due to post-TACE alteration in several vascular regulatory factors. Some authors advocate several treatment options to prolong survival, including adrenalectomy, ablation, or chemoembolization. However, if remain untreated, 1 year survival has been reported only as low as ± 5.4 months.
Conclusion: Adrenal metastasis in primary HCC might indicate poor prognosis. Further investigations are needed to improve patient's survival.

Abstract #22

Latent transforming growth factor-beta binding protein 1: molecular diagnostic marker for hepatocellular carcinoma in Egyptian patients

Olfat M. Hendy[1], Bishoy El-Aarag[2] and Mohamed Abdel-Samiee[3]

[1]Clinical Pathology Department, National Liver Institute, Menoufia University, Shebin Elkom, Menoufia, Egypt, [2]Biochemistry Division, Chemistry Department, Faculty of Science, Menoufia University, Shebin Elkom, Menoufia, Egypt, [3]Hepatology and Gastroenterology Department, National Liver Institute, Menoufia University, Shebin Elkom, Menoufia, Egypt

Introduction: Worldwide, hepatocellular carcinoma (HCC) consider the most common liver cancer and a leading cause of cancerrelated death. The latent transforming growth factor-beta binding protein 1 (LTBP-1) is a secreted protein and considers as a part of the extracellular matrix (ECM). In human malignant gliomas, the expression of LTBP-1 was gradually increased. Additionally, LTBP-1 expression was extremely strong in numerous malignant tumors.
Objectives: Therefore, the current study aims to evaluate the diagnostic role of LTBP-1 as a biomarker to distinguish HCC from Egyptian patients with liver cirrhosis.
Methods: The present study included 90 individuals; 40 HCC patients, 30 patients withcirrhosis, and 20 healthy volunteers as a control group. The serum level of LTBP-1 and AFP (alfa fetoprotein) were measured by enzyme-linked immunosorbent assay (ELISA). Receiver operating characteristics (ROC) curves and area under the curve (AUC) were calculated.
Results: revealed that the level of LTBP-1 was significantly higher in HCC patients than healthy and patients with cirrhosis. Furthermore, there was a significant ($p < 0.001$) association between the level of LTBP-1 and CLIP and BCLC inHCC patients. Moreover, LTBP-1 levels were significantly ($p = 0.01$) associated to child Pugh grade in patients withcirrhosis and HCC. ROC curve analyses revealed that LTBP-1 showed a better diagnostic performance (AUC = 0.970, Sensitivity: 82.50%, Specificity: 96.67%, PPV: 97.06%, NPV: 80.56%) in distinguishing HCC from cirrhosis patients, compared to AFP (AUC = 0.810, Sensitivity: 62.50%, Specificity: 93.33%, PPV: 92.59%, NPV: 65.12%). The level of LTBP-1 in HCC patients was significantly ($p < 0.001$) associated with CLIP score. Because, the LTBP-1 was gradually increased with CLIP score increasing, where LTBP-1 concentration in score 5 recorded 49.1 against to 19.4 in score 0. Conversely, AFP was not significantly (p = 0.098) associated with CLIP score. Regarding to BCLC, there was a significant ($p < 0.001$) association between the serum level of LTBP- 1 and BCLC score in HCC patients. The LTBP-1 level was gradually increased with the progress in BCLC score, where, the level was 46.8 in score 4 against 26.6 in score 0. Conversely, AFP level was not significantly ($p = 0.172$) associated with BCLC score.
Conclusion: Taken together, serum LTBP-1might be a potential serum marker to discriminate HCC from livercirrhosis patients due to its high sensitivity and specificity, compared to AFP. LTBP-1 might be a promising diagnostic biomarker for HCC. Further studies on large scale of patients are required to validate the attained results.

Table 1: Correlation between LTBP-1 and different clinopatholigical parameters in cirrhosis and HCC groups

Variable	LTBP-1			
	Cirrhosis (N=30)		HCC (N=40)	
	r	*P value*	*r*	*P value*
Age (Year)	-0.083	0.662	-0.264	0.100
AST (U/L)	0.306	0.100	0.361*	0.022
ALT (U/L)	0.131	0.491	0.104	0.522
ALP (U/L)	0.217	0.250	0.205	0.203
GGT (U/L)	0.225	0.232	-0.031	0.850
Total Bilirubin (mg/dl)	0.098	0.605	0.493**	0.001
Direct Bilirubin (mg/dl)	0.011	0.952	0.509**	0.001
Albumin (g/dl)	-0.328	0.077	-0.488**	0.001
Urea (mg/dl)	-0.114	0.547	0.399*	0.011
Creatinine (mg/dl)	-0.078	0.684	0.208	0.198
Prothrombin Conc.	-0.127	0.505	-0.447**	0.004
INR	0.127	0.503	0.401*	0.010

**. Correlation is significant at the 0.01 level
*. Correlation is significant at the 0.05 level

Table 2: Serum levels of AFP and TBP-1in association to CLIP score in HCC patients

CLIP score	*N*	AFP *Mean + SD*	*P- value*	LTBP-1 *Mean + SD*	*P- value*
0	7	117.8 ± 106.1	0.098	19.4 ± 0.7	< 0.001
1	8	593.5 ± 1004.3		26.0 ± 8.3	
2	5	1337.6 ± 2325.2		26.5 ± 2.4	
3	11	15791.6 ± 32407		31.9 ± 3.6	
4	5	949.4 ± 1218.7		38.2 ± 6.8	
5	4	33403.0 ± 39891.9		49.1 ± 5.7	

Table 3: Serum levels of AFP and TBP-1in relationship to BCLC score in HCC patients

BCLC score	*N*	AFP *Mean + SD*	*P- value*	LTBP-1 *Mean + SD*	*P- value*
0	4	599.3± 1051	0.172	26.6 ± 11.1	< 0.001
1	14	687.7± 1499.2		22.5 ± 4.5	
2	7	10591 ± 20256		33.1 ± 6	
3	11	21478.8± 37639.9		34.0 ± 6.5	
4	4	474.9± 909.8		46.8 ± 9	

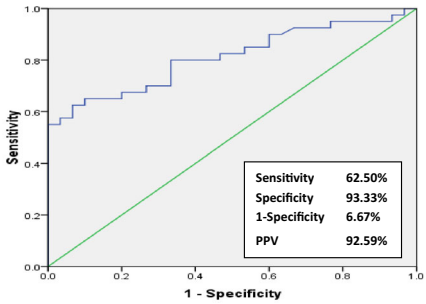


Figure 1: ROC curve analysis of AFP as a predictor of HCC between cirrhosis and HCC groups. At a cut-off value 42.8ng/ml, AFP had an area under the curve of 0.810 the percent of specificity and sensitivity was 93.3 and 62.5, respectively.

Abstract #83

Risk factors for hepatocellular carcinoma in men of northeast regions of Asia with high, medium, and low incidence rates

Malov Sergey[1,2], Baatarkhuu Oidov[3], Sleptsova Snezhana[4], Evgeniy Savilov Evgeniy[2,5], Rasulov Rodion[2], Malov Igor[1]

[1]Irkutsk State Medical University, Irkutsk, Russia, [2]Irkutsk State Medical Academy of Continuing Education, Irkutsk, Russia, [3]Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [4] North-Eastern Federal University, Yakutsk Russia, [5]Scientific Center of Family Health and Human Reproduction Irkutsk, Russia

Introduction: Hepatocellular carcinoma (HCC) is one of the most common forms of primary liver cancer. More than half of all HCC cases worldwide are reported in countries in Asia and Africa.
Objectives: To assess the significance of certain genetic and external risk factors for HCC in males of northeast regions of Asia with different incidence rates.
Patients and methods: The study was performed in the adjacent territories of northeast Asia: the Asian part of Russia (Rus-Asia), the Republic of Sakha (Yakutia) and Mongolia. 198 male patients diagnosed with HCC were examined, including 46 people from Rus-Asia, 44 from Yakutia, 108 from Mongolia. HCC risk factors were identified by analyzing medical records and questioning patients.
Results: The average incidence rate of HCC over the past 10 years in Rus-Asia was 4.9‰; in Yakutia—14.9‰; Mongolia—55.5‰. HBV, HDV or HCV markers were identified in Rus-Asia—72.8%, Yakutia—100%, Mongolia—96.2%. Incidence of co-infection (HBV ± HDV ± HCV) was found in Rus-Asia, Yakutia and Mongolia (9.1%, 25.0% and 15.7%, respectively). Among non-infectious factors, the highest prevalence of alcohol abuse (> 16 points on the Audit scale) was found in Rus-Asia (17.3%), obesity and diabetes mellitus—in Yakutia (20.5% and 6.8%, respectively).
Conclusion: the incidence of HCC is primarily associated with the prevalence of parenteral viral hepatitis. Obesity and alcohol consumption are additional risk factors that can be managed through healthy lifestyle promotion.

Abstract #85

Serum anti-14-3-3zeta autoantibody as a biomarker for predicting hepatocarcinogenesis in pre-malignant liver disease

Ting Wang[1], Sujun Zheng[1], Mei Liu[1]

[1]Beijing You'an Hospital, Capital Medical University, Beijing, China

Introduction: 14-3-3zeta protein is one of 14-3-3 protein family members which are involved in various cellular processes such as cell cycle regulation, apoptosis, proliferation, and differentiation. Studies have shown that over expression of 14-3-3zeta had been observed in a variety of tumor types including hepatocellular carcinoma (HCC). Our previous study found that the level of anti-14-3-3zeta autoantibody was significantly higher in the sera of patients with HCC than other chronic liver diseases and normal human sera. In addition, the anti-14-3-3zeta autoantibody had been detected in the sera from HCC patients at 9 months before the clinical diagnosis of HCC. Liver cirrhosis (LC), which comes from liver fibrosis, has been commonly considered as a pre-malignant liver disease of HCC, and 80–90% HCC patients were developed from LC. Thus, early detection of anti-14-3-3zeta autoantibody in LC may be significant in predicting hepatocarcinogenesis.
Objectives: To investigate the prevalence of serum autoantibody against 14-3-3zeta in pre-malignant liver disease and evaluate its feasibility in prediction of hepatocarcinogenesis.
Methods: Ninety three sera samples from liver cirrhosis (LC), 75 sera samples from chronic hepatitis (CH),60 sera from normal human controls (NHC) and 5 sera samples from one AFP negative HCC patient with serial bleeding samples were used in this study. Autoantibody against 14-3-3 zeta in serais evaluated by enzyme-linked immunosorbent assay (ELISA), western blot, and indirect immunofluorescence assay.
Results: The prevalence of autoantibody against 14-3-3zeta was 16.1% (15/93) in LC, which was significantly higher than that in CH, and NHS ($P < 0.01$). Serial serum samples showed the anti-14-3-3zeta autoantibody appeared in sera 9 months before the diagnosis of HCC and gradually increased as the size of the nodule increased,

which was subsequently proved to be a tumor nodule. Furthermore, univariate and multivariate analysis showed that anti-14-3-3zeta autoantibody was significantly associated with Child-Pugh grade ($p = 0.015$).
Conclusion: The prevalence of serum anti-14-3-3zeta autoantibody is high in patients with pre-malignant liver disease. Positive anti-14-3-3zeta autoantibody may be a biomarker for predicting hepatocarcinogenesis in pre-malignant liver disease.

Abstract #92

Perspectives in hepatocellular carcinoma management in a tertiary care centre in South India

Garg A[1], Mathew P[1], Kanni P[1], Pandey S[2], Ansari J[1], Gowda M[1]

[1]Department of Gastroenterology and Hepatology, VIMS and RC, Bangalore, India, [2]Interventional Radiologist, Department of Radiology, VIMS and RC, Bangalore, India

Introduction: Hepatocellular carcinoma (HCC) is a primary cause of liver cancer leading to death worldwide. Meanwhile, in a country like India where because of financial constraints for patients, Liver transplantation is not popular in spite of being offered to patients. Thus, HCC is managed with the best available treatment options.
Methods: Prospective study was conducted in which a total of 21 diagnosed cases of HCC patients were managed and treatment strategy was planned according to Barcelona Clinic Liver Cancer staging over a period of 3 years.
Results: Study showed male predominance (85%). Mean age was 65 ± 5 years. The Etiology was mainly Hepatitis B (70%), followed by Hepatitis C (25%). 60% patients were asymptomatic. Serum Alpha fetoprotein was raised in 45% of patients. Unresectable cases, underwent loco regional therapy. Transarterial Chemoembolization (TACE) was done in 9 patients, Radiofrequency Ablation (RFA) in 3 patients, TACE + RFA in 6 patients, TACE + Ethanol ablation in 1 patient, TACE followed by Curative Partial Hepatectomy in 1 patient and Only Sorafenib in 1 patient. Median Survival of patients is 2 years after TACE + RFA with no recurrence, TACE patients had a median survival of 6–8 months in which 44% had recurrence. RFA patient's survival is around 1 year, after which the patient developed recurrence. TACE + Ethanol and TACE + Surgery patients are on follow up with no recurrence.
Conclusion: HCC is potentially curable if discovered in its initial stages. Strategies for early diagnosis and treatment of HCC is a way to decrease mortality.

Abstract #137

Tumor size and survival outcomes after liver resection in patients with a solitary hepatocellular carcinoma without macroscopic vascular invasion

Shinkawa Hiroji[1], Tanaka Shogo[1], Takemura Shigekazu[1], Amano Ryosuke[1], Kimura Kenjiro[1], Yamazoe Sadaaki[1], Ohira Go[1], Nishioka Takayoshi[1], Tauchi Jun[1], Miyazaki Toru[1], Ishihara Atsushi[1], Eguchi Shinpei[1], Shirai Daisuke[1], and Kubo Shoji[1]

[1]Department of Hepato-Biliary-Pancreatic Surgery, Osaka City University Graduate School of Medicine, 1-4-3 Asahimachi, Abeno-ku, Osaka 545-8585, Japan

Objectives: The present study assessed the association of tumor size with the survival in patients with a solitary hepatocellular carcinoma (HCC) without vascular invasion.
Methods: We examined 638 patients who underwent initial and curative hepatic resection for a solitary HCC without macroscopic vascular invasion. A multivariate Cox proportional hazard model and propensity score matching (PSM) were used to evaluate the impact of tumor size on the survival outcome. The baseline tumor size was modeled using restricted cubic splines to allow for nonlinear associations. The tumor size cut-off was 5 cm for PSM analysis.
Results: The tumor size was significantly associated with a proportional increase in the prognostic risk for the overall survival (OS) ($p = 0.0032$); however, a multivariate analysis revealed no significant risk for recurrence-free survival ($p = 0.071$). After PSM, the OS of patients with tumors > 5 cm was significantly worse than in patients with tumors ≤ 5 cm ($p < 0.001$). The 2-year cumulative recurrence rates in patients with tumors ≤ 5 cm and > 5 cm groups were 24.8% and 48.1% ($p = 0.001$). Extrahepatic to total recurrence were noted in 11.1% of those with tumors ≤ 5 cm and 26.5% of those with tumors > 5 cm, respectively. Twelve of 40 patients (30%) in the ≤ 5 cm group and 18 of 36 (50%) in the > 5 cm group had multiple intrahepatic recurrence.
Conclusions: The tumor size was associated with recurrence within postoperative 2 years and poor OS in patients with a solitary HCC despite no vascular invasion being evident.

Abstract #138

Application of the herbal Fuzheng Jiedu Xiaoji decoction suppresses tumors via inhibition of SPARC protein in human hepatocellular carcinoma

Liu Yao[1], Feng Ying[1], Wang Xianbo[1]

[1]Center of Integrative Medicine, Beijing Ditan Hospital, Capital Medical University. Beijing, China

Introduction: The Fuzheng Jiedu Xiaoji decoction (FZJD) is a traditional Chinese herbal medicine developed by the Beijing Ditan Hospital for the treatment of hepatocellular carcinoma (HCC). According to a previous study, a combination treatment including FZJD contributed to significant improvement in the survival rate of patients suffering from HCC, compared to standard treatments alone. However, it is still necessary to determine the mechanisms underlying the effect of FZJD on tumor progression in HCC.
Objectives: The present study aimed at examining how FZJD suppresses the development of HCC, along with its potential mechanism of anticancer action.
Methods: We designed lentiviral vector plasmids that carried interference sequences required for the knockdown of secreted protein acidic and rich in cysteine (SPARC) in HuH-7 cells, in order to determine its tumor suppressive effect in a xenograft model. MTT, plate cloning, and transwell assays were used to characterize its biological functions in HCC cells. Immunoblotting analysis was utilized to quantitate protein expression.
Results: FZJD contributed to the inhibition of proliferation and metastasis of HCC cells at a non-toxic dose, as well as suppression of tumor growth in the xenograft murine model. As observed in both in vitro and in vivo experiments, FZJD remarkably weakened HCC cell proliferation and metastasis via decrease in levels of SPARC and phospho-extracellular signal-regulated kinases 1/2 (p-ERK1/2).
Conclusion: FZJD inhibits HCC cell proliferation and invasion via the SPARC-ERK1/2 pathway.

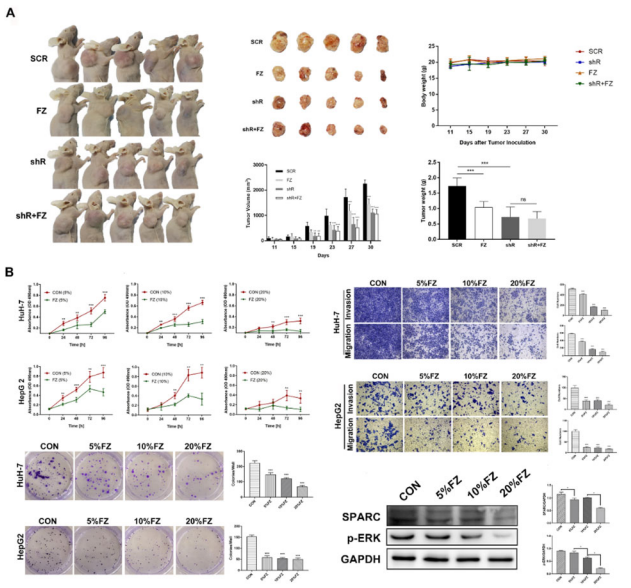


Figure. Fuzheng Jiedu Xiaoji decoction (FZJD) decreases tumor volume and weight in HuH-7 xenografts by acting on SPARC (A). FZJD inhibits the expression of SPARC and decreases level of p-ERK1/2, leading to suppression of HCC cell proliferation, invasion, and migration (B). *p < 0.05, **p < 0.01, and ***p < 0.001.

Abstract #197

The combined sorafenib for the individuals with intermittent stage hepatocellular carcinoma unresponsive to transarterial chemoembolization

Shou-Wu Lee[1], Teng-Yu Lee[1], Sheng-Shun Yang[1], Hong-Zen Yeh[1], Chi-Sen Chang[1]

[1]Division of Gastroenterology, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

Background: Intermittent stage hepatocellular carcinoma (HCC) is typically treated with transarterial chemoembolization (TACE), but its outcomes remain limited. The aim of this study was to determine the outcomes of intermittent stage HCC patients receiving combined sorafenib who were unresponsive to TACE therapy.
Methods: Data were collected from subjects with HCC, BCLC classification stage B, and who were receiving TACE alone, from January 2013 to June 2014, or TACE in combination with sorafenib, from January 2017 to June 2018, at Taichung Veterans General Hospital. The subjects who received TACE alone were classified as the monotherapy group, while those who received both sorafenib and TACE were classified as the combined therapy group.
Results: A total of 64 subjects, comprising 34 in the monotherapy group and 30 in the combined therapy group, were enrolled. The two groups' general data were similar. The mean therapeutic duration of sorafenib was 8.47 months. The patients in the combined therapy group displayed a significantly prolonged time-to-progression (TTP) (mean 14.46 vs. 6.39 months, p = 0.001), and had a non-significantly longer overall survival (OS) (mean 18.96 vs. 15.44 months, p = 1.000) compared with the monotherapy group. The mortality rate was significantly lower at 12–18 months in the combined therapy group, but after adjustment, there was no significant positive association.
Conclusion: The combination of TACE with sorafenib brings about a significantly better TTP than TACE alone for intermittent stage HCC patients who are unresponsive to TACE.

Abstract #210

A multicenter observational study of lenvatinib for unresectable hepatocellular carcinoma in Japan-interim analysis

Izumi Namiki[1], Motomura Kenta[2], Kudo Masatoshi[3], Inaba Yoshitaka[4], Katamura Yoshio[5], Kondo Yasuteru[6], Yabushita Kazuhisa[7], Motoyoshi Katsuaki[8], Furuse Junji[9]

[1]Department of Gastroenterology and Hepatology, Musashino Red Cross Hospital, Tokyo, Japan, [2]Department of Hepatology, Aso Iizuka Hospital, Fukuoka, Japan, [3]Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka, Japan, [4]Department of Diagnostic and Interventional Radiology, Aichi Cancer Center Hospital, Aichi, Japan, [5]Department of Gastroenterology, Onomichi General Hospital, Hiroshima, Japan, [6]Department of Hepatology, Sendai Kousei Hospital, Miyagi, Japan, [7]Department of Internal Medicine, Fukuyama City Hospital, Hiroshima, Japan, [8]Eisai Co., Ltd., Tokyo, Japan, [9]Department of Medical Oncology, Kyorin University Faculty of Medicine, Tokyo, Japan

Background: Lenvatinib has been available for treatment of unresectable hepatocellular carcinoma (uHCC) in Japan since March 2018. We conducted a multicenter prospective observational study to evaluate the safety of lenvatinib in clinical practice.
Methods: This study enrolled patients initially receiving lenvatinib for uHCC as systemic therapy who gave informed consent. From July 2018 through January 2019, 713 patients were registered at 133 clinical sites. Interim analysis was conducted on data collected up to August 2019.
Results: A total of 443 evaluable patients were included in this analysis. Their median age was 73 years (25–94), 96.6% had a PS of 0–1, 88.5% were in Child-Pugh class A, 52.8% were BCLC stage C, 96.2% had Vp 0–3, and 37.2% had extrahepatic metastasis. Previous treatment was TACE (72.7%), HAIC (11.5%) and TKI therapy (22.1%). Treatment-related adverse events (TRAEs) of any grade and ≥ grade 3 occurred in 79.2% and 33.4%, respectively. Common TRAEs (incidence rate ≥ 10%) were hypertension (17.8%), decreased appetite (17.6%), malaise (17.4%), palmar plantar erythrodysesthesia syndrome (14.9%), proteinuria (14.9%), hypothyroidism (12.6%), and diarrhea (10.4%). TRAEs ≥ Grade 3 with an incidence rate ≥ 5% were hypertension (5.9%) and proteinuria (5.4%). The 3–month treatment continuation rate was 68.8%. TRAEs led to discontinuation in 17.2%, including decreased appetite (3.4%) and malaise (2.5%).
Conclusion: This interim analysis showed that the safety and tolerability of lenvatinib in clinical practice were consistent with previous reports.

Abstract #256

Neonatal Streptozotocin treatment rapidly causes hepatocellular carcinoma without continuous hyperglycemia in 4CS mice fed a normal diet

Kobayashi Tomoko[1], Ichimura-Shimizu Mayuko[1], Tsuneyama Koichi[1]

[1]Department of Pathology and Laboratory Medicine, Graduate School of Medical Sciences, Tokushima University, Tokushima, Tokushima 770-8503, Japan

Introduction: Hepatocellular carcinoma (HCC) is one of the most frequent causes of cancer-related death. The etiology of HCC is

diverse, and many unclear points remain about the mechanism of cancer onset and progression. To analyze the carcinogenic mechanism of the liver, it is desired to develop a model animal that exhibits a histology close to human HCC.
Methods: We previously reported DIAR mice develop type 1 diabetes and HCC in a short period of time by neonatal streptozotocin (STZ) treatment. In this study, STZ-resistant 4CS mice were used. Newborn 4CS mice, as well as DIAR mice, were divided into two groups. At 1.5 days after birth, STZ was injected into the treated group, whereas the same volume of physiologic solution was injected into the control group. Mice in each group were assessed at 4, 8, 12, and 16 weeks of age.
Results: The blood glucose level of DIAR-nSTZ mice became high, but that of 4CS-nSTZ mice was almost normal. Pancreatic islets disappeared in DIAR-nSTZ, while many islets remain in 4CS-nSTZ mice. At eight weeks, three out of five DIAR-nSTZ mice and one out of ten 4CS-nSTZ mice exhibited dysplastic nodules. At 16 weeks of age, eight out of eight DIAR-nSTZ mice and eight out of eight 4CS-nSTZ mice exhibited well-differentiated HCC or high-grade dysplastic nodules.
Conclusions: STZ treatment itself induces HCC with or without hyperglycemia. Because 4CS-nSTZ mice did not show any other pathological changes, it is a useful chemical-induced HCC model to study the mechanism of liver carcinogenesis.

Abstract #273

Differentiation of small hepatocellular carcinomas from small benign nodules in cirrhotic liver on gadoxetic acid-enhanced and diffusion-weighted magnetic resonance images

Byun Jae Ho[1], Kim So Yeon[1], Won Hyung Jin[1], Kim Kyung Won[1], Shin Young Moon[1], Kim Pyo Nyun[1]

[1]Department of Radiology, Asan Medical Center, University of Ulsan, Seoul, Republic of Korea

Introduction: Gadoxetic acid enhanced magnetic resonance (MR) imaging offers hepatobiliary phase MR imaging that can provide superior lesion to liver contrast. Diffusion-weighted (DW) MR images offer better results to detect small liver lesions. Then, gadoxetic acid enhanced MR imaging and DW MR imaging can help to differentiate benign lesions from hepatocellular carcinoma (HCC)?
Objectives: To identify imaging characteristics which differentiate small less than 2 cm HCCs from small benign nodules in cirrhotic liver on gadoxetic acid enhanced and DW MR images.
Methods: On gadoxetic acid-enhanced and DW MR images, we analyzed signal intensity of 222 small HCCs and 61 benign nodules (diameter, 0.5–2 cm) at each sequence and rim enhancement during portal or equilibrium phases. Univariate and multivariate logistic regression analyses identified predictors of HCC. Combinations of significant MR findings in multivariate analysis were compared with American Association for the Study of Liver Disease (AASLD) practice guidelines.
Results: In multivariate analysis, arterial enhancement (adjusted odds ratio (aOR) = 8.6), T2 hyperintensity (aOR,5.8), and hyperintensity on DW images (aOR, 3.8) were significant for differentiating small HCCs from benign nodules. When two or all three findings were applied as diagnostic criteria for differentiating small HCCs from benign nodules, sensitivity and accuracy were significantly higher compared with AASLD practice guidelines (91% vs. 78% and 89% vs. 81%, respectively;each $p < 0.0001$).
Conclusions: On gadoxetic acid-enhanced MR imaging, arterial enhancement and hyperintensity on T2-weighted and DW MR images are helpful for differentiating small HCCs from benign nodules in liver cirrhosis.

Abstract #275

Preliminary results of RF ablation of hepatic dysplastic nodules

Shin Yong Moon[1], Lee So Jung[1], Kim So Yeon[1], Won Hyung Jin[1], Kim Pyo Nyun[1]

[1]Department of Radiology, Asan Medical Center, University of Ulsan, Seoul, Republic of Korea

Introduction: Radiofrequency ablation (RFA) is a good treatment modality for hepatocellular carcinoma (HCC) in liver cirrhosis. However, many nodules including dysplastic nodules are also commonly seen in cirrhotic liver. Usually dysplastic nodules are not indication of RFA, but sometimes, they are ablated because of suspicion of atypical HCC.
Objectives: Our purpose is to present the results of RF ablation of pathologically proven dysplastic nodules.
Method: 24 hepatic nodules were ablated in 24 patients (M: F = 19:5, Mean age = 59). Mean nodule size was 1.7 cm (range 0.9–2.5 cm). All nodules were pathologically confirmed as dysplastic nodules by percutaneous biopsy prior to ablation. 3 nodules showed arterial phase enhancement, and other nodules showed hypovascularity.
Results: All nodules were ablated technically successfully without significant complication. On follw up there was no local tumor progression. 13 cases presented intrahepatic metastasis of typical HCC.
Conclusion: Ablation of dysplastic nodules gives safe results with good prognosis.

Abstract #281

Significance of plasma levels of soluble programmed death-1 and soluble programmed death-ligand 1 in hepatocellular carcinoma

Gwang Hyeon Choi[1], Jung Wha Chung[2], Yun Suk Choi[1], Da woon Jeong[1], Soomin Ahn[3], Eun Sun Jang[1], Jin-Wook Kim[1], Sook-Hyang Jeong[1*]

[1]Departments of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Republic of Korea, [2]Departments of Internal Medicine, Wonkwang University Sanbon Hospital, Wonkwang University College of Medicine, Gunpo, Republic of Korea, [3]Departments of Pathology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Republic of Korea

Introduction: In contrast to tissue expression of programmed death-1 (PD-1) and its ligands (PD-L1), plasma levels of soluble PD-1 (sPD-1) and soluble PD-L1 (sPD-L1) were not clearly defined in hepatocellular carcinoma (HCC).
Objectives: To investigate plasma levels of sPD-1 and sPD-L1, and to evaluate their relationship with clinical factors and overall survival in HCC patients.
Methods: Using plasma samples obtained from the prospectively enrolled HCC patients (n = 242) and age-and sex-matched healthy-controls (n = 91), the plasma levels of sPD-1 and sPD-L1 were measured by commercial ELISA.
Results: The 242 HCC patients showed a mean age of 60.8 years, male in 80.6%, Child-Pugh class A in 84.7%, and BCLC 0/A in 57.0%. The plasma sPD-1 was detected in 35.2% of healthy control

and in 34.7% of HCC patients (median 244 vs 472, p = 0.25). The plasma sPD-L1 was detected in almost all the heathy-control and HCC group (median 371 versus 332 pg/mL, p = 0.13).
The proportion of Child-Pugh class B was higher in detectable-sPD-1 group (22.6%) than in non-detectable-sPD-1 group (14.4%, p = 0.04), and higher in high-sPD-L1 group (19.8%) than in low-sPD-L1 group (9.9%, p = 0.04). During mean follow-up of 4.6 years, the median overall survival was not significantly different between the non-detectable- and detectable-sPD-1 group (4.5 versus 5.2 years), and between the low- and high-sPD-L1 group (4.6 versus 4.4 years).
Conclusion: Though, detectable sPD-1 level or high sPD-L1 level were associated with poor liver function in HCC patients, either level may not be a useful biomarker for the diagnosis or prognosis of HCC.

Abstract #295

Efficacy and safety and patient satisfaction in percutaneous radiofrequency ablation with deep sedation

Koki Sato[1], Takamasa Ohki[1], Yukiyo Fukumura[1], Makoto Imai[1], Mayuko Kondou[1], Kaoru Takagi[1], Kentarou Kojima[1], Michiharu Seki[1], Nobuo Toda[1]

[1]Mitsui Memorial Hospital

Introduction: Percutaneous radiofrequency ablation (RFA) is a useful and safe procedure for treating hepatic neoplasm. However, it often causes severe pain.
Objectives: In this study, we performed RFA under deep sedation with midazolam and pentazocine and investigated its efficacy and safety, and patient satisfaction.
Methods: We conducted a retrospective study including 277 HCC and 88 metastatic liver tumor patients who received RFA treatments between June 2017 and July 2019 at our institution. The primary endpoint was the proportion of complete procedures, the patient's level of consciousness, and the frequency of patients' complaint of pain during RFA. In addition, the patient satisfaction using a 10-point visual analogue scale (VAS) for pain after the procedure and RFA complications were determined.
Results: All patients exhibited depressed consciousness and did not complain of pain during RFA under deep sedation. In addition, they completed the procedure. VAS score was recorded for all patients. The mean VAS of 0.07 ± 0.68. Regarding the major complications, intraperitoneal hemorrhage was observed in one patient. After transfusion, the patient sufficiently recovered under careful observation. There were no deaths.
Conclusion: Deep sedation using midazolam and pentazocine for RFA was safe and effective for patients with hepatic neoplasm. In addition, they were very satisfied with the quality of sedation.

Abstract #318

Drp1-mediated limited mitochondrial permeabilization contributes to liver tumorigenesis through DNA damage and genomic instability

Yang Qifan

Introduction: Mitochondrial dynamics are implicated in cell apoptosis. Mitochondrial fission mediated by Drp1 regulates mitochondrial outer membrane permeabilization (MOMP). The exact relationship between mitochondrial fission and liver tumorigenesis needs to be explored.
Objectives: In this study, we aim to confirm the relationship between Drp1 expression and limited mitochondrial permeabilization. Then we will demonstrate the mechanism that limited mitochondrial permeabilization engages caspase activity and DNA damage, promotes genomic instability and contributes to liver tumorigenesis.
Methods: We overexpressed Drp1 in HCC cell HepG2 and normal liver cell QSG-7701 with lentivirus vectors. The limited mitochondrial permeabilization was detected by Western Blot and immunofluorescence. Next, we quantified caspase-3 activity using assay kits and captureed activity-dependent precipitation of caspase-3. The cell proliferation was detected by EdU assay, CCK-8 assay and clonogenic survival assay after treated with caspase inhibitors. Then we used comet assay to measure DNA damage. The DNA damage in tumor tissues was determined by immunohistochemistry.
Results: The results of Western Blot and immunofluorescence showed Drp1 overexpression induced limited mitochondrial permeabilization and Cytochrome c release. Cytochrome c engages caspase activity. Treatment with the caspase inhibitor had adverse effects on cell proliferation. Caspase activity induces CAD activation through cleavage of its inhibitor ICAD, that trigger caspase-dependent DNA damage.
Conclusion: Drp1 overexpression induces limited mitochondrial permeabilization, engages limited caspase activity related to liver cell tumorigenesis. Drp1 overexpression induces caspase-dependent DNA damage, contributes to genomic instability and liver tumorigenesis.

Abstract #336

Expanding the potential roles of immune checkpoint inhibitors as hepatocellular carcinoma therapy: a systematic review and meta-analysis

Boby Pratama Putra[1], Ummi Maimunah[2]

[1]Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia, [2]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Dr Soetomo Teaching Hospital, Surabaya, Indonesia

Introduction: Hepatocellular Carcinoma (HCC) is the most common primary liver malignancies about 75–85% of total cases. HCC is one of malignancies whose bad prognosis and high mortality rates. Sorafenib has been established as HCC therapies, unfortunately did not meet expected outcomes. Previous studies and trials of Immune Checkpoint Inhibitors (ICIs) in HCC therapies showed promising results.
Objectives: This meta-analysis aims to evaluate descriptively efficacies of ICIs as HCC therapy.
Methods: We did comprehensive searching using predefined keywords in Pubmed, EMBASE, and the Cochrane Library for all relevant studies until November 10, 2019. We extracted data about overall survival (OS), progression-free survival (PFS), and objective responses rate (ORR) of each studies. Risk of bias was assessed using Cochrane tables. Quantitative analysis of OS, PFS, and ORR provided pooled mean and 95% Confidence Interval (CI) with random effects model.
Results: We included 5 studies (2 RCTs) about anti-Programmed-Death-1 (PD-1), 2 RCTs about anti-PD-1 Ligand (PD-L1), and 2 RCTs about anti-Cytotoxic-T-Lymphocyte-associated Protein-4 (CTLA-4). The pooled OS of RCTs only is 11.6 months (95% CI 7.9–15.2), while the pooled OS including non-RCTS is 11.1 months (95% CI 8.1–14.1). The pooled PFS of RCTs only and non-RCTs-included are 3.7 months (95% CI 2.6–4.8) and 3.6 months (95% CI 2.8–4.4). The pooled ORR of 6 studies was 22.2% (95% CI 8.4–35.9)

considered as primary outcomes. Sorafenib has lower OS, PFS, and ORR than ICIs.
Conclusion: ICIs showed promising outcomes as HCC therapy. However, further RCTs should be done to establish its efficacies.

Abstract #355

Fibrosis stage as a predictor of outcome after resection for hepatocellular carcinoma

Mahmoud H. Allam[1], Aliaa Sabry[1], Osama Higazy[2], Mohamed A. S. Kohla[1]

[1]Department of Hepatology and Gastroenterology, National Liver Institute, Menoufiya University, Egypt, [2]Department of Hepatobiliary Surgery, National Liver Institute, Menoufiya University, Egypt

Objective: To evaluate the relationship between liver fibrosis stage and the risk of postoperative hepatic decompensation in patients with liver cirrhosis undergoing hepatectomy for hepatocellular carcinoma (HCC).
Methods: This prospective study was conducted on forty adult patients with hepatitis C (HCV) related HCC eligible for hepatic resection. Liver stiffness measurement by Fibroscan® was prospectively done for all enrolled patients. Patients' demographics, comorbidities, laboratory and radiological data were collected.
Results: Hepatic decompensation occurred in 14 patients (35%) after liver resection. Analysis of ROC curve of liver stiffness measurement done before resection revealed a value equal to or higher than 15.4 KPa as the best cutoff value for liver fibrosis stage predicting postoperative hepatic decompensation with a sensitivity of 100%; specificity 100%, a positive predictive value 100% and negative predictive value of 100%.
Conclusion: Liver stiffness measurement by transient elastography (Fibroscan®) may be a reliable tool to predict hepatic decompensation after liver resection for HCC.

Abstract #358

Recurrence of hepatocellular carcinoma in chronic hepatitis C patients treated with direct acting antiviral agents (DAAs): a single center experience

Allam Mahmoud[1], Omar Yassmin[1], Assem Medhat[1], El Azab Gaser[1], Kohla Mohamed[1]

[1]Department of Hepatology and Gastroenterology, National Liver Institute, Egypt

Background: Chronic hepatitis C (HCV) infection is a leading risk factor for hepatocellular carcinoma (HCC) worldwide. The development or recurrence of HCC after successful therapy of HCV with Direct-Acting Antiviral agents (DAAs) was questionable. This prospective study was conducted on a cohort of 100 Egyptian patients with HCV-induced liver cirrhosis treated with DAA for HCV between December 2015 and December 2016. Patients were categorized into 2 groups: Group (I): included 50 patients with liver cirrhosis without any evidence of HCC. Group (II): included 50 patients with HCC on top of liver cirrhosis. These patients were included in the study after four weeks of successful intervention therapy for HCC aiming at cure, with no evidence of activity by dynamic imaging at time of inclusion in the study. All patients were treated with Sofosbuvir and Daclatasvir with or without Ribavirin. Patients were followed up by dynamic computed tomography (CT) of the abdomen every 12 weeks during and after treatment period by DAA.
Results: Most of patients in both groups were males (74 and 78% for group I and II respectively). Eleven patients (22%) in group II showed active nodules of HCC on repeated follow up after DAA therapy. Of these 11 patients, five patients (45.5%) developed local recurrence of a previous focal lesions, while six patients (54.5%) developed de-novo focal lesions. Two patients (18.2%) had vascular invasion and one patient (9.1%) had bone metastasis.
Conclusions: Treatment with a Sofosbuvir-based regimen was associated with a high rate of recurrence of HCC. Patients with HCC should be properly evaluated prior to antiviral therapy with DAAs and followed up carefully during and after therapy.

Abstract #386

The real-world systemic sequential therapy of sorafenib and regorafenib for advanced hepatocellular carcinoma: a multicenter retrospective study in Korea

Ji Hoon Kim

Background and aims: Regorafenib has been proved as 2nd line systemic therapy for hepatocellular carcinoma (HCC) patients through phase III trial. We analyzed the real-world data to assess clinical efficacy and safety.
Method: This study was a multicenter, non-comparative, retrospective cohort study. Between July 2017 and May 2019, 133 patients with HCC who received regorafenib after sorafenib therapy were eligible for inclusion in this study. Tumor response was assessed according to modified RECIST criteria. We evaluated time to progression (TTP), progression-free survival (PFS) and overall survival (OS) of regorafenib therapy including prediction factors for prognosis.
Results: Their median age was 60 years, and most patients (82%) were male. Hepatitis B virus infection (68.4%) was the most common etiology of HCC. Most of patients (98.5%) were classified as Child-Pugh A except 2. Eighty-four percent of patients had extrahepatic metastasis and Vascular invasion was presented in 45.1%. Three patients (2.7%) achieved complete response and 11 (9.8%) patients had a partial response resulting in objective response rate 12.5% in 112 available patients for response assessment. The disease control rate (DCR) was 34.8%. Median treatment duration of regorafenib was 2.6 months (1.5–4.7 months). During follow up, 38 patients died. On regorafenib, the median OS was 10.0 months (95% CI 8.4–11.6), the median PFS survival was 2.7 months (95% CI 2.5- 2.9 months), and the median TTP was 2.6 months (95% CI 2.4–2.8). The OS rate from the start of regorafenib at 6 months and 1 year were 71.2%, and 38.7%. In multivariate analysis, Child-Pugh score > 5 (HR 3.037 95% CI 1.46–6.314; $p = 0.003$), AFP > 400 ng/ml (HR 5.9; 95% CI 2.608–13.349; $p < 0.001$), and TTP on sorafenib $\geq$ median (HR 0.441; 95% CI 0.310–0.629; $p < 0.001$) were independently associated with OS. In exploratory analysis from the time of sorafenib administration, the median OS from sorafenib administration was 25.8 (95% CI 8.7–42.9 months). The 1 year and 2 years survival rate were 79.5% and 53.1%.
Conclusion: Regorafenib was effective in patients with advanced HCC who failed first-line sorafenib in real-life setting, consistent with previous clinical trial. Regorafenib may improve the prognosis of patients who had longer TTP on previous sorafenib therapy.

Abstract #401

Usefulness of serum PIVKA-II as a marker of radiological response and survival outcome in patients with hepatocellular carcinoma undergoing transarterial chemoembolization

Soohyun Yang[1], Sunghoon Kim[1], Taegyoon Kim[1], Wonhyeong Park[1]

[1]Department of Internal Medicine, Veterans Health Service Medical Center, Seoul, Korea

Introduction and objectives: We validated the predictive ability of change in protein induced by PIVKA-II as an indicator of tumor response after transarterial chemoembolization (TACE) in comparison of the AFP model.
Methods: We included 154 consecutive HCC patients with high baseline levels of PIVKA-II ($\geq$ 60 mAU/mL) and/or AFP ($\geq$ 200 ng/mL) who underwent TACE between 2012 and 2018. Radiological response was assessed by dynamic CT and/or MRI using mRECIST criteria. Serological response was defined as a decrease of $>$ 50% compared to baseline level during a series of repeated TACE sessions.
Results: Of 154 patients, 131 (85%) were male, and median patient age was 68 years (range 42–85). There were 39 patients (25%) with high baseline levels of both PIVKA-II and AFP, and 63 (41%) and 50 (32%) with high PIVKA-II and AFP levels alone. Serological responses had good inter-responder with radiological responses (κ values, 0.811 for PIVKA-II and 0.731 for AFP). Both PIVKA-II and AFP responders had better overall survival than nonresponders (hazard ratios, 3.4 and 4.7, respectively; $p < 0.001$), as did mRECIST responders (hazard ratio, 7.2; $p < 0.001$). The Cox's model revealed that PIVKA-II response was a significant predictor of overall survival of patients with high PIVKA-II level at baseline, independently of initial tumor and host factors (hazard ratio, 3.2; $p < 0.001$).
Conclusions: PIVKA-II response could be a surrogate endpoint of immediate and prolonged clinical outcomes following TACE along with AFP response, especially in HCC patients with elevated PIVKA-II.

Abstract #405

Percutaneous radiofrequency ablation as an initial treatment for hepatocellular carcinoma among extremely old-age patients using propensity score matching analysis

Kyohei Tsuchiya[1], Takamasa Ohki[1], Koki Sato[1], Mayuko Kondo[1], Nobuo Toda[1], and Kazumi Tagawa[1]

[1]Mitsui Memorial Hospital, Department of Gastroenterology, Tokyo, Japan

Introduction: Although radiofrequency ablation (RFA) is known as a minimal invasive treatment for early stage hepatocellular carcinoma (HCC), it is not well known whether RFA achieves favorable outcomes among extremely old-age patients.
Objectives: We conducted this study to clarify the efficacy and safety of RFA among them.
Methods: We enrolled 512 naïve HCC patients treated with RFA between January 2001 and December 2016. We divided them into two groups, extremely old-age group (equal to or over 80 year-old) and the controls (under 80 year-old). Primary end-point was overall survival (OS). Propensity score matching method was applied to adjust each patient background using sex, liver functions, tumor number, tumor diameter, and presence of HCV infection. Finally, 68 extremely old-age patients and 68 controls were extracted. We compared patients' backgrounds, primary end-point and secondary end-points between the 2 groups.
Results: In patients' backgrounds, there were significant differences about ALT levels and prothrombin time between the 2 groups. The cumulative OS rates were not differed between the 2 groups (P = 0.83); 98.5%, 87.9%, and 50.5% at 1, 3, and 5 years in extremely old-age group, 94.1%, 72.8%, and 49.3% in the controls, respectively. Age over 80 year-old was not a significant factor related to OS even in multi-variate analysis. Liver related deaths were observed in 17 of extremely old-age group, and 16 of the controls (P = 1.00). **Conclusions**: RFA is a safe and effective treatment even among extremely old-age HCC patients.

Abstract #410

Sorafenib treatment in patients with peritoneal metastasis from hepatocellular carcinoma

Eiichiro Suzuki

Background: Peritoneal metastasis (PM) has been connected with worst prognosis in many malignancies. In the era of systemic chemotherapy, we encounter peritoneal metastasis from hepatocellular carcinoma (HCC).
Objectives: The aim of this retrospective analysis was efficacy and safety of sorafenib in patients with PM from HCC in the real-world practice.
Patients and methods: Data of all sorafenib patients were collected between July 2009 and December 2013 and analyzed retrospectively.
Results: Eighteen HCC patients out of 185 (9.7%) receiving sorafenib treatment had PM. Main adverse Events were hand foot skin reaction (55.5%) and hypertension (44.4%) and no treatment-related death. Response rate was 22.2% (Partial response 4 cases) and Median overall survival and progression free survival, which showed 8.6 months and 2.7 months respectively, was not different from non-PM patients (OS, P = 0.97; PFS, P = 0.87).
Conclusions: Sorafenib treatment for HCC patients with PM was safe but the result was not satisfactory. These data were referential for future clinical trials.

Abstract #423

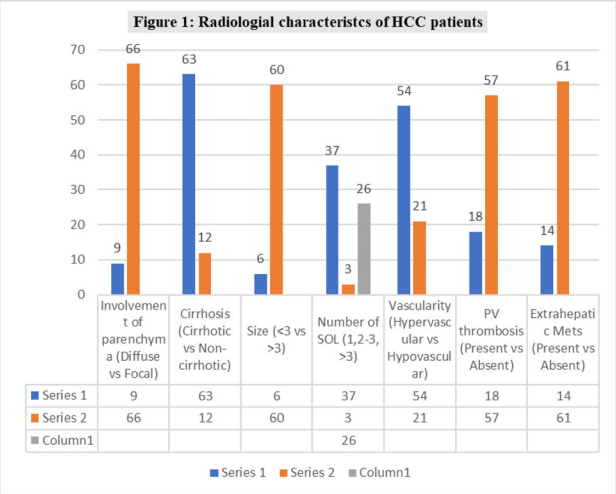
Correlation of alpha-fetoprotein (AFP) with cross-sectional radiological, virological features and BCLC stages of hepatocellular carcinoma

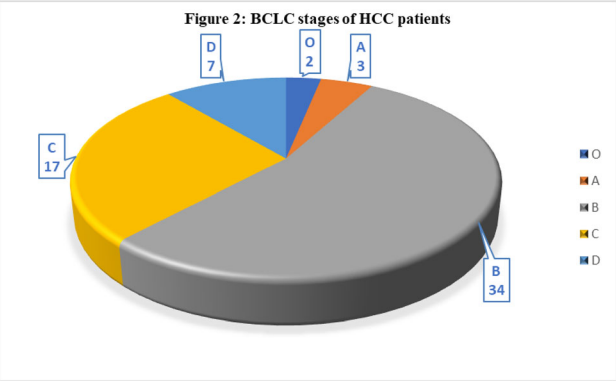
Roy Partho Pratik[1], Mahtab Mamun Al[2], Rahman Salimur[3]

[1]Shaheed Suhrawardy Medical College, Dhaka, Bangladesh, [2]Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, [3]Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Introduction: Hepatocellular carcinoma (HCC) is eighth most common malignancy in Bangladesh. Measurement of alpha-fetoprotein (AFP) can potentially be used for the diagnosis of HCC. Dynamic contrast-enhanced CT has almost 100% specificity and 78–98% sensitivity for diagnosis of HCC. But data regarding correlation between value of AFP and radiological features of HCC are lacking.
Objectives: To explore relationship between AFP and various radiological, virological variables and BCLC stages.
Methods: It was a cross sectional observational study which was done in department of Hepatology BSMMU from March 2016 to March 2017. Serum AFP levels were measured in 75 HCC patients.

Radiological features of HCC (Size, number of tumour, vascularity, portal vein thrombosis) were evaluated by Dynamic contrast-enhanced CT scan. Virological status (HBsAg), BCLC staging were also evaluated. Patients were divided into four groups according to different cutoff value of AFP (< 200, 201–1000, 1001–10,000, > 10,000 ng/ml) and analyzed with the variables.
Results: Median AFP value was 1583 ng/ml. Majority of patients were HBsAg positive (n = 50, 66.67%). On each cutoff value of HCC, higher number of patients were HBsAg positive. Around 90.9% tumours are ≥ 3 cm, most of them had AFP value between 1000 and 10,000 ng/mL. 54 (72%) patients showed contrast enhancement in arterial phase (Hypervascular), 31 of them had AFP value > 1000. 8 patients (44%) within 18 patients with PV thrombosis had AFP value > 10000, which was statistically significant (p = 0.020). Most of the patients belonged to BCLC stage B [n = 34 (54%)].
Conclusion: Portal vein thrombosis had strong correlation with raised AFP.





Abstract #440

Selective internal radiation therapy (SIRT) versus sorafenib in mongolian patients with advanced hepatocellular carcinoma

Oidoy Baatarkhuu[1,5], Munkhchuluun Batzaya[2], Khasbazar Ariunaa[2], Jazag Amarsanaa[3], Nachin Baasanjav[4,5]

[1]Department of Infectious Diseases, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [2]Department of Chemotherapy, National Cancer Center of Mongolia, Ulaanbaatar, Mongolia, [3]Mongolian Associations for Study of Liver Diseases, [4]Department of Surgery, Ach Medical University, Ulaanbaatar, Mongolia, [5]Mongolian Academy of Medical Sciences, Ulaanbaatar, Mongolia

Background: In Mongolia, primary liver cancer is the most common cancer, and 2000–2300 new cases have diagnosed each year. SIRT with yttrium-90 resin microspheres is one potential alternative treatment for locally advanced HCC. Sorafenib is an oral multikinase inhibitor with antiproliferative and antiangiogenetic effects.
Objective: To treat patients with advanced hepatocellular carcinoma with either of selective internal radiation therapy or sorafenib and compare the results.
Methods: Patients were randomly assigned 1:1 stratified and to receive either SIRT or, sorafenib800 mg/d orally. Outcome measures were physical examination, ECOG, CBC, liver function test AFP results and CT scan every 4, 8 and 12 weeks follow up visit after treatment initiation.
Results: Twenty patients were treated with SIRT and 19 patients were treated with sorafenib. Median OS and PFS rate were longer in sorafenib arm patients than in SIRT arm (15.56 and 9.17; HR 0.95, 95% CI 0.46; P = 0.889) and (8.51 months and 5.85 months; HR,1.07; CI 0.53–2.16). Tumor response results was greater in SIRT than sorafenib (68.8% vs 62.5%, P = 0.033). Of 2 (10%) patients CR, 2 (10%) patients got PR and 7 (43.8%) patients received stable responses. A total of 165 treatment emergent adverse events were reported (SIRT, 66; sorafenib, 99). Significantly fewer patients in the SIRT than sorafenib group had grade ≥ 3 adverse events.
Conclusion: In patients with locally advanced HCC, overall survival did not differ significantly between SIRT and sorafenib. But SIRT significantly increased tumor response and reduced the incidence of adverse events compared with sorafenib.

Abstract #453

Association between prothrombin induced by vitamin K absence-II (PIVKA-II) and barcelona clinic liver cancer (BCLC) stage, tumor size, portal venous thrombosis in hepatocellular carcinoma patients

Siregar Gontar Alamsyah[1], Zain Lukman Hakim[1], Lubis Masrul[1], Dairi Leonardo Basa[1], Ilhamd[1], Darmadi[1]

[1]Division of Gastroenterohepatology, Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

Introduction: Prothrombin induced by vitamin K absence-II (PIVKA-II) is an abnormal prothrombin protein that is increased in Hepatocellular carcinoma (HCC) patients. The validity of PIVKA-II as a tumor marker for HCC patients has been reported by many investigators.
Objectives: To investigate the association between prothrombin induced by vitamin k absence-II (PIVKA-II) and Barcelona Clinic Liver Cancer (BCLC) stage, tumor size, portal venous thrombosis in HCC patients.
Methods: A cross sectional study of 60 HCC patients. The diagnosis of HCC was confirmed by triphasic CT scan (arterial hypervascularity followed by venous and/or delayed phase "washout"). Serum level of PIVKA-II were examined using an ELISA kit. Cholangiocarcinoma, hemangioma, and liver metastasis patients were excluded from the study. HCC patients were classified according to Barcelona Clinic Liver Cancer criteria. Data analysis used the Kruskal Wallis H-test with the SPSS statistical program. Statistically significant if $p < 0.05$ with a confidence level of 95%.

Results: HCC patients with BCLC B (124 ng/mL), C (168 ng/mL), and D (168 ng/mL) had significantly higher PIVKA levels compared to BCLC A (46 ng/mL) ($p < 0.001$). HCC patients with portal venous thrombosis (168 ng/mL) had significantly higher PIVKA levels compared without portal venous thrombosis (89 ng/mL) ($p = 0.001$). HCC patients with tumor size > 5 cm (176 ng/mL) had significantly higher PIVKA-II levels compared to tumor size < 3 cm (58 ng/mL) ($p = 0.003$).
Conclusion: There were significant association between PIVKA-II level and BCLC stage, tumor size, portal venous thrombosis in HCC patients.

Abstract #455

Correlation of alpha-fetoprotein (AFP) and prothrombin induced by vitamin K absence-II (PIVKA-II) levels in hepatocellular carcinoma patients

Siregar Gontar Alamsyah[1], Zain Lukman Hakim[1], Lubis Masrul[1], Sungkar Taufik[1], Halim Sahat[1], Darmadi[1]

[1]Division of Gastroenterohepatology, Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

Introduction: The most commonly utilized biomarker in clinical practice for hepatocellular carcinoma (HCC) is α-fetoprotein (AFP). However, it is not recommended for routine screening because it lacks specificity. Prothrombin induced by vitamin k absence-II (PIVKA-II) is a specific marker for HCC and exhibits higher sensitivity and specificity than AFP in diagnosing HCC.
Objective: To evaluate the correlation between AFP and PIVKA-II in HCC patients.
Methods: A cross sectional study of 60 HCC patients. The diagnosis of HCC was confirmed by triphasic CT scan (arterial hypervascularity followed by venous and/or delayed phase "washout"). A 4 mL peripheral blood sample was collected in an EDTA tube from each patient. Plasma aliquots were stored at – 70 °C until measurement. Serum levels of AFP and PIVKA-II were examined using an ELISA kit. Cholangiocarcinoma, hemangioma, and liver metastasis patients were excluded from the study. Data analysis used the Spearman correlation test with the SPSS statistical program. Statistically significant if $p < 0.05$ with a confidence level of 95%.
Results: HCC patients had median AFP level of 536.9 ng/mL and PIVKA level of 149.5 ng/mL. There was a significant positive correlation between AFP and PIVKA-II levels in HCC patients, with weak correlation strength ($p = 0.048$, $r = 0.256$). The higher the AFP level, the higher the PIVKA-II level.
Conclusion: There was a weak positive correlation between AFP and PIVKA-II in HCC patients.

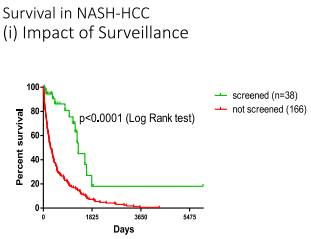
Abstract #467

Outcomes of non-alcoholic steatohepatitis (NASH)-related hepatocellular carcinoma (HCC) at New Zealand liver transplant unit (NZLTU) over last 2 decades

Hassan Ibrahim[1], Fahmi Hassan[2], Gane Edward[3]

[1]Hepatology registrar, New Zealand Liver Transplant unit (NZLTU), Auckland City Hospital, Auckland, New Zealand, [2]Medical registrar, Auckland City Hospital, Auckland, New Zealand, [3]Hepatologist and transplant physician, New Zealand Liver Transplant unit (NZLTU), Auckland City Hospital, Auckland, New Zealand

Introduction: due to the current obesity and diabetes epidemics and effective therapies for hepatitis B and C, NASH will soon become the leading cause of HCC globally. Patients with NASH without cirrhosis are at risk for HCC, because of persistently elevated proinflammatory cytokines and insulin levels and changes in the gut microbiota.
Objectives: to describes the outcomes of patients with NASH-related HCC and evaluates the benefits of HCC surveillance in this population.
Methods: all NASH-related HCC cases referred to NZLTU between 1999 and 2019 were included. Data on demographics, screening status, hepatitis B serology, treatment and survival were collected. Cirrhosis status was determined by clinical, laboratory, radiological features, or histologic criteria
Results: 204 patients with NASH-related HCC were identified: median age 71 years, 78% male, 67% European. 82% were obese, 75% diabetics, 78% hypertensive, and 66% had hyperlipidaemia. 20% had resolved HBV infection. 19% cases were detected through regular HCC surveillance, the remainder after onset of symptoms. Of surveillance-detected NASH-HCC cases, 68% received curative therapy compared to 20% of symptomatic cases ($p < 0.01$). Survival was higher in patients with surveillance-detected HCC compared to symptomatic cases ($p < 0.0001$). 70% of NASH-HCC cases were cirrhotic (21% on histology; 15% radiology; 34% clinical and radiology).
Conclusion: NASH-HCC has increased dramatically during the study period. Poor outcomes reflect lower rate of screening uptake and curative therapy in cirrhotic patients and absence of surveillance in non-cirrhotic cases. Identified risk factor for HCC includes age above 50, male gender, metabolic syndrome and positive anti-Hepatitis Bcore..



Abstract #514

A role of prospero homeobox 1 induce invasion and angiogenesis in hepatocellular carcinoma cells

Ji Yoon Hong[1], Min Woo Jung[1], Jae Hyen Yoon[1], Sun Young Park[1], Young Lan Park[1], Young Eun Joo[1], Sung Kyu Choi[1], Sung Bum Cho[1]

[1]Divsion of Gastroenterology, Departments of Internal Medicine, Chonnam National University Medical School, Gwangju, Korea

Background: Prospero homeobox 1 (PROX1) is a nuclear transcription factors that plays a major role during embryonic lymphangiogenesis and has recently been known as oncogenic roles in various cancer. However, the role of PROX1 is complex and unclear in hepatocellular carcinoma. We determined whether PROX1 affected the oncogenic behavior of hepatocellular carcinoma (HCC) cells and investigated its prognostic value in patients with HCC.
Methods: a small interfering RNA against PROX1 and pcDNA6-myc vector was used to control PROX1 gene expression in HCC cell lines HepG2 and Huh 7. Apoptosis, proliferation and angiogenesis were determined by performing the TUNEL assay and immunohistochemical staining for Ki-67, CD34, and D2-40. Invasion, migration and in vitro angiogenesis assay was also performed. A 62 HCC tissues

that obtained surgically resected were performed immuohistochemical stains of PROX1 and analyzed according to various clinical parameters.
Results: PROX1 knockdown suppressed tumor cell proliferation and inducing apoptosis by activating cleaved caspase-3. PROX1 knockdown induced cell cycle arrest in G2/M phase by increasing p21 and p27. Knockdown of PROX1 suppressed tumor cell migration and invasion. Knockdown of PROX1 suppressed tumor cell angiogenesis through inhibition of VEGF and activation of angiostatin. PROX1 positive group of HCC tissues was 69.4% (n = 43) and negative group was 30.6% (n = 19) by evaluating the area and intensity of immunohistochemical stain. However, no significant difference was observed between PROX1 expression and clinical parameters of histology, recurrence, survival.
Conclusions: PROX1 is associated with oncogenic roles of tumor cell proliferation, resistance to apoptosis and angiogenesis by inducing VEGF signaling in HCC cells.

Abstract #521

Efficacy of re-TACE after Lenvatinib treatment for TACE-refractory hepatocellular carcinoma

Sawako Uchida-Kobayashi[1], Ken Kageyama[2], Akira Yamamoto[2], Naoshi Odagiri[1], Kanako Yoshida[1], Kohei Kotani[1], Hiroyuki Motoyama[1], Etsushi Kawamura[1], Atsushi Hagihara[1], Hideki Fujii[3], Masaru Enomoto[1], Akihiro Tamori[1], Shigekazu Takemura[4], Shoji Kubo[4], Yukio Miki [2], Norifumi Kawada[1]

[1]Department of Hepatology, [2]Radiology, [3]Premier Preventive Medicine, and [4]Hepato-Billiary-Pancreatic surgery, Osaka City University Graduate School of Medicine

Introduction: Lenvatinib (LEN) has become available as a therapy in patients with unresectable and TACE-refractory hepatocellular carcinoma (HCC).
Objectives: We investigated the effects of re-TACE after LEN treatment for TACE-refractory hepatocellular carcinoma.
Methods: Thirteen patients who underwent re-TACE after LEN for TACE-refractory HCC from May 2018 to the end of March 2019 at our hospital were included. The background of the patients and effects of re-TACE after LEN treatment were examined.
Results: The age at the start of LEN was 76 (45–82) years. The average period from the first occurrence of HCC to the start of LEN was 3 years, the average number of TACE before LEN was 4 times, and all of them had a liver reserve of Child-Pugh A. The duration of LEN treatment was 177 (25–420) days, and the reasons for re-TACE were 9 in LEN refractory and 4 intolerant. Dynamic CT 1–3 months after re-TACE showed efficacy in 8 cases (61.5%). The post-re-TACE courses of 8 cases ware 1 patient with complete response who was able to complete the treatment, 3 patients with partial response who were able to switch from molecular targeted agents to radical therapy (hepatectomy, radio-frequency ablation and TACE), and 3 patients who were continuing molecular targeted agents for intrahepatic and/or extrahepatic lesions. The observation period after TACE was 209 ± 98 days, and there were 2 deaths.
Conclusion: Re-TACE after LEN treatment refractory/tolerance for TACE-refractory hepatocellular carcinoma can be an effective treatment option.

Abstract #522

Safety and local control of percutaneous microwave thermosphere ablation for liver cancer

Tamai Hideyuki[1], Okamura Junpei[1]

[1]Department of Hepatology, Wakayama Rosai Hospital, Wakayama, Japan

Introduction: Emprint™ ablation system with thermosphere™ technology (Covidien) is a new thermal ablation modality that produces predictable spherical ablation zone.
Objectives: This study aims to evaluate the safety and local control of percutaneous microwave thermosphere ablation for liver cancer.
Methods: This is a retrospective cohort study of patients who underwent percutaneous ultrasound guided microwave thermosphere ablation between December 2017 and August 2019. Treatment-related complications, local recurrence rate, and factors related local recurrence were analyzed.
Results: Three hundred eighty-eight tumors including 347 hepatocellular carcinoma (HCC) and 41 metastatic liver cancer in 299 patients were ablated. Of 388 tumors, 203 subcapsular, 112 perivascular, and 40 protrusive lesions were included. Median follow up period was 257 days. No treatment-related death within one month was seen. Thirty-five complications per patient (12%) occurred; bile duct injury (n = 15), bleeding (n = 14), seeding (n = 4), portal thrombosis (n = 1), liver abscess (n = 1). All seedings were found in patients with HCC over 3 cm in diameter. Multivariate analysis identified tumor size as the only factors independently related to local recurrence ($p < 0.05$). Cumulative 1-year local recurrence rate per lesion of overall, within 3 cm, and over 3 cm tumors was 5%, 4%, and 26%, respectively. Local recurrence rate was significantly higher in tumor over 3 cm than in within 3 cm ($p < 0.001$).
Conclusion: Percutaneous microwave thermosphere ablation is a safe and curative treatment for small liver cancer within 3 cm in diameter. However, this procedure should not be considered as first line treatment for liver cancer over 3 cm because of high risks of local recurrence and seeding.

Abstract #525

Expert-level recognizing hepatocellular carcinoma and beyond

Chen Wei-Ming[1], Fu Min[2], Zhang Cheng-Ju[3], Xing Qing-Qing[1], Zhou Fei[1], Lin Meng-Jie[4], Dong Xuan[1], Zheng Qi-Zhong[5], Hong Mei-Zhu6, Pan Jin-Shui[1]

[1]Department of Gastroenterology, Zhongshan Hospital Affiliated to Xiamen University, Xiamen, Fujian, China, [2]School of Aerospace Engineering, Xiamen University, Xiamen, Fujian, China, [3]Department of Anesthesiology, Zhongshan Hospital Affiliated to Xiamen University, Xiamen, Fujian, China, [4]Department of Pathology, Zhongshan Hospital Affiliated to Xiamen University, Xiamen, Fujian, China, [5]Department of Pathology, Xiamen Hospital of Traditional Chinese Medicine, Xiamen, Fujian, China, [6]Department of Traditional Chinese Medicine, Zhongshan Hospital Affiliated to Xiamen University, Xiamen, Fujian, China

Introduction: Human–based medical–image interpretation always falls into the predicament between specialized practitioners and expanding medical imaging.
Objectives: We aim at developing a diagnostic tool for medical–image classification by using transfer learning that can be applied to diverse image types.

Methods: In this multicentre study, images were retrospectively collected and prospectively analysed using machine learning. Microscopic images of liver tissue that show or do not show hepatocellular carcinoma were used to train the classification framework using a convolutional neural network. To evaluate the classification performance based on transfer learning, histological images from colorectal tissue and breast, and other types of images such as lung X-rays, and optical coherence tomography images were also collected.
Results: Accuracy, sensitivity, and specificity were reported and compared to human image interpretation and other artificial–intelligence (AI) image classification systems such as AlexNet and GoogLeNet. For the test dataset, sensitivity, specificity, and area under the curve of the AI framework were 99.1%, 98.0%, and 0.960, respectively. In human–machine comparisons, the accuracy of the AI framework was 98.5%, while the accuracy of human experts fluctuated between 93.0% and 95.0%. Based on transfer learning, the AI framework accuracy for colorectal carcinoma, breast invasive ductal carcinoma, pneumonia, and retinal diseases, were 96.8%, 96.0%, 97.0%, and 98.0%, respectively.
Conclusion: The performance of the proposed AI framework in classifying histological images with hepatocellular carcinoma is comparable to the classification by human experts. With limited training, the proposed AI framework has potential versatility and universality in medical–image classification.

Abstract #572

Mebatolic syndrome does not contribute to HCC recurrence after hepatic resection

Yijin Wang

Background and aims: Metabolic syndrome (MS) has been increasingly recognized a risk factor for hepatocellular carcinoma (HCC), however, whether MS play roles in HCC recurrence after hepatic resection remains unknown. We thus aimed to evaluate whether MS is a risk factor for HCC recurrence after resection.
Method: 506 HCC patients undergoing liver resection between 2012 and 2017 were recruited. MS, defined as presenting 3 or more metabolic abnormalities, including obesity, diabetes, hypertriglyceridemia, hypercholesterolemia and hypertension, were assessed at the time of tumor resection.
Results: The median patient age was 49 and 83.8% were men. The median follow-up time was 26 months. Interestingly, univariate analysis showed that patients with MS had a lower risk for HCC relapse within 2 years than those without ($p = 0.090$), although no statistical significance. After adjusting for age, cirrhosis status, tumor diameter, tumor number and hypertension, MS showed no association with HCC recurrence. Further analysis of recurrence incidence at different time points showed that the probability of HCC recurrence in patients with MS was 3.4%, 3.4% and 42.9% at 6 month, 12 month and 36 month, respectively. While the recurrence rates at the same time point in patients without MS was 13.3%, 22.7% and 52.3%, respectively ($p = 0.0973$). In multivariate analysis, cirrhosis (odds ratio [OR], 3.21; 95% CI 1.32–7.81; $p = 0.01$) large tumor size > 5 cm ([OR], 3.61; 95% CI 2.29–5.69; $p < 0.001$), and multiple tumors (odds ratio [OR], 3.59; 95% CI 1.51–8.55; $p = 0.004$) were found to be independent risk factors for HCC recurrence.
Conclusion: MS seems not associated with tumor recurrence in HCC patients with resection.

Abstract #575

CDCA levels are prognostic and diagnostic markers for hepatocellular carcinoma

Liao Yangjing[1], Li Wenchao[2], Yang Hongzhi[1]

[1]Department of Traditional Chinese Medicine, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China, [2]Department of General Surgery, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

Background: Little is known about the molecular mechanisms involved in the development and progression of hepatocellular carcinoma (HCC). Cell division cycle-associated (CDCA) genes, consisting of seven family members, are pivotal for cell mitosis and contribute to tumorigenesis in a variety of cancers.
Objectives: we aimed to evaluate the prognostic and diagnostic value of CDCA genes in HCC.
Methods: Multiple public databases integrating genetic, mRNA and proteomic microarray data were used to validate the survival and diagnostic value of CDCA genes in HCC. Furthermore, a functional analysis was conducted to predict the potential mechanisms involved.
Results: We observed significantly increased mRNA and protein levels in HCC tissues compared with normal tissues, and high CDCA mRNA expression indicated unfavorable overall survival (OS) and recurrence-free survival (RFS). In addition, Cox regression analysis showed that CDCA subunits acted as independent prognostic factors for patient OS. Receiver operating characteristic (ROC) curve analysis showed that CDCA levels were of great diagnostic value in HCC. The functional analysis revealed that CDCA proteins may regulate the biological activity of hepatoma through the AMPK and p53 signaling pathways.
Conclusion: CDCA levels are prognostic and diagnostic markers for HCC and deserve further study.

Abstract #582

Pembrolizumab induced acute on chronic liver failure in a patient with advanced hepatocellular carcinoma after trans-arterial radio embolization: a case report

Mehtani Rohit[1], Premkumar Madhumita [2], De Arka[3], Dhiman R K[4]

[1]Senior Resident, Department of Hepatology, Postgraduate institute of Medical Education and Research, Chandigarh, India, [2]Assistant Professor, Department of Hepatology, Postgraduate institute of Medical Education and Research, Chandigarh, India, [3]Assistant Professor, Department of Hepatology, Postgraduate institute of Medical Education and Research, Chandigarh, India, [4]Professor and Head, Department of Hepatology, Postgraduate institute of Medical Education and Research, Chandigarh, India

Introduction: advanced hepatocellular carcinoma (HCC) has limited curative treatment options and is associated with a poor prognosis. PD-1/PDL-1 inhibitor therapy has been approved by US-FDA as second line therapy for advanced HCC with preserved liver functions and performance status. However, various immune mediated adverse effects are a concern with immune checkpoint blockade.
Case: we report a case of 81-year-old gentleman with Non-alcoholic steatohepatitis (NASH) related cirrhosis with HCC in left lobe of liver with tumoral portal vein thrombosis. Patient underwent Yttrium-90 Trans-arterial radio-embolization (TARE) followed by 2 infusions of Pembrolizumab 200 mg at an interval of 4 weeks. He was also started on Lenvatinib 12 mg daily after TARE. After 2nd dose of

Pembrolizumab patient developed jaundice, ascites, oliguric acute kidney injury, shock and grade II hepatic encephalopathy. He was treated with intravenous fluids, broad spectrum antibiotics and intensive care following which his parameters improved to baseline values. Repeat triple phase CT scan showed significant reduction in the size of the lesion with residual lesion showing only subtle rim enhancement on arterial phase. His AFP level also normalized to 4.2 ng/mL from a baseline value of 298 ng/mL.

Conclusion: management of advanced HCC requires aggressive therapy to achieve response as was done in this case. Our case highlights the good response seen with combination of TARE, Lenvatinib and Pembrolizumab. However, it was complicated by the occurrence of acute on chronic liver failure which was managed effectively with intensive care.

Abstract #608

Change in the recurrence pattern and predictors over time after complete cure of hepatocellular carcinoma

Yeon Seok Seo[1]

[1]Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

Background/aims: We investigated the diagnostic performances of serum AFP, AFP-L3, PIVKA-II level, and the combination of these tumor markers for diagnosis of hepatocellular carcinoma (HCC).

Methods: Total 526 patients who underwent AFP and AFP-L3 tests were enrolled. We calculated the serum AFP-L3 level using the formula as follows: serum AFP-L3 level = serum AFP level (ng/mL) × serum AFP-L3 fraction (%) × 0.01. New diagnostic model, ALPs (AFP, AFP-L3 fraction, and PIVKA-II) score was developed as follows: ALP-II level = 1.7 × [serum AFP level (ng/mL) × AFP-L3 fraction (%) × 0.01] + 0.2 × PIVKA-II level (mAU/mL).

Results: 317 patients (60.3%) had chronic liver disease and 185 patients (35.2%) had liver cirrhosis. Most common cause of chronic liver disease was chronic hepatitis B in 185 patients (35.2%). HCC was diagnosed in 131 patients (24.9%). BCLC stage was stage 0 in 6 patients (4.6%), stage A in 64 patients (48.9%), stage B in 32 patients (24.4%), stage C in 29 patients (22.1%).

The AUROCs for the diagnosis of HCC of serum AFP level, AFP-L3 fraction, and PIVKA level were 0.772, 0.801, and 0.829, respectively. Diagnostic accuracy did not differ among these markers (all $P > 0.05$). The optimal cutoff values of serum AFP level, AFP-L3 fraction, and serum PIVKA-II levels were 4.0 ng/mL, 5.7%, and 35.0 mAU/mL, respectively. The AUROC of AFP-L3 level was 0.816. It was significantly higher than AUROC of serum AFP level ($P < 0.001$), while it did not differ with AUROCs of AFP-L3 fraction ($P = 0.210$) and serum PIVKA-II level ($P = 0.682$). The optimal cutoff value of AFP-L3 level was 0.26 ng/mL with sensitivity 72.5% and specificity 79.7%. The AUROC of ALPs score for the diagnosis of HCC was 0.877, which was significantly higher than those of serum AFP level ($P < 0.001$), AFP-L3 fraction ($P < 0.001$), PIVKA-II level ($P = 0.005$), and AFP-L3 level ($P = 0.004$). The optimal cutoff value of ALPs score was 5.05 with 82.4% of sensitivity and 82.8% of specificity. AUROCs for the diagnosis of early stage HCC of serum AFP level, AFP-L3 fraction, AFP-L3 level, PIVKA-II level, and ALP-II level were 0.689, 0.738, 0.754, 0.735, and 0.815, respectively. AUROC of ALPs score was significantly higher than those of serum AFP level ($P < 0.001$), AFP-L3 fraction ($P = 0.034$), and serum PIVKA-II level ($P = 0.007$), while there was a trend of higher AUROC of ALPs score than that of AFP-L3 level ($P = 0.060$). AUROC of ALPs score was significantly higher than that of serum AFP level ($P < 0.001$), while it did not differ with AFP-L3 fraction ($P = 0.470$) and serum PIVKA-II level ($P = 0.748$).

Conclusions: Diagnostic accuracy for the diagnosis of HCC was significantly improved with ALPs score, calculated using serum AFP level, AFP-L3 fraction, and serum PIVKA-II level. ALPs score was also very accurate for the diagnosis of early stage HCC. To confirm these results, validation study is needed.

Abstract #609

Natural killer cell activity correlates with the stage and the risk of recurrence after curative treatment of hepatocellular carcinoma

Han Ah Lee[1], Hyun Gil Goh[1], Tae Hyung Kim[1], Sun Young Yim[1], Young-Sun Lee[1], Sang Jun Suh[1], Young Kul Jung[1], Ji Hoon Kim[1], Yeon Seok Seo[1], Hyung Joon Yim[1], Jong Eun Yeon[1], Kwan Soo Byun[1], Soon Ho Um[1]

[1]Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

Background/aim: Natural killer (NK) cell dysfunction is recognized as significant mechanisms for the development and recurrence of hepatocellular carcinoma (HCC). However, clinical correlation of NK cell activity measured from peripheral blood mononuclear cell (PBMC) with the stage and the risk of recurrence after curative treatment of HCC has not been fully evaluated.

Methods: Patients with first-diagnosed and treatment-naive HCC who underwent curative treatment were enrolled. PBMC was isolated at the time of diagnosis, and at 1 month after treatment.

Results: In total, 80 patients with HCC were enrolled. Chronic hepatitis B virus infection was most frequent underlying liver disease (48 patients, 60.0%). Barcelona clinic liver cancer (BCLC) was 0 in 15 patients (18.8%), A in 38 patients (47.5%), and B, C, or D in 27 patients (33.8%).

Interferon (IFN)-γ producing NK cell proportion was significantly lower in patients with BCLC BCD than in those with BCLC 0 (56.8±16.8% in BCLC 0 vs. 42.9±21.2% in BCLC BCD, $P = 0.045$) and there was a trend of lower IFN-γ producing NK cell proportion in patients with BCLC BCD than in those with BCLC A ($P = 0.080$).

PBMC sample at 1 month after curative treatment was available in 42 patients. Type of treatment was surgical resection in 27 patients (64.3%) and RFA in 15 patients (35.7%). HCC recurred in 14 patients during the follow-up period. IFN-γ producing NK cell counts at baseline and at 1 month after treatment were 5509.4 ± 5824.2 cells and 7158.2 ± 6310.5 cells, respectively, and IFN-γ producing NK cell proportions at baseline and at 1 month after treatment were 50.5 ± 17.7% and 45.1 ± 16.8%, respectively.

There was no significant changes in total NK cell count (12620.9 ± 13778.4 cells vs. 16846.1 ± 15127.1 cells, $P = 0.218$), total NK cell proportion (9.6 ± 6.9% vs. 11.2 ± 7.4%, $P = 0.299$), IFN-γ producing NK cell count (5509.4 ± 5824.2 cells vs. 7158.2 ± 6319.5 cells, $P = 0.244$), and IFN-γ producing NK cell proportion (50.5 ± 17.7% vs. 45.1 ± 16.8%, $P = 0.108$) from baseline to 1 month after curative treatment.

When patients were classified according to the IFN-γ producing NK cell proportion (group 1, ≥45%; and group 2, < 45%). HCC recurrence rate did not differ according to the IFN-γ producing NK cell proportion at baseline ($P = 0.835$). While, it differed significantly according to the IFN-γ producing NK cell proportion at 1 month after treatment ($P < 0.001$). HCC recurrence rates were significantly lower in group 1 (0%, 4.2%, 25.8%, and 25.8% at 6, 12, 18, and 24 months, respectively) than in group 2 (32.8%, 66.4%, 66.4%, and 66.4% at 6, 12, 18, and 24 months, respectively). On multivariate analysis, BCLC

stage and IFN-γ producing NK cell proportion at 1 month after treatment were independent predictors for HCC recurrence.
Conclusion: NK cell activity is significantly associated with the stages at diagnosis and the recurrence of HCC after curative treatment.

Abstract #613

SMG9 is upregulated in hepatocellular carcinoma and correlated with poor prognosis.

Zhi-shuo Mo[1], Pei-Pei Wang[1], Zhe-bin Wu[1]

[1]Department of Infectious Disease, The Third Affiliated Hospital, Sun Yat-Sen University, Guangzhou, China

Introduction: SMG9 is a component of the nonsense-mediated mRNA decay (NMD) complex. It degrades mRNA with mutations at the DNA level or in RNA itself during transcription or processing. However, our knowledge about the role of SMG9 in hepatocellular carcinoma (HCC) is limited.
Objectives: The present study is aimed to investigate the role of AMG9 in the prognosis of hepatocellular carcinoma (HCC).
Methods: HCC expression data were obtained from TCGA and GEO. The results were analyzed using EdgeR and GraphPad Prism 7 software to find the related data of SMG9. SMG9 mRNA expression was assessed in 16 pairs of HCC samples and adjacent normal liver tissues (ANLTs) by reverse transcription-quantitative polymerase chain reaction (RT-qPCR). The clinical data were collected and analyzed. Statistical analysis was performed with SPSS version 23.0 (IBM).
Results: SMG9 was highly expressed in HCC tissues compared with normal liver tissues according to analysis of data from TCGA ($P < 0.05$) and GEO ($P < 0.01$). RT-PCR analysis of SMG9 expression in 16 pairs of HCC tissues and corresponding ANLTs verified up-regulation of SMG9 in HCC tissues ($P < 0.001$). SMG9 was closely interrelated to TNM stage, Number of tumors, Tumor size and AFP levels. Kaplan–Meier and Cox proportional hazards analyses indicated that high SMG9 expression was related to poor patient survival
Conclusion: The study shows that high SMG9 expression could be a predictive of poor prognosis in patients with HCC.

Abstract #618

Prognostic value of dynactin 2 in hepatocellular carcinoma

Li Wenchao[1], Xiong Zhiyong[1], Yao Zhicheng[1], Zhou Hui[1], Huang Shaozhuo[1], Liu Bo[1], Hu Kunpeng[1]

[1]Department of General Surgery, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

Background: Dynactin (DCTN), including six family members, are dynein acting proteins that can activate the cytoplasmic dynein, and drive the intracellular organelles transportation. DCTN subunits are related to a number of malignant tumors. Nevertheless, the functions and prognostic roles of DCTN in hepatocellular carcinoma (HCC) have not been explored.
Objective: We aim to investigate the roles of distinct DCTN subunits in HCC.
Methods: We explored the gene expression and prognostic values of DCTN subunits in HCC through a variety of databases, including The Cancer Genome Atlas (TCGA), UALCAN, Kaplan–Meier Plotter and cBioPortal databases. Receiver operating characteristic (ROC) were conducted to evaluate the predictive power of the DCTN subunits in HCC diagnosis. Besides, we verified these results from the databases by performing the Western Blots and qRT-PCR. Finally, plate clonality, migration and invasion analysis assays were performed to analysis the oncogenicity of DCTN2 in HCC.
Results: COX regression analysis suggested that DCTN2 (HR = 1.748, 95% CI 1.190–2.568, and $p = 0.004$) was an independently prognostic factor for overall survival in HCC patients. Besides, Western Blot analysis validated that DCTN2 was upregulated in HCC tissue and hepatoma cell lines. Moreover, the proliferation and invasion ability of hepatoma cell Huh7 are inhibited when knockdown the expression of DCTN2.
Conclusion: We propose that DCTN2 level can serve as prognostic marker for hepatocellular carcinoma.

Abstract #636

Prognostic indication of transarterial chemoembolization and multikinase inhibitors in patients with intermediate stage hepatocellular carcinoma

Shigeo Shimose

Background: Prognosis of patients with intermediate stage hepatocellular carcinoma (HCC) treated with transcatheter arterial chemoembolization (TACE) is unsatisfactory. We analyzed the indications for suitable TACE in patients with intermediate stage HCC. We also investigated whether further TACE or switching to multi-kinase inhibitors (MKIs) was more beneficial for patients with HCC recurrence after initial TACE.
Methods: This retrospective study enrolled 238 patients with intermediate stage HCC who were initially treated with TACE (median age, 74 years). A decision-tree analysis was employed to investigate the therapeutic effect profiles and overall survival rates.
Results: In the decision-tree analysis for overall survival, complete response (CR) by initial TACE was selected as the most important variable. In the decision-tree analysis for CR, < 3 liver segments with nodule, simple nodular type, and within the up-to-seven criteria were selected as the first, second, and third variables associated with a high CR rate (35–64%), respectively. In patients with HCC recurrence having ≥ 3 liver segments with nodule, out of the up-to-seven criteria, and Child-Pugh class A, the median survival time was significantly longer in those who were treated by switching to MKIs than further TACE (44.9 vs. 21.9 months; $P = 0.003$).
Conclusion: In intermediate stage HCC, the indications for suitable TACE criteria may be "$<$ 3 liver segments with nodule," "simple nodular type," and "within the up-to-seven criteria." Moreover, in patients who were ineligible for TACE criteria, the switch to MKIs may improve the prognosis than further TACE in cases of HCC recurrence after first TACE.

Abstract #663

Low expression of growth hormone receptor (GHR) is correlated with malignant progression and predicts a poor prognosis in human hepatocellular carcinoma

Zhong Zhaozhong[1], Xiong Zhiyong[1], Liang Hao[1], Yang Jiarui[1], Cao Mingbo[1], Deng Meihai[1]

[1]Department of Hepatobiliary Surgery, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

Introduction: Hepatocellular carcinoma (HCC) is the most common primary malignancy of liver and the third highest cause of cancer-

related death worldwide. Growth hormone receptor (GHR), Combining with signal factors to activate a cascade of signaling events, might play an important role in tumorigenesis through its effects on cell proliferation, differentiation and apoptosis. Substantial evidence implicated that aberrant expression of GHR is associated with increasing risk of tumor, including breast, prostate, lung, melanoma, endometrial, pancreatic, and colon cancer.

Objectives: We performed an analysis to identify low expression of GHR is correlated with malignant progression and predicts a poor prognosis in HCC.

Methods: RNA sequencing and clinical information of patients were gathered from The Cancer Genome Atlas (TCGA) database, Kaplan Meier-plotter were performed to explore it's correlation with overall survival (OS), Levels of GHR were quantified using QRT-PCR. GHR was knocked down or overexpressed in human hepatoma cell lines (QGY, Huh7, 97L, Bel-7404), cells were analyzed for proliferation, migration, and invasion.

Results: Based on TCGA's information, GHR was found to be low expressed in HCC, and was correlated with shorter survival times of patients. QRT-PCR showed the same expression pattern of GHR with the result of TCGA database. Knockdown of GHR in hepatpma cells promoted proliferation, migration, and migration. While Overexpression of GHR reduced proliferation, migration and invasion.

Conclusion: This study suggests that low expression of growth hormone receptor (GHR) is correlated with malignant progression and predicts a poor prognosis in human hepatocellular carcinoma.

Abstract #709

Comparison of prediction models for the occurrence of hepatocellular carcinoma in patients with chronic hepatitis b: a systematic review and meta-analysis of combining 83,752 patients

Shanshan Wu[1], Zhirong Yang[2], Jialing Zhou[1], Xiaoning Wu[1], Yameng Sun[1], Yuanyuan Kong[1], Feng Sun[3], Siyan Zhan[3], Jidong Jia[1], Hong You[1]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing Key Laboratory of Translational Medicine in Liver Cirrhosis, National Clinical Research Center of Digestive Diseases, Beijing, China, [2]Primary Care Unit, Department of Public Health and Primary Care, School of Clinical Medicine, University of Cambridge, Cambridge, UK, CB18RN, [3]Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Centre, Beijing, China, 100191

Objective: To systematically identify and validate the performance of published hepatocellular carcinoma (HCC) prediction models in patients with chronic hepatitis B (CHB).

Methods: Medline, Embase and The Cochrane Library were systematically searched until 10th September, 2019 to identify prediction models for HCC and independent external validation studies in CHB. Model performance to predict HCC within 3/5 years after enrollment was assessed through meta-analytic discrimination (C-statistic) and calibration index (total observed:expected ratio).

Results: Overall, 12 models were identified from 29 out of 1133 publications with 83752 patients. Of all, REACH-B, CU-HCC, GAG-HCC, PAGE-B, LSM-HCC and mREACH-B were validated most, with 22, 18, 11, 10, 6, 5 studies and totally 22653, 15241, 10672, 25244, 4733, 3370 patients, respectively. Other models included mPAGE-B, AASL-HCC, NGM1-HCC, NGM2-HCC, RWS-HCC and CAMD. Discrimination was comparable for all models, with combined C-statistic ranging from 0.72 to 0.79 for 3-year and 0.71 to 0.86 for 5-year. Total observed:expected ratio ranged from 0.49 (NGM2-HCC for 5-year) to 0.72 (REACH-B for 5-year) for all 3/5-year models. Compared with no-treatment, discrimination was worse in patients undergoing anti-viral therapy for REACH-B (0.61 and 0.64 for 3 and 5-year), while it was similar in other 5 leading models ranging from 0.74 to 0.82. Compared with non-cirrhotic patients, the most 6 leading models performed worse in cirrhotic patients, ranging from 0.60 (LSM-HCC) to 0.72 (mREACH-B) for 3-year and 0.59 (PAGE-B) to 0.69 (mREACH-B) for 5-year.

Conclusion: Several models performed relatively poor discrimination in patients with cirrhosis and anti-viral therapy. Nearly all models predicted higher HCC risk than in fact.

Abstract #734

Nucleos (t)ide analogs reduces hepatocellular carcinoma mortality in patients with low HBV-DNA levels

Wang Xinhui[1], Liu Xiaoli[1], Yu Lihua[1], Wang Peng[1], Wang Xianbo[1], Yang Zhiyun[1]

[1]Center of Integrative Medicine, Beijing Ditan Hospital, Capital Medical University, Beijing 100015, People's Republic of China

Aims: To evaluate whether antiviral therapy is useful in reducing mortality in patients with low HBV-DNA levels.

Method: A retrospective analysis was performed of 853 patients diagnosed with HBV-related HCC with HBV-DNA < 500 IU/mL between January 2008 and June 2017 at the Beijing Ditan Hospital. Patients were divided into antiviral group and non-antiviral group according to whether they were treated with Nucleos (t)ide Analogs (NA) in the first diagnosis of primary liver cancer in our hospital. We used 1:4 frequency matching to compare the antiviral group (n = 444) and non-antiviral group (n = 111). A Cox multivariate regression analysis was employed to evaluate the effects of NA therapy on the Hazard Risks (HR) value and Kaplan–Meier survival curve for mortality risk in HCC patients. A log-rank test was performed to analyze the effect of NA therapy on the survival time of HCC patients.

Results: After propensity score matching, the 1-, 3-, and 5-year overall survival rates for the antiviral group and the control group were 78.8%, 61.9%, 26.2%, and 63.1%, 49.5%, and 12.9%, respectively. The overall survival for the antiviral group were significantly better than the control group (P = 0.001, P = 0.023, P = 0.018, respectively). The l year progress free survival rates for the 2 groups were 63.3% and 54.1%, respectively (P = 0.081). After adjusting for confounding prognostic factors in a Cox model, the HR of death for antiviral treatment was 0.651 [95% CI 0.496– 0.856; P = 0.005]. Antiviral therapy was an independent protective factor of mortality.

Conclusion: In patients with low HBV-DNA levels, antiviral therapy significantly reduced HCC mortality.

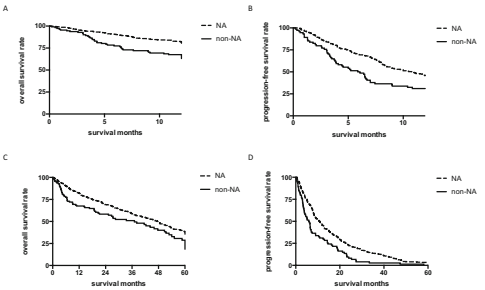


Fig.1 Kaplan–Meier curves of overall survival (OS) and progression-free survival (PFS) for total 853 of propensity-score- matched patients. (A) OS and (B) PFS for 1 year; (C) OS and (D) PFS for 5 years.

Table 1 Univariate and multivariate Cox analysis for 5 year OS of Hepatocellular Carcinoma in PS matched patients.

	Univariate analysis			Multivariate analysis		
	P	*HR*	*95%CI*	*P*	*AdjustHR*	*95%CI*
Gender	0.993	1.001	[0.770 1.302]			
Age	0.036*	1.357	[1.020 1.807]			
HBeAg	0.362	0.925	[0.783 1.093]			
antiviral	0.007*	0.681	[0.521 0.891]	0.002*	0.651	[0.496 0.856]
rGGT	0.000*	1.788	[1.390 2.300]	0.000*	1.661	[1.305 2.115]
MELD	0.000*	1.762	[1.361 2.280]	0.000*	1.601	[1.253 2.046]
AFP	0.026*	1.371	[1.039 1.811]	0.032*	1.736	[1.332 2.261]
Tumor Size	0.001*	1.600	[1.220 2.100]	0.000*	1.908	[1.464 2.486]
BCLCgroup	0.000*	1.865	[1.426 2.440]	0.000*	1.851	[1.721 1.990]

Abstract #738

A decision-tree analysis of prognostic factors in hepatic arterial infusion chemotherapy for advanced hepatocellular carcinoma exceeding up-to-7 criteria

Takashi Niizeki

Aim: To assess efficacy of HAIC using cisplatin (CDDP) suspended in lipiodol in combination with 5-fluorouracil (5-FU) (New FP) in patients with advanced HCC exceeding up-to-7 criteria and without EHS, and to determine good indication of New FP.
Methods: Between April 2008 and March 2017, total of 126 consecutive patients were enrolled. The primary and secondary endpoint in efficacy was median survival time (MST), and tumor response rate (RR) and CR rate, respectively. Clinical factors associated with CR were identified by a decision-tree analysis.
Results: In New FP therapy, MST, RR, and CR rate was 25.6 months, 74%, and 27%, respectively. Rate for CR, PR, SD, and PD was 27%, 47%, 13%, and 13%, respectively; and MST stratified by CR, PR, SD, and PD was 67, 26, 11, and 6.5 months, respectively. Treatment-related death was not observed. A decision-tree analysis of CR predictors revealed as follows: the number of liver segment where tumor localizes ≤ 2, responsiveness to TACE, and the number of tumors ≤ 4. In 59 cases with "(1) both the tumor-located segments ≤ 2 and responsiveness to TACE" or "(2) both the tumor-located segments > 3 and the number of tumors ≤ 4", MST, RR, and CR rate was 37 months, 85%, and 53%, respectively.
Conclusion: New FP therapy was tolerable and demonstrated robust efficacy. Regardless of tumor size and the status of macroscopic vascular invasion, the above conditions (1) and (2) are defined as good prognostic factors for New FP-treated locally advanced HCC.

Abstract #740

A Scoring system based on artificial neural network for predicting progression in HBV-related hepatocellular carcinoma

Liu Xiaoli[1], Hou Yixin[1], Wang Xinhui[1], Yu Lihua[1], Wang Xianbo[1], Jiang Li[2], Yang Zhiyun[1]

[1]Center of Integrative Medicine, Beijing Ditan Hospital, Capital Medical University, Beijing 100015, China, [2]Department of Hepatobiliary Surgery, Beijing Ditan Hospital, Capital Medical University, Beijing 100015, China

Objectives: Disease progression is an important factor affecting the long-term survival in hepatocellular carcinoma (HCC). This study aimed to explore the prognostic factors that affect the progression of HCC and establish an individualized prediction model.
Methods: We included 2890 patients with hepatitis B-related HCC hospitalized at Beijing Ditan Hospital, Capital Medical University and randomly divided into training and validation cohort. Cox multivariate regression was used to analyze independent risk factors affecting the 1-year progression of HCC, and an artificial neural network model was constructed. C-index, calibration curve, and decision curve analysis were used to evaluate the performance of the model.
Results: Cox multivariate regression showed smoking history, a tumor numeras ≥ 2, tumor size ≥ 5 cm, portal vein tumor thrombus, WBC, NLR, γ-GGT, ALP, and AFP ≥ 400 ng/mL were risk factors for 1-year progression-free survival (PFS), while albumin and CD4 T cell counts were protective factors in HCC patients. The AUROC of 1-year PFS in HCC patients was 0.866 (95% CI 0.848–0.884), which were higher than predicted by TNM, BCLC, Okuda, CLIP, CUPI, JIS, and ALBI scores ($P < 0.0001$). All patients were divided into high-, medium-, and low-risk groups, according to the ANNs model scores. Compared with the hazard ratios (HRs) of PFS in low-risk group, those in the high-risk group were 26.42 (95% CI 18.74–37.25; $P < 0.0001$) and 6.13 (95% CI 4.28–8.79; $P < 0.0001$) in the training and validation cohorts, respectively.
Conclusion: The ANNs model has good individualized prediction performance and is helpful to evaluate the disease progression of HCC in clinical practice.

Abstract #745

Prediction of long-term Survival of patients with Hepatocellular carcinoma based on NK Cells count novel model

Yu Lihua[1], Liu Xiaoli[1], Wang Xinhui[1], Yan Huiwen[1], Jiang Yuyong[1], Wang Xianbo[1], Yang Zhiyun[1]

[1]Center of Integrative Medicine, Beijing Ditan Hospital, Capital Medical University, Beijing 100015, People's Republic of China

Background and aims: Among all immune cells, NK cells, as the first line of defense against tumor, play a vital role. The purpose of our study is to observe whether the number of NK cells can predict the survival of patients with hepatocellular carcinoma (HCC).
Method: To develop a novel model, a retrospective cohort with HCC (n = 121) at Beijing Ditan Hospital was enrolled from January 2012 and June 2014. Furthermore, a prospective cohort (n = 58) was recruited to validate the association between NK cells count and survival in patients with HCC.
Results: The model used in predicting survival of HCC included four variables (namely, NK cells count, tumor size, tumor number, and AFP level). A simple assessment using a nomogram showed the 5-year OS rate of patients with HCC. The nomogram was divided into high, intermediate and low risk groups to predict the 5-years survival risk of HCC patients ($p < 0.001$), and there were significant differences in BCLC stage 0-B and BCLC stage C-D ($p = 0.002$, $p = 0.0042$). The decision tree showed that the 5-years death risk of HCC with low NK count (≤ 124.5) was 61.2%. In the prospective cohort, the contour line shows that low NK counts and high AFP level have more death of HCC. NK cells count in patients with advanced HCC was significantly lower than that in patients with early.
Conclusion: Our study emphasises the utility of NK cells count for exploring interactions between long-term survival and predictor variables.

Figure:

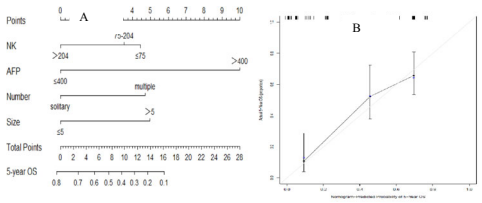


Figure1. Prognostic nomogram and calibration curves. Nomogram predicted overall survival (OS) (A) for HCC patients. To use the nomogram, the value of an individual patient is located on each variable axis, and a line is drawn upward to determine the number of points received for the value of each variable. The sum of these numbers is located on the total point axis, and a line is drawn downward to OS axes to determine the likelihood of 5-year OS. The calibration curves for 5-year OS (B) in the deriving cohorts were identified.

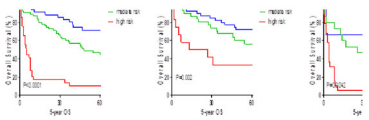


Figure2. The nomogram score is divided into low, medium and high-risk groups according to the interquartile spacing (low risk group, ≤ 3.5point; medium risk group, 3.5-14 point; high risk group, > 14 point). (A)Nomogram; (B)BCLC stage 0-B; (C)BCLC stage C-D.

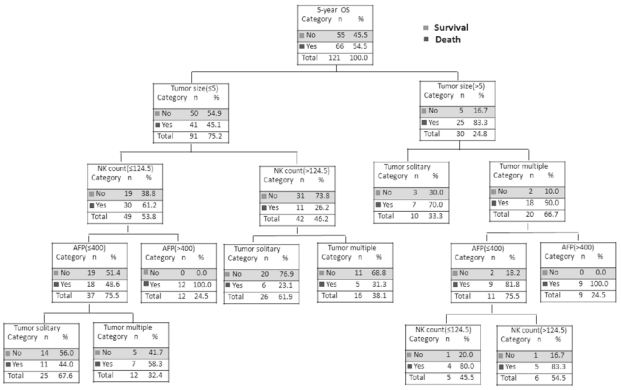


Figure3. Decision tree for model shows 5-year Survival rate of patients with Hepatocellular carcinoma

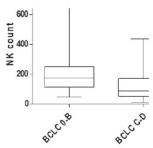


Figure 4. In the prospective cohort, NK cells count in patients with advanced HCC was significantly lower than that in patients with early.

Abstract #845

Sorafenib inhibits angiogenesis and reduces the growth of human hepatocellular carcinoma in cirrhotic mouse xenograft model

Huang Qingyao Daniel[1], Zhou Lei[2], Tan Wan Xin[2], Jumat Nur Halisah[2], Abbas Sakinah[2], Wee Aileen[3], Soon Gwyneth3, Pang Yin Huei[3], Madhavan Krishnakumar [4], Bonney Glenn[4], Kow Alfred[4], Iyer Shridhar Ganpathi[4], Dan Yock Young[1,2]

[1]Division of Gastroenterology and Hepatology, National University Hospital, Singapore, [2]Department of Medicine, National University of Singapore, Singapore, [3]Department of Pathology, National University Hospital, Singapore, [4]Department of Surgery, National University Hospital, Singapore

Introduction: Hepatocellular carcinoma (HCC) is one of the most common and deadly cancers worldwide, with a high prevalence in Asia due to endemicity of Hepatitis B. The effectiveness of chemotherapeutic agents for this tumor such as sorafenib and lenvatinib vary among patients. There is an unmet need for patient-derived xenograft (PDX) animal models that can accurately predict response to therapy. In this study, we describe a PDX that recreates the fibrotic and inflammatory microenvironment in cirrhosis and predicts response to sorafenib.
Methods: NOD Scid gamma (NSG) mice were treated with thioacetamide to induce liver fibrosis. The human HCC tissue was cut into small fragments, suspended in Corning Matrigel Matrix was injected into the mouse livers. Sorafenib (100 mg/kg) was administered orally, once daily in 16 days to the cirrhotic mice with PDX and compared with control (saline). MRI of the mouse livers was performed before and after administration of sorafenib. With the xenograft tissue, histology and Immunofluorescence for CD34, an endothelial cell marker, were performed.
Results: PDXs were developed in the cirrhotic livers in mice successfully and their morphological appearances were similar to the original human HCC. Non response to sorafenib in the PDX model predicted clinical non response to sorafenib. In other PDX HCC lines, MRI showed that Sorafenib significantly reduced PDX growth rate compared to control group ($p < 0.05$) in the model. Sorafenib responders showed downregulation of CD34. **Conclusion**: The cirrhotic PDX is able to predict response to sorafenib, which is mediated by effects on angiogenesis.

Abstract #850

Amniotic epithelial cell (AEC) exosomes modulate epithelial to mesenchymal transition in HCC cell line

Huang Qingyao Daniel[1], Tan Wan Xin[2], Zhou Lei[2], Jumat Nur Halisah[2], Abbas Sakinah[2], Raj Vaishnevi[2], Seet Bee Leng2, Lee Yi Xin Fiona[3], Choolani Mahesh[4], Dasgupta Ramanuj[3], Dan Yock Young[1,2]

[1]Division of Gastroenterology and Hepatology, National University Hospital, Singapore, [2]Department of Medicine, National University of Singapore, Singapore, [3]Genome Institute of Singapore, A*Star, Singapore, [4]Department of Surgery, National University Hospital, Singapore

Introduction: Epithelial to mesenchymal transition (EMT) plays a key role in hepatocellular carcinoma (HCC) development, and tumor invasion and metastasis. Exosomes are extracellular vesicles (EVs) and play an important role in cell signaling, cancer progression and metastases. In this study, we evaluated the effect of exosomes on HCC growth and invasiveness.
Methods: The exosome (EV, less than 100 nm) was obtained from the culture supernatant of human amniotic epithelial cells (AEC) by size exclusion chromatography. NOD Scid gamma mice were treated with thioacetamide and induced liver cirrhosis. HCC cells from HUH-7 or SK Hep-1 were orthotopically transplanted into the cirrhotic mouse livers to mimic the real HCC microenvironment in human. Exosomes were administrated to the transplanted mice for two weeks before animal organs were harvested. Immunofluorescence and western blot for vimentin, a mesenchymal marker was performed to evaluate the effects of the exosome on the HCC invasion and differentiation.
Results: The number of HUH7 colonies in mouse liver were significantly reduced in the exosome group compared to control ($p < 0.01$).

Exosomes also resulted in significant inhibition of SK Hep1 cell growth ($p < 0.05$) compared to control. Exosomes reduced SK Hep1 cell metastasis to the lung ($p < 0.05$). The vimentin expression in SK Hep-1 cells transplanted in mice in exosome group is significantly lower than that in control group ($p < 0.01$) by calculation of sum intensity value with immunofluorescence. The reduction of vimentin expression was confirmed by western blot ($p < 0.01$).
Conclusion: AEC exosomes inhibit HCC growth and invasion possibly by reversing epithelial to mesenchymal transition.

Abstract #905

Profile and characteristic demographic of hepatocellular carcinoma in west kalimantan: the first study

Frastica Michelle[1], Mulyadi Yustar[2]

[1]Internal Medicine Department, Dr. Soedarso General District Hospital, Pontianak, West Borneo, Indonesia, [2]Internal Medicine Department, Dr. Soedarso General District Hospital, Pontianak, West Borneo, Indonesia

Introduction: The prevalence and incidence of hepatocellular carcinoma (HCC) vary around the globe; however 72.5% of the new cases were from Asian countries. [1] Major risk factors of HCC are viral toxic, metabolic and immune-related.[3] This is the first study that examine the demographic characteristic or profile among patients with HCC in West Kalimantan, a region of Indonesia.
Objective: To explore the characteristics of HCC among patients in West Kalimantan
Methods: Restrospective study of 152 patients data, retrieved from the medical record, with HCC in the Dr Soedarso General Hospital, the highest referral hospital in West Borneo, Indonesia, between July 2016 to Februrary 2019 (30 months). The diagnosis of HCC was established through either histopathological examination or imaging modalities.
Result: Most of the subjects were males (n = 110), from 50 s age group (33.6%, n = 51) and came from Malay (34.2%) ethnic background. The majority had normal BMI (77%) and had no history of alcohol intake (88.2%). Liver viral infection was common in this study, at least one of the viruses responsible for chronic liver infection (HBV 59.2% or HCV 16.4) and was present in 71.7% of cases (n = 109).
Conclusion: The majority of HCC patients in West Borneo were male (n = 110), from 50 s age group (33.6%, n = 51), Malay (34.2%), had normal BMI (77%) and had no history of alcohol intake (88.2%). The most common viral liver infection found were hepatitis B (59.2%).

Abstract #958

Atypical clinical presentation of advanced hepatocellular carcinoma

Saut Horas H. Nababan[1], Wahyu Purnama[1], Ening Krisnuhoni[2], Irsan Hasan[1], Rino A. Gani[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia, [2]Department of Anatomy Pathology, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Background: Hepatocellular carcinoma (HCC) still pose diagnostic challenge, as 40% of HCC lesions do not show the typical wash-in wash-out pattern on dynamic CT or MRI.
Method: We reported a 69-year-old male admitted with melena, history of recurrent upper abdominal pain and weight loss of 3 kg within five months. Physical examination revealed hepatomegaly with ascites. HbsAg and AntiHCV were negative. Upper endoscopy showed gastric mass extending from proximal corpus to antrum with biopsy showed poorly differentiated adenocarcinoma. Multiphase abdominal CTScan showed multiple lesions on the right and left liver lobes with gradual centripetal enhancement, suggesting liver metastasis of gastric cancer. Tumor marker levels were very high for AFP (5691 ng/ml) with normal CEA and Ca 19-9 (2.7 ng/ml and 4.3 U/ml). At this point, liver biopsy was performed and the result was grade III HCC. The immunohistochemical staining from both liver and gastric tissues showed weak positivity for HepPar-1, strong positivity for glypican-3 and glutamine synthetase. The CEA and CK7 expressions were negative. The final diagnosis was HCC with gastric metastasis. The patient died one month after admission.
Discussion: This case illustrates the atypical imaging pattern of HCC with extrahepatic metastasis and the value of immunohistochemical evaluation. Histologically, poorly differentiated HCC has overlap features with metastatic adenocarcinoma or cholangiocarcinoma. In this case, an immunohistochemical panel can help to identify the hepatocellular differentiation of liver tumors.
Conclusion: In most cases of HCC, tissue diagnosis is unnecessary. However, in atypical HCC with extrahepatic metastasis, immunohistochemistry can help establish the diagnosis

Abstract #973

Role of Fibroscan for early detection of hepatocellular carcinoma (HCC) in hepatitis C Cirrhotic patients

Ahmed Elhosieny Ebrahim[1], Mona Ahmed Helmy Shehata[2], Sabry Abou-saif[2], Manal fathy Hamisa[3], Mohamed Yousef[2], Sherief Abd-Elsalam[2]

[1]Kafr-Elsheikh General Hospital, Kafr-Elsheikh, Egypt, [2]Department of Tropical Medicine, Tanta University, Tanta, Egypt, [3]Diagnostic Radiology Department, Tanta University, Tanta, Egypt.

Background and aims: Hepatocellular carcinoma (HCC) is ranked to be the fifth prevalent cancer worldwide and it is in the third place as the commonest cause of deaths due to cancer. The utility of Fibroscan in the evaluation of the risk for HCC has not been fully elucidated that is assessed in this work. The aim of this work was to study the role and clinical significance of Fibroscan for early detection of HCC in hepatitis C Cirrhotic patients.
Methods: This was a cross sectional study included Fifty (50) HCV patients. They were divided into two groups as the following: group I: Included 25 HCV cirrhotic patients with HCC and group II: Included 25 HCV cirrhotic patients without HCC. These patients have undergone thorough history, clinical examination; laboratory and radiological investigations and Fibroscan was done for all patients enrolled in the study.
Results: As regards binary logistic regression for predictors of HCC, it was found that Child C, AST, Fibroscan and AFP were predictors for developing HCC. Liver stiffness values were significantly high in all groups, and the determined cut-off value for HCC concurrence was more than 24 kPa in those with HCV. So, Liver stiffness of more than 24 kPa can be considered as an independent risk factor for new HCC development in HCV cirrhotic patients.
Conclusion: Liver stiffness of more than 24 kPa was an independent risk factor for new HCC development in HCV cirrhotic patients.

Abstract #978

The expression of leptin in type 2 diabetic rat induced hepatocellular carcinoma by dietylnitrosamine

Atmodjo-Wahyuni Lukita[1,2], Larasati-Young Othiwi[2], Nufika-Riska[2], Naomi-Steffi[3], Marlen-Stella[1], Sulistiawati-Erni[4]

[1]Faculty of Medicine, Universitas Pelita Harapan, Tangerang 15810, Indonesia, [2]Mochtar Riady Institute for Nanotechnology, Tangerang, Indonesia, [3]Indonesia International Institute for Life Science, Jakarta, Indonesia, [4]Vocational School, Bogor Agricultural University, Bogor, Indonesia

Introduction: People with type 2 diabetes commonly show a higher risk of developing hepatocellular carcinoma (HCC). Leptin which expressed in activated hepatic stellate cells (HSC) and neoplastic cells, has a potential role in HCC development. Although leptin level increased significantly in liver cirrhosis with HCC, however the expressions of leptin in liver cells of type 2 diabetic rat induced-HCC has not yet been explored clearly.
Objective: to explore the expressions of leptin in liver cells of type 2 diabetic rat induced-HCC.
Methods: Wistar rats were divided into 3 groups; (1) negative control group; (2) diabetic group given high fat diet (HFD) and Streptozotocin (STZ) injection 45 mg/kg BW two times in a week interval; and (3) diabetic-HCC group, diabetic rat injected with Diehylnitrosamine (DEN) 70 mg/kg BW every week. All groups were sacrificed 10 weeks after first DEN injection. The liver were stained immunohistochemically to evaluate the expression of leptin. Leptin expression were measured using ImageJ and analyzed using SPSS with p-value < 0.05 as statistically significance.
Result: In the control and diabetic rat liver, leptin was not expressed in either the parenchymal or non-parenchymal cells. However, high leptin expression was found in the cytoplasm of pre-neoplastic cells characterized with prominent nucleoli of diabetic-HCC liver. The difference level of leptin expression in diabetic-HCC rats showed significantly difference with $p \leq 0.005$ compared to diabetic and control group.
Conclusion: High level expression of leptin in pre-neoplastic cells of diabetic-HCC rats showed that leptin were involved in the liver carcinogenesis.

Abstract #989

Comparison of alpha-fetoprotein serum levels in patients with hepatocellular carcinoma with with etiology of hepatitis b or hepatitis c virus infection and hepatitis b non-virus and hepatitis c infection

Pravdani K. M.[1], Yusra[2]

[1]Medical student, Faculty of Medicine, Universitas Indonesia, Salemba, Jakarta, Indonesia, [2]Clinical Pathology Department, Faculty of Medicine, Universitas Indonesia, Salemba, Jakarta, Indonesia

Introduction: Hepatocellular carcinoma (HCC) is one of the highest rates of mortality in the world. Serum alpha-fetoprotein (AFP) levels can be used as a biomarker for early diagnosis. However, the comparison between serum AFP and HCC with viral infections etiology and non-viral etiology is unknown. This research aims to determine the comparison between serum AFP and HCC with viral infections etiology and non-viral aetiology.
Methods: A cross-sectional study conducted in Cipto Mangunkusumo Hospital, Jakarta in January to October 2018 by reviewing 287 medical records of patients diagnosed with HCC from 2013 to 2017 period of time.
Results: The median (minimum–maximum) value of AFP levels in HCC patients with the etiology of VHB or HCV infection is 419 (0.8–400,000). The median value (minimum–maximum) of AFP levels in HCC patients with the etiology of non HBV-HCV infection was 7.18 (0.6–90,944).
Conclusion: There were significant differences between AFP levels and KHS with the etiology of HBV or HCV infections and the etiology of non HBV-HCV infections (p value < 0.0001).

Abstract #1021

Comparison of 10-year mortality of HCC treated with RFA by a self-trained expert and a beginner, trained by dr. Shiina

Hitoshi Mochizuki

RFA is not necessarily a simple procedure. In this study, we compared the difference in the mortality of HCC treated by RFA conducted by an expert and a beginner. Expert has the experience of more than 800 cases for the past 7 years, but never had the experience of training. Therefore, he can be called a self-trained expert. Contrary, the other doctor who was 54 year old, went to Dr. Shiina's hospital and had he basic trainings for 6 months. The comparison study started 10 years ago. Totally, 92 cases were treated by RFA; 43 by beginner and 49 were by the experienced. Ages, gender, Child-Pugh score, virus types, mean number, diameter of the HCC nodules were no different. Pleural and peritoneal effusion techniques were used more often by a beginner (43.1% vs. 17.1% and 10.3% vs. 0%, respectively). Results: Local recurrence rate at one and two years were not different between the two doctors. Median survival time for the beginner was 5.4 years whereas that of experienced was2.8. Five year survival was 57% for the beginner and29% for the experienced, respectively. The difference was statically significant ($p = 0.04$). Conclusion: Ten year follow up study clearly indicate you need the basic training before starting RFA under the supervision of experts at high throughput institution.
Background/aims: Although RFA procedure has been employed so widely as treatment option for therapy of HCC, training system for the beginner has not been established.
Methods: Ninety-two consecutive HCC patients were randomly assigned to two board-certified hepatogastroenterologists. One (KH) has performed more than 600 cases of RFA in the past 12 years, but principally self-trained. He is called, here, as the *Experienced*. The other (HM) is also a board-certified gastroenterologist, never experienced ablation procedure for HCC in the past 30 years. Here, HM is called the *Beginner*. However, the *Beginner* had 6 months training session of RFA at high-throughput center before he stared to perform the ablation procedure.
Results: The *Beginner* (HM) and the *Expert* (KH) performed 43 and 49 ablations, respectively. There was no difference of background demographic and clinical feature of two patients cohort. The length of time required for ablation was longer (75 min) by the *Beginner* than by the *Experienced* (49 min). However, complication rate during and after the procedure and outcome of the treatment, namely Overall survaival rate within 10 years, were no different between the two operators. Differences noted were frequencies of employment of pleural effusion techniques, peritoneal effusion techniques by the *Beginner* and the *Experienced*, respectively.
Conclusions: This prospective study concluded that the proper training, including the experience of ultrasound guided needling with the help of pleural or peritoneal effusion methods helped to start safe and effective ablation treatment procedure by the *Beginner*.

Abstract #1070

Study on validity of biomarkers DKK1 and HBx-LINE1 in diagnosis and posttreatment mornitoring of hepatocellular carcinoma

Hieu Trung Le[1,3], Hai Trung Le[2,3]

[1]Military Central Hospital, [2]Hanoi General Hospital, [3] The Vietnamese Association for the Study of liver diseases

Objective: Evaluate validity of DKK1 and HBx-LINE1 in diagnosis and post-treatment of HCC/HBV and analyse relationship with clinical and paraclinical some characteristics.
Subject and method: Study on 114 HCC patients at Central Militay Hospital 108, Military Hospital 103 and Military Hospital 175 (1/2016 to 3/2018) with DKK1 and HBx-LINE1, re-examination after surgery.
Result: With DKK1 $\geq$ 2.15 ng/mL, the positive rates of serum protein DKK1 were significant increased when compared with those of AFP (97.37% and 62.92%, respectively). The mean of serum protein DKK1 of HCC was significant higher than it in liver cirrhosis patients with $p < 0.05$. Combination beetwen AFP and DKK1 expression will improved positive rates and help more diagnosis in 12.3% of HCC cases. Logistic regression analysis showed the risk of HCC will increased about 18.5 times when DKK1 $\geq$ 2.15 ng/mL.
Conclusion: Biomarkers serum protein DKK1 and DKK1 expression have validity in diagnosis and post-treatment of HCC, especially for AFP-negative patient. HBx-LINE1 fusion transcript was not identified in our study

Abstract #1075

The Relationship between adverse events caused by sorafenib treatment and microbiome in patients with advanced hepatocellular carcinoma

Kenta Yamamoto[1], Teiji Kuzuya[1], Takashi Honda[1], Takanori Ito[1], Yoji Ishizu[1], Masatoshi Ishigami[1], Mitsuhiro Fujishiro[1]

[1]Department of Gastroenterology and Hepatology, Nagoya University Graduate School of Medicine

Introduction and objectives: The microbiome has the potential to chemically modify drugs and bacterial metabolism associated with treatment effects and adverse events. Sorafenib is also influenced by the microbiome due to enterohepatic recycling. We evaluated the relationship between the microbiome of advanced hepatocellular carcinoma patients and hand foot syndrome (HFS) or diarrhea caused by sorafenib treatment.
Methods: Twenty-five patients with hepatocellular carcinoma were classified into two groups based on the presence of HFS or diarrhea. The microbiome was nalysed from a stool sample using the Illumina MiSeq sequencing platform targeting the V3–V4 region of 16 s rRNA before sorafenib treatment. Microbiome and bacterial functioning predicted by the Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt) were compared between the groups.
Results: The non-HFS group (n = 9) had a richer abundance of genus *Veillonella, Faecalibacterium, Lachnospira, Dialister, Bacillus, Enterobacter*, *Anaerostipes*, and family *Bacillaceae* than the HFS group (n = 16). Carotenoid biosynthesis (p = 0.018) and bacterial invasion of epithelial cells (p = 0.032) were enriched in the HFS group. The non-diarrhea group (n = 17) had a higher abundance of genus *Butyricimonas* and class *Erysipelotrichi*, and a lower abundance of *Citrobacter*, *Peptostreptococcus,* and family *Staphylococcaceae* than the diarrhea group (n = 7). Eight categories were detected by PICRUSt, with significant differences between the two groups.
Conclusion: The non-HFS group had much more oral bacteria, which facilitated dysbiosis in the gut. This dysbiosis may affect enterohepatic recycling of sorafenib. The non-diarrhea group may have a protective intestinal environment resulting from bacterial functionality.

Abstract #1095

Hepatitis virus induced hepatocellular carcinoma is associated with more severe cancer staging in recent years

Batbold Batsaikhan[1], Ganchimeg Dondov[1], Tulgaa Lonjid[1], Gantsetseg Gantumur[2], Chia-Yen Dai[3,4,5,6]

[1]Department of Internal Medicine, Institute of Medical Sciences, Mongolian National University of Medical Science, Ulaanbaatar, Mongolia,[2]Mongolian Association of Family Medicine Specialists, Mongolia, [3]Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, [4]Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [5]Faculty of Internal Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, [6]Health Management Center and Department of Occupational and Environmental Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

Objective: Barcelona Clinical Liver Cancer Research (BCLC) staging system is for the classification of hepatocellular carcinoma (HCC). Chronic hepatitis B induced HCC is associated with more severe cancer stage by BCLC. We aimed to analyze whether viral induced HCC have more severe cancer stage in two different time period.
Methods: Characteristics of 3391consecutive patients from single medical center admitted during 1993–2018 have been analyzed. Multiple comparisons of BCLC staging and clinical features were done.
Results: Hepatitis C virus (HCV) positive HCC showed 35.6%, hepatitis B virus (HBV) induced HCC was 41.2%, 18% showed negative for both HCV; HBV and 5.2% of patients had coinfection. Patients who diagnosed HCC after 2014 were older (65.4 ± 11.2 years versus 62.1 ± 11.9 years, $p < 0.001$) compared to the patients who diagnosed previously. Patients with viral induced HCC were associated with older age (hepatitis C virus—$p < 0.001$; hepatitis B virus—$p < 0.001$) but not in co-infected patients ($p = 0.055$). We used the Barcelona Clinic Liver Cancer staging system and stage C, D were increased in viral induced (HCV 43.4% to 55.6%, $p < 0.001$; HBV 40% to 60.5%, $p = 0.008$) HCC after 2014. However HBV plus HCV patients and non-viral induced patients were did not increased significantly after 2014.
Conclusion: Patients with viral induced HCC classified in more severe BCLC stage after 2014. However, the prevalence of viral induced HCC was decreased and it was associated with older age in patients who diagnosed after 2014

Abstract #1111

Combined hepatocellular-cholangiocarcinoma in liver cirrhosis HBV patient: a case report

Patriotika Ismail[1], Kemal Fariz Kalista[2]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo General Hospital, Jakarta, Indonesia, [2]Division of Hepatobiliary, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo General Hospital, Jakarta, Indonesia

Introduction: Combined hepatocellular-cholangiocarcinoma (CHC) is an infrequent primary hepatic malignancy with no clearly defined diagnostic criteria, and no guidelines regarding therapy.
Case report: Male 74 years old, with dull pain in the right upper abdomen since 6 months. Physical exam showed no jaundice and organomegaly. Platelet, PT, albumin, bilirubin, AFP and Ca 19-9 was normal. HBsAg (+), HBV DNA 4.35×10^4 IU/mL. Gastroscopy showed esophageal varices grade 2. Abdominal ultrasound showed isoechoic inhomogen mass in the right lobe. Multiphase Abdomen CT showed cirrhotic liver with hypervascular mass in S-IV, V and VIII with diameter 10 cm, enhanced in arterial phase, some part of the lesion showed more prominent enhancement in venous phase, other part of the lesion showed wash-out in venous phase, isodens in delayed phase and mass also cause biliary obstruction in proximal CBD level. Liver core biopsy showed highly differentiated hepatocellular carcinoma and moderately differentiated cholangiocarcinoma. (WHO Criteria classical type).
Discussion: CHC is a rare primary malignant liver tumor, accounts for 1.2% to 14.2%. The case we report of combined hepatocellular and cholangiocarcinoma in patient with HBsAg (+). Patient with CHC have same risk factor like HCC such as viral hepatitis and cirrhosis. CHC has more aggressive behavior and related with poorer prognosis. More cases should be accumulated to illuminate the feature diagnosis and therapeutic strategy of this unique tumor.
Conclusion: CHC with no diagnosis criteria and guideline for therapy, we need to perform a good examination including histological examination to confirm the diagnosis before proceed to treatment planning.

Abstract #1115

Unusual metastasis of hepatocellular carcinoma to the esophagus

Wahyu Purnama[1], Lucky Nosih[1], Nurhidayati[2]

[1]General Practitioner in Massenrempulu Hospital, Enrekang, South Sulawesi, [2]Internal medicine in Massenrempulu Hospital, Enrekang, South Sulawesi

Backgrounds: The most common sites of metastasis from Hepatocellular carcinoma are the lung, bone, intraperitoneal organ, and adrenal gland. The esophagus is the rare site of metastasis.
Case illustration: A male, 75-year-old with unusual metastatic of Hepatocellular carcinoma to esophagogastric junction causing diagnostic lemma. An endoscopic examination revealed an ulcerative lesion in the lower end of the esophagus. The biopsy specimen revealed the pseudoglandular arrangement of tumor cells. Ultrasound abdomen showed liver nodule with biopsy confirming HCC. Immunohistochemistry (IHC) of the esophageal mass showed positivity for Hep par 1, Glypican-3, Arginase, Ca-199, CK 19, CDX2, pCEA, SATB2, and Ki-67 having 70% positivity confirming the HCC.
Discussion: Among these IHC panels, all are specific markers of HCC, but CDX2 and SATB2 were aberrantly expressed in our case. He was started on six cycles of chemotherapy (apristar 125 mg, epirubicin 40 mg, oxaliplatin 100 mg, and capecitabine 500 mg). After 8 months of follow-up, he was symptomatically improved. However, later, the patient was lost to follow-up. The accurate pretreatment staging and then providing stage appropriate treatment is crucial in optimizing esophageal and hepatocellular cancer outcomes.
Conclusion: The case of premortem diagnosed esophageal metastasis from HCC is extremely rare. Our case was ideal for IHC, which plays an important role in arriving at proper cases. Furthermore, it confirmed and highlighted the rare manifestations of hepatocellular carcinoma.

Abstract #1122

Microwave ablation therapy vs radiofrequency ablation for primary hepatocellular carcinoma in cardinal santos medical center: a retrospective cohort

Tongo, Marco Angelo[1], Payawal, Diana A.[1]

[1]Section of Gastroenterology, Department of Internal Medicine, Cardinal Santos Medical Center San Juan City, Philippines

Introduction: In the Philippines, prevalence rate for hepatocellular carcinoma is 7.8% with mortality rate of 25%. Cases of poor post-operative recovery and post resection complications prompted development of local ablation techniques including Percutaneous Microwave Ablation (PMAT) Therapy, which was recently introduced in a tertiary hospital in the Philippines.
Objectives: This study aims to compare the liver function tests and alpha-fetoprotein (AFP) levels of patients who underwent Percutaneous Microwave Ablation Therapy (PMAT) with those who underwent Radiofrequency ablation (RFA).
Methods: Review of records from January to December 2018 was done yielding, a total of sixteen (16) patients with Primary Hepatocellular carcinoma who underwent local thermoablation, either RFA or PMAT at Cardinal Santos Medical Center. Data including pre- and post-procedural liver function tests, Alpha-feto protein (AFP), and imaging studies were reviewed.
Results: Improvement in AFP levels on one year follow up were statistically significant for those who underwent PMAT *($p = 0.031$)* and RFA *($p = 0.026$)*. Improvement in INR was statistically significant for patients who underwent RFA *($p = 0.010$)* while there was also a trend towards improvement among those underwent PMAT *($p = 0.056$)*. The widest diameter of tumors, as well as other laboratory parameters, did not change significantly from baseline for those who underwent either RFA or PMAT.
Conclusion: Percutaneous Microwave Ablation Therapy is a potentially viable treatment option for patients with primary hepatocellular carcinoma. The statistically and clinically significant improvements in AFP and INR indicate the potential benefit of Percutaneous Microwave Ablation Therapy among patients with Primary Hepatocellular Carcinoma however, further investigation is still warranted.

Abstract #1125

Clinical characteristics and therapeutic procedures followed in patients with HCC in Greece. Survival rates according to BCLC staging system

Pliarchopoulou F[1], Marantos T[1], Fillipiadis D[2], Reppas L[2], Psarakis C[1], Tziolos N[1], Paneta M[1], Vrentzos E[1], Pelekanou A[1], Chounta A[1]

[1]Hepatology Unit, 4th Department of Internal Medicine, National and Kapodistrian University of Athens, "ATTIKON" Hospital, [2]2nd Department of Radiology, National and Kapodistrian University of Athens, "ATTIKON" Hospital

Introduction: Hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide. The aim of this study is to determine the

clinical characteristics and therapeutic procedures in patients diagnosed with HCC as long as survival rates according BCLC staging system.
Methods: A retrospective analysis of medical records was performed on 201 patients with Hepatocellular Carcinoma (HCC) followed in the Outpatient Hepatology Department in "ATTIKON" University Hospital in Athens, Greece, during the period 2003–2019. Gender, age, stage of fibrosis, underlying disease where recorded from diagnosis. The patients with HCC were grouped according to stage BCLC and treatment procedures along with survival rates were recorded.
Results: 201 patients with HCC were studied retrospectively. 80% were above the age of 60, 80% were men and most of them (95.5%) had F4 stage of fibrosis. The underlying hepatic disease was predominately ASH (40%) followed by viral Hepatitis (HBV 24%, HCV 21%) and NASH 11.5%. During the decade 2009–2019 78.5% were diagnosed. The > 1 year survival rate was 51% for all groups of BCLC staging. Upon diagnosis of HCC, 40% were Child Pugh A score, 33.6% B, 7.5% C and in 18.5% CP score could not be determined. Stage A (according to BCLC staging system) was the 15% of patients, 100% of them CP score A. > 1 year survival rate was 90%. In this group of patients 33% were treated with Radiofrequency ablation, 13.3% underwent surgical resection and 13.3% received combined treatment with RF and Surgery, under liver transplantation were 6.6%, while 20% received no treatment. Stage B BCLC were 66% and the > 1 year survival rate was 44% in this group. CP score A were 39%, B 50%and C 11%. No treatment received 60% due to concomitant medical situations or de-compensated cirrhosis, TACE 21%, Sorafenib 13.6% and RF + TACE 4.5%. In stages C and D BCLC 7% and 4% respectively, only palliative treatment was administered while no therapeutic procedure was followed. The > 1 year survival rates were 35.7% and 37.5% respectively.
Conclusion: In the group of patients with HCC followed in our department most of them were over the age of 60, with cirrhosis and the predominant underlying disease was ASH and viral Hepatitis. Upon diagnosis, most patients were Stage B according to BCLC staging system and 60% received no treatment due to concomitant medical situations and cirrhosis, that didn't allow therapeutic interventions. > 1 year survival rate ranged from 90% to 35.7% according to BCLC stage. Early screening of cirrhotic patients might allow more treatment options in patients with HCC and improve survival rates.

Abstract #1153

Difference of vascular endothelial growth factor (VEGF) levels among Barcelona clinic liver cancer (BCLC) stages in hepatocellular carcinoma patients

Darmadi[1], Siregar Gontar Alamsyah[1]

[1]Division of Gastroenterohepatology, Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

Introduction: Angiogenesis involved in the development and pathogenesis of hepatocellular carcinoma (HCC). Vascular endothelial growth factor (VEGF) plays important roles in vascularization and the most potent of angiogenic protein known.
Objectives: To investigate the comparison of VEGF level in varying severity degree of HCC patients assessed with The Barcelona Clinic Liver Cancer (BCLC) System.
Methods: A cross sectional study of 60 HCC patients from January to December 2018 at Haji Adam Malik General Hospital Medan, Indonesia. The diagnosis of HCC was confirmed by triphasic CT scan (arterial hypervascularity followed by venous and/or delayed phase "washout"). Circulating VEGF levels were examined in serum using the Quantikine Human VEGF-ELISA. Cholangiocarcinoma, hemangioma, and liver metastasis patients were excluded from the study. HCC patients were classified according to BCLC criteria. Data analysis used the Kruskal Wallis H-test with the SPSS statistical program where $p < 0.05$ considered as statistically significant with 95% confidence interval.
Results: About 41.7% of HCC patients categorized as BCLC C followed by 35% BCLC B, 15% BCLC D, and 8.3% BCLC A. There were significant differences in VEGF levels among BCLC degrees in HCC patients ($p = 0.014$). HCC patients with BCLC C (1009.6 pg/mL) and BCLC D (1189.7 pg/mL) had significantly higher VEGF levels compared to BCLC A (578 pg/mL).
Conclusion: There was significant association between VEGF level and BCLC stage in HCC patients.

Abstract #1172

Hepatoma arterial-embolization prognostic (HAP) and its modificatios score as prognostic factor in hepatocellular carcinoma patients treated with transcatheter arterial embolization in Sardjito Hospital Yogyakarta Indonesia

Nuraida Wisudani[1], Neneng Ratnasari[2], Putut Bayupurnama[2], Fahmi Indrarti[2], Catharina Triwikatmani[2], Sutanto Maduseno[2], Siti Nurdjanah[2]

[1]Trainee in Division of Gastroenterology and Hepatology, Departemen of Internal Medicine, Medical Faculty Gadjah Mada University Dr. Sardjito Hospital Yogyakarta Indonesia, [2]Division of Gastroenterology and Hepatology, Departemen of Internal Medicine, Medical Faculty Gadjah Mada University Dr. Sardjito Hospital Yogyakarta Indonesia

Introduction: Transarterial chemoembolization (TACE) is the standard of care for patients with intermediate stage hepatocellular carcinoma (HCC). If applied correctly, TACE can produce survival benefits without adversely affecting hepatic functional reserve. Intermediate state of HCC came with a wide variation of patient, therefore selecting the right candidate for TACE was challenging. Hepatoma arterial-embolization prognostic (HAP) score and its modifications (modified HAP [mHAP] and mHAP-II), consisting of some or all of the factors have been found to predict outcomes after TACE for HCC. A-B class risk ini these scoring systems were considered a better candidate for TACE.
Objective: To evaluate if HAP score and its varians can be used as prognostic factors in HCC patient treated with TACE in Sardjito Hospital Yogyakarta
Methods: Retrospective cohort study in patients with HCC and first TACE at the Sardjito Hospital, Yogyakarta Indonesia, from January 2017 until December 2018. The HAP, mHAP, mHAPII score was applied, mortality and survival were observed with a follow-up until December 2019.
Result: We included 51 patients, mostly male (80.39%) and 96.07% were Child Pugh A. Patients with A-B class risk scores showed better survival than those with C-D class risk scores. The median OS were *13.6 vs 3.56 months* ($p = 0.069$) for mHAP-II, *13vs.2.86 months* ($p = 0.078$) for mHAP, and *9.7vs.2.7 months* ($p = 0.233$) for HAP. Mortality at 12 month also showed better result for A-B class risk with HR (95% CI) *1.485 for HAP, 2.111 for mHAP and 3.456 for mHAP-II.*
Conclusion: Although not statistically significant, *HAP score and its modification can be used to predict TACE outcomes.* Among all scoring, *mHAP II shows better assessment* in selecting the optimal candidate for TACE.

Abstract #1215

Diagnostic performance of CT/MRI liver imaging reporting and data system v2017 for hepatocellular carcinoma: a systematic review and meta-analysis

Sunyoung Lee, MD, PhD[1], Myeong-Jin Kim, MD, PhD[1]

[1]Department of Radiology and Research Institute of Radiological Science, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

Introduction: The liver Imaging Reporting and Data System (LI-RADS) is a comprehensive system for standardizing liver imaging in patients at high risk for hepatocellular carcinoma (HCC).
Objectives: We performed a meta-analysis to determine the diagnostic performance of the LR-5 category for HCC and the pooled proportions of HCCs in each LI-RADS category using CT/MRI LI-RADS v2017.
Methods: We searched multiple databases for original studies reporting on the diagnostic accuracy of CT/MRI LI-RADS v2017. Random-effects models were used to determine the summary estimates of the diagnostic performance of the LR-5 category and the pooled proportions of HCCs for each LI-RADS category. Risk of bias and concerns regarding applicability were evaluated with the Quality Assessment of Diagnostic Accuracy Studies-2 tool.
Results: Fourteen studies (3 prospective studies and 11 retrospective studies) were included in the final analysis, consisting of 2059 patients, 2592 observations, and 1695 HCCs. The pooled per-observation sensitivity was 67% (95% confidence interval [CI], 62%–72%) with specificity of 91% (95% CI 87%–94%) in the LR-5 category of CT/MRI LI-RADS v2017 for diagnosing HCC. The pooled proportions of HCCs were 0% (95% CI 0–0%) for LR-1, 4% (95% CI 0–8%) for LR-2, 34% (95% CI 23–44%) for LR-3, 67% (95% CI 53–81%) for LR-4, and 91% (95% CI 87–96%) for LR-5. The proportions of HCCs were significantly different among LI-RADS categories 1–5 ($p = 0.034$).
Conclusion: The LR-5 category of CT/MRI LI-RADS v2017 shows moderate sensitivity and high specificity for diagnosing HCC. Higher LI-RADS categories contained higher proportions of HCCs.

Abstract #1257

Routine blood tests ratio as prognostic for survival in hepatocellular carcinoma patients treated with transarterial chemoembolization in Sardjito Hospital Yogyakarta Indonesia

David Simanjuntak[1], Putut Bayu Purnama[2], Neneng Ratnasari[2], Fahmi Indrarti[2], Catharina Triwikatmini[2], Sutanto Maduseno[2], Siti Nurdjanah[2]

[1]Trainee in Division of Gastroenterology and Hepatology, Departement of Internal Medicine, Medical Faculty Gadjah Mada University Dr Sardjito Hospital Yogyakarta Indonesia, [2]Division of Gastroenterology and Hepatology, Departement of Internal Medicine, Medical Faculty Gadjah Mada University Dr Sardjito Hospital Yogyakarta Indonesia

Background: Transarterial chemoembolization (TACE) is the strandard care of patients with intermediate stage hepatocellular carcinoma (HCC). TACE can produce survival benefits without adversely affecting hepatic functional reserve. Limited number of studies have explored the association between blood-based inflammatory biomarkers collected from routine blood tests such as platelete-lymphocyte ratio (PLR), lymphocyte-neutrophil ratio (LNR) and lymphocyte-monocyte ratio (LMR) and their prognosis to HCC patients undergoing TACE.
Objective: To evaluate wether the LNR, PLR and LMR can be used as prognostic factors for survival in HCC patient treated TACE in Indonesian population.
Methods: Retrospective cohort study in patients with HCC and first TACE at Sardjito Hospital, Yogyakarta Indonesia, from January, 2017 until December, 2018. Patients were analyzed and assigned into 2 groups based on optimal cutoff value for LNR (low ≤ 0.48 or high > 0.48), PLR (low ≤ 157.5 or high > 157.5) and LMR (low ≤ 1.75 or high > 1.75).
Results: Patients with higher LMR had a longer overall survival (OS) than those with lower LMR (6.6 vs 11.7 months; HR 1.79; CI 95% 1.01–3.22; p 0.048). Patients with higher PLR had longer OS than lower PLR but no statistically significant (9.3 vs 10.3 months; HR 1.04; CI 95% 0.56–1.03; p 0.906). The higher and lower LNR shown no differences for OS (9.4 vs 9.9 months).
Conclusion: LMR is associated with the HCC patients treated TACE and may be a potential marker for survival prognosis but not with LNR and PLR.

Abstract #1270

Safe radiofrequency ablation for low platelet count patients with novel platelet count raising drug (lusutrombopag)

Hideo Yoshida

Background: Blood transfusion of platelet was the practical way to increase the number of platelet count before invasive hepatic procedure such as radiofrequency ablation (RFA) for liver cancer. Recently, novel drug which raises platelet count by acting on thrombopoietin receptor has become available.
Methods: Lusutrombopag was orally administered 3 mg daily for seven days for the patients underwent RFA for liver tumor with low platelet count (mainly less than 50 thousands/μL). Medication was started 7–19 days before procedure. We collected demographic data, liver function, and platelet count of the patients.
Results: Lusutrombopag was administered for 92 patients. Thirty-six were females and 56 were males. Median age was 71yo (range 36–90). Forty-two patients had HCV, 13 had HBV, 22 had alcoholic liver disease, 9 had NASH, and 6 had other disease as background liver disease. Median Child Pugh score was 7 (range 5–11). Forty patients were Child A Class, 47 were Child B, and 5 was Child C. Thirty-one patients had stage I tumor, 38 had Stage II, 12 had stage III, and 1 had Stage 4. Platelet count was elevated from $4.4 \times 10^4 \pm 1.4 \times 10^4$ to $8.5 \times 10^4 \pm 2.7 \times 10^4$. Eighty-four patients (91%) out of 92 need not platelet blood transfusion by Lusutrombopag administration. No patients had bleeding complication after RFA procedure. One had portal thrombosis after lustrombopag taking.
Conclusions: Lustrombopag administration made the number of patients who need platelet blood transfusion lower at the time of RFA procedure for liver cancer.

Abstract #1292

Symptom management for patients treated by continuous hepatic artery perfusion chemotherapy: a longitudinal study

Weixi Hong

Introduction: China is the country with the highest incidence and mortality of liver cancer in the world. Hepatic artery continuous

infusion chemotherapy is often used for treating patients with unresectable liver cancer or as an adjuvant treatment after liver cancer resection. However, due to the long time patients rest in bed, many discomfort symptoms occur in different periods. It is of great importance to use symptom management to reduce patients' discomfort, meanwhile improve patients´ quality of life.

Method: Research design was based on Dynamic Symptom Model. A prospective study was conduct on 126 patients with primary liver cancer who received treatment of continuous hepatic artery infusion chemotherapy at the First Affiliated Hospital of Jinan University from January 10, 2019 to December 10, 2019. Using general information and Memorial Symptom Assessment Scale (MSAS) to assess patients´ symptom experience at three times during treatment (before interventional surgery, during chemotherapy and after removing the chemotherapy tube). Exploratory factor analysis was used to extract the composition of symptom clusters.

Results: Symptom cluster before interventional surgery include emotional symptom cluster and fatigue symptom cluster. Symptom cluster during chemotherapy include pain-related symptom cluster, upper gastrointestinal symptom cluster, liver function impairment symptom cluster and psychological symptom cluster. Symptom cluster after removing the chemotherapy tube include sickness symptom cluster, upper gastrointestinal symptom cluster and psychological symptom cluster.

Conclusions: Liver cancer patients treating by Hepatic artery continuous infusion chemotherapy with symptom of different points can gather in groups. The symptoms cluster has certain srablity and dynamics.

Abstract #1345

Comparison of the risk of hepatocellular carcinoma in nucleos(t)ide analogue-naive chronic hepatitis b patients treated with entecavir versus tenofovir: a systematic review and meta-analysis

Oh Hyunwoo[1], Kim Yoon Jun[1], Jang Heejoon[1], Kim Sun Woong[1], Kim Albert Minseok[1], Lee Yun Bin[1,2], Cho Eun Ju[1,2], Lee Jeong-Hoon[1], Yu Su Jong[1], Yoon Jung-Hwan[1]

[1]Department of Internal Medicine and Liver Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea, [2]Biomedical Research Institute, Seoul National University Hospital, Seoul, Korea

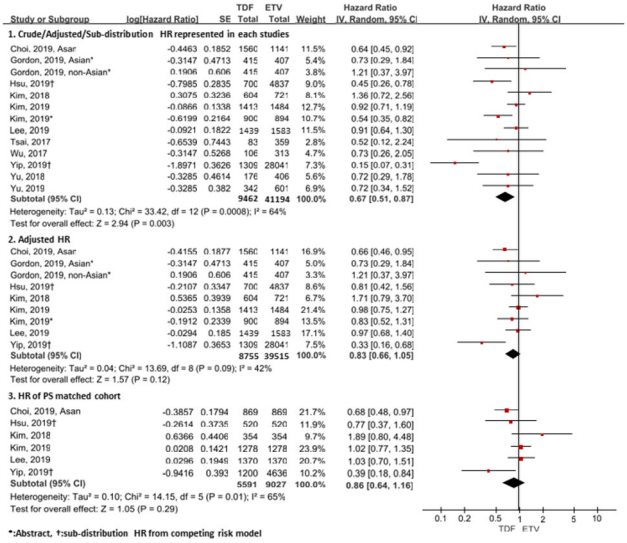
Introduction: Recently, efficacy for reducing incidence of hepatocelluar carcinoma (HCC) has become a critical concern in chronic hepatitis B (CHB) patients due to the long-term use of drugs. However, existing studies show conflicting results.

Objectives: This meta-analysis aims to assess the efficacy in reducing incidence of HCC comparing Tenofovir (TDF) monotherapy with Entecavir (ETV) monotherapy among CHB patients with hazard ratios (HRs).

Method: Two investigators independently searched the Cochrane Library, MEDLINE, and Embase databases for randomized controlled trials and nonrandomized studies (NRSs) using the keywords "Hepatocellular carcinoma", "Tenofovir", and "Entecavir", and additional references were obtained from the bibliographies of relevant articles published through October 2019. The quality of each study was assessed using the Newcastle-Ottawa scale and the Grading of Recommendations Assessment, Development and Evaluation criteria.

Results: Twelve NRSs enrolling 50,656 patients met the inclusion criteria. The incidence of HCC seems significantly low among the TDF group than ETV group [HR (95% CI) of 0.67 (0.51, 0.87), P = 0.003]. However, using adjusted HRs or HRs of propensity score (PS) matched subcohort in each studies, a statistically significant difference disappeared [Adjusted HR analysis: from 0.64 (0.41, 0.98), P = 0.04–0.83 (0.66, 1.05), P = 0.12] [PS matched subcohort analysis: from 0.64 (0.47, 0.92), P = 0.01–0.86 (0.64, 1.16), P = 0.29].

Conclusion: There was no statistical significant difference when using HR which reduce heterogeneity of the TDF and ETV groups. We need further research comparing the efficacy of two drugs with standardized protocols reducing heterogeneity.



Abstract #1370

Usefulness of tumor markers in patients with hepatocellular carcinoma

Seong Woo Nam[1], Jae Yoon Jeong[1], Jong Kyung Choi[1], Hyeok Choon Kwon[1], and Yong Bum Yoon[1]

[1]Department of Internal Medicine, National Medical Center, Seoul, Korea

Aims: To investigate the usefulness of tumor markers (AFP, PIVKA-II) according to size (< 3 cm, 3 ~ 5 cm and > 5 cm), type (single or multinodular, infiltrative and mass form) and metastasis in the diagnosis of hepatocellular carcinoma (HCC).

Methods: We retrospectively collected data on 398 enrolled patients with newly diagnosed HCC from April, 2009 to March, 2019.

Results: Under 3 cm, each tumor marker's availability for diagnosis were only 40 ~ 50%. But according to size in ≥ 3 cm, positive predictive value of tumor markers was increased. Especially PIVKA-II was more useful in > 5 cm. AFP levels were not depended on type, but PIVKA-II levels were changed according to type. Infiltrative form showed the highest PIVKA-II levels, and multinodular form showed the lowest PIVKA-II levels. Also, PIVKA-II/AFP ratio (≥ 5 and ≥ 100) showed differences according to type (infiltrative form, 77% and 43%; mass form, 66% and 28%; multinodular, 59% and 17%). In distinguishing between infiltrative form and non-infiltrative form in HCC patients, PIVKA-II had the highest AUC value among tumor markers (0.783; AFP, 0.679; PIVKA-II/AFP ratio, 0.627).

Conclusions: As the tumor size was larger or tumor was infiltrative, the usefulness of tumor markers in diagnosis in HCC increased

Abstract #1379

Evolution of etiology, presentation, management and prognostic tool in hepatocellular carcinoma

Chih-Chieh Ko[1,3], Shu-Yein Ho[1,3], Yi-Hsiang Huang[1,3,4], Ming-Chih Hou[1,4], Teh-Ia Huo[2,3,5]

[1]Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, [2]Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan;[3]Faculty of Medicine, [4] Institute of Clinical Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan, [5]Institute of Pharmacology, National Yang-Ming University School of Medicine, Taipei, Taiwan

Background: Hepatocellular carcinoma (HCC) is the leading cause of cancer-related death globally, but its current status is unclear.
Aim: To investigate the evolution of etiology, presentation, management and prognostic tool in HCC over the past 12 years.
Methods: Between 2004 and 2015, 3349 newly diagnosed HCC patients were consecutively enrolled and retrospectively analyzed. The comparison of survival was performed by the Kaplan–Meier method with log-rank test. Homogeneity and corrected Akaike information criteria (AICc) were used to evaluate the prognostic accuracy for different staging systems.
Results: Hepatitis B and C virus infection in HCC were continuously declining over the three time periods (2004–2007, 2008–2011, 2012–2015; $p < 0.001$). At diagnosis, single tumor detection rate increased to 73% ($p < 0.001$), whereas vascular invasion gradually decreased to 20% in 2012–2015 ($p < 0.001$). More patients (76%) had Child-Turcotte-Pugh class A in 2012–2015 ($p < 0.001$). Early stage HCC, as defined in most staging systems, also gradually increased from 2004–2007 to 2012–2015 ($p < 0.001$). The probability of patients receiving curative treatment increased from 2004–2007 to 2012–2015 ($p < 0.001$). Long-term survival significantly increased for patients in 2012–2015 as compared with other two cohorts. The Cancer of Liver Italian Program (CLIP) and Taipei Integrated Scoring (TIS) system are two more accurate staging systems among all.
Conclusions: The clinical presentations of HCC have significantly changed over the past 12 years. Hepatitis B and C-associated HCC became less common, and more patients were diagnosed at an early cancer stage. Patient survival increased due to early cancer detection that results in increased probability to undergo curative therapies.

Abstract #1387

ALBI grade transition in lenvatinib treatment for unresectable hepatocellular carcinoma

Yoshikawa Syuhei[1], Asano Takeharu[1], Mashima Hirosato[1]

Department of Gastroenterology, Saitama Medical Center, Jichi Medical University, Saitama, Japan

Intoduction: In patients with unresectable hepatocellular carcinoma, lenvatinib therapy requires long-term maintenance at a high dose. In many cases, however, the occurrence of side effects requires drug withdrawal or reduction.
Objective: Using the recently proposed ALBI score as a marker of residual liver function, we examined whether it could be an indicator of continuation of lenvatinib medication.
Methods: 34 patients with unresectable hepatocellular carcinoma who received lenvatinib in our hospital, who had been taken for more than 1 month and evaluated CT (mRECIST) 3–12 weeks after treatment was analyzed. We evaluated ALBI score during lenvatinib treatment.
Results: Before treatment, the ALBI score of subjects was 17 for Grade 1, 7 for Grade 2a, 11 for Grade 2b, and 1 for Grade 3. The median was − 2.52 (− 3.34 to − 1.13). Side effects of lenvatinib were hand-foot syndrome (52%), hypertension (52%), diarrhea (30%), anorexia (30%), hypothyroidism (24%), and proteinuria (12%). Image evaluation of treatment effect was PR (24%), SD (52%), and PD (24%). The change in ALBI score before and after treatment was median − 0.04 (− 1.16 to 0.82). After treatment, the grade of ALBI score decreased in 6 cases, of which 3 cases showed anorexia and 2 cases showed high proteinuria.
Conclusion: The disease control rate of lenvatinib is high at 76%. The side effect anorexia may be associated with a worsening of the ALBI score. In order to achieve long-term oral administration, countermeasures against anorexia, including nutritional guidance, were considered important

Abstract #1395

Role of tumor necrosis factor β polymorphism in hepatitis C virus related chronic liver diseases

Amr Mohammed Zaghloul

Introduction: HCV infection is a major public health problem, patients are at risk of developing chronic hepatitis, liver cirrhosis and hepatocellular carcinoma (HCC). Subjects with TNF gene polymorphisms may have a significantly higher risk of more severe liver disease. Genetic variations in different individuals may alter the function of cytokine proteins, influencing the risk and clinical outcomes of HCC.
Objective: To investigate the association of different TNF β genotypes with the degree of fibrosis in chronic hepatitis C patients and its contribution to the risk of HCC in these patients.
Material and Methods: One hundred and eight HCV patients were grouped into 3 groups: Group (1) 28 patients with chronic HCV, Group (2) 36 patients with HCV- related liver cirrhosis, Group (3) 44 patients with HCV-related liver cirrhosis with HCC. TNF-β gene polymorphism was detected by PCR- Restriction Fragment Length Polymorphism. (RFLP) technique.
Results: In total 108 patients were included (32 males) with mean age 56 ± 7.74 years
Multivariate binary logistic regression analysis confirmed that carriage of TNF β G/G genotype and platelet count were independent predictors for development of HCC in patients with HCV-related liver cirrhosis
Conclusion: There is a significant association between TNF β polymorphism (G/G genotype) and HCC development and disease severity in patients with HCV-related liver cirrhosis. The TNF β G/G genotype may be used as a molecular marker to predict the risk of HCC in patients with HCV-related liver cirrhosis

Abstract #1408

Prevalence of Hepatic and extrahepatic malignancies in an urban population of patients with diagnosis of cirrhosis

Jammu A[1], Dallali H[1], Lee J[1], Mahmood M K[1], Kausar S[1], Magnes M[1], Elkhashab M[1]

[1]Research, Toronto Liver Centre, Toronto, Canada

Background: The association between liver cirrhosis and HCC is well established. While risk factors for liver cirrhosis include chronic viral hepatitis, excessive alcohol, autoimmune liver disease and

NAFLD, the risk factors for cancer include conditions such as alcohol/tobacco use, hormonal imbalance, components of metabolic syndrome, obesity and poor diet. As such, risk factors for cancer overlap with factors which may lead to cirrhosis.
Objective: To analyze the presence of shared risk factors and the prevalence of hepatic/extrahepatic malignancies within this subset of population.
Methods: Retrospective review of 5748 charts at the Toronto Liver Centre was conducted to identify cases of cirrhosis (n = 470). Patient age, sex, comorbid condition history, hepatic/extrahepatic cancer history was analyzed.
Results: Of the 470 patients with positive cirrhosis history, 65% male and 35% female. In terms of age: < 30:0.2%, 31–40:1.3%, 41–50:6.8%, 51–60:21.9%, 61–70:27.9%, 71–80:18.5%, 81–90:18.7%, > 90:4.7%. Chronic HCV (42.3%), chronic HBV (17.4%), alcoholic liver disease (18.1%), NAFLD (3.6%), NASH (9.8%), autoimmune hepatitis (3.6%) was observed with the associated frequencies. Comorbid condition history: 202 patients had hypertension (43%), 165 had diabetes (35.1%), 129 had dyslipidemia (27.4%) and 121 had an obesity diagnosis (25.7%).
13.8% of patients developed HCC. In terms of extrahepatic malignancies (Figure 1), 8 patients (1.7%) developed breast cancer, 7 patients (1.5%) developed colorectal cancer, 4 patients (0.9%) developed non-Hodgkin's lymphoma. 22 of the patients (4.7%) have history of a liver transplant.
Conclusion: HCC was observed among 14% of the cohort and extrahepatic malignancies in 9%. The most commonly observed extrahepatic malignancies were breast and colorectal cancer. Various components of metabolic syndrome were prevalent: hypertension (43%), diabetes mellitus (35.1%), dyslipidemia (27.4%) and obesity (25.7%).

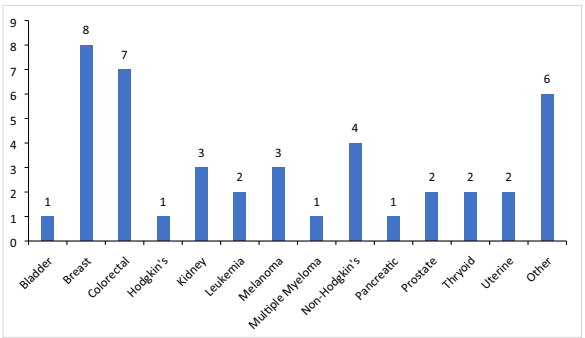


Figure 1: Prevalence of extra-hepatic malignancies among patient with a liver cirrhosis diagnosis (n=470).

Abstract #1409

Prevalence of hepatic and extrahepatic malignancies among an urban population with NAFLD and/or NASH and its correlation with the components of metabolic syndrome

Jammu A[1], Dallali H[1], Lee J[1], Mahmood MK[1], Kausar S[1], Magnes M[1], Elkhashab M[1]

[1]Research, Toronto Liver Centre, Toronto, Canada

Background: NAFLD/NASH is considered the hepatic manifestation of metabolic syndrome. Extrahepatic malignancy is considered one of the most common causes for mortality among patients with NAFLD/NASH. Obesity is a common cancer-inducing factor among NAFLD/NASH patients.
Objective: To investigate the prevalence of hepatic/extrahepatic cancers among patients with NAFLD/NASH and its correlation with different components of metabolic syndrome in an urban centre with patients from diverse ethnic backgrounds in Toronto, Ontario, Canada.
Method: Retrospective review of comorbidities for 2764 NAFLD/NASH patients. 1161 patients had obesity, 1074 patients with dyslipidemia, 618 with type-II diabetes mellitus and 909 with hypertension. A graphic representation was produced to visually analyze the proportion of patients with each cancer type relative to the number of individuals with comorbidities stated above. The description of demographics and proportions were done to identify the prevalence of comorbidities in relation to different cancers.
Results: 175 patients were diagnosed with some type of hepatic or extrahepatic malignancy. A large number of patients were diagnosed with metabolic syndrome (nearly half with obesity and over 1000 patients with dyslipidemia). Breast cancer was a most common extrahepatic malignancy. There were peaks in incidence in prostate, liver and thyroid cancers. Obesity and dyslipidemia combined were present in 2235 patients out of 2764 patients, which is the total cohort.
Conclusion: Hepatic and extrahepatic malignancies were present in about 6% of a cohort of patients with NAFLD/NASH. Breast cancer was highest in frequency. Majority of obese patients had higher prevalence of dyslipidemia, followed by type II diabetes mellitus.

Abstract #1431 **5-lncRNA prognostic signature for hepatocellular carcinoma from TCGA database**

Wang, Szu-Jen[1,2], Tsai, Ching-Yang[2], Dai, Chia-Yen[3], Yu, Ming-Lung[3]

[1]Graduate Institute of Clinical Medicine, Kaohsiung Medical University, Kaohsiung City, Taiwan, [2]Division of Gastroenterology, Department of Internal Medicine, Yuan's General Hospital, Kaohsiung City, Taiwan, [3]Hepatobiliary Division, Department of Internal Medicine, and Hepatitis Center, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung City, Taiwan

Introduction: Recent studies demonstrated that the dysregulated long noncoding RNAs (lncRNAs) expression profiles were related to the progression and survival in patients with various cancers including hepatocellular carcinoma.
Objectives: This study aimed to find a long non-coding RNA (lncRNA) signature for predicting hepatocellular carcinoma (HCC) prognosis from The Cancer Genome Atlas (TCGA) database.
Methods: LncRNAs expression profiles and corresponding clinicopathological data for 374 patients with HCC were obtained from The Cancer Genome Atlas (TCGA), including 374 tumor-part specimens and 50 non-tumor-part specimens. Differentially expressed lncRNAs (DELs) between tumor-part and non-tumor-part specimens of hepatocellular carcinoma (HCC) were identified using the edgeR package, using an false discovery rate (FDR) < 0.05 and log2 |fold change (FC)| > 2. The least absolute shrinkage and selection operator Cox (LASSO Cox) regression model was used to identify the lncRNA signature. Next, the key lncRNAs in Lasso Cox regression were further analyzed with a stepwise multivariate Cox regression model. The lncRNAs fitted in the multivariate Cox regression model and independently associated with overall survival were selected to construct a prognostic risk formula. The R software version 3.6.1 and the "edgeR", "glmnet", "survival", "timeROC" and "survminer" package were utilized to analysis. The risk scores were calculated based on the formula generated through the multivariate Cox regression model. Using the median risk score as the cutoff value, patients in the dataset were divided into low-risk or high-risk groups correspondingly. The efficiency of the predictive model was estimated by the Receiver operating characteristic curve (ROC curve) and Harrell's C-index statistic.

Results: Based on lncRNA expression profiling of 374 HCC patients from the TCGA database, a total of 1292 DELs were selected out including 80 down-regulated DELs and 1212 up-regulated DELs (Fig. 1). 6 lncRNAs were identified using LASSO Cox. Finally, 5 lncRNAs (AC015712.7, AC015722.2, LINC00462, LINC01297 and SRGAP3-AS2) were confirmed in multivariate Cox regression model (Fig. 2). According to this 5-lncRNAs signature, the corresponding AUC for the predictive model of 3-year and 5-year survival was 0.689 and 0.647, respectively (Fig. 3). It had a Harrell's C-index statistic of 0.679 (95% CI 0.54–0.81), indicating a near moderate predictive ability for survival time of HCC. Kaplan–Meier analysis revealed that for the TCGA cohort, the high-risk group had significantly poorer survival than the low-risk group (Log-Rank test p = 2.579e−0.5) (Fig. 4).

Conclusion: Our study constructed the 5-lncRNA model can be a biomarker to predict the prognosis of HCC. Further studies were needed to confirm this signature.

Fig.1 Volcano plot of the differentially expressed long non-coding RNAs between hepatocellular carcinoma tumor specimens and non-tumor specimens

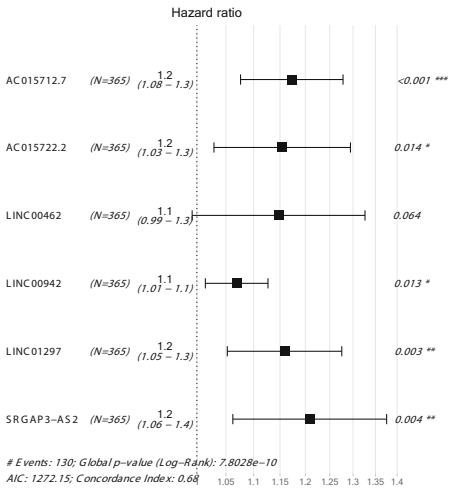


Fig.2 Identified lncRNAs of predictive prognosis in TCGA dataset of HCC

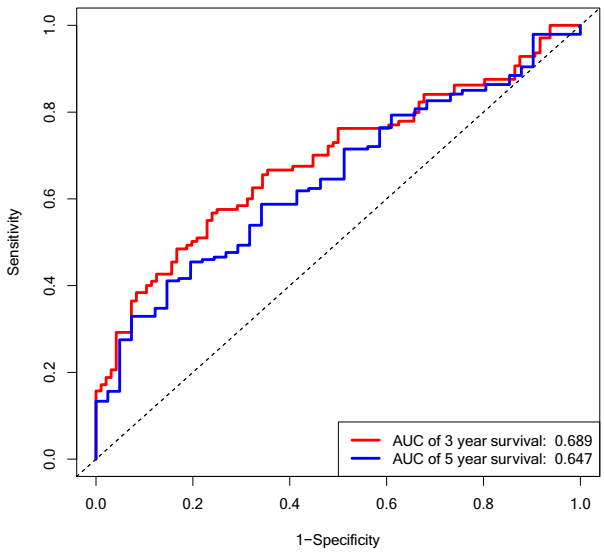


Fig. 3 ROC curve of 3-year and 5-year survival

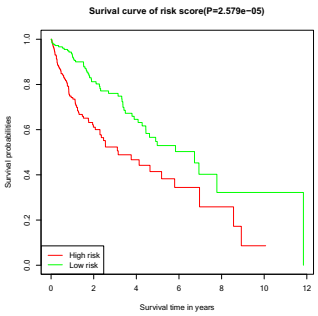


Fig.4 Kaplan Meier analysis indicated high-risk group exhibited significantly poorer survival than the low-risk group

Abstract #1457

The role of expression of cancer stem cell markers *cluster differentiation* 44 (CD44), CD90, CD133, *epithelial cells adhesion molecule* (EpCAM) and *alpha-fetoprotein* (AFP) serum level in patients with advanced liver disease

Mustika Syifa[1], Supriono[1], Wibowo Bogi Pratomo[1], Lesmana Cosmas Rinaldi A[2]

[1]Department of Internal Medicine, Gastroenterohepatology Division, dr.Saiful Anwar General Hospital, Faculty of Medicine Universitas Brawijaya, Malang,[2]Department of Internal Medicine, Hepatobiliary Division, Dr.Cipto Mangunkusumo National General Hospital, University of Indonesia, Jakarta

Introduction: The increasing of serum alpha-fetoprotein (AFP) often to be a marker for hepatocellular carcinoma (HCC) patients with advanced stage. Nowadays, cluster differentiation (CD)44, CD90, CD133, and Epithelial cell adhesion molecule (EpCAM) were cancer stem cells (CSCs) biomarkers which were predicted as an early marker for HCC and correlate with advanced liver disease progressiveness. Until now, none of CSCs research for HCC conducted in Indonesia.

Objective: To evaluate the role and expression of CD44, CD90, CD133, EpCAM and serum AFP levels in relation to advanced liver disease.
Methods: An observational study was conducted from the 0th to the 6th month, on 41 patients with chronic hepatitis B or C, liver cirrhosis, and HCC in dr. Saiful Anwar General Hospital. Expression of CD44, CD90, CD133, and EpCAM serum were measured using flowcytometry, and serum AFP levels using ELISA. Patients characteristic data were analyzed by bivariate and multivariate statistics. Data also analyzed by correlative test (Pearson and Spearman) and comparative test (One-way ANOVA, unpaired T, Mann-Whitney, Chi-square, Kruskal-Wallis) with significance value of $p < 0.05$. The prediction of factors influencing disease progression was analyzed using regression logistic tests.
Results: There were 16 subjects of chronic hepatitis, 15 subjects of liver cirrhosis, and 10 subjects of HCC at first observation. The expression of CSCs on early observation which significantly differ in all groups were $CD44^+/CD90^+$ ($p = 0.001$), $CD133^+/EpCAM^-$ ($p = 0.004$), and serum AFP ($p = 0.000$). In 6 months observation, there were 11 subjects of chronic hepatitis, 13 subjects of liver cirrhosis, and 4 subjects of HCC. Only AFP was significant in all groups ($p = 0.002$). The expression of $CD44^+/CD90^+$ and $CD133^+/EpCAM^-$ did not have significant result in 6th month ($p = 0.213$; $p = 0.669$; $p = 0.937$).
Conclusions: The expression of $CD44^+/CD90^+$, $CD133^+/EpCAM^-$ were significantly different in early observation of advanced liver disease patient groups but inconsistent with later observation. Only serum AFP level significantly differs on early and later observation of advanced liver disease patient groups. Yet, the correlation between CSCs marker expression with disease progressiveness is still unproven.

Abstract #1465

Serial case: exophytic hepatocellular carcinoma mimicking gastrointestinal stromal tumour (GIST) in non cirrhotic liver

Cecilia OP[1], Hery DP[1], Agung P[1], Paris B[2], Erick P[2], Maya N[3], Devia E[4]

[1]Division of Gastroenterohepatology, Department of Internal Medicine, Diponegoro University, Dr. Kariadi Hospital, Semarang, Indonesia, [2]Division of Digestive Surgery, Diponegoro University, Dr. Kariadi Hospital Semarang, Indonesia, [3]Department of Radiology, Diponegoro University, Dr. Kariadi Hospital, Semarang, Indonesia, [4]Department of Histopathology, Diponegoro University, Dr. Kariadi Hospital, Semarang, Indonesia

Introduction: Exophytic/Pedunculated Hepatocellular Carcinoma is very rare. The diagnosis presents a challenge due to the uncertainty of the tumour origin.
Case report: We report three patients (47-year-old female, 47-year-old male, and 33-year-old female) presented with a lump and pain in the left upper quadrant abdomen. A bulky mass was palpated in the epigastric extended to the left upper quadrant abdomen, large, immobile, solid in palpable, and no bruit. There was no sign of cirrhosis. AFP level was high in 2 patients with HBsAg positive, one patient had normal AFP level and HBsAg negative. Abdominal CT scan showed mixdensity lesion on gastric fundus and duodenum suspected as GIST. Quadruple-phase MDCT showed lobulated mass in left upper quadrant abdomen with necrotic area inside which enhanced in early arterial and late arterial phase, and washout in venous and delayed phase. The patients underwent left lobe hepatectomy and resection of the neoplasm. Pathological examination revealed a malignant epithelial tumour, highly suggestive of hepatocellular carcinoma moderately differentiated. Immunostaining result was negative for CK7 and CK20. The patients are on regular follow up and doing well for more than 3 years.
Discussion: Three young, non-cirrhotic patients presented with large mass in left upper quadrant abdomen. Quadruple-phase MDCT, pathological findings, and negative CK-7 and CK-20 supported the diagnosis of HCC. Surgical therapy showed good survival in these patients.
Conclusion: Exophytic hepatocellular carcinoma is difficult to diagnose. Therefore, when a bulky mass is discovered and is in contact with the surface of liver, this diagnostic possibility should be considered.

Abstract #1466

Radiological spectrum of hepatocellular carcinoma in Pakistan. Are we diagnosing too late?

Umair Shafqat, Shahid Rasool, Ahmad Nawaz Babar, Nayab Alia, Ayman Rehman

Background: Hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide and the third cause of cancer-related deaths. Chronic liver disease due to chronic viral hepatitis is the major cause and burden is increasing especially in the developing countries including Pakistan. Early diagnosis of HCC is the key to the cure of the disease.
Objective: This study was done to look for the spectrum of HCC on multiphasic CT scan at the time of diagnosis. These CT scan reports were evaluated for a potential candidacy for curative therapy.
Methods: All multiphasic CT scans done at our institute from January 2017 to December 2018 with a diagnosis of new HCC were evaluated. Demographic data like age, gender, presence of liver cirrhosis, cause of liver cirrhosis, size and site of the tumor, portal vein thrombosis, and presence of metastasis were noted. Data were analyzed for the potential candidacy of curative treatment like hepatic resection, radiofrequency ablation, and liver transplant.
Results: 106 cases of HCC were found. 73 (69%) were male with a median age of 49.6 ± 12.3 years. 97 patients (92%) had radiological evidence of liver cirrhosis and HCV infection, 76 (71.7%) was the major cause followed by NBNC 24 (22.6%) and HBV 6 (5.6%) infection.48 cases (45.3%) have involvement of both lobes of the liver, 46 (43.4%) have involvement of right lobe while 8 (7.5%) have involvement of only left lobe of the liver. 44 (41.5%) patients have evidence of portal vein thrombosis at the time of diagnosis proving vascular invasion of the tumor. 6 (5.6%) patients have evidence of distant metastasis while 23 (21.7%) had evidence of lymphadenopathy. According to the latest guidelines for the treatment of HCC, only 39 (36.8%) were potential candidates for curative therapy i.e. tumor resection, RFA or liver transplant on the bases of radiological findings.
Conclusion: HCC is a serious and common complication of liver cirrhosis. We need to strengthen our surveillance strategies to diagnosis earlier so a cure could be offered to these patients.

Abstract #1481

Epidemiological characteristics and etiology among hepatocellular carcinoma in cambodia: One National hospital, Khmer-Soviet Friendship Hospital, Phnom Penh

MIM Vanda[1], CHEA Khang[3,4], CHEA Ong[1,2]

[1]University of Health and Sciences, Cambodia, [2]Liver and GI unit at Khmer-Soviet Friendship Hospital, Phnom Penh, Cambodia, [3]Liver

and GI unit at Calmettre Hospital, Phnom Penh, Cambodia, [4]Ekip liver and GI specialist clinic, Phnom Penh, Cambodia

Introduction: Hepatocellular carcinoma (HCC) still remains as one of cancer-related death in the world. The etiology varies in different geographical. In Cambodia, HBV and HCV has been known as the etiology frequent in HCC.
Objectives: The aim of this study is to evaluated the etiology among HCC.
Methods: It was retrospective mono-center study of 127 patients who were diagnosed with HCC during 6 months from January 2019 to June 2019. The judgment Criteria based on clinical, biological and imagery. The epidemiological characteristics and the etiology of HCC were analyzed.
Results: The mean age was 55.94 years old with male predominance (68.5%). Cirrhosis represented 88.2% of cases. The etiologies were dominated by viral hepatitis B 60.6%, alcohol 38.6%, and viral hepatitis C 20.5%. Abdominal Pain (71.64%) was the most common chief complaint. Most of patient had Child-Pugh scale in class B (43.3%) and AFP > 400 ng/dl was 67.7%. 68.96% of patients had nodule > 3 cm and 40.9% had portal thrombosis. Ascites, upper GI bleeding and hepatic encephalopathy represented 63%, 13.4% and 11% respectively.
Conclusions: HBV still remains the main cause of HCC while alcohol becomes the second rank. Most of the patient visited doctor in advance stage which is possible for palliative treatment only. Health check-up and medical care are still not accustomed in our country. Further prospective with multiple center should be done to find out the risk factors of HCC among our population, in order to make an appropriate strategy to reduce the incidence and the rate of mortality.

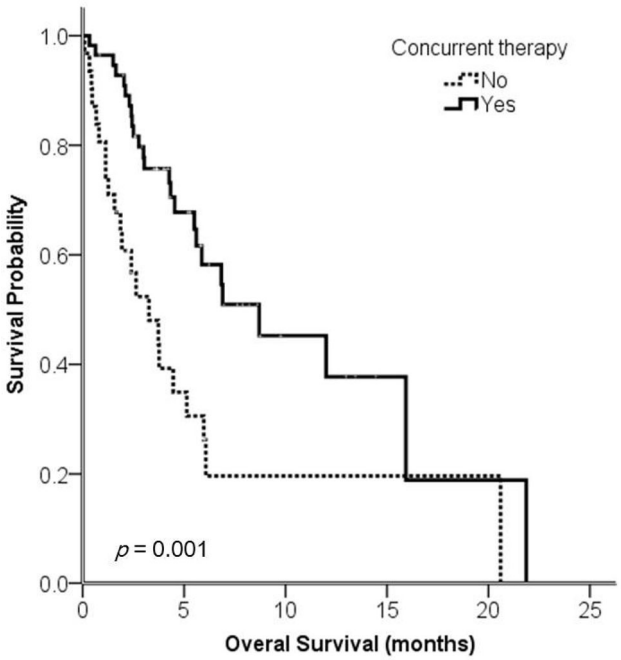
Abstract #1482

Nivolumab for hepatocellular carcinoma: a combined experience at two hospitals in Central Taiwan

Wei-Fan Hsu[1,2], Po-Heng Chuang[1], Cheng-Kuo Chen[3], Hsueh-Chou Lai[1,4], Cheng-Yuan Peng[1,5], Chun-Che Lin[1,5], Guan-Tarn Huang[1,5], Jaw-Town Lin[1,5]

[1]Center for Digestive Medicine, Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan, [2]Graduate Institute of Biomedical Science, China Medical University, Taichung, Taiwan, [3]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Asia University Hospital, Taichung, Taiwan, [4]School of Chinese Medicine, China Medical University, Taichung, Taiwan, [5]School of Medicine, China Medical University, Taichung, Taiwan

Introduction: Immuno-oncology agents are emergent therapeutic options for hepatocellular carcinoma (HCC), but the real-world experience is limited.
Objectives: To evaluate clinical characters, adverse effects, and factors associated with objective response and survival to nivolumab in patients with HCC.
Methods: From 2017 May to 2019 Dec, 87 consecutive HCC patients were enrolled in this retrospective study from China Medical University Hospital and Asia University Hospital.
Results: Of 87 patients, seven, 9, 65, and 6 patients belonged to Barcelona Clinic Liver Cancer (BCLC) stage A, B, C, and D, respectively. Most patients received prior (74.7%) and concurrent therapy (64.1%). The numbers of patients with complete response (CR), partial response (PR), stable disease (SD), progressive disease, and not evaluable were 9, 8, 17, 28, and 25, respectively. The objective response rate (ORR, CR + PR) and disease control rate (CR + PR + SD) were 19.5% and 39.1%, respectively. Overall survival (OS) was 3.73 (2.10–6.03) months. Cancer of the Liver Italian Program (CLIP) ≥ 3 (hazard ratio [HR] 2.698, 95% confidence interval [CI] 1.140–6.385, p = 0.024) and concurrent therapy (HR 0.308, 95% CI 0.150–0.636, p = 0.001, figure), were independent predictors of shorter OS by multivariate Cox regression. Patients with longer OS (> 6 months) had a lower CLIP score (p < 0.001) and smaller maximal tumor size (p = 0.041) compared to those with shorter OS. Three patients expired due to severe immune-related adverse effects (irAEs).
Conclusions: Nivolumab was effective in a proportion of patients with HCC. ORR and OS to nivolumab were associated with both hepatic functional reserve and tumor burden.



Abstract #1507

The efficacy of hepatic artery infusion chemotherapy for hypovascular hepatocellular carcinoma

Lu-Chiaming

Background: Hypovascular hepatocellular carcinoma (HCC) is not unusual in clinical practice and a challenge for hepatologsits. Some studies reported the presence of hypovascular HCC to be a negative predictor in HCC patients receiving TACE/TAE which are usually not recommended for the treatment of hypovascular HCC. However, the efficacy of hepatic artery infusion chemotherapy for hypovascular HCC remains unclear.
Aims: This retrospective study aims to evaluate the efficacy of HAIC in patients with or without hypovascular HCC.
Methods: From 2005 to 2017, HCC patients who received initial HAIC were retrospectively analyzed. Hypovascular HCCs were detected by dynamic computed tomography or magnetic resonance imaging before starting HAIC. Baseline data, treatment response and overall survival were compared between patients with and without hypovascular HCC.
Results: A total of 311 patients were enrolled, including 63 patients with and 248 patients without hypovascular HCC. Except smaller tumor size in patients with hypovascular HCC (9.4 cm versus 10.8 cm, p = 0.03), the other baseline data was comparable between

the two groups. The overall response rate was 19% (complete response: 6.3% partial response: 12.7%) and 19% (complete response: 7.3% partial response: 11.7%) in patients with and without hypovascular HCC (p = 0.56). The disease control rate was 25.4% and 37.9% in patients with and without hypovascular HCC (p = 0.08). The overall median survival were 6 and 8 months in patients with and without hypovascular HCC (p = 0.70). The 3-month, 6-month, and 12-month survival rate were 72.8%, 50.2%, 32.3% in patients with hypovascular HCC and 80.1%, 55.5%, 37.8% in patients without hypovascular HCC (p = 0.53).
Conclusions: The treatment outcomes of HAIC seemed to be similar in patients with and without hypovascular HCC.

Abstract #1515

Correlation of platelet to lymphocyte ratio (PLR), neutrophil to lymphocyte ratio (NLR), and child pugh (CP) score with survival in hepatocellular carcinoma (HCC) patient

Syifa Mustika[1], Sri Utami[1]

[1]Gastroenterohepatology Division, Department of Internal Medicine, dr. Saiful Anwar Hospital, Medical Faculty of Brawijaya University, Malang, Indonesia

Introduction: The Platelet to Lymphocyte Ratio (PLR) and Neutrophil to Lymphocyte Ratio (NLR) is new systemic inflamations markers for diseases and malignancy. HCC, is one of the cancer which had worse prognosis and survival.
Objectives: We evaluated the use of PLR, NLR, and Child Pugh (CP) score for prediction of survival in patients with HCC.
Methods: A total 24 patients with HCC in this cohort retrospective study. Complete blood count and liver function test were used to determine the PLR, NLR, and CP score. The patients were divided into two groups according to one years survival. Statistic analysis PLR or NLR with CP score were using Spearman, for analysis of survival were using Fisher and C-Square methods with significantly if $p < 0.05$. We are also measuring area under the curve (AUC) for determining the cut-off PLR or NLR in relationship with survival.
Result: The correlation of NLR with CP score were strongly positive (p = 0.013, r = 0.498) but in contrary for PLR with CP score (p = 0.604, r = − 0.111). A cut-off value of PLR for survival is 131.6 (p = 0.035) with sensitivity and specificity were 85% and 75%. A cut-off value of NLR for survival is 5.8 (p = 0.020) with sensitivity and specificity were 70% and 100%, with strong AUC of 86%. The assosiation of CP class with survival HCC (p = 0.002).
Conclusions: The using of PLR, NLR, and CP score useful parameter for prediction of survival HCC patients.

Abstract #1550

Epidemiological characteristics and survival of advanced hepatocellular carcinoma patients in Cipto Mangunkusumo Hospital a Tertiary Referral Center in Indonesia

Juferdy Kurniawan[1], Gita Aprilicia[1], Monica Raharjo[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Epidemiological characteristics and survival of advanced hepatocellular carcinoma (HCC) in Indonesia has not been well reported.
Objectives: This study was done to describe characteristics and survival of Barcelona Clinic Liver Cancer class C (BCLC C) HCC patients and identify factors associated with 1-year mortality in these patients.
Methods: A retrospective study was done in Cipto Mangunkusumo Hospital. We performed a retrospective HCC registry review on all patients in the registry (patients diagnosed with HCC from August 2015-September 2019). Bivariate analysis with Chi-Square test and multivariate logistic regression analysis were performed.
Results: 158 patients were included in this study. 126 patients (79.7%) were male. Mean age was 54 years old. Hepatitis B virus infection is the most common etiology (68.4%). 90 patients (57%) had multiple tumor and 110 patients (69.6%) had portal vein involvement and/or metastasis at diagnosis. Median tumor size was 98 mm. 128 patients (81%) received supportive care. 85 patients (53.8%) died within a year. Bivariate analysis found that Child-Pugh class B, tumor size $\geq$ 50 mm, and receiving only supportive care were associated with 1-year mortality. After performing multivariate analysis, only Child-Pugh class B and receiving supportive care were associated with 1-year mortality. Median survival time was 3 months. Survival was significantly lower in patients with Child-Pugh class B compared to class A and patients receiving supportive care compared to palliative treatment.
Conclusion: Advanced BCLC C HCC patients have poor survival, especially patients with Child-Pugh class B or receiving only supportive care.

Abstract #1561

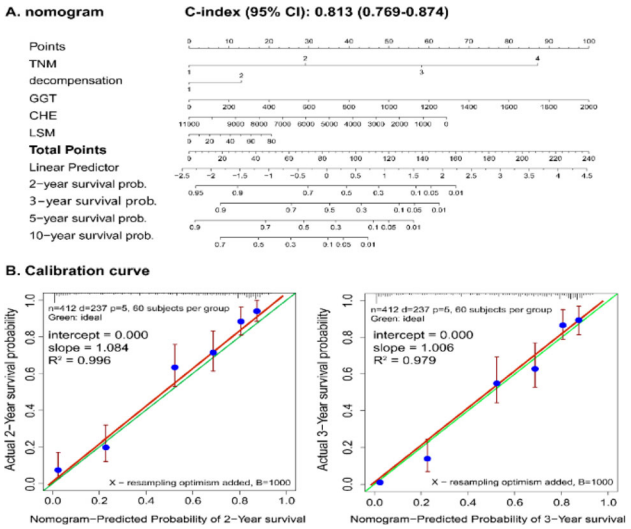
Nomogram to predict mortality in CHB patients with hepatocellular carcinoma in Chinese

Dong Ji[1], Yihui Rong[2], Song-Hai Chen[1], Yu-dong Wang[3], Yiying Lu[4], Guofeng Chen[1], George Lau[1,3]

[1]Second Liver Cirrhosis Diagnosis and Treatment Center, The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China, [2]Infection Disease Center, Peking University International Hospital, Beijing, China, [3]Humanity and Health Clinical Trial Center, Humanity and Health Medical Group, Hong Kong SAR, China, [4]Comprehensive Liver Cancer Center, The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China

Background and aim: In China, hepatocellular carcinoma (HCC) is the most commonly diagnosed cancer in individuals under the age of 60 years, and approximately 60–80% of HCC are attributable to chronic HBV infection. We develop a nomogram to predict mortality related to CHB with HCC in a real-world setting.
Methods: We retrospectively enrolled CHB Chinese patients with HCC, referred to Second Liver Cirrhosis Diagnosis and Treatment Center, The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China between Jan 2008 and Jan 2019. All the patients had at least 3 time of follow-up at an interval of 3–6 months. The zero time was the date when the diagnosis of HCC was made in accordance to ASPAL HCC guideline and censored time was the time of death of the patients. Liver stiffness measurements (LSM), alpha-fetoprotein (AFP), and other serum parameters were examined at each visit. Overall survival was measured and multivariate Cox proportional hazards regression was used to identify the independent risk factors associated with mortality and then a nomogram was synthesized.
Results: Totally, 412 CHB-HCC patients were enrolled. Resectable cases underwent surgery unless medically unfit. For unresectable cases, TACE was the primary treatment. 84.2% was male, mean age was 53.9 ± 9.0 years old, 58.5% (n = 241) did not receive any anti-HBV treatment before the diagnosis of HCC, 34.0% were HBeAg positive (n = 140), and 39.8% had decompensated liver

cirrhosis (n = 164). Median follow-up time was 57.0 (51.0–67.0) months and median survival time was 40.0 (29.0–57.0) months. Overall, 57.5% (237 cases) death occurred during follow-up and the 2-, 3-, and 5-year survival rates were 57.3%, 51.4% and 42.1%, respectively. Cox proportional hazards model showed that hepatic decompensation, high LSM value (≥ 17.0 kPa), low cholinesterase and TNM staging were risk factors associated with higher mortality due to HCC. The nomogram for prediction of mortality achieved good concordance indexes (C index) of 0.813 (95% CI 0.769–0.874) in both resectable and unresectable cases. The predictive performance of the nomogram was also measured by calibration with 1000 bootstrap samples to decrease the overfit bias, and results showed the well-fitted calibration curves regarding 2- and 3- year survival rates with slopes of 1.084, and 1.006, respectively.
Conclusions: The nomogram could predict mortality in CHB- related HCC patients. Using the model, the therapeutic strategy might be modified according to risk factors.



Abstract #1562

Transition of the postoperative prognosis in hepatocellular carcinoma according to the hepatitis virus infection status

Yukiyasu Okamura

Background: The Japanese nationwide survey revealed that hepatocellular carcinoma (HCC) patients with negative for hepatitis B (HB) surface antigen and hepatitis C (HC) antibody (NBNC-HCC) had a significantly lower risk of recurrence than those with HB virus-positive (B-HCC) and HC virus-positive (C-HCC). However, the postoperative prognosis in C-HCC patients has been improved introducing direct acting antivirals (DAAs). We aimed to reveal the latest postoperative prognosis according to the hepatitis virus infection status.
Methods: From 2002 to 2018, 552 primary HCC patients who underwent hepatectomy were included. We divided the treatment period before and after 2014 because DAAs could be administered from 2014. The postoperative prognosis was compared between the two periods.
Results: There were 380 and 172 patients in the former and latter periods, respectively. The distribution of hepatitis virus infection status between the two periods was significantly different ($P < 0.001$). In the former period, the number (175) and rate (47%) of C-HCC was the most. However, the number (91) and rate (54%) of NBNC-HCC was the most in the latter period. Relapse-free survival of C-HCC patients in the latter period was significantly better than that in the former period (P = 0.03). In contrast, there were no significant differences of survival in B-HCC and NBNC-HCC patients.
Conclusions: The present study suggested that the postoperative prognosis has changed according to the hepatitis virus infection status. The rate of NBNC-HCC patients has been increasing, but the prognosis has not been improved. The treatment strategy for NBNC-HCC patients is needed to be established in the future.

Abstract #1567

Intrabiliary hepatocellular carcinoma diagnosed from endoscopic retrograde cholangiopancreatography: a case report

Chieh Sian Koo[1], Khek Yu Ho[1], Qingyao Daniel Huang[1]

[1]Department of Gastroenterology and Hepatology, National University Hospital, Singapore

Introduction: Hepatocellular carcinoma (HCC) is the most common primary malignant hepatic neoplasm. Extrahepatic invasion into the biliary ducts is rare. We report an unusual case of a patient who was diagnosed with intrabiliary HCC from an endoscopic retrograde cholangiopancreatography (ERCP).
Case: A 87 year old Chinese male presented with right upper quadrant pain and obstructive jaundice for 1 day. He had a significant background of recurrent gallstone cholangitis, previous cholecystectomy, hyperlipidemia and diabetes mellitus. He was a non-drinker. Laboratory workup showed a total bilirubin of 81 μmol/L, alanine aminotransferase of 125 U/L, aspartate aminotransferase of 127 U/L, alkaline phosphatase of 141 U/L, albumin of 38 g/L, white blood cell count of 6.55×10^9/L, platelet count of 148×10^9/L, international normalised ratio of 1.25, and an elevated alphafetoprotein of 611 μg/L. Hepatitis B and C serology was negative. A triphasic computed tomography scan of his abdomen showed dilatation of the intrahepatic biliary tree and common duct with filling defects suggestive of stones, and a 3 cm segment 3 lesion suggestive of HCC. An ERCP was performed which demonstrated a dilated left intrahepatic duct with amorphous filling defects obstructing its distal end. Balloon trawling during the ERCP extracted the intraductal lesions, which appeared to be tumour-like tissue. Histology showed necrotic tumour tissue with residual viable tumour cells staining diffusely positive with HepPar, Arginase, and CAM5.2, compatible with HCC. Lenvatinib was initiated after discussion at a multidisciplinary meeting in view of his age and preferences.
Conclusion: Intrabiliary HCCs represent a rare but important differential in patients with obstructive jaundice

Abstract #1583

Comparing outcomes of Milan criteria, University of California San Fransisco Criteria, and expansion of both criteria in hepatocellular carcinoma patients undergoing liver transplantation

Juferdy Kurniawan[1], Budiman Syaeful Anwar[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related deaths worldwide. Currently, liver transplantation for HCC is the only hope for a cure from the tumor and from end-stage

liver disease (ESLD). Recently, there was interest in expansion of the Milan criteria because it's too stringent.
Methods: Three selected articles are found through Pubmed, Science Direct and Cochrane Lib according to clinical questions. The selection of articles is based on inclusion and exclusion criteria.
Results: These three selected articles revealed that overall survival rate and tumor-free rate in 5 years using Milan criteria range from 74–77% and 73–90.2%, University of California San Fransico (UCSF) criteria 74–75% and 71–86%, ASAN criteria 67–72% and 74–83%, Valencia criteria 76 and 72%, CUN criteria 75.8% and 71.7%, and Hangzhou criteria 72.5 and 67.8%, respectively.
Conclusion: The expansion of Milan criteria and UCSF criteria is an alternative criterion for the candidate's liver transplantation. The presence of vascular invasion can affect the HCC recurrence rate and survival rate. Further research needs to be done.

Abstract #1584

Efficacy and safety of DEB-TACE versus cTACE in patients with hepatocellular carcinoma

Juferdy Kurniawan[1], Mustika Dian Permana[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Background: Drug-eluting beads (DEBs) have been imposed as novel drug delivering agents for trans arterial chemoembolization (TACE) within the target tumor with lower systemic concentrations compared to conventional TACE (cTACE). It is still controversial in clinical practice as to whether DEB-TACE is superior to cTACE in terms of overall survival and treatment response.
Methods: Two selected articles are found through Pubmed and EBSCOHost according to clinical questions. The selection of articles is based on inclusion and exclusion criteria.
Results: Jing Huai Zou et al reviewed that DEB-TACE increase the complete response rate (OR, 1.38; 95% CI 1.01–1.89) and overall survival rate (OR 1.41; 95% CI 1.01–1.98) with less common adverse events (OR 0.59, 95% CI 0.41–0.84). Meanwhile, Peng Chen et al reviewed that overall survival were significantly higher in DEB-TACE group.
Conclusion: DEB-TACE has a higher complete response rate and a higher overall survival rate in patients with hepatocellular carcinoma compared to cTACE. Furthermore, DEB-TACE is safer and has less common adverse events than cTACE.

Abstract #1601

Efficacy of radiofrequency ablation in the treatment of patients with hepatocellular carcinoma and compensated liver disease: a pathological evaluation of liver explants

Waleed Al-hamoudi[1,2], Issam Salih[2], Sarra Yousif[2], Khalid Bzeizi2, Saleh Alqahtani[2], Ali Benmousa[2], Mark Sturdevant[2], Dieter Broering[2], Hamad Alsuhaibani[3]

[1]Department of Liver Transplantation and Hepatobiliary Surgery, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia, [2]Departement of Medicine, College of Medicine, King Saud University, Riyadh, Saudi Arabia, [3]Department of Radiology, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia

Introduction: Radiofrequency ablation (RFA) is a safe and effective treatment for patients with limited hepatocellular carcinoma (HCC).
Objectives: To correlate the radiological tumor response of RFA with the histopathologic examination of explanted livers following liver transplantation (LT).
Methods: All compensated patients treated with RFA prior to LT at our institution from 2007 to 2018 were included in this study. Patients data were collected from our prospectively collected database.
Results: 29 patients were treated with RFA prior to LT. 12 (41%), 12 (41%), and 5 (18%) of patients had a single, two, or three lesions, respectively. 17 (58.6%), 8 (27.6%), 3 (10.3%), and 1 (3.4%) received 1, 2, 3, and 4 sessions, respectively. When comparing RFA for single or multiple HCC with no lesion more than 3 cm pathological cure was significantly higher, 85% (12/14) of cases vs 46% (7/15) in patients with lesions exceeding 3 cm (p-value = 0.027). Pathological cure was 100% (4/4) in patients with a single lesion less than 3 cm. Furthermore, 6 patients had lesions on the explant examination that were not demonstrated on the pretransplant imaging. Two patients developed new lesions on follow up imaging prior to LT. None of the included patients developed post-transplant HCC recurrence during the post-LT follow up period (54 months, range 1–131 months) and the overall survival was 76%.
Conclusion: The HCC histopathologic characteristics in the explanted liver at the time of LT has a dual function in both reflecting the efficacy of preoperative locoregional therapy and as a predictive factor for HCC recurrence.

Abstract #1606

Hypoxia suppresses miR-98 maturation via Lin28B/miR-98 negative feedback and promotes autophagy and malignancy in hepatocellular carcinoma

Qing Li[1,2], Xuehao Wang[1,2]

[1]School of Medicine, Southeast University, Nanjing, China, [2]Hepatobiliary Center, The First Affiliated Hospital of Nanjing Medical University, Key Laboratory of Liver

Introduction and objectives: Hypoxia suppresses miR-98 maturation via Lin28B/miR-98 negative feedback and promotes autophagy and malignancy in hepatocellular carcinoma.
Method: Gain- and loss-of-function experiments were employed to determine the effects of miR-98 on autophagy in HCC cell lines (Hep3B and SMMC7721) under hypoxia. Autophagy was detected using western blotting, immunofluorescence, immunohistochemistry, and transmission electron microscopy. The growth of xenograft tumors in nude mice was also recorded to confirm the effects of miR-98 in vivo.
Results: We found that hypoxic stress induced Lin28B to bind to primary transcript of miR-98 (pri-miR-98), thereby blocking miR-98 maturation in HCC, decreasing the binding ability of mature miR-98 to the 3' UTR of Lin28B mRNA, and degrading its transcript. Thus, more Lin28B was available to block miR-98 maturation. This Lin28B/miR-98 negative feedback loop played a crucial role in promoting autophagy in HCC cells by increasing autophagy-related gene ATG16L1. Xenograft tumors in nude mice transfected with anti-miR-98 had smaller necrotic area, more autophagic cells, and faster growth rate. Furthermore, exosomal miR-98 might serve as a sensitive and specific biomarker for detection of HCC.
Conclusion: We demonstrated a novel regulatory mechanism of autophagy in which Lin28B/miR-98 negative feedback loop suppressed miR-98 maturation under hypoxia

Abstract #1614

Prolonged fever as a rare manifestation of paraneoplastic syndrome in hepatocellular carcinoma: a case report

Rosatya Imanuela[1], Kemal Fariz Kalista[2], Taufik Agung[3]

[1]Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia, [2]Hepatobiliary Division, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia, [3]Department of Radiology, Cipto Mangunkusumo National General Hospital, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia

Introduction: Hepatocellular carcinoma (HCC) can cause paraneoplastic syndrome such as fever. The presence of fever in HCC signify an advanced disease with unfavorable prognosis.
Case Illustration: A 62-year-old male presented with prolonged fever for the last three months and painful upper abdomen. He was referred due to liver nodule finding in ultrasound and blood culture resulted a growth of Methicillin-Resistant Staphylococcus Aureus (MRSA). He had achieved sustained viral response (SVR) after direct acting antiviral (DAA) therapy for his hepatitis C infection three years prior to admission. Physical examination showed a palpable 4 cm mass on his right upper abdomen. Dynamic abdominal CT scan showed a mass of HCC characteristics sized 10.2 × 10.6 × 7.6 cm in the 6th- 8th hepatic segments, a thrombus in main portal vein, and multiple lung nodules. α fetoprotein (AFP) was 3959 ng/ml. Despite 14 days of intravenously given Vancomycin and subsequent blood culture resulted no microbial growth, the fever persisted.
Discussion: HCC, although uncommon, can also present as fever. The pathophysiology is unclear but it is hypothesized that it is related to pyrogens (IL-8, IL-6, and TNFα) produced by cancer cells. HCC with fever had a propensity for larger tumor size, poor tumor differentiation, vascular invasion, and metastasis.
Conclusion: This case demonstrates a rare case of HCC patient presented with prolonged fever which related to poorer prognosis.

Abstract #1629

Diagnostic performance of alpha fetoprotein in advanced liver disease patients: an observational study between 0th and 6th months

Novita Apramadha Kartika Sari[1], Syifa Mustika[2]

[1]Faculty of Medicine, Brawijaya University, Malang, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine, Brawijaya University-dr. Saiful Anwar Hospital, Malang, Indonesia

Introduction: Alpha fetoprotein (AFP) is tumor marker that is widely used to detect hepatocellular carcinoma (HCC). It is widely available in hospitals and inexpensive. However, its role in diagnostic and screening is still being debated.
Objective: To analyze the accuracy of AFP in advanced liver disease in the 0 and 6 months observations.
Methods: Study was done in 0th and 6th months of 41 patients with chronic hepatitis B and or/C, liver cirrhosis and HCC at Saiful Anwar General Hospital, Malang. AFP levels were measured by ELISA. Data on patient characteristics were analyzed using bivariate and multivariate analysis (One way ANOVA, Mann-Whitney, Chi-Square, Kruskal-Wallis). The accuracy of AFP was analyzed using receiver operating characteristic (ROC).
Results: At initial observation, there were 16 patients with chronic hepatitis, 15 patients with liver cirrhosis and 10 patients with HCC. The area under curve (AUC) of AFP was 0.971 (95%, CI 0.93–1.00) with optimum cut-off value of 144.3 ng/ml indicating that sensitivity was 70%, specificity was 100%, positive predictive value (PPV) was 100% and negative predictive value (NPV) was 96.8%. In the 6th month, one of chronic hepatitis patients progressed to liver cirrhosis, and 5 HCC patients passed away. The AUC of AFP was 1.00 (95%, CI 1.00) with optimum cut-off value of 105 ng/ml indicating that sensitivity, specificity, PPV and NPV was 100%.
Conclusion: AFP can be used as HCC screening tool, although sub-optimal sensitivity was obtained at initial observation. It can be enhanced by the use of other modalities.

Abstract #1634

Clinical study of xiaochaihu decoction plus on the regulation of immune function after transarterial chemoembolization treatment for primary liver cancer

Qiao Bing[1], Zhou Yong[1], Chen Peng[1], Gou Wei[1], Li Jinjin[1], Shi Changhe[1]

[1]Qingdao Hospital of Infectious Diseases, Qingdao Liver Disease Institute, Shandong Qingdao, 266033

Objective: To observe the TCM syndromes, liver function, and immune-related indicators of patients with primary liver cancer after Transarterial chemoembolization Treatment, to explore the effects of Xiao Chaihu Decoction Plus (XCDP) on the immune function, the TCM syndromes, liver function and related indicators of patients with primary liver cancer after Transarterial chemoembolization Treatment.
Content: 80 patients with liver cancer who were admitted to our hospital from January 2019 to December 2020 were selected. They were divided into control group (40 cases), Xiao Chaihu Decoction Plus treatment group (40 cases), both groups were given conventional symptomatic supportive treatment. XCDP group added Xiaochaihu Decoction plus on the basis of the control group. Liver function (ALT, AST), AFP, DCP, CK18, and immune-related IgG, IgA, T lymphocytes (CD3 +, CD4 +) and the improvement of TCM symptom score were measured before and after treatment in 4 weeks. And carry out scientific statistical analysis.
Results: Both the XCDP group and the control group can improve the TCM symptom score, reduce ALT, AST, AFP, DCP, CK18, immune-related IgG, IgA levels, and increase the number of T lymphocytes (CD3 +, CD4 +) ($P < 0.05$), the XCDP group had better effect in TCM syndrome scores, ALT, CK18, IgG, and IgA due to the control group ($P < 0.05$).
Conclusion: Xiao Chaihu Decoction Plus can improve immune function, protect liver function, improve the clinical symptoms and promote the prognosis of patients with primary liver cancer after Transarterial chemoembolization Treatment.

Abstract #1660

Aspartate transaminase to platelet ratio index (APRI) and albumin–bilirubin Grade (ALBI) predict postoperative morbidity following hepatectomy for hepatocellular carcinoma: a multicenter cohort study

Li-Yang Sun BA[1,2*], Lei Liang MD[1*], Hao Xing MD[1*], Chao Li MD[1*], Ming-Da Wang MD[1], Ya-Hao Zhou MD[3], Wei-Min Gu MD[4], Hong Wang MD[5], Ting-Hao Chen MD[6], Yong-Yi Zeng MD[7], Wan Yee Lau MD, FRCS, FACS, FRACS (Hon)[1,8], Meng-Chao Wu MD[1], Feng Shen MD, PhD[1], Tian Yang MD[1]

[1]Department of Hepatobiliary Surgery, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, China, [2]Department of Clinical Medicine, Second Military Medical University, Shanghai, China, [3]Department of Hepatobiliary Surgery, Pu'er People's Hospital, Yunnan, China, [4]The First Department of General Surgery, the Fourth Hospital of Harbin, Heilongjiang, China, [5]Department of General Surgery, Liuyang People's Hospital, Hunan, China, [6]Department of General Surgery, Ziyang First People's Hospital, Sichuan, China, [7]Department of Hepatobiliary Surgery, Mengchao Hepatobiliary Hospital, Fujian Medical University, Fujian, China, [8]Faculty of Medicine, the Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, China

Background and aims: Postoperative morbidity following hepatectomy remains high, and understanding its risk factors is important to improve perioperative outcomes. We aimed to identify the role of two non-invasive markers—albumin-bilirubin (ALBI) and aspartate transaminase to platelet ratio index (APRI)—in predicting postoperative morbidity following hepatectomy for hepatocellular carcinoma (HCC).
Methods: A multicenter data of patients undergoing hepatectomy for HCC at 8 centers were retrospectively analyzed. These patients were divided into normal and high groups according to preoperative ALBI and APRI scores. ALBI and APRI's predictive accuracy of postoperative 30-day overall and major morbidity were evaluated by the area under the receiver operating characteristic curve (AUC) and compared with two conventional scores: Child-Pugh grade and model for end-stage liver disease (MELD).
Results: In 2301 patients, 866 (37.6%) and 400 (17.4%) were in the high ALBI and APRI groups, respectively. There were significant differences of postoperative overall morbidity between the normal and high ALBI groups (26.2% vs. 40.1%, $P < 0.001$), as well as between the normal and high APRI groups (29.2% vs. 42.4%, $P < 0.001$). The AUCs of the ALBI and APRI scores for predicting overall morbidity are greater than those of Child-Pugh grade and MELD score. Multivariable analyses revealed that ALBI and APRI were independent predictors of overall morbidity in both preoperative and postoperative prediction models. Similar results existed in predicting postoperative major morbidity.
Conclusion: Preoperative ALBI and APRI could predict postoperative 30-day overall and major morbidity following hepatectomy for HCC before or after surgery

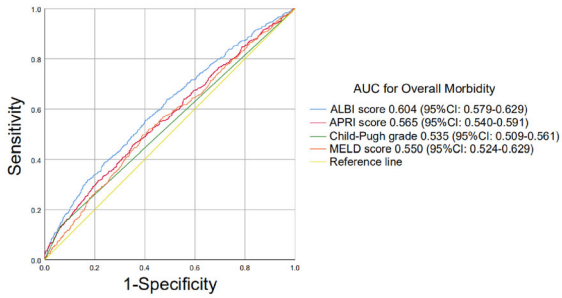


Figure 1. Receiver operating characteristic (ROC) curves of ALBI, APRI, Child-Pugh grade and MELD score for predicting postoperative 30-day overall morbidity after hepatectomy for hepatocellular carcinoma. (AUC, Area under the curve of ROC; CI, Confidence interval)

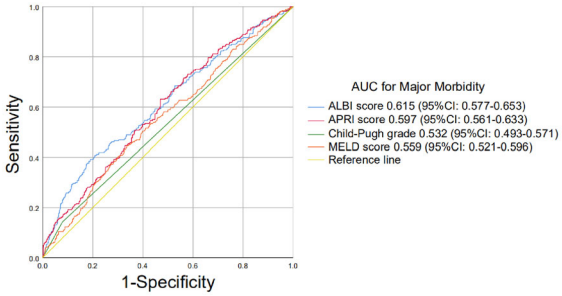


Figure 2. Receiver operating characteristic (ROC) curves of ALBI, APRI, Child-Pugh grade and MELD score for predicting postoperative 30-day major morbidity after hepatectomy for hepatocellular carcinoma. (AUC, Area under the curve of ROC; CI, Confidence interval)

Abstract #1668

Difference in the clinical phenotype and overall survival among patients with nonalcoholic fatty liver disease-associated hepatocellular carcinoma (NAFLD-HCC) versus hepatocellular carcinoma of other etiology

NL Ong[1], IHY Cua[1], JL Gopez-Cervantes[1]

[1]St. Luke's Medical Center, Quezon City

Background: NAFLD-HCC has a slowly increasing trend and known with different carcinogenesis. This study aims to investigate the difference in the clinical phenotype of patients with NAFLD-HCC and other etiologies.
Methods: Study Design: Retrospective, cohort; Study Population: Patients with HCC; Exposure: Etiology of HCC; Outcome/Statistical Analysis: Chi-squared and Mann-Whitney test (p-value); Kaplan Meier curve.
Results: 167 patients were included in the study, 46 (26.7%) NAFLD, 94 (56.3%) HBV, 15 (8.98%) HCV and 11 (6.6%) ALD. Compared HCC of other etiology, NAFLD-HCC had a higher proportion of females and older at presentation (p-value < 0.001); higher incidence of hypertension (p-value 0.004), diabetes mellitus (p-value < 0.001), dyslipidemia (p-value < 0.001), and liver cirrhosis (p-value < 0.001). NAFLD-HCC had the same ECOG and Karnofsky performance status, Child's and MELD-Na Score at baseline, incidence of gastrointestinal bleeding (p-value 0.393), ascites (p-value 0.359), hepatorenal syndrome (p-value 0.368), SBP (p-value 0.412), hepatic encephalopathy (p-value 0.321), portal vein thrombosis (p-value 0.826), serum AFP (p-value 0.586), and presence of solitary or multiple tumors at diagnosis (0.988). However, mean size of the largest tumor at diagnosis was larger (p-value 0.001) and presence of distant metastasis higher (p-value 0.022) in the group of HCC of other etiology. The overall survival was identical (p-value 0.053) among both groups; approximately 4.1 years.
Conclusion: Our study showed that NAFLD-HCC patients are older, more comorbid conditions, same degree of liver function and complications, less severe tumor characteristics and metastasis compared to a HBV predominant HCC population. However, this only translated to a statistically non-significant survival advantage of approximately 53 days.

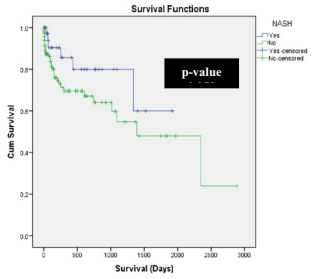


Figure 2. Kaplan-Meier curve showing the survival in days of HCC patients. NASH-HCC showing in blue, other-HCC shown in green. (p-value 0.053)

Abstract #1673

A pilot association study of the MARCO gene polymorphisms and susceptibility to hepatocellular carcinoma

Zhenzhen Su[1], Bei Cai[1], Limei Luo[1], Xiaojuan Wu[1], Bin Wei[1], Lu Wang[1], Lanlan Wang[1]

[1]Department of Laboratory Medicine, West China Hospital of Sichuan University, Chengdu 610041, China

Objectives: Macrophage receptor with collagenous structure (MARCO) is constitutively expressed on macrophage. Previous studies have reported that macrophages play a key role in host anti-tumor defenses in hepatocellular carcinoma (HCC) and less expression of MARCO is associated with HCC development and progression. Impaired expression of MARCO may due to its gene variations. Therefore, we sought to investigate whether polymorphisms in MARCO could contribute to HCC risk.
Method: A total of two single nucleotide polymorphisms (SNPs, rs17009726 and rs6761637) were genotyped in 420 HCC patients and 519 benign liver disease controls (HBV related fibrosis/ cirrhosis and hepatic hemangioma) using a hospital based case-control association study.
Result: Although we found no significant differences in the frequency distributions of the two SNP alleles or genotypes between the two groups. The rs17009726 AG genotype was observed slightly more common in HCC group [106 (25.2%) patients vs 105 (20.2%) controls, p = 0.074, adjusted odds ratio (AOR) = 1.383, 95% confidence interval (CI) = 0.969– 1.974 in a codominant model]. Meanwhile, rs6761637 TC genotype was also observed more frequent in HCC group [105 (25.0%) patients vs 105 (20.2%) controls, p = 0.081, AOR = 1.374, 95% CI = 0.962– 1.961 in a codominant model].
Conclusion: Our pilot study indicates that individuals carrying the specific MARCO genotype may have a possible tendency towards HCC. However, we need include more samples to confirm this finding

Abstract #1691

Synergistic anticancer effect of metformin in combination with immunosuppressant on hepatocellular carcinoma cell lines

Suk-Won Suh[1], Yoo-Shin Choi[1]

[1]Department of Surgery, Chung-Ang University College of Medicine

Introduction: After liver transplantation (LT), immunosuppression is needed to avoid rejection and graft loss, however, it can stimulate hepatocellular carcinoma (HCC) recurrence and progression. Previous studies have shown that metformin had an anticancer effect on several cancers, including HCC.
Objectives: The aim of this study was to evaluate the interactions between metformin and immunosuppressive agents including sirolimus, tacrolimus and mycophenolate mofetil (MMF) for antitumor activity.
Methods: Three cell lines (Huh7, HepG2 and Hep3b) were tested. Cell viability was determined using a MTT assay and Western blot analysis for mammalian target of rapamycin (mTOR) pathway related proteins were performed to reveal their mechanism.
Results: Metformin and sirolimus had synergistic antiproliferative effect and sirolimus plus metformin supplemented with MMF also showed synergistic antiproliferative effect in specific HCC cells. Synergistic effect of metformin and sirolimus through the inhibition of mTOR and its down-stream, p70S6K, and p-4EBP1 were demonstrated. Metformin and sirolimus also showed synergistic effect for the down-regulation of Livin and Survivin expressions in HepG2 and Hep3b cells.
Conclusion: Metformin had synergistic interactions with sirolimus in terms of anticancer effects for HCC cells and the mechanism explaining this synergistic inhibition might be related with mTOR pathway. These results may provide a foundation for further studies for patients with HCC who underwent LT in clinical era

Abstract #1696

Disulfiram induces apoptosis of hepatocellular carcinoma Huh7 cells via protein poly-ubiquitination and caspase signaling pathway

He YuLin[1], Meng ZhongJi[1], Li RuiMing[1], Wei ZhiQiang[1], Cheng Bin[1], Liu GuoHua[1]

[1]Institute of Biomedical Research, Taihe Hospital, Hubei University of Medicine, Shiyan, China

Introduction: Disulfiram (DSF) is a clinically available drug for alcohol dependence. Recent studies have demonstrated the copper (Cu)-dependent antitumor properties of DSF in various types of cancers.
Objectives: The aim of the current study was to investigate the anti-tumor effect and molecular mechanism of DSF on hepatocellular carcinoma Huh7 cells.
Methods: Huh7 cells were treated with DSF in the presence or absence of copper at different concentrations. The effect of DSF/Cu on the viability of Huh7 cells was evaluated by MTT assay, early and late apoptosis assays were performed using flow cytometry with annexin V/PI staining, and the percentages of the annexin V-positive cell population were quantified. The levels of the Caspase signaling pathway-related proteins were analyzed by Western blotting.
Results: Huh7 cells became rounded in shape and detached from the substratum after incubation with DSF/Cu. In addition, a significant reduction in cell viability was observed at a DSF concentration of 1 μM with Cu (1 μM) 24 hrs post treatment. Annexin V/PI staining identified a significant increase in the numbers of early and late apoptotic cells, accompanied by increased levels of cytochrome c, caspase-3 activation and PARP cleavage. Additionally, DSF/Cu treatment led to accumulation of poly-ubiquitylated proteins in Huh7 cells.
Conclusion: The results indicated that DSF/Cu has a potential anti-tumor activity in Huh7 cells. Mechanistically, DSF/Cu-induced cytotoxicity was closely associated with protein poly-ubiquitynation and Caspase signaling pathway.

Abstract #1701

Comparison of the effects of ultrasound alone and ultrasound, CT, and MRI combination on surveillance in high-risk patients with hepatocellular carcinoma

Heejoon Jang[1], Minseok Albert Kim[1], Hyunwoo Oh[1], Sun Woong Kim[1], Yun Bin Lee[1], Eun Ju Cho[1], Jeong-Hoon Lee[1], Su Jong Yu[1], Jung-Hwan Yoon[1], Yoon Jun Kim[1]

[1]Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Korea

Introduction: Many clinical guidelines suggest ultrasonography at six-month intervals for patients at high risk for hepatocellular carcinoma (HCC). Nevertheless, in clinical practice, surveillance is often performed by combining ultrasound with other imaging tests such as computed tomography (CT) and magnetic resonance imaging (MRI).
Objectives: This study analyzed the differences in clinical outcomes between patients who followed HCC surveillance guidelines and those who did not.
Methods: Patients who were diagnosed from January 2010 to December 2014 with chronic hepatitis B or cirrhosis and who underwent 2 or more imaging tests at 6 ± 1 month intervals for HCC surveillance were included. The cumulative incidence of HCC, overall survival, cause-specific HCC survival, and stage of HCC were compared between the group of patients who received only ultrasound (USG group) and the group of patients who received a combination of ultrasound, CT and MRI (UCM group).
Results: A total of 794 patients were analyzed. Cumulative incidence of HCC was higher in the UCM group than in the USG group (adjusted hazard ratio [aHR] = 2.07, 95% confidence interval [CI] = 1.21–3.54; log-rank P = <0.01), but overall survival (aHR = 1.06, 95% CI = 0.49–2.26; log-rank P = 0.52) and cause-specific HCC survival (aHR = 2.00, 95% CI = 0.53–7.56; log-rank P = 0.13) were not significantly different between the two groups. HCC at the very early stage of the Barcelona clinic liver cancer staging system was significantly higher in the UCM group (Fisher's exact test P = 0.03).
Conclusion: Liver ultrasound may be sufficient for surveillance to date in terms of survival, but the combination of CT and MRI can detect earlier stage HCC.

Abstract #1708

The prognostic value of neutrophil-to-lymphocyte ratio in advanced stage hepatocellular carcinoma treated with sorafenib: an evidence-based review

Rasco Sandy Sihombing[1], Saut Horas H Nababan[1]

[1]Hepatobiliary Division, Internal Medicine Department, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

Background: Systemic inflammation is associated with poor prognosis and hepatocellular carcinoma (HCC) recurrence. Previous studies showed a correlation between neutrophil-to-lymphocyte ratio (NLR), as an inflammation biomarker, with HCC prognosis.
Aim: To summarize current evidence on the prognostic role of the NLR in advanced HCC patients treated with sorafenib.
Methods: Literature searching was conducted by using the PubMed database from 1st Jan 2013 to 31st Dec 2019 to identify studies that evaluate NLR as a survival predictor in advanced HCC patients treated with sorafenib. Studies meeting the selection criteria were reviewed. The quality of the papers was rated using the Centre for Evidence-based Medicine (CEBM) critical appraisal tool for prognostic study.
Results: Six publications were identified for this systematic review. Three studies from Europe, two studies from Asia and one from Latin America. Two studies included patients treated with sorafenib, either as first and second-line therapy. One study also reported the changes in the NLR as outcome predictor. Overall, all studies consistently showed that lower NLR was associated with improved overall survival in sorafenib-treated advanced HCC. However, the optimal cutoff value of NLR was not fully defined.
Conclusion: Based on this review, the NLR parameter can be useful in determining the prognosis of advanced hepatocellular carcinoma (HCC) patients treated with sorafenib.

Abstract #1709

Humeral metastasis in a patient with advanced hepatocellular carcinoma: a rare clinical entity

Siregar L.[1], Loho I. M.[1], Waspodo A. S.[1], Elaine S.[1], Swadari R.[1], Basuki A.[1], Setyarani M.[1], Rayhani F.[1]

[1]"Dharmais" Cancer Hospital, Indonesian National Cancer Center, Jakarta, Indonesia

Introduction: The most frequent sites of hepatocellular carcinoma (HCC) metastasis are the lungs, the abdominal lymph nodes, and the bone. Humeral metastasis of hepatocellular carcinoma is very rare and to date only one case has been reported in the literature.
Case report: A 32-year-old male was referred to our hospital for further treatment of advanced HCC. He was accidentally diagnosed with HCC during exploratory laparotomy due to acute abdominal pain one year before, which revealed the presence of small amount of blood in the peritoneal cavity. Histopathology of the liver mass was suggestive of HCC. Two months after surgery, he got a right humerus bone fracture after an accidental fall, but denied any further treatment for his fracture. Three months after surgery, he received three sessions of TACE and the swelling of humeral bone fracture became progressive. On admission in our outpatient clinic, we found a bulging mass on his shoulder (dimensions 30 × 27 × 13 cm). Laboratory examination showed hemoglobin level of 5 g/dL, HBsAg non-reactive, anti HCV total non-reactive, and alpha feto-protein level of 9,363,410 ng/mL. Abdominal CT revealed a mass in segment 7–8 of liver (15 × 13.3 cm) with typical HCC pattern and portal vein thrombosis. Due to progressive decrease of hemoglobin level, a decision of immediate forequarter amputation was made. However, the patient suffered from 3500 mL of blood loss during surgery, which was treated with cauterization. Histological examination was consistent with metastatic HCC and the tumor cells were positive for Ki-67 and AFP, while negative for synaptophysin, chromogranin, CD56, glypican-3, and vimetin on immunohistochemical staining. After surgery, he received sorafenib and had performed well.
Conclusion: Humeral bone metastasis from advanced HCC is a very rare case, but carries a risk of heavy bleeding. Embolization of feeding artery to the tumor may be a good solution to prevent severe hemorrhage during amputation.

Abstract #1726

Ramucirumab after lenvatinib failure for patients with advanced hepatocellular carcinoma: initial experience

Teiji Kuzuya[1], Masatoshi Ishigami[1], Takanori Ito[1], Yoji Ishizu[1], Takashi Honda[1], Mitsuhiro Fujishiro[1]

[1]Department of Gastroenterology and Hepatology, Nagoya University Graduate School of Medicine, Nagoya, Japan

Introduction: With the positive results of the REACH-2 trial, ramucirumab have become available as second-line treatment for advanced hepatocellular carcinoma (HCC) patients with AFP levels of $\geq$ 400 ng/ml. However, in the REACH-2 trial, since the first-line treatment was sorafenib, the outcomes of ramucirumab used after lenvatinib failure is unknown.
Objective: We aimed to investigate the outcomes of ramucirumab treatment in advanced HCC patients after lenvatinib failure in clinical setting.
Methods: Patients consisted of 5 males and 5 females, with a median age of 75 years. There were 7 patients with an ECOG-PS of 0, 5 patients with a Child–Pugh score of 5. Median AFP level was 3421 ng/mL (633–82429). Radiologic antitumor response at 6 weeks, time to progression (TTP), treatment duration, changes in AFP and safety were evaluated.
Results: The antitumor response (CR/PR/SD/PD) at 6 weeks according to RECIST was 0/0/8/2 (ORR; 0%, DCR; 80%). Median TTP was 94 days. The frequency of patients with AFP reduction of AFP were as followed: 50% at 2 weeks and 30% at 6 weeks, respectively. Median treatment duration was 139 days. The most common adverse events (AEs) were appetite loss (n = 5) and proteinuria (n = 5). The frequency of AEs of grade 3 or more was low.
Conclusions: Early outcomes of ramucirumab treatment could have therapeutic potential after lenvatinib failure.

Abstract #1732

Hepatocellular carcinoma in a 36-year-old thalassemia patient: a case report

Monica Raharjo[1], Patriotika Ismail[1], Kemal Fariz Kalista[2], Taufik Agung[3], Marini Stephanie[4]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [3]Department of Radiology, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [4]Department of Anatomic Pathology, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Increased survival of β-thalassemia patients made it possible for them to develop long-term liver complications such as hemosiderosis, cirrhosis, and hepatocellular carcinoma (HCC).
Case Illustration: A 36-year-old transfusion dependent β-thalassemia patient was admitted with complaints of abdominal enlargement over the past month. The patient was diagnosed with thalassemia at 2 years old and has been receiving regular blood transfusions every two weeks. He underwent total splenectomy at 15 years old. He has not been taking deferiprone or deferoxamine in the past two months. Physical examination showed conjunctival pallor, scleral icterus, and hepatomegaly. Laboratory examination showed anemia (6.9 g/dl), hyperbilirubinemia (3.9 mg/dl), hypoalbuminemia (2.1 g/dl), and normal prothrombin time. Ferritin was elevated (15,405 ng/ml) and alpha-fetoprotein was normal (5.82 ng/ml). Abdominal ultrasound revealed a hyperechoic lesion in the left lobe of the liver. Consistent with ultrasound, multiphase computed tomography revealed a hypodense mass with arterial enhancement and washout during venous and delayed phase in segment III of the liver, hemosiderosis, and biliary dilatation. Atypical cells and iron deposits were found on liver biopsy. The patient succumbed to his disease before further work-up can be done.
Discussion: We present a case of HCC in a thalassemia patient. Iron overload due to periodic blood transfusions is a major risk factor for development of liver cirrhosis and later HCC. Ultrasound is the preferred method of HCC screening in thalassemia patients as alpha-fetoprotein can be normal at diagnosis.
Conclusion: HCC screening should be done in thalassemia patients with iron overload and liver cirrhosis.

Abstract #1733

Progression of portal vein thrombus involving superior mesenteric vein in a patient with hepatocellular carcinoma: a case report

Monica Raharjo[1], Rebekka Martina[1], Wahyu Purnama[1], Fathony Arsyad[1], Kemal Fariz Kalista[1], Sahat B. R. E. Matondang[2]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Department of Radiology, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Portal vein (PV) thrombus occurs in 35–50% of patients with hepatocellular carcinoma (HCC). However, superior mesenteric vein (SMV) thrombus along with PV thrombus is rare.
Case illustration: A 55-year-old male patient was admitted with worsening abdominal pain in the last 3 weeks. He also complained of abdominal enlargement accompanied by weight loss of 9 kilograms within the last 3 months. The patient has been previously diagnosed with hypertension and dyslipidemia. Elevated blood pressures, scleral icterus, abdominal tenderness, and hepatosplenomegaly were found upon physical examination. He had a reactive anti-HCV and his alpha-fetoprotein was $>$ 20,000 ng/ml. Multiple hypodense lesions in segment V-VIII of the cirrhotic liver (largest lesion 9.4 $\times$ 7.1 $\times$ 6.7 centimeters) with arterial enhancement and washout during venous and delayed phase can be seen on multiphase computed tomography (CT) along with SMV and PV thrombus, para-aortic lymphadenopathy, and splenomegaly. The patient was treated with intravenous unfractionated heparin maintaining a two to threefold prolongation of the activated partial thromboplastin time after performing esophageal band ligation of high-risk varices. Abdominal pain resolved after anticoagulation. The patient was discharged and continued on oral anticoagulant rivaroxaban. He is scheduled for follow-up CT during his next visit.
Discussion: We present a case of SMV and PV thrombus in a patient with HCC. This condition should be suspected in patients with abdominal pain and prompts long-term anticoagulation. Risk factors for thrombosis include portal hypertension and malignancy.
Conclusion: Anticoagulation may be useful in managing abdominal pain of HCC patients with progressing PV thrombus.

Abstract #1792

Tumor microenvironment modification effect multikinase inhibitors in allograft mouse hcc model

Kanayama Kengo

Background: The antitumor effect of multikinase inhibitors (MKIs) is caused not only by direct inhibition of tumor cells, but also by modification of the tumor microenvironment (TME). In this study, we

examined the effect of MKIs on TME using allograft mouse HCC model.
Methods: Mouse hepatoma cell line Hepa1-6 (5×10^6 cells) were subcutaneously implanted in 6-week old male B57/B6NCr mice. When the tumor diameter reached 10 mm, sorafenib (SOR) (30 mg/kg daily) or lenvatinib (LEN) (10 mg/kg daily) were administered. After 7 days of drug administration, PD-L1 expression on tumor cell, fractions of T lymphocytes and mononuclear cells were evaluated by flow cytometry. In addition, immunohistochemical analysis of microvessel was performed with CD34 antibody.
Results: In cultured Hepa1–6 cells, PD-L1 expression was reduced by SOR but remained unchanged by LEN. On the other hand, PD-L1 expression in tumor cells from mouse model was reduced in both groups. The number of CD4 and CD8-positive T cells, regulatory T cells, myeloid-derived suppressor cells, and macrophages did not change in both groups, but the PD-1 + Tim3 + fraction in CD8-Tcells (exhausted T cells) increased in the LEN group. In immunohistochemical analyses, CD34-positive microvessel area did not change in the SOR group, but increased 3.1 times in the LEN group.
Conclusion: The effects of SOR and LEN on tumor cells showed a similar tendency, but an increase in exhausted T cells was observed in the LEN group. LEN administration significantly increased the microvascular area, suggesting that hypoxia could be involved in indirect antitumor effects

Abstract #1802

Metagenomics approach identified diversity and composition of tumor-infiltrating microbiota in hepatocellular carcinoma

Yosuke Hirotsu[1], Yuji Iimuro[2], Hitoshi Mochizuki[1,3], Masao Omata[3,4]

[1]Genome Analysis Center, Yamanashi Central Hospital, Kofu, Japan, [2]Department of Surgery, Yamanashi Central Hospital, Kofu, Japan, [3]Department of Gastroenterology, Yamanashi Central Hospital, Kofu, Japan, [4]The University of Tokyo, Tokyo, Japan

Introduction: Metagenomics analysis revealed the relationship between bacteria and tumor development. Recently, diversity and composition of microbiome is associated with the prognosis and influences the host immune response in pancreatic cancer (Riquelme at l. Cell, 2019). However, it remains under investigation whether the tumor-infiltrating microbiota related to the development of HCC.
Objectives: We aim to examine the presence of bacteria in HCC, composition of microbiota and influences of carcinogenesis
Methods: We conducted amplicon-based next generation sequencing targeting variable regions in 16S ribosomal RNA according to according the Earth Microbiome Project (X) and NIH-Human Microbiome Project. We mapped single-end sequencing reads to the dataset (Greengenes and MicroSEQ) and identified tumor-infiltrating bacteria. Diversity of microbiome were analyzed QIIME and observed taxonomic unit (OTU).
Results: PCR amplified the variable regions of 16S ribosomal RNA using template DNA extracted from formalin-fixed paraffin embedded tumor tissues. Adaptor-ligated PCR product was subjected to the microbiome analysis and in-house developed pipeline successfully. We identified several types of microbiome subgroups and diversity of bacteria in HCC.
Conclusion: Metagenomic analysis showed the presence of bacteria in hepatocellular carcinoma Composition and diversity is different between each subjects. Tumor-infiltrating microbiome may associated to interaction between microbiota and host immune response.

Abstract #1830

Management of hyperammonemia in patients with hepatocellular carcinoma who underwent lenvatinib therapy

Yoji Ishizu

Background and aim: Hepatic encephalopathy (HE) is sometimes seen in patients with advanced hepatocellular carcinoma (HCC) who underwent lenvatinib therapy. And, once it developed, lenvatinib therapy was discontinued, thus, management of hyperammonemia is important.
The aim of this study is to clarify the clinical course and factors associated with hyperammonemia in patients with HCC who underwent lenvatinib therapy.
Methods: 49 patients with advanced HCC who were treated by lenvatinib were enrolled in this study. Hyperammonemia was defined when NH3 levels increased $\geq$ 80 (μmol/L). 23 patients were BCLS stage B and 26 were C.
Results: NH3 was significantly increased from 28.8 ± 14.7 μmol/L at baseline to 42.5 ± 22.3 μmol/L at one week after starting lenvatinib therapy (1 W) ($p < 0.01$) and hyperammonemia were seen in three patients at 1 W. High ammonia levels and the presence of previous treatment history for esophagogastric varices (EGV) were associated with the development of hyperammonemia. ALBI score also significantly increased from -2.19 ± 0.47 at baseline to -1.97 ± 0.49 at 1 W ($p < 0.001$) and delta changes of ALBI score and ammonia levels were marginally and weakly correlated ($R = 0.267$, $P = 0.07$). 11 patients with ammonia levels of > 42 μmol/L (an upper limit of ammonia levels at our institute) were received ammonia lowering therapy, and ammonia levels significantly decreased after starting ammonia lowering therapy (from 71 ± 21.2 μmol/L to 48.1 ± 26.5 μmol/L, $p < 0.001$).
Conclusions: Low liver function or previous treatment history for EGV were risk factors for developing hyperammonemia during lenvatinib therapy in patients with HCC. Ammonia lowering therapy was effective for hyperammonemia caused by lenvatinib therapy.

Abstract #1844

Progression pattern after lenvatinib therapy in patients with advanced hepatocellular carcinoma

Naoya Kanogawa, Sadahisa Ogasawara, Naoya Kato

Introduction: Lenvatinib is the second front-line agent for advanced hepatocellular carcinoma (HCC) according to the results of the REFLECT trial. However, clinical outcomes and treatment findings regarding progression after lenvatinib therapy have not been standardized. The present study aimed to clarify the clinical outcomes according to the progression patterns of HCC with lenvatinib therapy.
Methods: We retrospectively collected data regarding lenvatinib therapy from patients with advanced HCC at seven Japanese institutions between March 2018 and March 2019. According to previous findings, the progression patterns with lenvatinib therapy were classified as follows: intrahepatic growth, new intrahepatic lesion, extrahepatic growth, and new extrahepatic lesion. Radiological assessments were performed using the modified RECIST.
Results: Among 116 patients, who received lenvatinib as front-line treatment, the median age was 73 years, 78% were male, and 86% were classified as Child-Pugh class A. Macrovascular invasion and extrahepatic metastasis were observed in 28% and 35% of patients, respectively. The objective response rate of the present cohort was 44%, including a complete response rate of 3%. During follow-up, 60 patients (52%) were confirmed to have radiological progression. The

median post-progression survival (PPS) was 5.4 months. The PPS was shorter in patients with new extrahepatic metastasis than in the other patient population (5.4 months vs. 6.4 months, P = 0.189); however, the difference was not significant.
Conclusion: Patients with advanced HCC who had new extrahepatic metastasis at the time of progression after lenvatinib therapy might have a short PPS, similar to the finding with sorafenib.

Abstract #1917

Outcome of Yttrium-90 selective internal radiation therapy (Y90-SIRT) in unresectable hepatocellular carcinoma: a 6-year experience from a tertiary care center

Chaikajornwat J.[1], Tanasoontrarat W.[2], Pinjaroen N.[2], Chaiteerakij R.[3]

[1]Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [2]Vascular and Interventional Radiology Unit, Department of Radiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [3]Division of Gastroenterology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Introduction: Although with reported improved local tumor control in non-Asian population, the efficacy of Y90-SIRT in Thai patients is currently unknown. We aimed to determine survival benefit and identify predictors of response in HCC patients after Y90-SIRT.
Methods: 52 unresectable HCC patients treated with Y90-SIRT at our tertiary center between 2014 and 2019 were retrospectively enrolled. Response was determined using the mRECIST criteria. Overall survival (OS), progression-free survival (PFS), and predictive factors were evaluated by Kaplan–Meier method and Cox-proportional hazard analysis.
Results: 81% were male with a median age of 63.5 years. 83% had Child-Pugh class A, while 14% and 2% had Child-Pugh class B and C, respectively. Underlying etiologies were mainly hepatitis B (44%) and cryptogenic (22%). 71% and 29% had BCLC stage C and B HCC, respectively. 64% had portal vein thrombosis. The median number of Y90-SIRT session was 1 (range 1–3). No pulmonary or visceral toxicity was observed. 35% had treatment response. OS and PFS were 11 months and 2.4 months, respectively. ECOG score, multifocal lesion, Child-Pugh score, AFP $\geq$ 200 IU/mL and infiltrative lesion were significantly associated with poor survival. By multivariate analysis, multifocal lesion, AFP $\geq$ 200 IU/mL, Child-Pugh score and ECOG score remained significantly associated with poor survival, adjusted HR 6.9 (1.7–28.0), 5.5 (2.1–14.8), 4.1 (1.2–14.2), and 3.2 (1.1–9.9), respectively, $p < 0.05$ all.
Conclusion: Thai patients with HCC treated with Y90-SIRT had comparable outcomes to those previously reported. Single lesion, AFP $<$ 200 IU/mL, good liver reserve and good performance status were significant predictors of favorable response.

Abstract #1943

Heterogenenity plays roles in the results of transarterial chemoembolization in patients with intermediate stage hepatocellular carcinoma

Waspodo A.[1], Siregar L.[1], Loho I. M.[1], Swadari R.[1], Hermawan R.[2], Fachri A.[2], Fransisca T.[1], Ferino F.[1]

[1]Department of Gastroenterology and Hepatology, "Dharmais" Cancer Hospital, Indonesian National Cancer Center, Jakarta, Indonesia, [2]Department of Radiology, "Dharmais" Cancer Hospital, Indonesian National Cancer Center, Jakarta, Indonesia

Introduction: Transarterial chemoembolization (TACE) is currently recommended as the standard of care in patients with intermediate stage hepatocellular carcinoma (HCC). However, due to the heterogeneity of the patient population in this stage, TACE may not be suitable for all patients.
Methods: A retrospective study was conducted among 19 patients with intermediate stage HCC who received TACE with doxorubicin and gelfoam® between January 2016 and December 2018 in our institution as the initial treatment. All patients were followed-up for a minimum of one year. Cumulative survival rates were calculated using the Kaplan–Meier method. Contributing factors to survival could not be analyzed due to inadequate sample size.
Results: There were 12 males and 7 females with a median age of 65 years (range 36–78 years) included in this study. The primary causes of HCC were hepatitis B (11 patients) and non-B non-C (5 patients). Eighteen of our patients had good liver function (Child-Pugh A). According to Bolondi subclassification, there were 7 patients in stage B2 and 12 patients in B4. During the follow-up period, 16 patients died. Overall median survival of the cohort was 4.5 months. Of three patients who survived, two patients were non-B non-C HCC with initial tumor size above 15 cm and normal serum alpha-fetoprotein (AFP) at diagnosis, while one patient was hepatitis B positive with initial tumor size of 9 cm. Each patient who survived had 2, 4, and 6 cycles of TACE, respectively.
Conclusion: Careful selection of patients for TACE is essential to gain survival benefit.

Abstract #1953

ROTEM (rotational thromboelastometry) in hepatobiliary malignancies—is it warranted?

Varadarajan annapoorani[1], Bihari chhagan[1]

[1]Department of Hematology, Institute of Liver and Biliary Sciences, New Delhi

Introduction: Hepatobiliary malignancies can potentially affect coagulation. ROTEM is the recent tool to study coagulation abnormalities.
Objectives: To study the coagulation abnormalities in hepatobiliary malignancies by ROTEM
Methods: A review of our prospectively collected database was performed to identify patients with neoplastic etiology. The study was conducted among patients with primary or secondary neoplasms of the liver presenting between January 2018 to December 2019. The exclusion criteria included patients with alternative diagnosis, neoplasms not affecting liver and those with incomplete data. The various ROTEM parameters were studied to identify the coagulation abnormality.
Results: Out of all Records available during the study period, 15 patients had neoplastic etiology. The mean age was 59.3 yearsand M:F ratio was 14:1. The most common diagnosis was Hepatocellular carcinoma (10cases)followed by secondaries liver (2 cases)and one case each of Lymphoma liver, Hilar cholangiocarcinoma, carcinoma gall bladder. The most common coagulation abnormality was deficiency of Vitamin K dependent clotting factors (7 patients) followed by Disseminated intravascular coagulation (DIC likepicture -stage 2)in 3 patients. The mean CT (Clotting time), CFT (Clot formation time), A 10 (Amplitude at 10 mins), MCF (Maximum clot firmness) were112.5seconds,116 seconds,46 mm,50.7 mm,52 mm in patients with clotting factor deficiency. Remaining patients had either platelet or fibrinogen deficiency

Conclusion: ROTEM is useful in identifying coagulation abnormalities in hepatobiliary malignancies and the most common abnormality was deficiency of Vit K dependent clotting factors

Abstract #1954

Clinical significance of preoperative ^{18}F-FDG-PET/CT in hepatocellular carcinoma patients treated with curative resection

Hyun Beom Kim[1], Suk Bae Kim[1], Jai Hyuen Lee[2], Il Han Song[1]

Departments of [1]Internal Medicine and [2]Nuclear Medicine, Dankook University College of Medicine, Dankook University Hospital, Cheonan, Korea

Introduction: Positron emission tomography/computed tomography with fluorine-^{18}fluorodeoxyglucose (^{18}F-FDG-PET/CT) has proven to be a valuable tool in pre- and post-treatment work-up of several solid tumors. However, there has been a matter of debate whether the potential use of ^{18}F-FDG-PET/CT is informative in hepatocellular carcinoma (HCC).
Objectives: This study aims to investigate clinical significance of preoperative ^{18}F-FDG-PET/CT in HCC patients who have received curative resection.
Methods: A total of 60 HCC patients who underwent ^{18}F-FDG-PET/CT before surgical resection were selected for retrospective review of medical records. The HCCs' metabolic activity displayed on ^{18}F-FDG-PET/CT was incorporated into clinical characteristics and outcomes.
Results: Thirty-six HCCs revealed a hypermetabolic activity on ^{18}F-FDG-PET/CT: 24 (66.7%) moderately differentiated (MD) and 12 (33.3%) poorly differentiated (PD), while twenty-four HCCs showed a isometabolic activity/low FDG uptake on PET/CT: 4 (16.6%) well differentiated, 19 (79.2%) MD, and 1 (4.2%) PD. Standardized uptake value (SUV) of PD HCCs on PET/CT was significantly higher than that of MD HCCs (5.2 ± 2.4 vs. 3.8 ± 1.2, $p = 0.045$). The serum PIVKAII level and tumor size in HCC patients showing a hypermetabolic activity were significantly larger than those in isometabolic HCC patients (log PIVKAII 2.9 ± 1.0 vs. 1.6 ± 0.7, $p < 0.001$; tumor diameter 6.6 ± 4.5 vs. 2.9 ± 2.0 cm, $p < 0.001$). The SUV was positively correlated with tumor size ($r = 0.340$, $p = 0.043$) and serum alpha-fetoprotein level ($r = 0.556$, $p < 0.001$). HCC recurrence and disease-free survival were not correlated with SUV on PET/CT.
Conclusion: Preoperative ^{18}F-FDG-PET/CT seems to be clinicopathologically informative in aspects of tumor size, differentiation, tumor markers, but not tumor recurrence and disease-free survival in HCC patients treated with curative resection.

Abstract #1955

Targeting HBx by CRISPR/Cas9 system effectively reduces the proliferation, invasion, EMT and stemness characteristics of hepatoma cells

Preety Rawal, Dinesh M Tripathi, Vikrant Nain, Savneet Kaur.

Introduction: Previously, we have shown that hepatitis B-X protein (HBx) encoded in hepatitis B virus (HBV) genome induces cancer stemness and epithelial to mesenchymal transition in hepatoma cells.
Objective: Our aim was to design a novel HBx gene specific single guide RNA (sgRNA) with CRISPR/Cas9 system and evaluate its knock-down effects on HBx-induced tumorigenic and functional properties of hepatoma cells in vitro.
Method: In silico, we designed sgRNA against HBx by CRISPOR web based tool with minimal off-target activity. In vitro, HepG2-2.15 (stable hepatoma cell line with a HBV expression) was transfected with HBx-CRISPR or control vector (PX459). Functional properties of hepatoma cells including proliferation, migration, invasion, and EMT were studied in all study groups. Flow cytometry and 3D-spheroid culture assays were performed to study stemness properties.
Results: HBx knockdown cells showed significant decrease in tumorigenic properties including proliferation, chemotaxis and invasion in HBx-CRISPR cells as compared to control cells ($p < 0.05$). Flow cytometry data showed the epithelial marker (E- cadherin) was increased while the mesenchymal marker (vimentin) and stemness marker (CD133) were decreased in HBx-CRISPR transfected cells as compared to that observed in the control cells. 3D spheroid cultures established that HBx-CRISPR cells formed lesser ($p < 0.01$) and smaller-sized ($p < 0.001$) spheroids in culture as compared to control cells.
Conclusion: The study shows that targeting HBx by CRISPR/Cas9 system effectively reduces the proliferation, invasion, stemness and mesenchymal characteristics of hepatoma cells.

Abstract #1985

Alpha-fetoprotein level correlated with staging of BCLC hepatocellular carcinoma

I. Nyoman Yogi Wiraguna[1], Muhammad Luthfi Parewangi[1], Fardah Akil[1], Nu'man AS Daud[1], Rini Rachmawarni Bachtiar[1], Susanto H. Kusuma[1], Amelia Rifai[1]

[1]Centre of Gastroenterology-Hepatology HAM Akil/DR. Wahidin Sudirohusodo General Hospital, Division of Gastroenterology-Hepatology, Department of Internal Medicine, University of Hasanuddin, Makassar-Indonesia

Introduction: Hepatocellular Carcinoma (HCC) is a major health concern worldwide and the third most common cause of cancer related-death in Asia-Pacific region. The Barcelona Clinic Liver Cancer (BCLC) staging classification is commonly used for HCC, and assumes the coexistence with cirrhosis. Alpha-Fetoprotein (AFP) levels is known as independent prognostic value in HCC patients.
Objectives: To analyze the correlation between AFP level with staging of HCC cirrhotic or non-cirrhotic.
Methods: A total of 592 HCC patients were enrolled between June 2014-December 2019. Demography, liver biochemistry, and radiology data were collected. Staging of HCC was based on BCLC classification (A/B/C/D) and AFP levels were divided into 4 category: < 20, 20–200, 201–400, > 400 ng/ml. Data analysis using *Chi Square* and one-way Anova ($p < 0.05$ significant).
Results: We found 476 (80.4%) male and 116 (19.6%) female, with mean age 53.8 ± 12.4 years. Common etiology was HBV 434 (73.3%), followed by unknown etiology 136 (22.9%), HCV 14 (2.4%), HCV/HBV 4 (0.7%) and NAFLD 4 (0.7%). Based on BCLC staging B/C/D 320 (54.1%)/240 (40.5%)/32 (5.4%). Cirrhosis with HCC was found in 137 (23.1%) and without cirrhosis 455 (76.9%); Child-Pugh A/B/C 128 (21.6%)/378 (63.9%)/86 (14.5%), respectively. There is a significance correlation of AFP with BCLC staging ($p = 0.004$), it was observed that AFP level were higher > 400 ng/ml in advance stage BCLC as compared with the initial stage. HCC BCLC staging were significantly correlated with AFP levels in non-cirrhotic compare cirrhotic patients ($p = 0.026$).
Conclusion: Serum AFP has significant correlation with HCC BCLC staging especially on non-cirrhotic HCC. AFP level may serve as a useful marker for detection of HCC and to differentiate between early and advance stage.

Abstract #1986

Hepatic arterial infusion chemotherapy with reservoir for advanced hepatocellular carcinoma, results of under indication limit

Shinpei Sato[1], Toshihiro Kawai[1], Yuji Kondo[1], Yoshihiro Isomura[1], Miho Kanda[1], Takahisa Sato[2], Shuntaro Obi[2]

[1]Kyoundo Hospital, Gastroenterology, [2]Teikyo Chiba Medical Center, Gastroenterology

Background: From 2000 to 2014, 1026 patients with unresectable advanced hepatocellular carcinoma (HCC) who underwent hepatic arterial infusion chemotherapy with reservoir were performed. Good prognosis is expected in Child A, B and no case of intractable ascites. Since 2016, we established a standard for indication of HAIC was not enforced for Child C and refractory ascites, but only one shot infusion chemotherapy.
Aim: We retrospectively examined the therapeutic effect of HAIC (Low dose FP) satisfying the adaptation criteria.
Method: Between 2011 and 2016, HAIC was performed in 211 cases. Treatment effect was evaluated for each course, and 2–4 courses of treatment until for PD were continued. Median survival time (MST) stratified liver function, response rate, survival rate by response (Kaplan–Meier method) were compared. And we compared with the results before the limit of adaptation.
Result: HAIC performed for 211 cases (169 males), average age 66.3 years (30–82), median observation period 11.2 months, Patient background HBV/HCV/nonBnonC is 45/100/68 cases, Child A/B is 125/86 cases, portal vein tumor invasion (VP 0/1/2/3/4) is 47/5/39/64/56 cases, extrahepatic metastases in 37 cases. before adaptation restriction. MST was 9.1 months (6.9 months), MST in CR was 28.7 months, PR 12.1 months, SD 8.6 months, PD 5.6 months. The response rate was 29.3% (29% before the restriction of adaptation), 31 cases (15%) in CR, 31 cases in PR (15%), 46 cases in SD (22%), 103 cases in PD (49%).
Conclusion: Response rate did not change by restricting therapeutic indications, but MST was prolonged for 2 months and better results were obtained than before.

Abstract #2001

Hepatocellular carcinoma: a 20 years experience at a tertiary cancer care centre in India

Rupal Tripathi[1], Swarnima Jaitley[1], K S Rana[1], Dinesh Chandra Doval[1]

[1]Rajiv Gandhi Cancer Institute and Research Centre, Delhi, India

Introduction: Hepatocellular carcinoma (HCC) accounts for the majority of the liver cancers worldwide. This major health burden with a very poor prognosis is largely a problem of the less developed regions of the world. The present study assessed the epidemiology of HCC over a period of 20 years at a tertiary cancer care centre in India.
Methodology: All patients who enrolled in the Institute during the period 1996–2015 with a confirmed diagnosis of HCC were included in the study. Details of each patient related to their demographic profile, tumor characteristics and treatment information were recorded.
Results: A total of 139634 registered patients in the Institute were diagnosed with malignancy. Among these patients, a total of 2166 cases were diagnosed with HCC, of which 1607 (74.2%) patients were males. It was most commonly observed in the age group of 55–64 years (723 cases). Histopathology and cytology was the mode of diagnosis in 1090 and 387 patients, respectively. A total of 1470 patients did not take any kind of treatment in the hospital. Surgery, radiotherapy and chemotherapy alone were given in 66, 52 and 223 patients, respectively. Hospital deaths occurred in 2.49% patients.
Conclusion: HCC is a disease with multiple etiologies and with time, the incidence and mortality of these patients is also on the rise. Larger prospective studies are required to study the incidence patterns and regional differences in the different geographical regions of the world including the variations at the molecular level

Abstract #2063

Clinical manifestation and prognosis of combined hepatocellular-cholangiocarcinoma

Primasari Deaningtyas[1], Andri Sanityoso S[2], Chyntia O Jasirwan[2]

[1]Internal Medicine Resident Faculty of Medicine University of Indonesia, [2]Staff of Hepatology Division Faculty of Medicine University of Indonesia

Introduction: Combined hepatocellular-cholangiocarcinoma (CHC) is a rare hepatobiliary neoplasia with incidence ranging from 1.0 to 4.7%. This tumor has poor prognosis and hardly to diagnose preoperatively.[1]This is a presentation CHC, related prognosis factor and disease progression monitoring.
Case ilustration: A 42 years old male came with abdominal discomfort in right hipocondrium quadrant since 3 months prior to hospital visit. There was insignificant weight loss. His USG showed hepatic mass. There was absence history of hematemesis melena, diabetes, and jaundice. He is overweight with normal sclera, and mild abdominal pain. He diagnosed with hepatitis B infection and mild elevation of alpha fetoprotein (69.67 mg/dL. His abdominal CT scan revealed a hypodense lesion $3.3 \times 3.8 \times 4$ cm with mesenterium lymphadenopathy and abdominal anterior wall defect. He passed hepatectomy and right hemicolectomy. His biopsy showed combined hepatocellular-cholangiocarcinoma, ileocolitis and no lymphadenopathy infiltration. Tenofovir was administer to the patient. Two months after surgery, there is new lesion in liver segmen 5 and 7 with diameter 1.6 cm and 2.8 cm.
Discussion: The 1-, 3-, and 5-year survival rates of CHC after liver resection were 73.9, 41.4, and 36.4%. Tumor, node, metastasis system stage (hazard ratio 1.27, $p = 0.003$) and radical liver resection (hazard ratio 0.31, $p = 0.004$) were independent prognostic factors.[2,3,4] In line with previous researchs, this patient shows progressive disease in spite of no involvement of lymphadenopathy and small size tumor.
Conclusion: Although rare occurrence, CHC still can be managed if discovered in early stage. Its progressive character and poor prognosis demand close monitoring to improve its survival.

Abstract #2065

A 62-year-old man with hepatocellular carcinoma and type 2 diabetes mellitus and profile transarterial embolization ablation (TEA) therapy in DR. Moewardi Hospital Surakarta: a case report

Adi P. R.[1], Didik P.[2], Aritantri D.[3], Paulus K.[4], Triyanta Y.P.[5]

[1]Resident of Internal Medicine FK UNS/dr. Moewardi Hospital Surakarta, [2]Division of Gastroenterology and Hepatology of Internal Medicine Department, FK UNS/dr. Moewardi Hospital Surakarta

Background: Transarterial Embolization Ablation (TEA) is an interventional therapy for patients with Hepatocellular Carcinoma (HCC). The eligible HCC patients in dr. Moewardi Hospital who received TEA therapy on the period of December 2017–December 2019 were 13 patients (11 patients had received cTACE and the rest received TAELE). Based on the profile, 9 patients was male and the rest was female, the average age of 60.2 years old. The risk factors were 10 patients had hepatitis B, 2 patients had diabetes mellitus and a patients had hepatitis C. The average levels of SGOT and AFP were 157.7 U/L and 231.07 IU/ml.
Case description: A 62-year-old male patient diagnosed with HCC BCLC B with a history of diabetes more than 20 years. The laboratory data showed SGPT 19 u/l and AFP 275 IU/ml, non-reactive viral marker, the ultrasound showed a mass in the right liver lobe and the abdominal CT scan showed a solid nodule in the right lobe with a size of 15.3 × 12.1 × 15.5 cm which appeared wash in the arterial phase and wash out in the venous phase. He received 4 times of TAELE with an average distance of 6 weeks of each treatment.
Discussion: The evaluation after TAELE, there are improvement in laboratory and CT scan showing shrinked mass and partial response from the mass.
Conclusion: TAELE has gained attention as intervention for unresectable HCC. In this case TAELE intervention shows a positive result for our patient.

Abstract #2087

The effect of metformin on survival of diabetic liver cancer patients

Irsan Hasan[1], Fitria[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Liver cancer is one of the leading malignancies worldwide. Diabetes mellitus is a common chronic disease encountered in liver cancer. Anti-cancer effects of metformin through activation of adenosine monophosphate activated protein kinase (AMPK) containing tumor suppressor gene liver kinase B1 (LKB1) has been studied. However, clinical studies regarding effects of metformin adjuvant treatment on survival of diabetic liver cancer patients are conflicting.
Objectives: This study compares the survival of diabetic hepatocellular carcinoma (HCC) patients receiving metformin compared to no metformin.
Methods: Online search of PubMed and EBSCOhost led to four relevant articles. Only cohort studies involving patients with confirmed HCC and diabetes comparing patients treated with metformin and no metformin were included. Animal and in vitro studies were excluded. Critical appraisal was performed with the Oxford Center for Evidence Based Medicine criteria.
Results: Schulte el al and Seo et al reported that metformin significantly increases median overall survival (mOS; in months) of patients receiving metformin compared to no metformin, 22 vs 15 ($p = 0.018$) and 92.4 vs 51.6 ($p < 0.01$) respectively. Casadei et al reported that metformin significantly decreases mOS of patients receiving metformin compared to no metformin, 9.3 vs 20.5 ($p = 0.0001$). Bhat et al reported no significant difference of mOS in patients receiving metformin and no metformin, 22.8 vs 32.4 ($p = 0.77$).
Conclusion: The effect of metformin on OS of diabetic HCC patients remains controversial. Further studies should be done.

Abstract #2091

A rare case of Hepatoid Adenocarcinoma of the stomach in a 23 year old male

Maria Joscel D. Torres

Introduction: Hepatoid Adenocarcinoma of the stomach (HAS) is a rare aggressive tumor with hepatoid differentiation. HAS often produces alpha fetoprotein (AFP) and metastasizes to the lymph nodes and the liver. The term "Hepatoid Adenocarcinoma of the Stomach" signifies a primary gastric carcinomas that are characterized by both hepatoid differentiation and the production of large amounts of AFP. The stomach is one of the most common sites in which hepatoid adenocarcinomas have been detected. The hepatoid type of gastric adenocarcinomas seems to be the most aggressive, with the highest tendency toward liver metastases. Hepatoid Adenocarcinoma of the Stomach has a poor prognosis, even if diagnosed early. Our patient was diagnosed with Hepatoid Adenocarcinoma of the stomach, a rare clinical disease.
Clinical Presentation: A case of 23 year-old male with unremarkable past medical history presented with abdominal pain localized in the right upper quadrant, anemia and easy fatigability. Patient was initially diagnosed with Hepatocellular Carcinoma based on the CT scan findings of Hepatic mass and an elevated AFP. An upper GI endoscopy revealed fungating, ulcerated mass at the proximal fundus which is soft and friable on biopsy. A final diagnosis of Hepatoid Adenocarcinoma of the Stomach was made based on the histologic features and a positive CKAE1/CKAE3.
Outcome: Patient underwent Chemotherapy with Oxaliplatin, Folinic Acid and 5FU with partial response on the first cycle. However, patient continued to deteriorate and eventually expired after 29 days of Hospital stay.
Recommendation: The need for further research on the efficacy of chemotherapy in Hepatoid Adenocarcinoma of the Stomach is important to increase the survival rate of patients diagnosed with the disease.

Abstract #2107

Survival outcomes for patients with hepatocellular carcinoma after stereotactic body radiotherapy in Dr.Cipto Mangunkusumo Hospital, Jakarta

Eka Indah Pratiwi[1], Angela Giselvania[1], Soehartati Gondhowiardjo[1]

[1]Department of Radiation Oncology, National General Hospital of Dr. Cipto Mangunkusumo Universitas Indonesia, Jakarta

Introduction: Hepatocellular carcinoma (HCC) is the fourth leading cause of cancer mortality worldwide. The application of the latest technologies in radiotherapy, such as stereotactic body radiotherapy (SBRT) for HCC has been increased.
Objectives: This study aims to evaluate the survival outcomes of patients with HCC after SBRT.
Methods: This retrospective study evaluated patients with HCC who underwent SBRT in Radiation Oncology Department of Dr.Cipto Mangunkusumo Hospital between January 2016 and March 2019. All patients had Barcelona Clinic Liver Cancer (BCLC) stage B-C and Child Turcotte Pugh (CTP) Class A5-B8. Overall survival (OS), progression free survival (PFS), and prognostic factors were evaluated.
Result: A total of 39 patients were included with a median follow-up of 41 weeks (95% CI 4–172 weeks). The median age was 61 years, 79.5% were males, and their CTP were Class A5 (66.7%), A6

(15.4%), B7 (7.7%), and B8 (10.2%) before SBRT. The dose ranged from 28 to 50 Gy in 4–10 fractions, and the mean tumor diameter is 11,057 cm (± 4046). The 1-,2-,3-year overall survival (OS) and progression-free survival (PFS) were 56%, 43.1%, 28.7%, and 26.3%, 22.1%, 0%, respectively. The overall response rate was 44.4% (complete response 3.7% and partial response 40.7%) within 3 months after SBRT. However, the multivariate analysis revealed that CTP class, the presence of main portal vein tumor thrombosis, and therapy before radiation, were an independent factor for OS.
Conclusions: SBRT may be useful for patients with HCC that is inoperable or unsuitable for other locoregional therapies, with good survival outcomes

Abstract #2121

Profile of protein induced by vitamin K Absence-II (PIVKA-II) levels in patients with hepatocellular carcinoma

Siregar L.[1], Loho I. M.[1], Waspodo A. S.[1], Swadari R[1], Harijanto S.[2], Widiasih T. K.[2], Nandika G. I.[2], Fransisca T.[1], Ferino F.[1]

[1]Department of Gastroenterology and Hepatology, "Dharmais" Cancer Hospital, Indonesian National Cancer Center, Jakarta, Indonesia, [2]Department of Clinical Pathology and Laboratory Medicine, "Dharmais" Cancer Hospital, Indonesian National Cancer Center, Jakarta, Indonesia

Background: Serum level of prothrombin induced by vitamin K absence-II (PIVKA-II) has been used to diagnose hepatocellular carcinoma (HCC) as well as to monitor treatment response and predict prognosis. This study aims to assess the profile of PIVKA-II levels in patients with various stages of HCC before treatment and their survival.
Methods: A retrospective study was conducted among patients with HCC between October 2017 and November 2018. Patients with available serum level of PIVKA-II and a minimum follow-up period of one year were included.
Results: Serum level of PIVKA-II at diagnosis was available for 13 patients. All patients were male with a median age of 58 years (range 30–88 years). There were 9, 3, and 1 patients who were classified as Child Pugh A, B, and C, respectively. Liver cirrhosis was present in 9 patients, while portal vein thrombus was found in 3 patients. The main etiology of HCC was hepatitis B virus, which was found in 9 patients. According to BCLC classification, there were 7, 3, and 3 patients with intermediate, advanced, and terminal stage, respectively. Median overall survival of the cohort was 73 days. In one-year period of follow-up, death occurred in 10 of 13 patients. Median level of PIVKA-II was 15446 AU/L (range 36.41–101753 AU/L). Of 3 patients who survived, only 1 patient was found to have PIVKA-II level below 40 AU/L at diagnosis.
Conclusion: The prognostic role of serum PIVKA-II level in patients with HCC should be studied further with larger sample size.

Abstract #2151

Benefits of oral L-Carnitine on liver functions after transarterial chemoembolization (TACE) in intermediate stage hepatocellular carcinoma (HCC) patients

Malak Mohamed, MD[1], El-Sayed Ramy, MD[2]

[1]Department of Internal Medicine, Sohag Faculty of Medicine, Sohag, Egypt, [2]Department of Tropical Medicine and Gastroenterology, Sohag Faculty of Medicine, Sohag, Egypt

Background: Transarterial chemoembolization (TACE) is the standard treatment for intermediate stage hepatocellular carcinoma (HCC) and usually followed by hepatic dysfunction. L-carnitine is recently studied as hepatoprotective agent.
Objective: We evaluated L-carnitine effects against the deterioration in liver functions after TACE.
Methods: 53 sequential patients with intermediate stage HCC were enrolled. All patients were treated by TACE and assigned into two groups; L-carnitine group (26 patients) who received L-carnitine 300 mg tablet twice daily from 2 weeks before to 12 weeks after TACE and Control group (27 patients) without L-carnitine therapy. Liver functions were evaluated for all patients at 2 weeks before, 1, 4, 12 weeks after TACE.
Results: L-carnitine suppressed deterioration in serum albumin at 1 week after TACE. There were significant differences between L-carnitine group and control group in mean serum albumin change from baseline to 1 week and 4 weeks after TACE ($p < 0.05$). L-Carnitine maintained Child-Pugh score at 1 week after TACE and exhibited significant improvement at 4 weeks after TACE ($p < 0.01$ compared to 1 week after TACE). Interestingly, L-carnitine displayed improvement in prothrombin time (PT) from baseline to 1 week, 4 weeks ($p < 0.05$) and 12 weeks after TACE. There were significant differences between L-carnitine and control groups in PT mean change from baseline to 1 week ($p < 0.05$) and 4 weeks after TACE ($p < 0.05$).
Conclusion: L-carnitine therapy maintained and improved liver functions after TACE and may be offered as a new liver support tool in HCC patients.

Abstract #2191

The effect of stem cell hepatocyte on VEGF and cytology patient of hepatocellular carcinoma (HepG2)

Asih Sasamijati Lestari Suprapto Putri[1], Paulus Kusnanto[1]

[1]Internist, Gastroenterologist-Hepatologist, Moewardi General Hospital/Faculty of Medicine UNS, Surakarta, Central Java, Indonesia

Introduction: Hepatocellular Carcinoma is the most common liver malignancy, with survival rates ranging from 6 to 20 months. Of all the malignant liver tumors that has been diagnosed, 85% are HCC, 10% CC and 5% are other types. Hepatocellular Carcinoma (HCC) ranks second as the most common cause of death from cancer worldwide and is the fifth most common cancer in the world in men. In Indonesia, HCC ranks fourth as the most common cancer in men after lung, colorectal and prostate cancer, with an age-standardized rate of 13.4 per 100,000 population. Stem cells, especially stem cell hepatocyte, are cell products that work as anti-fibrosis, anti-inflammatory (immunomodulation), apoptotic activation, proliferation and anti angiogenesis.
Objective: The aim at this study is to prove whether there is an influence of stem cell hepatocyte in the impairment of VGEF as a marker in the process of angiogenesis and cytology of patients with hepatocellular carcinoma (HepG2).
Methods: This research is an experimental study with the object of HepG2 cell line culture research which is divided into 6 groups, namely the control group, and several treatment groups, then analyzed for VEGF and cytology. With each treatment group differentiated between dosing of stem cells. We do the post-test only with control design method. Each group will then be analyzed statistically using the Shapiro-Wilk parametric test of normality tests and in the VEGF group an abnormal data is obtained so for statistical testing using Kruskal-Wallis which is then continued with the Mann Whitney test.

Likewise in the cytology group of a significance limit: the P value was significant if $p < 0.05$.
Results: The results showed that the administration of stem cells with different doses—in patients with hepatocellular carcinoma had a significant effect on cell cytology, but for VEGF gave a decrease but not significant. In the control group it was found in grade IV, whereas in the treatment groups it was found to be decrease in grading from the sample after stem cell administration by 15 thousand. The effective dose in this study to reduce grading from HCC was found in the administration of 20 thousand stem cells, and in the 25 thousand dose group the results were not as good as in the administration of 20 thousand stem cell doses. In the VEGF treatment group, the results were not different from the control group and the treatment groups and the results from the VEGF smear were +3.
Conclusion: From the results of the study it can be concluded that there is an effect of stem cell hepatocyte administration on changes in cytology of patients with hepatocellular carcinoma, but in VEGF administration of stem cell hepatocyte does not have a significant effect.

Abstract #2222

Combination of alpha-fetoprotein and neutrophil lymphocyte ratio for screening hepatocellular carcinoma

Gita Aprilicia[1], Steven Zulkifly[2], Sheila Rizky Melati[2], Rino Alvani Gani[2]

[1]Department of Epidemiology, Faculty of Public Health Universitas Indonesia, Depok, Indonesia, [2]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia/Dr. Cipto Mangunkusumo National General Hospital, Jakarta 10430, Indonesia

Introduction: Serum alpha-fetoprotein (AFP) is commonly used for hepatocellular carcinoma (HCC) surveillance. However, serum AFP has a low sensitivity (about 41–65%) for predict HCC. Systematic inflammation may be associated with development of HCC. The neutrophil-to-lymphocyte ratio (NLR) is simple marker that reflects of systemic inflammatory respons.
Objective: To investigate the combination of AFP and NLR for screening HCC.
Method: This study used National HCC Registry from tertiary hospital in Jakarta between August 2015 until December 2019. Patients with new diagnosed of HCC and liver cirrhosis (LC) as control group were enrolled in this study. Serum AFP, neutrophil, and lymphocyte were obtained from complete blood count examination. The diagnostic value of AFP and NLR were analysed by using receiver operation characteristic (ROC) curve.
Results: A total of 459 patients were included in this study, including 289 HCC and 170 control patients. This population match in sex, while age of LC was lower than HCC (51 ± 11.01 vs. 55 ± 12.46). Median serum AFP was higher in HCC (209 ng/ml) group compared with LC (4.29 ng/ml). The AUC value for NLR were 0.71 (95% CI 0.67–0.76) and AFP were 0.82 (95% CI 0.77–0.85) with the best cut-off values of 3 and 10 ng/ml, respectively. The highest AUC value was combination of AFP-NLR 0.85 (95% CI 0.81–0.88). The sensitivity and specificity of AFP-NLR were 78.2% and 76.5%, while sensitivity and specificity of AFP were 73.7% and 74.1%.
Conclusion: The AUC value AFP-NLR was more superior than AFP alone for screening HCC.

Abstract #2223

Comparison of alpha-fetoprotein in viral and non viral etiology of hepatocellular carcinoma

Gita Aprilicia[1], Krisnawati Bantas[1], Rino Alvani Gani[2]

[1]Department of Epidemiology, Faculty of Public Health Universitas Indonesia, Depok, Indonesia, [2]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia/Dr. Cipto Mangunkusumo National General Hospital, Jakarta 10430, Indonesia.

Introduction: Pattern of etiology hepatocellular carcinoma (HCC) has been changed. Non-viral HCC etiology tend to be increasing. Serum alpha-fetoprotein (AFP) is marker that commonly used for screening HCC. However in non-viral HCC, serum AFP tend to be normal.
Objective: To observed variation of AFP level with difference etiology for screening HCC.
Method: Data from HCC Registry in tertiary hospital between August 2015 until December 2019 were obtained. Patients with liver cirrhosis (LC) were enrolled as control group. Etiology of liver disease was determined by viral serology examination. Non viral etiolgy was defined by negative serum Anti-HCV and negative HBsAg surface antigen. Serum AFP level and performance of AFP in difference etiology was evaluated by Mann Whitney Test and receiver operation characteristic (ROC) curve.
Results: A total of 289 HCC patients and 170 LC patients were included in this study. Non-viral etiology was found in 21.8% LC group and 22.1% HCC group. Both of LC and HCC group, median serum AFP was lower in non-viral etiology compared with viral etiology, 2.9 vs. 4.9 ng/ml, 34 vs. 370 ng/ml, respectively. The AUC value of AFP in non-viral etiology more lower than viral etiology, with non viral 0.76 (95% CI 0.67–0.86) vs. viral 0.84 (95% CI 0.80–0.88). The best cut off in viral etiology was 20 ng/ml, with sensitivity 74.7% and specificity 78.9%. While in non-viral etiology, cut of 20 ng/ml has lower sensitivity 53.1% and higher specificity 94.6%.
Conclusion: Serum AFP was poor indicator for screening non-viral HCC.

Abstract #2237

Tumor lysis syndrome in hepatocellular carcinoma: a rare but major complication of transarterial chemoembolization (TACE)

Navarro, Marc Julius H.[1] Tan, Charles Cua[1], Ian Homer Y.[1]

[1]Department of Medicine; Institute of Digestive and Liver Diseases; St. Luke's Medical Center, Quezon City, Philippines

Significance: Transcatheter arterial chemoembolization (TACE) is the standard of care for intermediate stage hepatocellular carcinoma (HCC). It is recommended for asymptomatic, large (greater than 3 cm) or multifocal hepatocellular carcinoma without vascular or extra-hepatic metastasis. Tumor lysis syndrome (TLS), particularly in solid tumors is a rare occurrence. It results from the destruction of malignant cells and the abrupt release of intracellular ions, nucleic acids, proteins and their metabolites into the extracellular space.
Clinical presentation and management: A 66 year old male with Hepatocellular Carcinoma secondary to Hepatitis C Infection with large liver mass, measuring $13.0 \times 12.0 \times 12.8$ cm, came in for TACE. Initial physical examination and diagnostics was unremarkable. Transcutaneous arterial catheterization showed a large tumor

staining hypervascular mass with neovascularization almost occupying the entire right hepatic lobe, chemoembolization with 30 mg cisplatin, 30 mg doxorubicin and 30 mg mitomycin C with 10 cc lipiodol was facilitated. 24 hours post-TACE, he developed loss of urine output, acidotic breathing and deranged electrolytes where he was diagnosed with TLS. Vigorous hydration was continued and sodium bicarbonate IV was given. Primed for renal replacement therapy but was not continued due to hypotension despite inotropic support. The patient's condition gradually declined and arrested.
Recommendations: In patients with HCC more than 5 cm in size who will undergo TACE; patients should be closely monitored for decrease in urine output and serum potassium, calcium, phosphorous, urea nitrogen, creatinine and uric acid evaluated up 72 hours post-treatment. Prompt management with vigorous hydration and allopurinol should be started once with suspicion of TLS.

Other Hepatobiliary Neoplasia

Oral Presentations

Abstract #555

A rare case of hepatic epithelioid hemangioendothelioma: case report

J. K. Tan[1], Adnan S. A.[1], H. L. Tan[2], Salmi A.[3], Omar H.[1]

[1]Hepatology Unit, Department of Medicine, Selayang Hospital, Kuala Lumpur, Malaysia, [2]Department of Radiology, Selayang Hospital, Kuala Lumpur, Malaysia, [3]Histopathology Unit, Department of Pathology, Selayang Hospital, Kuala Lumpur, Malaysia

Introduction: Hepatic epithelioid hemangioendothelioma (HEHE) is a rare vascular tumor of unknown etiology. Its incidence peaks in the fourth decade and clinical symptoms include upper abdominal pain or discomfort, weight loss, jaundice and/or fever but up to 25% may present asymptomatically with only incidental findings on radio-imaging. We examine a patient with painless jaundice and constitutional symptoms whom was diagnosed eventually with primary HEHE, to our knowledge, the first such case in our country.
Case report: 47-year-old gentleman with background hypertension and impaired fasting glucose presented with fever, lethargy and passing tea coloured urine for two weeks. Laboratory tests showed marked hyperbilirubinemia and transaminitis. Viral screening and leptospira serology were non reactive and alpha fetoprotein was not raised. Peritoneal tapping done yield a transudative fluid with no malignant cells. Workup for tuberculosis was negative. Liver biopsy of the left lobe performed revealed fibrosis but no obvious malignant cells. Oesophagogastroduodenoscopy showed pangastritis with duodenitis and colonoscopy showed prominent swollen ileo-caecal valve with small polyps (benign) and diverticulum at caecum. His condition deteriorated further and a decision to repeat the liver biopsy was made as the sample was taken from a site with minimal lesion. A repeat liver biopsy was done at the right lobe lesion with findings consistent with epithelioid hemangioendothelioma.
Conclusion: HEHE should be kept in mind when faced with a middle-aged patient with a suspected malignancy. Investigations and radio imaging are important in identifying the pathology and if suggestive, a biopsy for histopathological examination.

Abstract #1441

Genetic profiling using resected samples of juvenile-onset human cholangiocarcinoma: SKI gene regulates expressions of ERK1/2 and p21 resulting in cell cycle inhibition

Etsushi Kawamura[1], Tsutomu Matsubara[2*], Moe Higuchi[2], Atsuko Daikoku[1], Sayuri Takada[1, 2], Sanae Deguchi[1], Naoshi Odagiri[1], Tokuji Ito[3], Masahiko Kinoshita[4], Hideto Yuasa[2], Hayato Urushima[2], Misako Sato-Matsubara[1], Shogo Tanaka[3], Shigekazu Takemura[3], Keiko Iwaisako[5], Masaru Enomoto[1], Yoshiki Murakami[6], YH Taguchi[7], Akihiro Tamori[1], Shoji Kubo[3], Kazuo Ikeda[2] and Norifumi Kawada[1]

Departments of [1]Hepatology, [2]Anatomy and Regenerative Biology and [3]Hepato-Biliary-Pancreatic Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan, [4]Hepatobiliary and Pancreatic Surgery, Osaka City general Hospital, Osaka, Japan, [5]Department of Medical Life Systems, Doshisha University Graduate School of Life and Medical Sciences, Kyoto, Japan, [6]Department of advanced nucleic acid therapy, Tokyo Medical University, Tokyo, Japan, [7]Department of Physics, Chuo University, Tokyo, Japan.

Introduction: Oligonucleotide therapeutics are promoted as next generation chemotherapy. We focused on high risk cholangiocarcinoma (CCA) oncogenes obtained from juvenile-onset samples including printing workers exposed to 1, 2-dichloropropane (carcinogenic group 1 of International Agency for Research on Cancer).
Methods: To reveal microRNA (miR) profile in control of gene expression in CCA, microarray was performed with non-HBV/HCV 24 hepatobiliary resected human tumor samples [10 CCAs (under 60-year-old, including 4 printing workers)/14 controls (hepatocellular carcinoma 10 /benign 4)].
Results: Based on the array results and target database for miRs, we have extracted 5 miRs and their 5 target onco-transcripts of digestive cancer with the exception of CCA according to references; miR-3648 targeting SKI, miR-5787 targeting HNF4A, miR-4286 targeting RALA, miR-7977 targeting CD44 and miR-4508 targeting DNM1L. Of these five, SKI mRNA and miR-3648 showed highest target effectiveness on the database. Our results suggested that SKI overexpression inhibited the proliferation of human CCA cell line OZ, phosphorylation of extracellular signal-regulated kinase (ERK) 1/2 proteins expression, and promoted cyclin-dependent kinase inhibitor $p21^{Waf/Cip1}$ proteins expression. Conversely, SKI knockdown promoted OZ proliferation. MiR-3648 overexpression down-regulated SKI protein expression in the OZ, while miR-3648 knockdown up-regulated it.
Conclusion: This study demonstrated that SKI inhibited proliferation of human CCA, indicating the possibility that axes of SKI-ERK and SKI-p21 become attractive targets for therapy in the way of oligonucleotides including miR-3648.

Abstract #155

Diagnostic problem in isolated splenic tuberculosis with histology mimicking inflammatory pseudotumor in a spleen tumor patient

Viryani N. M.[1], Widodo B.[2], Kholili U.[2], Maimunah U.[2], Purbayu H.[2], Sugihartono T.[2], Setiawan P. B.[2], Nusi I. A.[2], Rahniayu A.[3]

[1]Resident of Internal Medicine Department, Universitas Airlangga, Dr.Soetomo General Academic, Surabaya, Indonesia, [2]Division of Gastroenterology and Hepatology, Internal Medicine Department, Universitas Airlangga, Dr.Soetomo General Academic, Surabaya,

Indonesia, [3]Department of Anatomical Pathology, Universitas Airlangga, Dr.Soetomo General Academic, Surabaya, Indonesia.

Introduction: Isolated Splenic Tuberculosis is rare, even more in an immunocompetent individual. It is likely to be misdiagnosed as lymphoma due to vague non-specific symptoms and imaging findings.
Case illustration: A 41-yo man presented with recurrent pain in the right upper quadrant abdominal, fever and nausea. There is no cough, weight loss and visible mass. His medical history did not include tuberculosis and HIV infection. Splenomegaly is found in physical examination. Computed Tomography of abdomen showed solid mass size 5.4 × 6.7 × 6.2 cm with necrotic area in spleen similar to lymphoma. Laboratory revealed LDH 389 U/l and β2 M 1.96 mg/L. The patient undergoes splenectomy and the specimen was read as a group of histiocyte cell form a granuloma with areas of necrosis and no sign of lymphoma. After surgery the patient still complain mild fever, so we sent the histology slide to review in another center. The reading revealed as Inflammatory pseudotumor-like follicular/fibroblastic dendritic cell sarcoma. However, as EBER (−), CD163 (+), CD34 (−) and acid-fast bacilli (−), this result leads toward reactive lesion. So, we test for IGRA and the result was positive. The patient now treated with Anti-Tuberculosis drugs first categories for nine months.
Discussion: TB and lymphoma can be present with night sweat, hepatosplenomegaly and elevated LDH. Nodule in the spleen should be differentiated into malignancy or infection. Histopathological examination is expected to be the final determinant for diagnosis. In this case, immunohistochemistry showed inconclusive result, therefore we test for IGRA and the result was positive. The patient then diagnosed as Isolated Splenic Tuberculosis.

Abstract #263

Percutaneous trans-hepatic biliary drainage: A descriptive cross sectional study from a tertiary care hospital in Pakistan

Parkash Om[1], Ali Mahrukh[1], Sulaiman Anjiya[1]

[1]Department of Medicine, Aga Khan University Hospital Karachi, Pakistan

Introduction: Percutaneous trans-hepatic biliary drainage (PTBD) is an image-guided procedure which involves insertion of a small plastic tube through skin into the biliary system and drainage of obstructed system. This is reserved as a second line therapy after endoscopic drainage fails.
Objective: The aim of this study is to determine the major indications, outcomes and complications of PTBD.
Methods: A retrospective review of patients who underwent PTBD from January 2015 to December 2018 was performed. Patient data was extracted from the hospital's electronic database and case records.
Results: Data from 210 patients showed 100 (47.6%) had no comorbids, 43 (20.5%), more than one. Diabetes (26, 12.4%), hypertension (22, 10.5%). Cholangio-carcinoma was in 57 (27.1%), pancreatic carcinoma 53 (25.2%), metastatic carcinoma 29 (13.8%), CBD stones 28 (13.3%), CBD leak 14 (6.7%), stricture 18 (8.6%). Major indications included hemodynamic instability 75 (35.7%), failed ERCP 73 (34.8%), and high obstruction 59 (28.1%). No post procedure complications were seen in 151 (71.9%) patients. Infection was the most common seen in 18 (8.6%) patients, catheter/stent occlusion or displacement 14 (6.7%), bleeding 6 (2.9%), and prolonged hospital stay (> 5 days) 21 (10%). 179 (85.2%) patients showed clinical improvement, 21 (10%) died in the hospital, PTBD failed in 10 (4.8%). Re-admission within 6 months in 47 (22.4%). Rendezvous ERCP was performed for 12 (5.7%).
Conclusion: Major indications for PTBD were patient fitness for ERCP and ERCP failure. The complications rate was low. Mortality was majorly because of advanced diseases and ongoing sepsis. PTBD was found to be a safe and useful approach to relieve obstruction in a setting where other modalities like Endoscopic ultrasound (EUS) are not available.

Abstract #287

Diagnostic value of brush cytology alone and in combination with tumor marker in malignant biliary stricture

Ansari J[1], Mathew P[1], Kanni P[1], Garg A[1], Gowda M[1]

[1]Department of Gastroenterology and Hepatology, VIMS and RC, Bangalore, India

Background: The aim of our study is to determine the yield of brush cytology alone and in combination with tumor maker in patients with suspected malignant stricture.
Methods: 68 patients with suspected malignant biliary obstruction based on clinical presentation and evidence of biliary obstruction in the form of stricture or pancreatic/biliary mass on contrast CT underwent brush cytology with onsite cytology analysis. The final diagnosis was approved based on the histological examination of the tissue taken surgically or by EUS–FNA.
Results: A total of 68 cytological specimens were included. The mean age of the patients was 52.03 ± 10.47 years. 52.9% of the patients had distal CBD stricture. Out of the 52 patients with malignant stricture confirmed with histology, 46 patients had positive brush cytology. The sensitivity and specificity of brush cytology with on site analysis in diagnosing malignant stricture in our study was 80.77% and 75% respectively ($p < 0.001$). The sensitivity of brush cytology in diagnosis of malignancy in distal CBD stricture was 92.31%. The sensitivity and specificity of brush cytology in combination with Ca19.9 was 96.2%and 62.5% respectively ($p < 0.001$).
Conclusion: Brush cytology has high sensitivity and specificity when performed with good technique and with on site analysis of the sample. The accuracy of the test is further enhanced while used in combination with tumor markers. Thus making the notion that brush cytology with on site analysis and in combination with tumor marker is a reliable method of diagnosing malignant biliary strictures

Abstract #408

A phase 3, randomized, double-blind, placebo-controlled, international study of durvalumab in combination with gemcitabine plus cisplatin for patients with advanced biliary tract cancers: TOPAZ-1

Do-Youn Oh[1], Li-Tzong Chen[2], Aiwu Ruth He[3], Takuji Okusaka[4], Shukui Qin[5], Steve Chin[6], Nana Rokutanda[7], Mallory Makowsky[6], Hyosung Kim[7], Arndt Vogel[8], Juan W. Valle[9]

[1]Seoul National University Hospital, Seoul, South Korea, [2]National Institute of Cancer Research, National Health Research Institutes, Tainan, Taiwan, [3]Georgetown University Medical Center, Division of Hematology and Oncology, Washington, DC, USA, [4]National Cancer Center Hospital, Tokyo, Japan, [5]PLA Cancer Center, Jinling Hospital, Nanjing, China, [6]AstraZeneca, Gaithersburg, MD, USA, [7]AstraZeneca, Osaka, Japan, [8]Hannover Medical School, Hannover, Germany, [9]The University of Manchester, Division of Cancer SciencesǀThe Christie NHS Foundation Trust, Department of Medical Oncology, Manchester, UK

Background: Advanced, unresectable biliary tract cancer (BTC) represents an area of unmet medical need due to its aggressiveness, limited treatment options, and poor prognosis. BTCs express PD-L1 and high levels of soluble PD-L1 correlate with poor prognosis in BTC patients (pts) treated with chemotherapy. PD-1/PD-L1 antagonists such as durvalumab (D; an anti–PD-L1 mAb) in combination with cytotoxic chemotherapy may contribute to a more effective antitumor immune response.
Objective: Early clinical data support evaluation of D combined with gemcitabine (G) and cisplatin (C) for treatment of pts with previously untreated, unresectable locally advanced, recurrent or metastatic BTC in the first-line setting.
Methods: TOPAZ-1 (NCT03875235) is the first large, phase 3, randomized, double-blind, placebo-controlled, international study to evaluate immunotherapy + chemotherapy in pts with BTC. Approximately 474 pts will be randomized 1:1 to Arm A (D + G/C for up to 8 cycles, then D until progressive disease [PD]) or Arm B (placebo + G/C for up to 8 cycles, then placebo until PD). Stratification factors are disease status and primary tumor location. Eligibility criteria include previously untreated disease if unresectable or metastatic at initial diagnosis (and recurrent disease > 6 months after curative surgery or completion of adjuvant therapy), and WHO/ECOG PS of 0 or 1. Pts with ampullary cancer or prior locoregional therapy are excluded; major surgery must have been completed > 28 days prior to the study. The primary endpoint is overall survival for Arm A vs Arm B. Secondary endpoints include progression-free survival, and objective response rate by investigator assessment using RECIST v1.1.
Results: None, Trial in Progress
Conclusions: None, Trial in Progress

Abstract #550

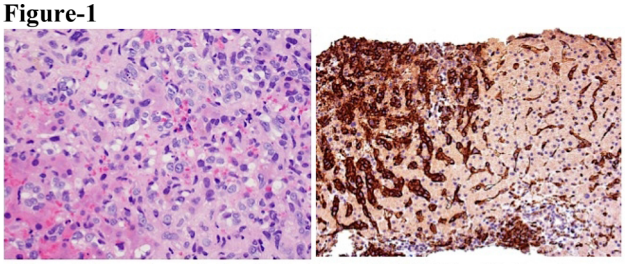
Hepatic angiosarcoma: case report

Htay Myat Thet[1,3], Tan Poh Seng[1], Kyaw Soe Tun[3], Aileen Wee[2], Pang Yin Huei[2]

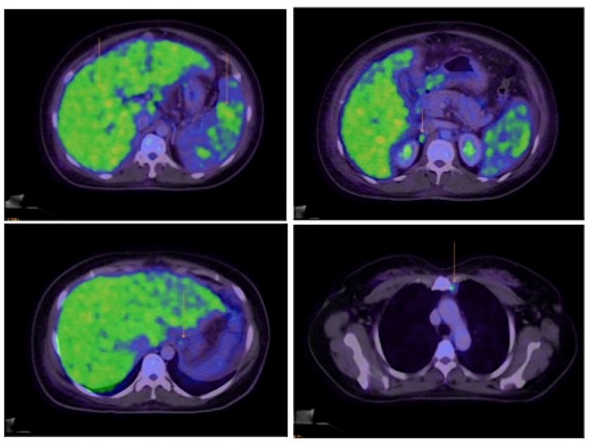
[1]Division of Gastroenterology and Hepatology, University Medicine Cluster, National University Health System, Singapore, [2]Department of Pathology, National University Health System, Singapore, [3]Department of Hepatology, PanHlaing Siloam Hospital, Yangon, Myanmar

Introduction: Hepatic angiosarcoma is a rare mesenchymal malignant tumor of the vascular endothelium with poor prognosis. High index of suspicion is required as diagnosis is challenging and often delayed with no specific clinical and liver imaging features.
Methods: Case description
Result: We report a rare case of primary hepatic angiosarcoma with unusual presentation. A 38 year-old woman with no past medical history presented with abdominal pain, elevated transaminases and jaundice, followed by pedal oedema and ascites 1–2 months later. Hepatosplenomegaly was detected on physical examination as well as on contrasted MRI but no discrete mass was seen. Her liver function gradually worsened (Table 1) with leucocytosis and thrombocytopenia. Investigations showed elevated igG (22.2 g/L), ANA (> 1:640) and anti-SMA (31 U) but were negative for other liver diseases including viral hepatitis. Tumor markers were normal. Presumptive diagnosis of autoimmune hepatitis was considered. Liver biopsy was performed and unexpectedly showed diffuse and extensive infiltration of the liver by malignant cells. Much of the hepatocytes were lost with no presence of cirrhosis. Further immunohistochemistry staining of the malignant cells showed strong nuclear positivity with ERG and membrane staining with CD31, positive CD117 and Ki 67 cell proliferation index of ~ 20% (Figure-1) but negative for epithelial markers of CD3, CD20, lysozyme, CD43, S100 protein, CD34, CD56, and Ber-EP4. Subsequent PET-CT (Figure-2) showed diffuse hepatic angiosarcoma with metastases to spleen and lymph nodes. Despite chemotherapy, patient succumbed to the disease.
Conclusion: Primary hepatic angiosarcoma could mimic decompensated liver disease due to autoimmune hepatitis. Liver biopsy is required to clinch diagnosis.

Figure-1



Histology - H&E showed tumor cells with residual hepatocytes and CD31 highlights proliferating malignant endothelial cells permeating and expanding the sinusoids



PET CT: Hepatomegaly with diffuse heterogenous appearance with FDG uptake with lymph nodes and splenic metastases

Table 1

	10/6/19	19/7/19	5/8/19	5/9/19	19/9/19	1/10/19	1st cycle chemotherapy on 04.10.2019	5/10/19	7/10/19	10/10/19	11/10/19	13/10/19
Total-Bilirubin (umol/l)	18	25	29	45	63	85		92	130	244	306	378
Conj-Bilirubin (umol/l)	-	-	-	-	27	42		45	64	137	167	284
Albumin (U/L)	-	-	-	31	31	29		30	29	26	23	22
AST	69	184	125	205	191	213		166	162	373	226	340
ALT	76	109	58	133	101	117		104	117	220	155	149
ALP	104	-	158	307	313	299		268	304	419	480	311
LDH	-	-	-	-	878	784		714	1359	2381	2975	4109
INR	1.06	-	-	1.32	1.23	1.25		-	-	-	1.64	-
WBC	15.5	12.3	-	12.8	14.8	13		-	-	107	87	70
Hb%	12	12	-	10.7	11.3	10.9		-	-	10.9	9.9	8.5
Platelets	101	133	-	111	99	100		-	-	33	29	39
Creatinine (umol/L)	-	-	-	68	86	74		-	-	87	94	305

Abstract #785

The role of preablation serum liver enzymes in predicting survival of patients with colorectal cancer liver metastasis after ultrasound-guided percutaneous microwave ablation

Huang Mingzhe[1,2], Huang Pinzhu[1,2], Qin Si[3], Peng Shaoyong[1,2], Liu Guangjian[3], Zhou Jiaming[1], Chen Zhiliang[4], Huang Meijin[1,2]

[1]Department of Colon and Rectum Surgery, The Sixth Affiliated Hospital (Guangdong Gastrointestinal and Anal Hospital), Sun Yat-

sen University, Guangzhou, Guangdong, China, [2]Guangdong Institute of Gastroenteroloy, Guangdong Provincial Key Laboratory of Colorectal and Pelvic Floor Disease, The Sixth Affiliated Hospital (Guangdong Gastrointestinal and Anal Hospital), Sun Yat-sen University, Guangzhou, Guangdong, China, [3] Department of Ultrasound, The Sixth Affiliated Hospital (Guangdong Gastrointestinal and Anal Hospital), Sun Yat-sen University, Guangzhou, Guangdong, China, [4]Department of General Surgery, Affiliated Dongguan People's Hospital, Southern Medical University (Dongguan People's Hospital), Dongguan, Guangdong, China

Introductions: Microwave ablation (WMA) was widely accepted for treatment of colorectal cancer liver metastasis (CRCLM). However, prognostic system designed for CRCLM patients undergoing WMA was rarely reported. Thus, an efficient predictor is required. Gamma glutamyltransferase (GGT), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are routine analysis for liver damage. Herein, the relationship between preablation liver enzymes and survival is studied.

Methods: We selected 192 CRCLM cases with WMA. Tumor burden score (TBS), defined as $TBS^2 =$ (maximum size of lesions)^2 + (number of metastasis)^2, was used to evaluate tumor burden. The prognostic value was explored by Kaplan–Meier method and Cox-regression model.

Results: All enzymes levels and ratios weren't correlated with TBS. ALT and AST displayed no relation to progression-free survival (PFS) and liver progression-free survival (LPFS) (all $P > 0.05$). In univariate analysis, improved levels of GGT, GGT/ALT, GGT/AST and ALT/AST were associated with poorer PFS (P = 0.003, 0.040, 0.003 and 0.039 respectively), while GGT and GGT/AST (P = 0.013 and 0.004) were correlated with LPFS. Further, GGT and TBS showed prognostic values for PFS (P = 0.001 and 0.002) and GGT/AST and TBS for LPFS (P = 0.001 and 0.003) in multivariate analysis. Unexpectedly, no liver enzymes predicted for overall survival (OS) in multivariate analysis. By subgroups, there was statistical significance of GGT/AST for the people treated with pre-chemotherapies and operations for primary tumors (all $P < 0.05$).

Conclusions: Preoperative GGT and GGT/AST were independent factors for recurrence of CRCLM under WMA. Even in patients with preoperative hepatotoxic drugs, GGT/AST was a promising predictor

Abstract #807

Atypical clinical manifestation of a hepatic perivascular epithelioid cell neoplasm (PEC-oma) with a multiple liver abscesses

Karolina Rostkowska-Białas[1,2], Marcin Czarnecki[1,3], Anna Szymanek-Pasternak[1,2], Krzysztof Simon[1,2], Dariusz Patrzałek[4]

[1]Department of Infectious diseases and Hepatology, Wrocław Medical University, Wrocław, Poland, [2]Department of Infectious diseases and Hepatology, Regional Specialistic Hospital im. Gromkowskiego, Wrocław, Poland, [3]Department of Infectious diseases, Liver Diseases and Acquired Immune Deficiencies, Wrocław Medical University, Poland, [4]Department of General, Vascular and Transplantological Surgery, University Teaching Hospital, Wrocław, Poland

Introduction: Perivascular epithelioid cell neoplasms (PEC-omas) is a rare group of mesenchymal tumors with liver being a very rare location for these neoplasms to grow.

Case descriptions: We report a case of 52 years old caucasian male with a 2 years history of intermittent fever with arthralgia, hyperaesthesia of the scalp, anorexia and increased sweating which turned out to be caused by a multiple liver abscesses most likely secondary to a liver PEC-oma. Prior to admission to our Department patient had been broadly diagnosed, including abdomen CT scans showing multiple lesions suggestive for abscesses which remained stable after prolonged antibiotic therapy. On admission abdomen CT scan was performed showing multiple focal hypodense lesions in the liver with local bile ducts widening suggesting liver abscesses and cholangitis. During hospitalization patient developed symptoms as written above with the increase in levels of inflammation markers. On the control CT scan we observed a large liver abscess, not seen on the previous scan. Patient was referred to a surgery unit where laparotomy was performed and two abscesses were drained. Histopathological analysis of the liver biopsy revealed neoplastic tissue, characterized as perivascular epithelioid cell neoplasm after immunohistochemical analysis. Pus culture was sterile. Up to this moment the treatment and diagnostic process is still ongoing

Abstract #932

Lymphoepithelioma-like hepatocellular carcinoma: a case report

Dina M. Sweed[1], Nermine A. Ehsan[1], Mervat M. Sultan[1], Asmaa M. Mosbeh[2], Yahya A. Fayed[3], Eman Abdelsameea[4], Imam Waked[4], Mohamed H. Abdel-Rahman[1,5,6]

[1]Pathology department, National Liver Institute, Menoufia University, Menoufia, Egypt, [2]Researcher of Pathology and Molecular Medicine, National Liver Institute, Menoufia, Egypt, [3]Hepato-pancreatobiliary Surgery and Liver Transplantation, National Liver Institute, Menoufia University, [4]Hepatology and gastroenterology, National Liver Institute, Menoufia University, [5]Ophthalmology department, The Ohio State University, Columbus, Ohio, US, [6]Division of Human Genetics, The Ohio State University, Columbus, Ohio, US, Menoufia, Egypt.

Introduction: Hepatic lymphoepithelioma like carcinoma (LELC) is a rare primary hepatic tumor that includes LEL-hepatocellular carcinoma (HCC), LEL-cholangiocarcioma (CC) and mixed types. Most LEL-HCC is associated with hepatitis C virus infection (HCV) with negative Epstein-Barr virus (EBV) infection.

Case descriptions: We report a case of LEL-HCC in a 41-year-old man with chronic HCV infection with negative serum AFP. The mass showed typical diagnostic criteria for HCC on computed tomography (CT). Histopathological examination showed sheets and cords of malignant epithelial cells intermixed with heavy lymphoid infiltrate than 100 tumor infiltrating lymphocyte (TILs) per 10 HPF. Immunohistochemical studies showed positive staining for HepPar 1 and glypican 3, focal positive for CK7 in the malignant cells. TILs were highly positive for CD3 with an equal ratio of CD4/CD8. The patient was recurrence free at 25 months after surgery as evident by CT findings and serum AFP level.

Conclusions: LEL-HCC is a rare variant of HCC with a relative better prognosis, so recognizing this rare subtype is important. Exploring the potential for immune modulator based therapy in this subset of tumors is highly recommended.

Abstract #950

A case of transcatheter arterial embolization using microspheres for painful bone metastasis of cholangiocellular carcinoma

Prasetyo D.[1,2], Morita S.[1], Suda T.[1], Hoshi T.[1], Abe S.[1], Yagi K.[1], and Terai S.[3]

[1]Department of Gastroenterology and Hepatology, Uonuma Institute of Community Medicine Niigata University Hospital, Niigata, Japan, [2]Division of Gastroenterology and Hepatology, Internal Medicine Department of RSUD dr. Moewardi Surakarta/Medical Faculty Universitas Sebelas Maret, Indonesia, [3]Division of Gastroenterology and Hepatology, Graduate School of Medical and Dental Sciences, Niigata University, Niigata, Japan

Case illustration: A 70-year-old Japanese man was provided the best supportive care for cholangiocellular carcinoma. Computed tomography examination of his left shoulder pain showed a soluble metastatic lesion of the left scapula. Oral morphine 90 mg/day and bisphosphonates were administered and external irradiation (20 Gy) was performed, but it was difficult to control cancer pain, and the visual analogue scale (VAS) was 7/10 at rest and 9/10 at raising the upper limb. After obtained informed consent, transcatheter arterial embolization (TAE) was performed for pain relief. Left brachial artery angiography showed a tumor stain from the thoracoacrominal artery and the circumflex scapular artery. The tumor was embolized with Embosphere® that the size was 300–500 μm from the each arteries and terminated with an embolization rate of about 80%. The frequency of temporary analgesics increased for post embolism pain until two days after TAE, but then gradually decreased and improved to VAS 4/10 (at rest) 10 days after TAE. There were no other adverse events.
Discussion: The number of patients with painful bone metastasis is increasing and the prognosis is prolonged due to advances in treatment. External radiation, opioid analgesics, bone modifiers, and surgery are recommended for pain relief, but many cases are difficult to control. There are cases in which TAE is effective for pain relief.
Conclusion: TAE using microspheres was useful in the treatment for painful bone metastasis of cholangiocellular carcinoma. Although clinical efficacy is expected, there are no reports with high evidence level, and prospective study is expected

Abstract #1073

Plastic stenting is an effective treatment for unresectable malignant hilar biliary obstruction

Koncoro H, Mayasari M, Maulahela H

[1]Department of Internal Medicine St. Carolus Hospital Jakarta, [2]Department of Digestive Surgery St. Carolus Hospital Jakarta, [3]Department of Internal Medicine Cipto Mangunkusumo Hospital Jakarta

Introduction: Bile duct carcinomas, or cholangiocarcinomas (CCs), is the second most frequent liver malignancy. While these tumors have a low incidence, they have high mortality rates because the level of compromise is advanced when they appear. Approximately 60–70% originate in the hepatic duct confluence. Palliative drainage is the primary treatment option for unresectable malignant hilar biliary obstruction to improve the prognosis and quality of life. Herein, we report a technique that consists of placing stent in the common bile duct for the treatment of hilar cholangiocarcinoma.
Case illustration: A 77-year-old man presented with jaundice and was diagnosed with Bismuth type I Klatskin tumor. On abdominal CT-scan we can find severe dilatation of right and left intrahepatic bile duct with sudden stenotic in hepatic hilum suspicious of neoplasm with differential diagnosis of Klatskin tumor and pancreatic head mass. There were no any common bile duct dilatation. The patient was diagnosed with cholestatic jaundice caused by Klatskin tumor and cholangitis. Because curative surgical resection was not possible, we placed stent in the proximal common bile duct. The patient was treated with Cefoperazone-Sulbactam 1 g every 8 hours. This technique was feasible and could be considered for the treatment of patient with hilar cholangiocarcinoma.
Conclusion: Plastic stent placement resulted in effective palliation in patients with unresectable malignant hilar biliary obstruction.

Abstract #1116

A rare liver malignancy: angiosarcoma

Introduction: Primary hepatic angiosarcoma is very rare and constitutes 2% of all primary liver malignancies. It is very aggressive, associated with vinyl chloride exposure, nonspecific multipl involvement in the liver and CD31 (+). In this case, we present a rare hepatic angiosarcoma with multiple liver involvement with vinyl chloride exposure.
Case: A 55-year-old male patient presented with complaints of fatigue, weight loss and jaundice. Her history included DM and HT. He worked in a plastic window workshop. On physical examination, skin and sclera were icteric and HSM was positive. HGB: 9.1 g/dL MCV: 89 fL, WBC: 24.02 $\times$ 10^3/μL, PLT: 48 $\times$ 10^3/μL, Glucose: 216 mg/dL, urea: 204 mg/dL creatinine: 1.93 mg/dL, AST: 59.42 U/L, ALT: 55 U/L, ALP: 207.1 U/L, LD: 682 U/L, Direct Bilirubin: 7.1 mg/dL, Total Bilirubin: 11.9 mg/dL, Albumin: 1.8 g/dL, CRP: 31 mg/L, INR: 1.92, Coombs +, direct coombs (Ig G): + 1, direct Coombs −. Peripheral smear showed 1–2% blast. Bone marrow biopsy was unremarkable. Viral markers were negative. Abdominal USG showed diffuse infiltration of the liver parenchyma with a large number of hypoechoic areas measuring 16 mm in diameter. Craniocaudal axis of liver was measured approximately 200 mm. Spleen dimensions increased to 170 $\times$ 73 mm. The splenic parenchyma is infiltrated. In a subsequent liver biopsy, immunohistochemical study reported that CD31 was potent (+) and vascular neoplasia (primarily angiosarcoma) was considered. The patient's ex-status worsened during follow-up.
Conclusion: Angiosarcoma is a rare disease with poor prognosis and limited treatment options. Angiosarcoma should be considered in patients with exposure to vinyl chloride who have multiple hepatic involvement in the liver.

Abstract #1216

Magnetic resonance imaging findings of biliary adenofibroma

Sunyoung Lee, MD, PhD[1,2], Kyoung Won Kim, MD, PhD[1]

[1]Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea, [2]Department of Radiology and Research Institute of Radiological Science, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

Introduction: Biliary adenofibroma is a rare tumor of bile duct origin characterized by a complex tubulocystic non-mucin secreting biliary epithelium with abundant fibrous stroma. Magnetic resonance imaging (MRI) features of biliary adenofibroma are not yet well established.
Case illustrations: Herein, we reported regarding two patients with biliary adenofibroma and reviewed the literature focusing on MRI findings. A well-circumscribed multicystic tumor with septal enhancement and no intrahepatic bile duct communication may be characteristic MRI findings of biliary adenofibroma.

Abstract #1298

Diagnostic problem in a patient with obstructive jaundice suspect periampullary carcinomas

Nabilah[1], Titong Sugihartono[2]

[1]Resident of Internal Medicine Department, Universitas Airlangga, Surabaya, Indonesia, [2]Division of Gastroenterology and Hepatology, Internal Medicine Department, Universitas Airlangga, Dr. Soetomo General Academic, Surabaya, Indonesia

Introduction: Determining the precise etiology of periampullary malignancies can be a challenge. Periampullary carcinomas exhibit diferent clinical behaviors according to their site of origin and it can determines five-year disease free survival.
Case illustration: A 79-yo man presented with jaundice throughout the body in 2 weeks, recurrent pain in the upper quadrant abdominal, with visible mass, and loss of body weight. There is also pale stool and dark urine. Palpable mass around 4 cm in upper quadrant abdomen is found in physical examination, solid, no tenderness. MRCP showed a solid mass, irregular edge, size 2.34 × 2.45 × 2.85 cm in the region of T1W1 and T2W1, severe distal CBD obstruction leading to proximal CBD dilatation, right IHBD, left IHBD, and GB hydrops may still be caused by periampullary lesion. Endoscopy showed mass in ampulla vatery with bulging, and the biopsy presented villous adenoma with moderate dysplasia. Laboratory revealed CA19-9 295.41 U/ml and ALP 574 UL. Patient will undergo a Whipple procedure. If unresectable, a biliodigestive bypass will be performed and the patient will be transferred to digestive surgery. However, in the course of the patient's condition worsened and died before surgery.
Discussion: Many of the difficulties in the treatment of periampullary carcinomas result from the difficulty in diagnosing the disease in its early stages. This patient laboratory and MRCP finding leads to a periampullary carcinoma, with histopathological as villous adenoma. The therapy could be Whipple procedure, bypass billiodigestive, or palliative.

Abstract #1460

Paraneoplastic hypoglycemia in hepatocellular carcinoma

Wahyu Purnama[1], Fathony Arsyad[1], Monica Raharjo[1], Rebekka Martina, Kemal Fariz Kalista[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Non-islet tumor hypoglycemia (NICTH) is a rare case of paraneoplastic complication, especially in the setting of hepatocellular carcinoma (HCC) but many patients are unaware of their hypoglycemia.
Case report: A 34-year- old man presented with epigastric pain, and weight loss of 3 kilograms in 2 months. He had chronic hepatitis B. The patient had a history of unconsciousness over 2 weeks ago. Physical examination revealed ascites, large protruding mass in the epigastrium, lower extremity edema and an ECOG performance status of 4. Laboratory tests tend to hypoglycemia with POCT (73–77–36–22–85 mg/dL). The patient was treated with drip dextrose 40% infusion, Metilprednison 2 × 62.5 mg iv. His alpha-fetoprotein was > 80.000 ng/mL. An abdominal CT scan showed heterogeneous arterial enhancement with portal/delayed phase washout, consistent with multifocal multicentric HCC.
Discussion: In this case, the patient had treated with dextrose 40% infusion and glucocorticoid, counter-regulatory hormone but remained persistently hypoglycemic. The cause of hypoglycemia in HCC is either from impaired gluconeogenesis due to the decompensated liver (glucose underproduction) or high insulin-like growth factor II (IGF-II) level produced by the tumor.
Conclusion: The diagnosis of HCC with paraneoplastic manifestation must be considered in a patient with chronic liver disease who presents with refractory hypoglycemia. Cytoreduction is the most effective method for treating hypoglycemia associated HCC, and while steroids are frequently used, they aren't effective in the majority of cases.

Abstract #1488

Case report: diagnostic approach to malignancy ascites patient who missdiagnosed as tuberculosis abdominal

Sang Ketut Widiana[1], Budi Widodo, Herry Purbayu, Titong Sugihartono, Iswan A. Nusi[2]

[1]Student of Internal Medicine Departement, Airlangga University-Dr. Soetomo General Hospital, Surabaya, Indonesia, [2]Gastroenterology and Hepatology staff of Internal Medicine Departement, Airlangga University-Dr. Soetomo General Hospital, Surabaya, Indonesia

Introduction: Ascites is an accumulation of free fluid with an abnormal amount (> 100 ml) in the peritoneal cavity. The causes of ascites are hepatic cirrhosis (75–80%), malignant ascites (10%) and the remaining 5% (mixed ascites ex infection Tuberculosis). Malignant ascites is a pathological condition caused by primary abdominal (ovarian cancer by 35%, colorectal by 30%, stomach by 10%, and followed by pancreatic and peritoneal cancers) and extra-abdominal malignancies (breast, lung and lymphoma cancer).
Case: A man, 41 years old, came with an enlarged stomach since the last 2–3 months, pain in the abdomen fever, decreased appetite accompanied by weight loss > 20 kg (72 kg to 50 kg) with change in bowel habit in the last 3 months. At first patient was diagnosed as abdominal tuberculosis (TB) and taking Tuberculosis Drug regimen (Isoniazid/Rifampin/Pyrazinamide/Ethambutol). Patient went to RS Sutomo and underwent several examinations and laboratorium, the results ledto colon cancer
Discussion: The etiological diagnosis of ascites is a major and very difficult problem and almost 20% of all patients have no known primary tumor. Distinguishing the cause of ascites is very important for planning appropriate management.

Abstract #1615

Radiofrequency ablation to metastatic liver nodules, improves survival in advance colorectal cancer patient

Mustika Dian Permana[1], Kemal Fariz Kalista[2]

[1]Department of Internal Medicine, Faculty of Medicine, University of Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, University of Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia.

Introduction: Liver metastases occur in up to 60% of patients with colorectal cancer, and the control of liver metastases is considered to be of primary importance because it is a critical factor in determining prognosis. Radiofrequency ablation (RFA) is an alternative therapy for hepatocellular carcinoma and liver metastases when resection cannot be performed. RFA has the advantage of being a relatively

low-risk minimally invasive procedure used in the treatment of focal liver tumors.
Case report: A 58-year-old man with colorectal cancer (CRC) pT3N2M0 St IIIc that diagnosed 2 years ago, found metastatic liver nodules one month after finished tumor resection followed by radiation and systemic therapy. He had no complaint and no co morbidity diseases. Physical examination revealed no significant abnormality and an ECOG PS 0. Laboratory test showed that the patient had a good liver function. A MRI showed metastatic lesion in segment 5/8 of the liver with 2 cm diameter. Then RFA was done to the liver nodules, and showed successfully complete response after two cycles of procedure, and sustained in 18 months after follow-up.
Discussion: In this case, the patient preferred to get RFA other than surgery procedure. Some reported that patients who received RFA had survival rates similar to surgical groups, while others found that survival rates were better among patients undergoing surgical resection. A more recent study reported that the overall survival and disease-free survival did not differ between patients treated with resection or RFA in patients with a solitary colorectal metastasis < 3 cm; however, in patients with a solitary metastasis > 3 cm, the disease-free survival was significantly lower in the RFA group as compared with the resection group.
Conclusion: The successful management of liver metastases from CRC can be obtained with RFA. RFA has a potential to achieve the same overall and disease-free survival rate as surgical resection in selected patients.

Abstract #1715

Liver abscess masking primary hepatic epitheloid angiomyolipoma: a case report

Leong Wen Hao[1], Justin Tan Xia[1], Huang Andrew[1], Salazar Ennaliza[1]

[1]Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore

Introduction: Hepatic angiomyolipomas (AML) are rare mesenchymal tumors composed of heterogeneous elements of blood vessels, lipocytes and smooth muscle with a young median age of onset. Numerous subtypes exist, of which the epitheloid type is a rare type distinct from classical AML in its malignant potential.
Case presentation: A 46-year-old man presented with five-day history of fever with epigastric pain and nausea. On admission, his temperature was 37.4C HR-90 BP-108/63 mmHg. Laboratory results showed abnormal liver function test (Albumin-37 g/L Bilirubin-25 μmol/L ALP-298 units/L ALT-247 units/L AST-344 units/L), Total White 4.73×10^9/L, CRP 39.6. The initial clinical suspicion was hepatobiliary sepsis and intravenous ceftriaxone commenced. CT Abdomen showed an ill-defined hypodense focus in Segment 4A/8 (4.5×3.5 cm) with minimal fluid component concerning for a developing abscess or phelgmon. Images reviewed by radiology showed minimal fluid for percutaneous drainage. MRI performed revealed a solid mass with nodular areas of arterial enhancement and washout, suspicious of neoplasm. Ultrasound-guided liver biopsy of the lesion was performed. Histology showed histiocyte rich epithelioid neoplasm consistent with epitheliod variant of angiomyolipoma. Immunohistochemical staining was positive for Human Melanoma Black 45, Melan-A and Cluster of Differentiation 68. He underwent liver resection of segment 4A/8 successfully after six weeks of antibiotics.
Conclusion: While there are unique radiological features of classical angiomyolipoma such as intra-tumour fat, hyperenhancement with draining hepatic vein during arterial phase and prolonged enhancement pattern, they are difficult to diagnose preoperatively and can be misdiagnosed as hepatocelluar carcinoma. Biopsy is useful for histological diagnosis. In view of the malignant potential, surgical resection should be considered.

Abstract #1781

Persistent hypoglycemia in patient with liver tumors: a case series

Hanum Citra Nur Rahma[1], Kemal Fariz Kalista[2]

[1]Faculty of Medicine, Universitas Indonesia, [2]Division of Hepatobiliary, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo General Hospital

Abstract
Introduction: The patients with large liver tumor have higher chance to suffer hypoglycemia. The hypoglycemic itself can be fatal if not detected and treated immediately.
Objectives: The purpose of this case series is to review characteristic profile of patient with liver tumor present with hypoglycemia.
Results: In this case series, 15 patients with liver tumor presented with hypoglycemia. Hepatocellular carcinoma was diagnosed in 8 patient, metastatic liver disease in 2 patient and 5 patient with undiagnosed liver mass. Mean age was 46 y.o and male predominance (71.4%). Jaundice was found in 57% and hepatomegaly was found in 95.6% patients. Initial blood glucose mean was 45.2 mg/dL. Child Pugh Score mean score was 10 (C class). Based on imaging tumor diameter mean was 12 cm, multiple tumor (93.3%), diffuse tumor (80%) and involving only right lobe (60%). Treatment for hypoglycemia were oral/enteral feeding, intravenous glucose and steroid. No treatment were given for the tumor because all the patients were in advanced stage. Treatment result was 42.6% blood glucose controlled, 50% refractory and 7.4% persistent.
Conclusion: In case of liver tumor, hypoglycemia occurs due to failure of the liver to meet glucose demand from the rapidly growing tumour and tumor secreting Insulin Growth Factor (IGF). In our case, the size of tumour was varied and we were not able to test the serum insulin level and IGF 1 level. Despite of treatment for hypoglycemia, treatment for tumor it self should be done to control the hypoglycemia.

Abstract #1782

Liver metastatic in non-functioning pancreatic neuroendocrine tumor: a case report

Marcel Sibarani[1], Andri Sanityoso Sulaiman[2], Saut Horas Hatoguan Nababan[2], Taufik Agung[3]

[1]Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Faculty of Medicine Universitas Indonesia, Jakarta, [2] Hepatobiliary Division, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Faculty of Medicine Universitas Indonesia, Jakarta, [3] Department of Radiology, Cipto Mangunkusumo National General Hospital, Faculty of Medicine Universitas Indonesia, Jakarta

Introduction: Pancreatic neuroendocrine tumors (PanNET) are rare neoplasms that arise in the endocrine tissues of the pancreas. PNET may be classified as either functional or non-functional. Between 50–70% of pancreatic NETs are nonfunctioning. Clinical presentation may vary from a slow-growing and non-infiltrative tumor to locally invasive and rapidly metastasizing. Metastases occur in 50–58% of cases predominantly in the liver.

Case presentation: A 53 years old male was referred from another hospital presented with enlarged stomach gradually over the past 2 years. He also reported fatigue, reduced appetite along with weight loss of 11 kg. Laboratory tests showed mild anemia, transaminase and jaundice index were normal, nonreactive hepatitis markers and tumor markers (CEA and AFP) were negative. Abdominal CT revealed enlarged liver size around 22 cm especially in the left lobe of the liver irregular with lobulated edges, a multiple solid cystic lesion and no visible focal lesion on the pancreas. A percutaneous liver biopsy was obtained and showed pieces of tumor tissue arranged trabecular and solid with rounded tumor cells, mild pleomorphic, hyperchromatic and eosinophilic cytoplasm histologically can be accordance with neuroendocrine tumor. Immunohistochemistry was positive for Chromogranin, AE1-E3, CK7, and CK19, non-specific for synaptophysin, negative CD56 with a Ki-67 proliferation marker of 10%. The patient was referred to digestive surgery, but due to the large tumor burden it was decided that the tumor was inoperable. The patient began chemotherapy with Carboplatin, Paclitaxel and Sandostatin for four cycles. The chemotherapy was discontinued because the CT-Scan showed stable disease.
Conclusion: Pancreatic neuroendocrine tumors are a heterogenous group of neoplasms that arise form progenitor islet cells. The diagnostic approach is still challenging, and the treatment should be guided multidisciplinary team.

Abstract #1874

Obscure gastrointestinal bleeding in a pancreatic neuroendocrine tumor patient

Nuarwenty M.[1], Widodo B.[2], Purbayu H.[2], Sugihartono T.[2], Rahniayu[3], Kristian I.[4]

[1]Resident of Internal Medicine Department, Universitas Airlangga, Surabaya, Indonesia, [2]Division of Gastroenterology and Hepatology, Internal Medicine Department, Universitas Airlangga, Dr. Soetomo General Academic, Surabaya, Indonesia, [3]Department of Anatomical Pathology, Universitas Airlangga, Dr. Soetomo General Academic, Surabaya, Indonesia, [4]Digestive Surgery Department, Universitas Airlangga, Dr. Soetomo General Academic, Surabaya, Indonesia.

Introduction: Obscure GI bleeding (OGIB) is defined as occult or overt bleeding of unknown origin that persists or recurs after an initial negative endoscopic evaluation. Pancreatic neuroendocrine tumors (PNETs) is a group of endocrine tumors arising in the pancreas.
Objective: To present a rare case of PNETs manifested by OGIB.
Methods: A 44-yo man presented with episodic abdominal pain in the right upper quadrant, vomiting, jaundice, melena, and weight loss of two months duration. His past medical history revealed type 2 diabetes mellitus. Physical examination found a palpable mass in the right side of the abdomen. Laboratory revealed anemia and increased in direct bilirubin. Abdominal CT scan showed malignant mass size $6.1 \times 4.4 \times 4.8$ cm that extends to the periampular to the duodenal part II (D2) causing dilatation of biliary system, without evidence of liver metastasis. MRCP showed dilatation of biliary system due to pancreatic head mass of $57.7 \times 42.2 \times 43.1$ mm, mass infiltration of D2–3. Gastroscopy showed ulcer with clean based at D2. Colonoscopy showed no source of bleeding. The source of bleeding may came from the proximal portion of the terminal ileum to D2. The patient undergoes Whipple procedure and duodenectomy. Histopathologic and immunohistochemical (synaptophysin, CD56, chromogranin, Ki67) result were PNETs grade 2. This patient's symptoms resolved after surgery.
Results: Mid-GIB comprises a majority of OGIB. Bleeding in the small bowel distal to Vater's papilla and reach as far as the terminal ileum is termed mid-GIB. PNETs can be classified into functioning (F-PNETs) and non functioning (NF-PNETs) based on hormonal secretion. Clinical presentation of F-PNETs are characterized by the hypersecreted hormones produced by the tumor, whereas the symptoms of NF-PNETs appear when they cause compression, invasion of adjacent organs, or when they metastasize. OGIB in this patient due to the large size of the tumor and extent of local invasion to duodenum. Grade 1 and 2 PNETs are well differentiated and the primary treatment are surgical resection.
Conclusion: OGIB mostly occurred in mid-GIB which can be caused by PNETs.

Abstract #1961

Clinical features of breast cancer patients with liver metastases

Siregar L[1], Loho IM[1], Waspodo AS[1], Elaine S[1], Budi E[1], Swadari R[1], Ferino F[1], Fransisca T[1]

[1]Department of Gastroenterology and Hepatology, "Dharmais" Cancer Hospital, Indonesian National Cancer Center, Jakarta, Indonesia

Introduction: Liver metastases in patients with breast cancer have been associated with very poor prognosis.
Objectives: This study aims to explore the clinical features of patients with breast cancer liver metastases and the time interval of liver metastases development after primary treatment for breast cancer.
Methods: Medical records of 660 patients diagnosed with breast cancer between September 2018 and November 2019 in our institution were retrospectively analyzed. Baseline characteristics and time of liver metastases detection were reviewed.
Results: The incidence of liver metastases in this study was 7.7%, with a total of 51 female patients with median age of 47 years. Of 51 patients, five patients exhibited metastasis only in the liver, while 43 patients were found to have multiple metastases. Presence of liver metastases upon initial diagnosis of breast cancer was found in six patients. As many as 22, 10, 8, and 5 patients were classified as luminal A, luminal B, triple negative, and HER2 + respectively. Six patients had incomplete data to be classified as any subtype. The predominant histological type was invasive carcinoma of no special type, which was found in 35 patients. Surgery was the main treatment modality in 44 patients and complete response was achieved in 18 patients. Of the 18 patients, liver metastases were detected within 5 years after surgery in 15 patients.
Conclusion: Liver metastases usually occurred concurrently with other distant sites metastases. Further study should be conducted to determine optimal surveillance schedule for detection of liver metastases in breast cancer

Abstract #1962

Innovative management of pancreatic neuroendocrine tumor using endoscopic ultrasound radiofrequency ablation (EUS-RA): a case report

Cosmas Rinaldi A. Lesmana[1,2,4], Aru W. Sudoyo[1,3,4], Laurentius A. Lesmana[1,4]

[1]Digestive Disease and GI Oncology Center, Medistra Hospital, Jakarta, Indonesia, [2]Department of Internal Medicine, Hepatobiliary Division, Dr. Cipto Mangunkusumo National General Hospital, Medical Faculty, Universitas Indonesia, Jakarta, Indonesia, [3]Department of Internal Medicine, Hematology-Oncology Division,

Dr. Cipto Mangunkusumo National General Hospital, Medical Faculty, Universitas Indonesia, Jakarta, Indonesia, [4]Mochtar Riyadi Comprehensive Cancer Center (MRCCC) Siloam Semanggi Hospital, Jakarta, Indonesia

Background: Pancreatic Neuroendocrine Tumors (PNETs) are a rare type of cancer involving the pancreas. Current medical treatment does not give satisfactory results. Meanwhile, surgical treatment option such as the Whipple procedure is sometimes not suitable anymore or resisted by the patient. Recently, therapeutic intervention endoscopic ultrasound (EUS), such as EUS radiofrequency ablation (RA), has been used to treat liver and pancreato-biliary disorders.
Case Illustration: A forty-eight years old female was referred for EUS-FNAB with incidental finding of pancreatic mass at the uncinate area with a diameter of 3 × 3.5 × 3.4 cm on abdominal MRI evaluation during medical check-up. No clinical symptoms were found. There was also no evidence of jaundice, biliary obstruction, or metastases. The biopsy result was consistent with neuroendocrine tumor. The patient was offered to undergo Whipple operation; however, she refused to undergo the surgery. After discussing with the patient, she agreed to undergo EUS-RA. There were no complications found after treatment procedure such as gastrointestinal hemorrhage, perforation, severe acute pancreatitis, or infection.
Conclusion: EUS-RA is a promising tool for PNETs management; however, further studies with larger samples should be done to evaluate long-term outcome after treatment, especially in tumor of larger size.

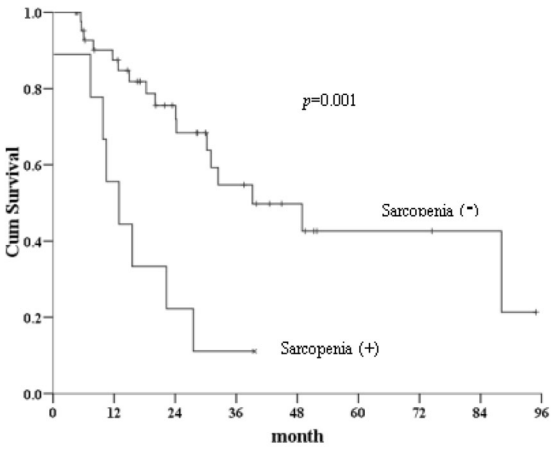
Abstract #2007

Prognostic value of sarcopenia in patients with synchronous colorectal liver metastases undergoing hepatic resection

Chao-Hung Hung[1], Yueh-Wei Liu[2], Chien-Chang Lu[3], Ching-Di Chang[4]

[1]Division of Hepatogastroenterology, Department of Internal Medicine, Chiayi Chang Gung Memorial Hospital, Chiayi, Taiwan, [2]Liver Transplant Center, Department of Surgery, Kaohsiung Chang Gung Memorial Hospital, and Chang Gung University College of Medicine, Kaohsiung, Taiwan, [3]Department of Colorectal Surgery, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan, [4]Department of Radiology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

Introductions: The prognostic significance of sarcopenia has been widely studied in different cancer patients. This study aimed to analyze the influence of sarcopenia on long-term survival in patients with synchronous colorectal liver metastasis (CRLM) undergoing hepatic resection.
Methods: A retrospective analysis of 119 patients undergoing hepatic resection for synchronous CRLM was performed. Sarcopenia was determined using the Hounsfield unit average calculation (HUAC), a measure of muscle quality-muscle density at preoperative abdominal computed tomography scans. Sarcopenia was defined as an HUAC score of less than 22 HU calculated using receiver operating characteristic analysis. The prognostic relevance of clinical variables and overall survival (OS) and recurrence-free survival (RFS) was evaluated.
Results: Patients with sarcopenia were older ($p < 0.001$) and had higher body mass index (BMI) ($p = 0.028$) and neutrophil-to-lymphocyte ratio ($p = 0.029$) compared to those without. Sarcopenia was not significantly associated with OS and RFS. Multivariate Cox's regression analysis showed that multinodularity (> 3) (hazard ratio (HR) 2.612; 95% confidence interval (CI), 1.352–5.045; $p = 0.004$), lymph node metastasis (N2) (HR 2.306; 95% CI, 1.225–4.339; $p = 0.010$) and blood loss (≥ 300 cc) (HR 2.054; 95% CI, 1.081–3.901; $p = 0.028$) were independent factors associated with OS. However, in subgroup analyses, sarcopenia was a significant factor of poor OS in the patients with multinodularity ($p = 0.001$) or higher BMI (≧ 25) ($p = 0.031$). Multinodularity was the significant factor associated with RFS by univariate and multivariate analyses (HR 1.98; 95% CI, 1.24–3.18; $p = 0.004$).
Conclusion: Despite no significance in whole cohort, sarcopenia was predictive of worse OS in selected patients with CRLM after partial hepatectomy. Sarcopenia was a significant factor of poor overall survival in the patients with multinodularity



No. at risk

Sarcopenia (+)	9	5	2	1	0	0	0	0
Sarcopenia (-)	41	33	21	12	7	3	3	2

Abstract #2023

Hemangioma mimicking hepatocellular carcinoma findings: a case report

Bonita Effendi[1], Ihsanul Rajasa[1], Kemal F. Kalista[2]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, [2]Division of Hepatobiliary, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia

Introduction: Radiological imaging plays an important role in diagnosis of hepatocellular carcinoma (HCC). It is noninvasive diagnosis of HCC in high-risk patients by typical imaging findings. However, its increased sensitivity of the imaging to detect small lesion, might cause false-positive HCC diagnosis. In several case of HCC may present with atypical contrast enhancement pattern mimicking benign liver masses.
Case presentation: A 65-year-old female presented with epigastric and right upper quadrant abdominal pain over the past 4 months. Ultrasonography showed multiple hepatic nodules. Hepatitis serology showed non-reactive. Abdominal CT scan demonstrated, there were 2 lesions with size 2.85 cm × 2.72 cm in segment 5, and size of 4 × 3.47 cm in segment 6 with wash in appearance during arterial phase and washout during venous phase and delayed. Differential diagnosis based on CT was HCC or hemangioma. Since the lesion size were > 1.5 cm and suspicious result, further examination was conducted. MRI with gadoxetic acid showed nodular lesion on segment 5 suspected to be HCC and lesion found on segment 6 suspected to be hemangioma. In addition, fine needle aspiration biopsy was conducted with MSCT guiding aspiration. Nodular lesion proven to be benign lesion, hemangioma.

Conclusion: Radiologic hallmarks from contrast imaging supported in diagnosing HCC. Hemangiomas are detected frequently during HCC surveillance and potentially mimicking HCC especially when the lesion is small. The degree of enhancement of hemangiomas are usually equivalent to that of aorta in the arterial phase and blood pool in the portal venous phase or later phase on multiphasic contrast enhancement CT and MRI using gadoxetic acid.

Abstract #2029

Noncirrhotic portal hypertension due to myelofibrosis in a 50-year-old man: a case report

Rebekka Martina[1], Monica Raharjo[1], Wahyu Purnama[1], Fathony Arsyad[1], Kemal Fariz Kalista[1], Saut Horas H. N.[1], Juferdy Kurniawan[1], Sahat B. R. E. Matondang[2]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Department of Radiology, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Myeloproliferative neoplasm (MPN) is a hematologic disorder that consists of polycythemia vera (PV), essential thrombocythemia (ET), primary myelofibrosis (PMF). in myelofibrosis, portal hypertension (PHT) often results from portal and/or hepatic vein thrombosis.
Case report: A 50 year old man presented with hematemesis and melena. He had no history of viral hepatitis, alcohol, the patient smokes. The patient has a history stomach feels enlarged and bloated. Physical examination revealed that the spleen was palpable in shuffner 3. Laboratory tests showed a decreased hemoglobin concentration of 7.8 g/dl. Hepatitis B virus and anti-hepatitis C virus were negative. Evaluation on JAK2 mutation was performed and the result is JAK2V61 mutation. Abdominal ultrasound and abdominal computed tomography showed the splenomegaly, minimal ascites, portal vein thrombus, mesenteric vein, splenic vein, portal hypertension, varicose veins in the perisplenic region, perigastric, esophageal pars, periumbilical. endoscopy confirmed that upper gastrointestinal bleeding was caused by esophageal varices grade 3, moderate porta hypertension gastropathy.
Discussion: A splenorenal shunt was planned. But over discussion in our department. The shunt cannot be done because of the broad thrombus, the splenic vein is covered by the splenorenal thrombus. PHT has been related to an increased intrahepatic resistance due to the myeloid metaplasia, and/or to marked portal flow increase, as a consequence of massive splenomegaly.
Conclusion: Thrombosis in portal vein, mesenteric, and splenic is relatively common complication in myelofibrosis patients. management for this patient because splenorenal shunt cannot be done is the administration of propanolol and hydroxyurea group, ligation endoscopy

Abstract #2035

Female 64 years old with mild polycystic liver disease and autosomal dominant polycystic kidney disease: a case report

Witjaksana, R.A[1], Pratama, A.A[2], Christiandari, Y[3]

[1]Medical Intern in Prima Husada Hospital, Malang, East Java, Indonesia, [2]Medical Doctor in Prima Husada Hospital, Sukorejo, East Java, Indonesia, [3]Internist in Prima Husada Hospital, Sukorejo, East Java, Indonesia

Introduction: Polycistic Liver Disease (PLD) is a collection of rare human disorders that result from structural changes in the biliary tree development. Hepatic cysts are the major clinical feature in Isolated Polycistic Liver Disease (PCLD) and the most frequent extra renal manifestation in Autosomal Dominant Polycystic Kidney Disease (ADPKD).
Case presentation: We report a case of 64-year-old female with PLD and ADPKD. The patient presented with a major complaint of abdominal pain in the epigastric region since 5 months ago. We already performed an ultrasound examination in August 2019 and only get polycystic of the liver as the result with maximum diameter was 9 × 9 cm. In December 2019 we perform abdominal CT Scan with contrast and get multiple liver cyst with maximum diameter was 10 cm urged the gaster and multiple bilateral ren cyst. The lack of knowledge of past family history makes us unable to ascertain whether or not there is a family history of illness. Due to limited facilities, we have not been able to do an MRI on patients.
Conclusion: Asymptomatic simple cysts maybe do not require intervention but patients with symptomatic PLD and hepatomegaly there is an unmeet for treatment. Somatostatin Analogues (SAs) is the first choice for inhibiting cyst growth and delaying complications. In these patients further examination becomes necessary if the complaint is getting worse

Abstract #2071

Pancreatic pseudocysts associated with primary hyperparathyroidism in a 28-year-old man: a case report

Akhmad Fajrin Priadinata[1], Rebekka Martina[2], Monica Raharjo[2], Wahyu Purnama[2], Fathony Arsyad[2], Kemal Fariz Kalista[2], Saut Horas Hatoguan Nababan[2], Sahat B. R. E. Matondang[3]

[1]Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [3]Department of Radiology, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Pancreatic pseudocysts are complications of pancreatitis. Primary hyperparathyroidism (PHPT) is rarely associated with pancreatitis. Hypercalcemia plays a major role in the pathogenesis.
Case report: A 28-year-old man with a history of alcoholism since 18 years old, presented with epigastric pain after meals and fever. Pancreatic pseudocyst was documented during his last admission from abdominal tomography and abdominal ultrasound examination. Percutaneus Transhepatic Biliary Drainage (PTBD) was performed to drain the fluid from the pancreatic cyst. He often experience pain in the bones, especially in the spine. Laboratory results reported calcium level was 12.8 mg/dl, parathyroid hormone levels 372 pg/ml, increased levels of amylase and lipase of 78 U/l and 133 U/l. Physical examination revealed palpable mass on the left neck, specifically on the left thyroid lobe, sized 0.3 × 0.3 cm × 0.1 cm.
Discussion: After 2 months of drainage attachment, PTBD still continuously producing fluid, but the pseudocyst diameter was reduced compared to the previous size of 2.28 × 2.63 cm. Elevated parathyroid hormone and high serum calcium levels could be responsible for calcium deposit in the pancreatic ducts and activation of pancreatic enzymes, which may be the main risk factors for

developing acute pancreatitis, which can cause pancreatic pseudocyst as complication.
Conclusion: The occurrence of pancreatic pseudocysts hyperparathyroidism is rare. When it occurs, it is associated with severe pancreatitis which need more attention and be subject to complementary explorations to search a benign or malignant cause

Abstract #2117

Liver cystic metastasis in a patient with gastric adenocarcinoma

Monica Raharjo[1], Rebekka Martina[1], Wahyu Purnama[1], Fathony Arsyad[1], Kemal Fariz Kalista[1], C. Rinaldi A. Lesmana[1], Taufik Agung Wibowo[2], Marini Stephanie[3]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Department of Radiology, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [3]Department of Anatomic Pathology, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Liver cystic metastasis are rare and are not immediately suspected in patients with cystic hepatic lesions unless there is a history of malignancy. We report a patient with liver cystic metastasis previously diagnosed as a hydatid cyst.
Case Illustration: A 65-year-old previously-well female farmer was admitted with abdominal pain, nausea, and decreased appetite for the past one month. Hepatomegaly and tenderness in the upper abdomen were found on abdominal examination. Multiple cystic lesions with mixed cystic and solid parts occupying both lobes of the liver were visualized on ultrasonography. Multiphase computed tomography also revealed partly septate and partly solid multiple cystic lesions in both lobes of the liver. Solid parts of the lesion in segment V, VII, and VIII of the liver were enhanced. Hepatomegaly, para-aortic lymphadenopathy, and diffuse thickening of the gastric mucosa were also seen. Aspiration of cyst was performed yielding 500 ml of reddish-brown exudate negative for microorganisms. Atypical cells were found on fluid cytology. The patient was discharged and treated with albendazole before readmission. Esophagogastroduodenoscopy, done due to melena, revealed a gastric mass (biopsy consistent with well-differentiated gastric adenocarcinoma). No improvement of hepatic cyst was observed on follow-up imaging. Two consecutive cyst aspirations were done yielding 900 ml and 1000 ml of fluid respectively. Repeat fluid cytology also found atypical cells. Chest computed tomography revealed multiple nodules in both lungs. The patient received palliative care.
Conclusion: The diagnosis of cystic metastasis should be considered in patients with multiple cystic lesions of the liver.

Abstract #2138

Role of rapid on-site evaluation of fine needle aspirate under ultrasound guidance in characterisation of hepatic lesions: 10-year experience

Patil N

Introduction: Fine needle aspiration (FNA) under image guidance has been accepted as the diagnostic procedure of choice for hepatic lesions. Rapid on-site assessment improves the diagnostic accuracy and guides in sample triaging for several ancillary studies.
Objective: To analyse the diagnostic accuracy of on-site cytologic assessment in the detection and correct subtyping of hepatic lesions.
Methods: Retrospecctive evaluation of 1539 consecutively registered patients with hepatic lesions who underwent ultrasound guided FNA during the period 2010–2019 was done. Age, gender, number of passes, adequacy, methods of confirmation of diagnosis were recorded. An average of 2–3 passes was carried out. May Grunwald Giemsa (MGG) stain was used as rapid stain. Rapid on-site assessment of the smears was done by the pathologists who made a preliminary diagnosis of positive or negative for malignancy for each lesion. Subtyping was attempted in every case. Material was also taken for cell block preparation whenever feasible. Immunohistochemical (IHC) staining was carried out for confirmation of diagnosis.
Results: With immediate cytologic analysis, 1041 malignant lesions were correctly identified as malignant and 179 benign lesions. Rest of the 318 cases were inadequate for diagnosis. Biopsy was available in 158 cases. Among them, 76 cases were true negatives and 82 cases false negative.
Conclusion: On-site evaluation of FNA of hepatic lesions has high accuracy (93.1%), specificity (100%), positive predictive value (100%) in diagnosing a lesion as malignant versus benign. Cell blocks and IHC assisted in further characterisation of the lesions

Abstract #2146

Assessment of the risk factors for severity in post endoscopic retrograde cholangiopancreatography pancreatitis

Malak Mohamed[1], El-Sayed Ramy[2]

[1]Department of Internal Medicine, Sohag Faculty of Medicine, Sohag, Egypt, [2]Department of Tropical Medicine and Gastroenterology, Sohag Faculty of Medicine, Sohag, Egypt.

Introduction: Post endoscopic retrograde cholangiopancreatography pancreatitis (PEP) is an unavoidable endoscopic complication for pancreatobiliary systems. There are many reports about these risk factors; however, there are few reports to assess the risk factors of severe PEP (sPEP).
Objectives: Our aim was to determine the risk factors of sPEP retrospectively and clarify the indication of prophylactic treatments.
Methods: At our hospital, endoscopic retrograde cholangiopancreatography (ERCP) was performed on 1250 patients from May 2015 to May 2019. Of these patients, we enrolled all 125 patients that were diagnosed with PEP. Fourteen of 125 patients diagnosed as sPEP were analyzed.
Results: Forty-one patients had contrast media remaining in the pancreatic duct after completion of ERCP. Seventy-one patients had abdominal pain within three hours after ERCP. Ten patients had past history of pancreatitis. These were significant differences for sPEP ($p < 0.05$). The median of Body mass index, the median time for ERCP, the median serum amylase level of the next day, past history including drinking and smoking, sphincter of Oddi dysfunction, whether emergency or not, expertise of ERCP procedure, diverticulum nearby Vater papilla, whether there was sphincterotomy or papillary balloon dilation, pancreatic duct cannulation and transpapillary biopsies had no significant differences with sPEP.
Conclusions: Contrast media remaining in the pancreatic duct after completion of ERCP and the appearance of abdominal pain within three hours after ERCP were risk factors of sPEP. The presence of these findings is an indication of early therapeutic intervention for sPEP.

Abstract #2149

Pseudomyxoma peritonei: a rare cause of ascites

Nadim Marchian Tedyanto[1], Kemal Fariz Kalista[2]

[1]Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta Indonesia, [2]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia.

Introduction: Pseudomyxoma peritonei (PMP) is a a poorly understood and rare malignant growth condition characterized by accumulation of gelatinous material in the abdominal and pelvic cavity along with mucus-secreting (mucinous) tumor cells over the peritoneum and omentum. We present two cases of pseudomyxoma peritonei as an unusual cause of ascites.
Case report 1: A 60-year-old man presented with recurrent abdominal pain and marked abdominal distension since 6 months ago. Physical examination revealed a massive ascites of unknown origin. The abdominal CT-scan found massive ascites with multiple components of solid density and "scalloping" appeareance of liver and spleen.
Case report 2: A 57-year-old man presented with recurrent abdominal distension since 2 months ago. Physical examination found a significant ascites. The abdominal CT-scan found massive ascites with displacement of colon and "scalloping" appeareance of liver.
Discussion: In these two cases, the patients were diagnosed with PMP after CT-scan results revealed pathognomonic findings for PMP. Classic "scalloping" of visceral surfaces of the liver and spleen can also be found which distinguishes mucinous from fluid ascites. Both patients were referred for percutaneous placement of a pigtail catheter drainage for the management of ascites.
Conclusion: The unusual behaviour of PMP tend to lead clinician to advocate no active treatment. However, it is increasingly obvious that most patients with untreated PMP will progress to terminal starvation through intestinal obstruction by mucinous ascites. Recent evidences suggest that the initial high morbidity and mortality observed with cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC) decreases with increasing experience

Abstract #2185

Non-Hodgkin lymphoma as a cause of obstructive jaundice: a rare case report

Wahyu Purnama[1], Fathony Arsyad[1], Monica Raharjo[1], Rebekka Martina, Kemal Fariz Kalista[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Hepatobiliary involvement by malignant lymphoma is usually secondary manifestation of systemic disease while Non-Hodgkin's lymphoma of the extrahepatic biliary duct is an extremely rare entity.
Case report: A 40-year-old man was admitted with progressive jaundice. The patient had performed needle biopsy of the neck mass and was diagnosed with Tuberculosis. On physical examination showed jaundice with scleral icterus, hepatomegaly. The laboratory showed pancytopenia, a total bilirubin level of 20.13 mg/dL, direct bilirubin level of 18.10 mg/dL, indirect bilirubin level of 2.03 mg/dL, elevated transaminase levels (SGOT, 472 IU/L and SGPT, 678 IU/L), alkaline phosphatase 613 IU/L, lactate dehydrogease (LDH) of 561 IU/L. Abdominal ultrasonography and computed tomography revealed intrahepatic and common hepatic ducts dilatation while magnetic resonance cholangiopancreatography showed a mild common bile duct stricture. Histopathology and immunohistochemistry revealed a large B cell non-Hodgkin's lymphoma.
Discussion: Non-Hodgkin lymphoma as caused of a biliary obstruction accounts 1–2% of all cases. It's very difficult to diagnose primary lymphoma of the bile ducts from other causes of obstructive jaundice. Ali Zakaria study, 2017 et al revealed there is no consensus on the best treatment modality to used but surgery is important for establishing the diagnosis and removing the lymphoma, that subsequent chemotherapy and or/ radiotherapy after initial surgery might be effective.[1,2]
Conclusion: It's very important to differentiate non-Hodgkin's lymphoma of the bile ducts as caused of obstructive jaundice. Despite it's a rare case, we would be considered as differential diagnosis.

Abstract #2192

Cirrhotic portal hypertension and normochromic normocytic anemia due to myelofibrosis in a 65-year-old man: a case report

Rebekka Martina[1], Monica Raharjo[1], Wahyu Purnama[1], Fathony Arsyad[1], Baiq Kirana Dyahningrum Mandasari[1] Kemal Fariz Kalista[1], Saut Horas H. N[1], Andri Sanityoso Sulaiman[1], Irsan Hasan [1], Sahat B. R. E. Matondang[2]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Department of Radiology, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Patients with Myelofibrosis might develop Portal Hypertension (PH). Exact mechanisms leading to are still controversial. variceal bleeding and ascites, anemia are the most common presentations.
Case report: A 65-year old man presented with abdominal pain, fatigue. No history of viral hepatitis, alcohol. Patient as a history stomach feels enlarged and bloated, melena. Physical examination revealed that the spleen was palpable in shuffner 6, positive shifting dullness. Laboratory tests showed a decreased hemoglobin concentration of 6.7 g/dl, MCV (84.7), MCHC (33.7). Hepatitis B virus, antihepatitis C virus were negative from bone marrow biopsy obtained myelofibrosis results. Abdominal ultrasound and abdominal computed tomography showed the splenomegaly, ascites, liver cirrhosis, portal hypertension. Endoscopy confirmed that upper gastrointestinal bleeding was caused by esophageal varices obliteration, moderate porta hypertension gastropathy. Patient underwent variceal eradication with endoscopic ligation.
Discussion: When thrombosis is absent, sinusoidal narrowing due to the myeloid metaplasia can be seen on liver biopsy so through a discussion in our department a liver biopsy was requested. An intense reactive bone marrow fibrosis that leads to ineffective erythropoiesis and extramedullary hematopoiesis in multiple organs, predominantly the spleen also in the liver resulting in hepatomegaly and splenomegaly.
Conclusion: In absence of thrombosis, both enhanced portal flow from the enlarged spleen and intra-hepatic sinusoidal obstruction have synergistic effects, so that even a slight increase in resistance in the face of enhanced portal flow might produce clinically significant PH. management for this patient because anemia which caused by upper bleeding is blood transfusion, propanolol, sucralfat, spironolakton, lactulac, antibiotic.

Abstract #2193

Pancreatic tuberculosis mimicking head of pancreas carcinoma

Widodo B[1], Viryani NM[1], Nuarwenty M[1] Rahniayu A[2] Septarendra D[3]

[1]Division of Gastroenterology and Hepatology, Internal Medicine Department, Universitas Airlangga, Dr. Soetomo General Academic, Surabaya, Indonesia, [2]Department of Anatomical Pathology, Universitas Airlangga, Dr. Soetomo General Academic, Surabaya, Indonesia, [3]Digeastive Surgery Department, Universitas Airlangga, Dr. Soetomo General Academic, Surabaya, Indonesia

Introduction: Tuberculosis (TB) is serious health problems worldwide, usually involves lung and extra pulmonary. TB of the pancreas is extremely rare and in most of the case mimics pancreatic carcinoma
Methods: To present case of Pancreatic Tuberculosis Mimicking Head of Pnacreas Carcinoma
Result: A 71-yo man presented with recurrent epigastric pain, fever, vomiting, weight loss since 4 month ago. The symptoms followed by jaundice, dark urine and pale of stool and palpable mass in epigastric. History pass illness in 1980 was diagnosed pulmonary TB and recieved specific treatment for 6 month. Physical examination of the palpable mass in the epigastric. Laboratory result was increase ol bilirubin levels, normal Ca 9–9, slight increase of CEA. Abdominal ultrasound was mass in the head of pancreas causes common bile duct (CBD) dilatation. Abdominal CT scan was enhancing solid mass with size 4 × 4.1 × 5.9 cm in the head of pancreas with dilated pancreatic duct and CBD. Patient was diagnosed with head of pancreas carcinoma and peritoneal seeding T3N0M1 underwent double bypass billiodigestive. Biopsy speciment was granulomatic of pancreas with positive Ziehl–Neelsen (ZN) staining and acid fast bacilli (AFB). The patient was given anti tuberculosis drugs for nine months.
Conclusion: Pancreatic TB commonly present with non specific symptoms such as abdominal pain, jaundice, vomiting, anorexia, loss of body weight, it usually involves the head and uncinate process of the pancreas carcinoma. The diagnosis pancreatic TB is a challenge because of the rarity cases. The suspicion of malignancy lead to an unwarranted resection as many cases are diagnosed after surgical. Presence of caseating granulomatous inflammation and acid fast bacilli sugestive of TB.

11. Metabolic and Genetic Diseases

Oral Presentations

Abstract #696

Development and evaluation of a DNA microarrray for detection of *ATP7B* mutations in patients with Wilson disease

Zhou, Donghu[1,2], Jia, Siyu[1,2], Li, Xiaojin[1,2], Zhang, Wei[2,3,4], Wu, Zhen[2,3,4], Zhang, Bei[1,2], Ou, Xiaojuan[2,3,4], You, Hong[1,2,3,4], Huang, Jian[1,2,3,4]

[1]Experimental Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [2] Clinical Research Center for Rare Liver Diseases, Capital Medical University, Beijing, China, [3]Liver Research Center, National Clinical Research Center for Digestive Diseases, Beijing, China, [4]Beijing Key Laboratory of Translational Medicine on Liver Cirrhosis, Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China. On behalf of China Registry of Genetic/Metabolic Liver Diseases (CR-GMLD) Group

Introduction: Wilson disease (WD) is an autosomal recessive copper metabolic disorder caused by mutations in the *ATP7B* gene. Currently, sequencing of the *ATP7B* gene was commonly used for the identification of ATP7B mutation. However, as the *ATP7B* gene contain 21 exons, the sequencing of the entire *ATP7B* gene is complex and time-consuming, other simple assay is urgently needed.
Objectives: We aimed to develop a microarray system, which is easy to operate, for the rapid detection of *ATP7B* mutation characterized by Chinese WD patients.
Methods: Genomic DNA is amplified by a three-tube multiplex and asymmetric polymerase chain reaction, and the fragmented products is hybridized with known nucleic acid probes stabilized on the carrier chip. The mutation loci were recognized by the analysis of fluorescent signals. Vectors containing target loci were constructed for the optimization of reaction conditions and quality control for the microarray. The accuracy of the microarray was evaluated by screening 50 WD patients of which the tested *ATP7B* mutations were confirmed by sequencing.
Results: Thirteen sets of primer and ninety-six probes were designed to develop a microarray for the detection of 24 most common *ATP7B* pathogenic mutations including p.R778L, covering up to 70% of Chinese WD patients reported in China. A reliable detection system with approximately 4 hours testing time was established. The overall consistency rate between the sequencing and microarray is 100%.
Conclusion: The WD microarray can conveniently be customized for high throughput detection of the *ATP7B* mutation and can be easily adapted for WD genetic diagnosis.

Abstract #718

Role of a recurrent *DENND3* p.L708V mutation in Chinese patients with hereditary haemochromatosis

Li Yanmeng[1,2,3,4], Zhang Chunpan[1,2,3,4], Zhang Wei[1,2,3], Wu Liyan[1,2,3], Jia Siyu[2,3,4], Su Yu[1,2,3], Xu Anjian[2,3,4], Jia Jidong[1,2,3], Huang Jian[1,2,3,4]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing Key Laboratory of Translational Medicine on Liver Cirrhosis, Beijing, China, [2]Clinical Research Center for Rare Liver Disease, Capital Medical University, Beijing, China, [3]National Clinical Research Center for Digestive Diseases, Beijing, China, [4]Experimental Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China

Introduction: Hereditary haemochromatosis (HH) is defined as a systemic iron overload disease with genetic heterogeneity. However, there has been a considerable proportion of unexplained cases in China. In our previous study, exome sequencing identified a recurrent p.L708V mutation in Differentially Expressed in Normal and Neoplastic cells Domain (DENND) 3 gene in primary iron overload cases. The DENND3 has been known acting as an activator of small GTPase Rab12, which regulates transferrin receptor (TFR) degradation. However, the role of *DENND3* p.L708V in the pathogenesis of HH remains unknown.
Objectives: We aimed to investigate the frequency and pathogenicity of the *DENND3* p.L708V mutation in HH in China.

Methods: Patients were analyzed for *DENND3* p.L708V mutation and TFR2 cellular localization by Sanger sequencing and immunohistochemical assay respectively. *DENND3* and *DENND3* L708V vectors were constructed and transfected in Huh7 and HepG2 cells with holo-transferrin treatment to analyze the alteration of Rab12, TFR2 and hepcidin expression, and BMP/SMAD pathway. Immunofluorescence assay was performed for co-localization of lysosome marker LAMP-1 and TFR2.
Results: Of 28 unrelated cases with primary iron overload, 6 cases (6/28 21.4%) harbour the *DENND3* p.L708V mutation. Mislocalization and the decrease expression of TFR2 were shown in the patients with *DENND3* p.L708V mutation. In vitro studies showed the mutant p.L708V led to increased expression of Rab12, and the degradation of TFR2 in lysosome, and the down-regulation of the BMP/SMAD pathway and hepcidin.
Conclusion: The *DENND3* p.L708V mutation is involved in the haemochromatosis and may represent a novel pathogenic factor of HH in China.

Abstract #1623

Early hepatic proteomic signatures reveal metabolic changes in high fat induced obesity in rats

Abhishak C Gupta[1], Adil Bhat and Shiv K Sarin[1]

[1]Department of Molecular and Cellular Medicine (MCM), Institute of Liver and Biliary Sciences (ILBS), New Delhi

Prevalence of diet induced obesity has dramatically increased globally, making it essential to understand its accompanying metabolic changes in the liver. Obesity causes many health issues, both independently and in association with other chronic diseases such as diabetes, insulin resistance and nonalcoholic fatty liver disease and also considered as the major risk factor for development of Nonalcoholic steatohepatitis and liver cirrhosis. In the present study we aimed to understand the molecular mechanisms underlying hepatic alterations in the pathophysiology of high fat diet induced obesity in rats. Hepatic proteins profile of normal and high fat fed induced obesity at 24 weeks were analyzed using two-dimensional difference gel electrophoresis (DIGE) and mass spectrometry for protein identification. Fifty two protein spots were identified by MALDI-TOF and computer-assisted DIGE image software analysis showed 18 major proteins significantly differentially expressed between the comparable groups more than 2.0 to 4.0 fold changes. These proteins were modulated in response to the high-fat diet. Differentially expressed proteins were involved in important metabolic pathways including lipid metabolism, energy metabolism, detoxification, urea cycle and calcium homeostasis in the liver. Further, western blot and immunohistochemistry of liver specific Arginase-1 showed significantly over expression in high fat fed rat liver ($p > 0.01$). Interestingly, Arginase-1 expression differentiates NASH progression. High fat in the diet might influence changes in metabolic pathways in the liver such as lipid metabolism, urea cycle and mitochondrial dysfunction could be the therapeutic targets in management of obesity related liver disease. Arginase 1 expression might be a potential pathological marker to assess liver disease progression.

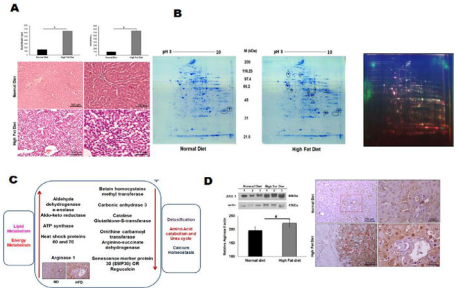


Figure: A. Graphical representation of Body weight and Aspartate aminotransferase (AST) levels in normal and high fat fed rat. Liver sections from normal and high fat fed rats are stained for Hematoxylin and Eosin (H & E). **B.** Preparative 2D Gel electrophoresis images for differentially expressed proteins in the respective groups for MALDI-TOF protein identifications. Fluorescent 2DE image is showing protein expression profile of normal and high fat fed rat liver (DIGE). C. Differentially expressed liver proteins in comparable groups. **D.** Western Blot of arginase-1 expression in Liver homogenate of comparable groups and representative quantitative Graph of Arginase-1 expression. Immunohistochemical staining for arginase-1 in liver sections of normal diet and High fat diet rat model.

Abstract #2100

Uncoupling protein-2 is involved in the development of non-alcoholic steatohepatitis via impairing mitochondrial function

Li Dongdong[1,2], Dong Shiming[1,2], Zhao Dandan[1,2], Du Jinghua[1,2], Zaid[1,2], Yuan Xiwei[1,2], Nan Yuemin[1,2]

[1]Department of Traditional and Western Medical Hepatology, Third Hospital of Hebei Medical University, 050051 Shijiazhuang, China, [2]Director of Hebei Provincial Key Laboratory of liver fibrosis in chronic liver diseases

Background and aim: Patients with Non-alcoholic fatty liver disease (NAFLD) exhibit serios hepatic steatosis and inflammation. Mitochondrial dynamics plays an important role in abnormal lipid metabolism, oxidative stress and the development of inflammation in NAFLD development. However, the regulator of mitochondrial dysfunction in NASH remains unclear. Studies found that uncoupling protein-2 (UCP-2) played a crucial role in inhibition of hepatic inflammation of NASH. Our study is aimed to clarify the mechanism of UCP-2 in regulation of mitochondrial dynamics through animal models, cultured hepatocytes and patients with NASH.
Methods: Sixty NASH patients and 30 healthy controls were enrolled. The serum UCP-2 and HO-1 levels were determined by ELISA. The male wild-type (WT) C57BL/6 J mice at 8 weeks were fed with methionine and choline deficient (MCD) diet for 4 weeks or high fat-high carbohydrate-high cholesterol (HFHC) diet for 16 weeks to induce steatohepatitis (6 $\sim$ 7 mice per group). Oil Red O, H & E staining were performed for observation of hepatic and cell steatosis inducing by palmitic acid (PA) and inflammation in human hepatocytes. The changes of mitochondrial ultrastructural and structure were assessed by TEM and Mito-Tracker respectively. The mRNA and protein expressions of UCP-2, apoptosis and inflammation related genes were detected by RT-PCR, Western blot, IFT and IHC, and apoptosis by flow cytometry. Hepatic levels of ROS, 8-OH-dG and ATP were examined by assay kit, respectively.
Results: The serum levels of UCP-2 in NASH patients were notably increased and HO-1 were decreased compared to the healthy controls (9.11 ± 0.36 vs. 12.59 ± 0.32, $P < 0.01$; 17.00 ± 3.30 vs. 9.09 ± 2.19, $P < 0.05$, respectively). As compared to control mice, MCD or HFHC mice significantly aggravated liver injury, which companied decreased expression of mitochondrial function genes MFN1, MFN2 and OPA1 in the NASH mice. Similar changes were observed in cultured hepatocytes, which companied increased expressions of the mitochondrial function genes and suppression of inflammation and apoptotic genes (TNF-α, IL-6, IL-1β, Bid, Bcl-2, caspase 3). Under confocal microscopy, swelled and fusion disappeared mitochondria were presented in cells. The mitochondrial dynamics was evidenced by reduced membrane potential and ATP

content, increased mitochondrial ROS, 8-OH-dG accumulation in PA group.
Conclusion: UCP-2 plays a crucial role in the pathogenesis of steatohepatitis. It is certified that UCP-2 might be a potential serum biomarker for the selective, diagnosis and personalized therapy of NASH.

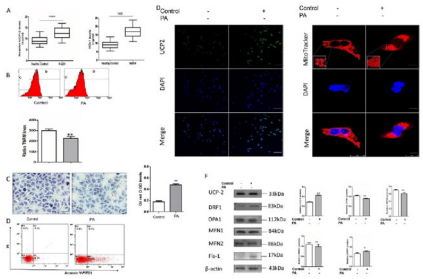


Fig. UCP-2 is involved in the mitochondrial dysfunction in the non-alcoholic fatty liver disease *in vivo* and *vitro*

Poster Presentations

Abstract #100

Spectrum of Budd-Chiari syndrome in a tertiary care center in india with special reference to endovascular management

Ansari J[1], Mathew P[2], Kanni P[3], Pandey S[4], Garg A[1], Gowda M[1]

[1]Senior Resident, Department of Gastroenterology and Hepatology, VIMS & RC, Bangalore, India, [2]Professor, Department of Gastroenterology and Hepatology, VIMS & RC, Bangalore, India, [3]Associate Professor, Department of Gastroenterology and Hepatology, VIMS & RC, Bangalore, India, [4]Associate Professor and Interventional Radiologist, Department of Radiology, VIMS & RC, Bangalore, India, Electronic address: jaseem10ansari@gmail.com

Background: Budd-Chiari syndrome (BCS) is characterized by hepatic venous outflow tract obstruction at various levels from small hepatic veins (HV) to inferior vena cava, resulting from thrombosis or its fibrous sequellae. Here we evaluate the patterns of obstruction, etiological spectrum and the various technical approaches to the endovascular management of patients with BCS in India.
Methods: 7 cases of BCS who presented with jaundice, ascites and pain abdomen were evaluated. All patients were subjected to radiological intervention via jugular route or femoral route or both depending on the morphology of inferior vena cava (IVC) and/or HV obstruction.
Results: Mean duration of symptoms were 18 ± 6 months. HV thrombosis (HVT) was present in 4 cases (57.14%), combined hepatic vein stenosis and IVC obstruction was seen in 2 cases (28.57%) and IVC thrombosis in 1 case (14.28%). Of the cases tested for hypercoagulability, 5 (71.42%) were positive for hypercoagulable states. Radiological intervention was technically successful in 7/7 (100%): HV angioplasty and stenting in 2 cases (28.57%), direct intrahepatic portosystemic shunt (DIPS) in 1 case (14.28%), transjugular intrahepatic portosystemic shunt (TIPS) in 1 case (14.28%), combined IVC angioplasty—HV angioplasty with stenting in 2 cases (28.57%) and IVC balloon angioplasty in 1 case (14.28%). None of the cases had complications during follow-up.
Conslusion: In our series, HVT was the predominant cause of BCS. All the patients underwent complex endovascular intervention which were successful and were also evaluated for the etiology of BCS.

Abstract #342

Non-cirrhotic hyperammonemia causing periodic behavioral changes: a case report

Theodorus Rinaldo, MD[1,3], Marc Julius H. Navarro[2,3], Angelica Joy Alonte[2,3]

[1]Department of Medicine, [2]Institute of Digestive and Liver Diseases, [3]St. Luke's Medical Center, Quezon City, Philippines

Significance: One of the most common causes of emergency room presentation is an acute or progressive deterioration inmental status. Any case of acute altered mental status should prompt a consideration of hyperammonemia as a potential cause. While hyperammonemia in adults is related to severe, often cirrhotic, liver disease in 90% of cases.
Clinical presentation: A 68-year-old woman with periodic behavioral changes presenting as decreased verbal output, slurring of speech and laughing spell which attributed with constipation. Physical examination was unremarkable with no stigmata of chronic liver disease.
Management: Diagnostics were done, she had unremarkable complete blood count, kidney function, electrolytes, capillary blood glucose and thyroid function test. She also has unremarkable brain MRI, EEG results and cerebrospinal fluid studies with negative blood culture results. Her liver function test showed unremarkable results with negative results for hepatitis B and C with normal liver elastography with Vs value of 1.44 m/s and 6.72 kPa.. Her ammonia was elevated as high as 138 µmol/L. She was diagnosed as a case of non-cirrhotic hyperammonemia secondary to a probable slow transit type of constipation and started on L-Ornithine L-Aspartate drip, lactulose, and rifaximin with noted markedly improvement of her sensorium as well as serum ammonia level.
Recommendations: The diagnosis of hyperammonemia may be challenging and requires a high index of suspicion. Awareness of hyperammonemia in absence of severe hepatic disease may lead to lifesaving prompt diagnosis and treatment. Aggressive management with reducing ammonia generation and uptake and increase ammonia removal is warranted.

Abstract #375

Risk factors of pancreatic cancer patients in Dr. Cipto Mangunkusumo National Referral Hospital Jakarta during 2014–2019

Renaldi Kaka[1], Septianto Teddy[1], Makmun Dadang[2]

[1]Gastroenterology Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia

Introduction: Pancreatic cancer is a very rare human cancer with age-adjusted rates ranging from about 5 to 10 new cases per 100,000 persons per year. Pancreatic cancer has one of the worst prognoses of any type of cancer, with a 5-year survival rate of only 4.6%. The major risk factors were smoking, a family history of pancreatic cancer, obesity, pancreatitis, diabetes mellitus, and alcohol consumption.
Objectives: To identify the prevalence of risk factors in pancreatic cancer patients at the dr. Cipto Mangunkusumo National Referral Hospital (RSCM), Jakarta.
Method: This descriptive study involved pancreatic cancer patients admitted in RSCM during 1 January 2014–1 January 2019. Data was obtained from the patient's medical record and Endoscopic

Retrograde Cholangiopancreatography (ERCP) data stored at the RSCM Gastrointestinal Endoscopy Center

Results: There were 123 patients with newly diagnosed with pancreatic cancer during the study period. The mean age of all patients was 52 years old. Pancreatic cancer was more common in men (53%) than women (47%). The results showed that the most common risk factor was smoking (29%), followed by obesity (27.9%), and a history of diabetes mellitus (19.5%). Risk factors with a low prevalence included alcohol consumption (9.7%) and chronic pancreatitis (2.4%). Interestingly, no family history of pancreatic cancer was found in the subjects.

Conclusion: This study showed that the common risk factors identified in pancreatic cancer patients were smoking, obesity and diabetes. On the other hand, risk factors with low prevalence were chronic pancreatitis, alcohol consumption, and family history of pancreatic cancer.

Abstract #529

The frequency of identified genetically determined thrombophilia in patients with portal vein thrombosis in the «National Research Oncology Center», Hepatology & Gastroenterology, Nur-Sultan, Kazakhstan

Zhanasbayeva M.[1], Prokopenko Y.[1], Baromyko N.[1], Kairalapova A.[1], Aginbay A.[1], Ashimkhanova A.[2]

[1]National Research Oncology Center, Hepatology and Gastroenterology, Nur-Sultan, Kazakhstan, [2]Nazarbayev University School of Medicine, Medicine, Nur-Sultan, Kazakhstan

Introduction: For the period from September 2017 to December 2018, 14 patients with presinusoidal portal hypertension in the presence of chronic portal vein thrombosis were examined at the Department of Gastroenterology, Hepatology and General Therapy "NROC". Among the examined were 4 men and 9 women. The average age was 31 years (from 19 to 51 years).

Aims & Methods: TVV verification was carried out using ultrasound dopplerographic examination of the vessels of the portal system, as well as computed or magnetic resonance imaging, or a combination thereof. Most of the patients were referred with a diagnosis of "presinusoidal portal hypertension" (64.3%), "cirrhosis of unclear etiology" (21.4%), "liver cirrhosis in the outcome of viral hepatitis C (7.14%), "portal vein thrombosis" (7.14%). In our center, a differential diagnostic search for the etiology of portal vein thrombosis was carried out. After excluding the acquired causes of thrombosis (antiphospholipid syndrome, myeloproliferative diseases, paraneoplastic process, inflammatory diseases of the abdominal organs, injuries/surgical interventions), the patients were referred to a molecular genetic study of thrombophilia predisposition genes

Results and conclusion: Among 14 patients, 8 (61.5%) were found to have mutations in the blood coagulation system genes. The most common mutations were gene polymorphisms of significant thrombophilia, such as heterozygous factor V gene polymorphism (Leiden), found in 7 patients (87.5%). This is followed by polymorphism G20210A of the factor II gene, detected in 6 patients (75%). 5 patients (62.5%) have polymorphism of the methylenetetrahydrofolate reductase gene. The most common combination of mutations was the polymorphisms of the factor V (Leiden) genes in the heterozygous state, the G20210A polymorphism of the factor II gene, the C 677T UTYF MTHFR gene in the heterozygous state.

Abstract #595

Mutation frequency and genotype-phenotype correlation of *SLC40A1* gene in hemochromatosis in China

Zhang Wei[1,2], Wu Liyan[1,2], Li Yanmeng[2,3], Xu Anjian[2,3], Wang Xiaoming[1,2], Wang Yu[1,2], Duan Weijia[1,2], Zhao Suxian[4], Nan Yuemin[4], Huang Jian[2,3], Ou Xiaojuan[1,2], You Hong[1,2], Jia Jidong[1,2]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [2]National Clinical Research Center for Digestive Diseases, Beijing, China, [3]Experimental Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [4]Department of Traditional and Western Medical Hepatology, Third Hospital of Hebei Medical University, Shijiazhuang, China

Introduction: Hemochromatosis type 4 is an autosomal dominant genetic disorder caused by pathogenic mutations in the *SLC40A1* gene, which encodes ferroportin. It can be classified as type 4A due to "loss of function" mutations and type 4B caused by "gain of function" mutations. However, the mutation frequency and genotype-phenotype correlation of *SLC40A1* in hemochromatosis in China is not clear.

Objectives: Tried to investigate the mutation frequency and the genotype-phenotype correlation of *SLC40A1* in hemochromatosis in China.

Methods: Patients with primary iron overload were detected for mutations in the *HFE*, *HAMP*, *HJV*, *TFR2*, and *SLC40A1* genes by Sanger sequencing. The correlation of clinical phenotype and genotype was analyzed.

Results: Of 28 unrelated cases with primary iron overload, nine cases (9/28, 32.1%) were identified with *SLC40A1* heterozygous mutations: three cases with p.Y333H, two cases with IVS1-8C>G, and the other four cases with p.N144D, p.V162del, p.V511I and IVS3 + 10delGTT, respectively. The average age was 51 ± 9 years, and five patients were male. Only the patient with p.V162del manifested with hyperferritinemia (5949 ng/ml) and low transferrin saturation (TS) (28%), a typical feature of mutations with "loss of function". The other eight patients presented with hyperferritinemia (median: 4076 ng/ml (685, 15000)) and high TS (median: 94% (71%, 97%)), a typical feature of mutations with "gain of function". All the patients presented iron overload in the liver on MRI, liver biopsy of 7 patients showed severe iron overload in hepatocytes, these characteristics were similar to hemochromatosis type 4B.

Conclusion: *SLC40A1* mutations were recurrently identified in patients with primary iron overload in China, and with the phenotype of hemochromatosis type 4B.

Abstract #603 ***HFE*-related hemochromatosis in a Chinese patient: the first reported case**

Zhang Wei[1,2], Wang Xiaoming[1,2], Duan Weijia[1,2], Huang Jian[2,3], Ou Xiaojuan[1,2], You Hong[1,2], Jia Jidong[1,2]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [2]National Clinical Research Center for Digestive Diseases, Beijing, China, [3]Experimental Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China

Introduction: Hereditary hemochromatosis (HH) is a most common genetic iron overload disease in European populations. It is reported that the *HFE* p.C282Y mutation is present in 1/10 people of northern European descent. However, *HFE* p.C282Y mutation is virtually absent among East Asians. Here we report a case of HFE-related

hemochromatosis caused by compound heterozygosity HFE p.C282Y/p.R71X in China.

Methods: Cases with primary iron overload were detected for mutations in the *HFE*, *HAMP*, *HJV*, *TFR2*, and *SLC40A1* genes by Sanger sequencing. Genetic determinations were also performed in his parents for pedigree analysis.

Results: A 28-year-old male was admitted to our department complaining of having persistent abnormal liver function test results for 8 years, without any symptoms. He denied taking supplemental iron and consuming excess alcohol. Physical examination was normal. Laboratory tests results were as follows: ALT 106U/L, AST 41U/L, ferritin 3033 mg/L, transferrin saturation 86.4%. Serum markers for viral hepatitis and autoimmune liver disease were normal. MRI showed severe iron overload in the liver. Liver biopsy showed severe iron deposited predominantly in hepatocytes. Genetic detection showed the patient carried two heterozygous mutations p.C282Y, and p.R71X in the *HFE* gene, no mutations were identified in the other HH-related genes. The patient's father and mother carried a heterozygous mutation p.C282Y or p.R71X in the *HFE* gene, respectively, indicating the mutation pattern of p.C282Y/p.R71X in the *HFE* gene in this case.

Conclusion: *HFE*-related hemochromatosis was identified in a Chinese hemochromatosis patient for the first time. Although very rare in Asians, this diagnostic possibility should not be ignored.

Abstract #640

A case report of rare cause of abnormal liver function: sitosterolemia

Shen Yi, Fan Xiaoli, Men Ruoting, Yang Li

Department of Gastroenterology and Hepatology, West China hospital, West China School of Medicine, Sichuan University, Chengdu, China

Introduction: Gene mutation of ABCG8 and concomitant abnormal liver function are rarely seen in Sitosterolemia.

Objective: To report a patient with sitosterolemia.

Method: The patient was a 27-year-old male, he began to have epistaxis and gingival bleeding 7 years ago. Then, he came to local hospital to treat sever epistaxis, and examinations showed that he had splenomegaly and abnormal liver function. Thereupon, splenectomy and liver biopsy were performed, but he still had intermittent epistaxis. And the cause of abnormal liver function was unknown. Then, the patient was transferred to our hospital. Examinations showed his body mass index was 19.05 Kg/m^2, and blood tests found some abnormality (see Table 1). The second liver biopsy was performed and it showed about 20% hepatocytes have vesicular steatosis and considered as chronic hepatic inflammation (G2/3S2). However, the diagnosis was still unclear. So the genetic screening was continued, and homozygous mutation in ABCG8 was finally found. Therefore, the patient was confirmed of sitosterolemia. Then, we tested his serum plant sterols and found campesterol and β-sitosterol increased significantly. In addition, many stomatocytes were presented in his peripheral blood smear. Results All of these findings were consistent with sitosterolemia. After the diagnosis, ezetimibe was given immediately, to our surprise, no epistaxis occurred any more to the patient. And his peripheric platelet count had returned to normal, liver function began to improve.

Conclusion Genetic screening should be considered when the cause of abnormal liver function cannot be determined by routine examinations.

Table 1. Results of blood tests

Parameter	Results	Reference range
Platelet	94 *10^9/L	100-300
Hemoglobin	139 g/L	130-175
Total bilirubin	21.1 umol/L	5-28
Direct bilirubin	6 umol/L	<8.8
Alanine aminotransferase	203 IU/L	<50
Aspartate aminotransferase	114 IU/L	<40
Alkaline phosphatase	234 IU/L	51-160
Glutamyl transpeptidase	9 IU/L	<60
Total bile acid	16.5 umol/L	<15
Triglyceride	0.72 mmol/L	0.29-1.83
Cholesterol	4.24 mmol/L	2.8-5.7
Campesterol	44.56 umol/L	0.01-10
β-sitosterol	108.03 umol/L	1-15
Prothrombin time	13.2 s	9.6-12.8
International normalized ratio	1.21	0.88-1.15

Abstract #655

Alagille syndrome with a novel identified mutation site in a 16-old patient: a case report

Qi Wang[1], Rui Ding[1], Wen Xie[1]

[1]Center of Liver Diseases, Beijing Ditan Hospital, Capital Medical University, 100015 Beijing, China

Alagille syndrome (ALGS) is an autosomal dominant genetic disease mainly caused by JAG1 gene mutation. Second-Generation Sequencing of the patient's is conducive to the diagnosis of ALGS, but the evidence of correlation between genotype and phenotype is still very limited. This paper reports a case of novel gene mutation and significant clinical characteristics. The patient was a 16-year-old male from China. After he was born, he was repeatedly treated for jaundice, but the condition continued to progress. Physical examination showed that the patient had stunting, special face, decompensated cirrhosis, hypoproteinemia, portal hypertension, ascites, and ocular changes. Ultrasound-guided liver biopsy pathological examination showed that Intrahepatic bile duct loss, chronic cholestasis. The patient and his mother's second-Generation sequencing of peripheral blood DNA showed that heterozygous mutation of c.1156G>A of JAG1 gene resulting in p.G386R. The HGMD database suggested the gene locus might be pathogenic. Above all, we thought he should be diagnosed ALGS clearly. After 18 months of follow-up, the patient developed upper gastrointestinal bleeding, hepatic encephalopathy, and eventually died of liver failure. Summary: early gene testing of cholestasis in adolescents and infancy is recommended for early diagnosis of ALGS.

Abstract #680

Insertion of LINE-1 retrotransposon inducing exon inversion causes a rotor syndrome phenotype

Zhou Donghu[1,2,3], Qi Saiping[1,2,3], Zhang Wei[2,3,4,5], Wu Lina[2,3,4,5], Zhang Bei[1,2,3], Ou Xiaojuan[2,3,4,5], Huang Jian[1,2,3,4,5], You Hong[1,2,3,4,5]

[1]Experimental Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [2]Clinical Research Center for Rare Liver Diseases, Capital Medical University, Beijing, China, [3]National Clinical Research Center for Digestive Diseases, Beijing Friendship Hospital, Beijing, China, [4]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [5]Beijing Key Laboratory of Translational Medicine on Liver Cirrhosis, Beijing Friendship Hospital, Beijing, China, On behalf of China Registry of Genetic/Metabolic Liver Diseases (CR-GMLD) Group

Introduction: Rotor syndrome is caused by biallelic pathogenic mutations in both SLCO1B1 and SLCO1B3. Insertion of the long

interspersed element-1 (LINE-1) into gene loci can interfere with gene expression, or lead to aberrant splicing and frameshift mutations. To date, only a few mutations have been identified, and no information was reported in Chinese patients.
Objectives: To screen mutations in Chinese patients with Rotor syndrome and explore whether an exon 4 inversion in SLCO1B3 could cause a Rotor syndrome phenotype.
Methods: Sanger sequencing was used to identify mutations in SLCO1B1 and SLCO1B3 in a patient with Rotor syndrome. A genome walking strategy was used to identify the unknown sequence between SLCO1B3 exons 3 and 5. The pET-01 vector was used as a splicing reporter to analyze whether exon 4 was present in the mature mRNA.
Results: An exon 4 inversion in SLCO1B3 was identified in a patient with Rotor syndrome, combined with a nonsense variant (SLCO1B1, p.R580X). Genome walking analysis showed that a 1,184 bp DNA segment, containing the entire exon 4 and adjacent intron sequence, was reversed end-to-end in SLCO1B3, which may generate a premature termination codon (p.Y120X). A LINE-1 was inserted upstream of the inverted DNA fragment. RT-PCR showed that the inverted exon 4 was absent from the mature mRNA.
Conclusion: We identified a novel exon 4 inversion in SLCO1B3 of a patient with Rotor syndrome, which may be induced by the insertion of a LINE-1 retrotransposon into SLCO1B3 intron 3.

Abstract #776

Gall stone is "active" in elderly males

Sun Chunyan, Wang Xuedong, Xiang Canhong, Gong Lei, Shi Jun, Zeng Jianping, Yang Shizhong, Wang Liang, Huang Yuan, Han Dongdong, Lu Qian, Tang Rui, Yan Jun, Yang Ming, Feng Xiaobin, Xu Guangxun, Zhang Lin, Zhang Yuewei, Wei Lai, Dong Jiahong

Hepatopancreatobiliary Center, Beijing Tsinghua Changgung Hospital, Tsinghua University, Beijing, China

Introduction: Complicated gall stone disease (GSD) is a common surgical entity worldwide. However, the age distribution of complicated GSD has not been well described.
Objectives: To study the age distribution of complicated GSD in both males and females, and compare the metabolic traits between the complicated GSD group and the non-complicated group.
Methods: We consecutively assembled a retrospective cohort of patients with GSD at Beijing Tsinghua Changgung Hospital from 1/11/2015 to 1/10/2019.
Results: Out of the 1395 patients, 859 (42.6% male) and 536 (35.6% male) patients were with and without complicated GSD. The number of females with complications peaked in the fifth decades, so did that without complications ($p = 0.217$). However, the age distribution in males was significantly different ($p = 0.005$). The number of males with complications peaked in the seventh decades, while the peak of that without complications appeared in the fifth decades. The frequency of complicated GSD was higher among males aged > 60 years than that among males aged ≤ 60 years (72.7% vs. 61.3%, $p = 0.006$). 36.7% and 21.6% female patients aged ≤ 60 years with and without complicated GSD had dyslipidemia ($p = 0.000$). The percentages in the males aged ≤ 60 years were 55.5% and 34.8% ($p = 0.000$). In females or males aged > 60 years, there was no significant difference in the two groups (42.1% vs. 32.4%, $p = 0.092$ and 47.4% vs. 41.4%, $P = 0.423$). Nor hypertension or diabetes were significantly different between the groups with and without complications.
Conclusion: GSD is "active" in elderly males. Patients aged ≤ 60 years were more likely to develop complications with dyslipidemia.

Abstract #1331

New *JAG1* mutation *c2519delA* causing alagille syndrome combined with giant hepatic regenerative nodule

Li XH[1], Huang R[1], Liu F[1], Wang XX[1], Wei L[1,2*], Rao HY[1*]

[1]Peking University People's Hospital, Peking University Hepatology Institute, Beijing Key Laboratory of Hepatitis C and Immunotherapy for Liver Diseases, Beijing International Cooperation Base for Science and Technology on NAFLD Diagnosis, Beijing 100044, China, [2]Department of Hepatobiliary and Pancreatic Center, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University, Beijing 102218, China

Alagille syndrome is a multisystem disease with variable phenotypic penetrance caused by heterozygous gene mutations in *JAG1* and *NOTCH2*, which encode the basic components of the Notch signaling pathway. In this report, we present the case of a 15-year-old Chinese man diagnosed with Alagille syndrome due to chronic cholestasis, vascular anomalies, facial characteristic, bile duct paucity, and gene analysis-confirmed *JAG1* mutation. Abdominal enhanced magnetic resonance imaging showed a benign giant hepatic regenerative nodule adjacent to the right portal vein, with its branch crossing through. Gene analysis revealed an unreported gene mutation of *c2519delA* in *JAG1*, causing p.N840Mfs*30 in amino translation, encoding a truncated protein. This gene mutation was not found in the patient's father and younger brother. This case broadens new pathogenic mutation in *JAG1* and reports the existence of a benign regenerative nodule in a patient with Alagille syndrome, which has not been mentioned in previous studies in the Chinese population.

Abstract #1382

Role of vitamin E and vitamin C for the treatment of Nonalcoholic steatohepatitis in non-diabetic patients

Barbakadze G.G.[1,2], Khachidze T.G.[1,2], Sulaberidze G.T.[1], Burnadze K.G.[2], Jebashvili M.I.[1]

[1]Tbilisi State Medical University, [2]Enmedic Clinic

Background and aim: Nonalcoholic steatohepatitis (NASH) is a frequent liver disease that can progress to cirrhosis and for which effective therapy is still lacking. Despite an important role of oxidative stress in the pathogenesis of NASH, antioxidant approaches have not been investigated sufficiently. The aim of the study was to detect the efficacy of vitamin E and vitamin C combination in non-diabetic patients with nonalcoholic steatohepatitis.
Methods: Patients with elevated aminotransferase levels and drinking, less than 40 g alcohol/week with NASH diagnose were randomly assigned to receive vitamin E 800 mg/day plus vitamin C 500 mg/day (group B) for 12 months and control group, which did not receive any medical treatment. Lifestyle modification was advised to both groups. The primary study end point was improvement in alanine transaminase (ALT) levels, secondary end points were improvement in steatosis score and improvement in fibrosis score.
Results: 72 patients were included 52 in the group A and 20 in control group. Baseline characteristics were not significantly different between groups. After 12 months treatment with vitamin E plus C, was associated with a significant reduction of mean alanine

aminotransferase (ALT) levels. Similarly, there was significant reduction of both mean steatosis score and fibrosis score.
Conclusion: Vitamin E plus C combination is an effective, safe and inexpensive treatment option in patients with NASH and may be useful to reduce damage from oxidative stress and slow the process leading to cirrhosis.

Abstract #1666

Severe jaundice due to rotor syndrome: a rare case report

Andi Alfian[1], Wahyu Purnama[1], Fathony Arsyad[1], Monica Raharjo[1], Rebekka Martina, Andri Sanityoso Sulaiman[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Backgrounds: Rotor syndrome is a rare, benign and inherited cause of hyperbilirubinemia which is often misdiagnosed with Dubin Johnson syndrome.
Case illustration: A 40-year old man was admitted due to asymptomatic persistent jaundice. The family history was unremarkable. Physical examination revealed icteric sclerae without hepatosplenomegaly. Laboratory findings showed increased serum bilirubin with direct bilirubinemia. A urine coproporphyrin exhibited an elevation and histology of the liver showed no pigmentation.
Discussion: Rotor syndrome is a rare case autosomal recessive disorder, which is benign and asymptomatic. Rotor syndrome occurs due to a defect in the hepatic storage of conjugated bilirubin, which then leaks into the plasma, leading to hyperbilirubinemia. Rotor syndrome can be diagnosed using measured urinary coproporphyrin excretion. An increased value of urinary porphyrins for more than 65 percent is useful to rule out Dubin Johnson syndrome, another rare cause of benign hyperbilirubinemia.
Conclusion: Conjugated hyperbilirubinemia is the main manifestation of two similar congenital syndromes, Dubin-Johnson and Rotor Syndrome, which can later be differentiated using urinary coproporphyrin excretion.

Abstract #1734

Abernethy malformation presenting with splenomegaly in a 30-year-old woman: a case report

Andi Alfian[1], Monica Raharjo[1], Rebekka Martina[1], Wahyu Purnama[1], Fathony Arsyad[1], Andri Sanityoso Sulaiman[2], Taufik Agung Wibowo[3]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [3]Department of Radiology, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Abernethy malformation or congenital extrahepatic portosystemic shunt (CEPS) is a rare congenital anomaly in which the portal vein is absent, partially or completely, and splanchnic venous blood bypasses the liver draining into systemic circulation through an extrahepatic portosystemic shunt.
Case illustration: A 30-year-old previously-well woman came to the hepatobiliary clinic with complaints of worsening abdominal fullness, vague abdominal discomfort, and progressive enlargement of the abdomen over a one-month period. The patient has been previously treated for her abdominal complaints in the past 8 years before presentation without significant improvement. Her spleen was palpable at Schuffner 4. Abdominal ultrasound revealed splenomegaly with dilatation of the splenic artery and vein. Grade I-II esophageal varices were found on esophagogastroduodenoscopy. Abdominal computed tomography angiography revealed absence of the portal vein with a splenorenal shunt (shunting of the splenic vein and left renal vein). The patient was diagnosed with type II Abernethy malformation.
Discussion: Common clinical manifestations of CEPS include hepatic encephalopathy, hepatopulmonary syndrome, or hepatic lesions (benign lesions, adenomas, or hepatocellular carcinoma). Cardiac and genitourinary anomalies are congenital anomalies often associated with this condition. CEPS is usually diagnosed in children under the age of 18. Therefore, it is very rare that CEPS remains asymptomatic during childhood and then later manifests for the first time in adulthood. We present a case of Abernethy malformation in a 30-year-old woman presenting with splenomegaly and no associated anomalies.
Conclusion: Abernethy malformation may be asymptomatic during childhood and present its first clinical manifestation in adulthood.

Abstract #1938

A case of Wilson's disease with hepatitis B

Xiaoyan Zheng

Wilson's disease (WD) is an autosomal recessive disorder of copper metabolism with chronic progressive liver disease and/or extrapyramidal symptoms as the main manifestations and is one of the few curable genetic diseases. Mutations in the *ATP7B* gene, which is involved in copper transport, can lead to WD. With the deepening of study on this disease, reports of WD patients with advanced age gradually increased. Here we reported a patient of 36-year-old initially diagnosed with viral hepatitis B, who was determined to have WD upon research-related exome sequencing. This new diagnosis, confirmed clinically by 24 h urine copper quantification (121 μg/24 h), liver copper staining and liver copper level (407 μg/g dry weight), led to a change in the therapy from lifestyle counseling to directed treatment with a copper chelating agent. ATP7B 18 exon heterozygous mutation (c.3889 g>a; P. V12971), a rarely reported site, found in this case might be a novel important mutation related to WD. In this case, the likelihood of making the correct diagnosis and thereby choosing the appropriate treatment was increased by exome sequencing and careful interpretation.

Abstract #1963

Glycogen storage disease type Ia in a patient with type II diabetes: a rare case report

Wahyu Purnama[1], Fathony Arsyad[1], Monica Raharjo[1], Rebekka Martina, Kemal Fariz Kalista[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Backgrounds: Glycogen storage disease type Ia is a genetic disorder associated with persistent hypoglycemia thus it will have a paradoxical effect for individuals with type II diabetes.
Case illustration: A 49-year old woman with palpable mass in the upper right abdomen since 4 months. The patient had type II diabetes since 5 years ago. Physical examination showed normoweight and

hepatomegaly (palpable 2 fingers below the right costal margin and 3 fingers below the xiphoid process). Laboratory tests were significant hypertriglyceridemia of 365 mg/dL, elevated transaminase levels, fasting blood glucose of 319 mg/dL and Hba1C of 11.9%. The pathological examination suggested a deposition of glycogen in hepatocytes with fibroblast.
Discussion: Typically, the patient with GSD-1a and type 2 DM is very rare. The paradoxical nature of the two conditions presents itself as a challenge to glucose homeostasis. A recent study describes a possible correlation between GSD-1a and the development of metabolic syndrome which could explain the propensity for our patient to develop diabetes. Our patient presented as a dilemma for treatment, requiring modulation of both fasting hypoglycemia from her GSD, as well as post-prandial hyperglycemia secondary to her diabetes. No guidelines exist on how to treat hyperglycemia in patients with GSD-1a.
Conclusion: The management of glycemic control remains a clinical challenge due to the risk of hypoglycemia from her underlying glycogen storage disease.

Abstract #1988

Analysis of *UGT1A1* variants and their correlation with hyperbilirubinemia in Chinese patients with Gilbert and Crigler-Najjar syndrome

Lina Wu[1], Siyu Jia[1], Yanmeng Li[1], Yi Song[1], Donghu Zhou[1], Anjian Xu[1], Wei Zhang[1], Hong You[1], Jidong Jia[1], Jian Huang[1], Xiaojuan Ou[1]

[1]Liver Research Center, Experimental Center, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, P.R. China

Objectives: Inherited unconjugated hyperbilirubinemia includes Crigler-Najjar syndrome (CNS) and Gilbert syndrome (GS), of which the pathogenic variants in uridine diphosphoglucuronate glucuronosyltransferase (*UGT1A1*) are mainly A $(TA)_7TAA$ in European populations. In the present study, we evaluated the *UGT1A1* genotypes in a large cohort of Chinese inherited unconjugated hyperbilirubinemias patients.
Methods: We enrolled CNS or GS patients from China. Peripheral blood samples were collected to screen mutations in the gene *UGT1A1* by PCR and subjected to Sanger sequencing. Correlations of *UGT1A1* variants with hyperbilirubinemia were analyzed.
Results: We enrolled 252 patients (183 men and 69 women, from 11 to 74 years old) including 192 GS and 60 CNS-II. Total of 13 variants were identified, according to the allele frequency, the most common variants in GS were A $(TA)_7TAA$ (50.1%), p.G71R (29.7%), p.Y486D (8.4%), p.P364L (6.9%) and p.P229Q (4.9%); whereas in CNS-II, the most common variants were p.G71R (32.2%), A $(TA)_7TAA$ (31.4%), p.Y486D (27.3%), p.P364L (5.8%) and p.P229Q (3.3%). In addition, five novel variants were also identified: p.P62L, p.L123R and p.G374D with unknown allele frequency; p.L179Q and p.V498I with allele frequency of 4.065e−06 and 8.148e−06 in normal population, respectively. Median of serum total bilirubin was 122 μmol/L for homozygous p.Y486D mutation which was identified predominantly in CNS patients, and below 66 μmol/L in the other variants.
Conclusion: The spectrum of *UGT1A1* variants in Chinese patients was distinct from European populations. Our study expands the knowledge associated with the spectrum of *UGT1A1* variants and contributes to profile genotype-phenotype correlations in hyperbilirubinemia patients.

Abstract #1995

Portal vein thrombus noncirrhotic portal hypertension with splenorenal shunt procedure

Nindy Jayatri[1], Kemal Fariz Kalista[2], Saut Horas Nababan[2], Sahat Matondang[3], Febiansyah Ibrahim[4]

[1]Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [3]Interventional Radiology Division, Department of Radiology, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [4]Digestive Surgery Division, Department of Surgery, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Backgrounds: Noncirrhotic portal hypertension (NCPH) comprises a broad group of disorders characterized by elevated portal pressures in the absence of cirrhosis. NCPH is an infrequent cause of portal hypertension worldwide. Portal vein thrombosis (PVT) is one cause of extrahepatic portal venous obstruction characterized by the obliteration of the portal vein supply leading to portal hypertension.
Case illustration: We report the case of a 36-year-old man with the recurrent esophageal variceal haemorrhage. Hepatitis B and C were negative. Two months ago, an esophagogastroduodenoscopy (EGD) conducted showed large esophageal varices in the distal esophagus and isolated gastric varices in the fundus of the stomach. The patient was performed ligation dan hystoacril injection. Computed tomography of the abdomen showed normovolume of the liver with the appearance of chronic parenchymal changes, no visible focal lesions in the liver, thrombus along the main porta vein and branches intrahepatically along the splenic vein, massive collateral formation in the cavernous venous transformation, collateral in the peripancreatic, splenic hilum, perigastric, and anterior abdominal wall up to the lower abdomen, cholelitiasis about 4 mm, and moderate to severe splenomegaly. The laboratory showed normal value of Protein C, Protein S, and platelet aggregation. From examination, patient was diagnosed portal vein thrombus and performed splenorenal shunt.
Conclusion: Important components in the management of NCPH include controlling episodes of acute gastrointestinal bleed, and preventing further episodes. Patients with NCPH typically have better overall survival, this is typically attributed to the former having preserved synthetic function.

Abstract #2064

Effect of hemoglobinopathies on outcome of chronic liver disease

Shashidhara Nagaraghatta Ashwini[1], Bihari Chhagan[2]

[1]Senior Resident, Department of Clinical Hematology, ILBS, Delhi, India, [2]Associate Professor, Department of Clinical Hematology, ILBS, Delhi, India

Introduction: Chronic liver diseases (CLD) are frequently associated with anemia of diverse etiology. Hemoglobinopathies lead to a state of chronic anemia causing tissue hypoxia and oxidative stress which may increase the severity of liver disease. The extent of the impact of hemoglobinopathies on the outcome of chronic liver disease is not well studied.
Objective: To study the effect of hemoglobinopathies on the severity and outcome of chronic liver disease.

Methodology: We retrospectively analyzed 201 samples from patients with chronic liver disease (CLD) sent for High Performance Liquid Chromatography for suspected hemoglobinopathy work up from January 2018 to December 2019. Clinico-pathological characteristics and outcomes were assessed. Liver biopsy was available for 70 patients of which 31 had hemoglobinopathy.
Results: Of 201 cases of CLD, 89 cases had hemoglobinopathies. Beta thalassemia trait (63/89, 70%) was most common. Hemoglobin ($p < 0.00$) was lower, total bilirubin levels ($p < 0.00$) and hemoglobinopathy. Serum creatinine ($p < 0.01$) and International Normalized Ratio ($p < 0.001$) were higher in CLD patients with hemoglobinopathies. On histology, ballooning degeneration was higher ($p < 0.04$). Outcome measures such as Model for End-stage Liver Disease (MELD) ($p < 0.001$), MELD sodium ($p < 0.04$), Child score ($p < 0.006$) were higher and survival ($p < 0.04$) was lower in patients with hemoglobinopathies.
Conclusion: Chronic liver disease patients with underlying hemoglobinopathies have greater severity of disease and poorer outcome.

Abstract #2190

Genetic counselling in polycystic liver disease: a case report

Fias[1], Ruswhandhi[2]

[1]Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Division of Gastroenterohepatology, Department of Internal Medicine, Gatot Soebroto Army Hospital, Jakarta, Indonesia

Introduction: Genetic counselling polycystic liver disease (PLD) with or without kidney cysts. PCLD 1 is caused by heterozygous mutation PRKCSH gene (177060) on chromosome 19p13, PCLD 2 gene, caused mutation in the SEC63 gene (608648) on chromosome 6q21, PCLD 3 caused mutation in ALG8 gene (608103) on chromosome 11q14, PCLD 4, caused mutation in the LRP5 gene (603506) on chromosome 11q13.
Case illustration: Male 75 years old, admitted to our hospital with increase abdominal girth, pain in the right upper abdomen and right flank, and early satiety. He had difficulties bending over and could neither cut her toenails nor tie her shoe lace. Underwent a computed tomography (CT) scan. Incidentally, multiple liver lesions characterized as cysts were detected with the largest size $6.2 \times 46.16 \times 4.23$ cm. Laboratory testing demonstrated SGOT (37 U/L, normal: < 35 U/L), hemoglobin (10.2 g/dl, normal: 13.0–18.0 g/dl), Albumin: 2,7 g/dL, CEA: 11,6 ng/ml, AFP: 2.66 ng/dl, and Ca 19-9: < 3 nl/ml
Discussion: The patient should be informed of the consequences of genetic testing, especially on children or asymptomatic family members. Clinical heterogeneity among patients with ADPLD may be partially explained by the different effects of each mutation on PC1 expression, as well as on other proteins that contributes to the process of cystogenesis. Radiological imaging is the first means to diagnose ADPKD or ADPLD in at-risk individuals or asymptomatic first-degree relatives. Referral for genetic counselling should be considered, especially in patients with ADPKD, permiting an informed choice about diagnosis and screening.

Abstract #2200

Fulminant hepatitis in hyperthyroidism

Syuhada Dan Adnan[1]

[1]Hospital Sultanah Nur Zahirah, Malaysia

Objective: Hyperthyroidism can cause liver derangement from mild to severe liver failure. It is infrequently reported and its pathophysiology is poorly understood. We hereby report a case of fulminant hepatitis due to hyperthyroidism.
Methods: A 29-year-old female with no known medical illness presented with 2 weeks history of jaundice. She was later diagnosed with hyperthyroidism. She was noted to have a large, non-tender thyroid gland with bruit; thyroid function tests were consistent with uncontrolled hyperthyroidism.
Results: After initiating treatment with steroids, Lugol iodine, propanolol and lithium she improved. Once clinically stable, she underwent thyroidectomy as a definitive treatment of her Graves disease.
Conclusion: The occurrence of fulminant hepatitis in patients with hyperthyroidism has rarely been reported in the literature and is associated with high mortality. Hyperthyroidism has been hypothesized to injure the liver through several mechanisms which we will discuss in this case report.

Non-Alcoholic Fatty Liver Disease

Oral Presentations

Abstract #24

MicroRNA-29a mitigates CD36 to ameliorate high fat diet-induced steatohepatitis and liver fibrosis in mice

Ying-Hsien Huang

Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan, 833, R.O.C.

Background: MicroRNA-29 (miR-29) has been shown to play a critical role in reducing inflammation and fibrosis following a liver injury. Non-alcoholic fatty liver disease (NAFLD) occurs when fat is deposited (steatosis) in the liver due to causes other than excessive alcohol use and is associated with liver fibrosis. In this study, we asked whether miR-29a could reduce experimental high fat diet (HFD)-induced obesity and liver fibrosis in mice.
Methods: We performed systematical expression analyses of miR-29a transgenic mice (miR-29aTg mice) and wild-type littermates subjected to HFD-induced NAFLD.
Results: The results demonstrated that increased miR-29a not only alleviated HFD-induced body weight gain but also subcutaneous, visceral, and intestinal fat accumulation and hepatocellular steatosis in mice. Furthermore, hepatic tissue in the miR-29aTg mice displayed a weak fibrotic matrix concomitant with low fibrotic collagen1α1 expression within the affected tissues compared to the wild-type (WT) mice fed the HFD diet. Increased miR-29a signaling also resulted in the downregulation of expression of the epithelial mesenchymal transition-executing transcription factor snail, mesenchymal markers vimentin, and such pro-inflammation markers as il6 and mcp1 within the liver tissue. Meanwhile, miR-29aTg-HFD mice exhibited significantly lower levels of PPARα, TFAM, and mitochondria DNA content in the liver than the WT-HFD mice. An in vitro luciferase reporter assay further confirmed that miR-29a mimic transfection reduced fatty acid translocase CD36 expression in HepG2 cells.
Conclusion: Our data provide new insights that miR-29a can improve HDF-induced obesity, hepatocellular steatosis, and fibrosis, as well as

highlight the potential of miR-29a targeted therapy for treating NAFLD.

Abstract #218

Validation of the diagnostic accuracy of magnetic resonance elastography (MRE) for the detection of advanced fibrosis due to NASH across multiple phase 2 and 3 clinical trials

Rohit Loomba[1], Naim Alkhouri[2], Mazen Noureddin,[3] Jie Zhang[4], Bryan J. McColgan[4], C. Stephen Djedjos[4], Robert P. Myers[4], Michael Middleton[5], Zachary Goodman,[6] Kris Kowdley,[7] Atsushi Nakajima,[8] Stephen A. Harrison,[9] Zobair Younossi,[6] Eric J. Lawitz,[2] Vincent Wong,[10] Keyur Patel[11]

[1]NAFLD Research Center, University of California San Diego, La Jolla, CA, USA, [2]Texas Liver Institute, University of Texas Health San Antonio, San Antonio, TX, USA, [3]Cedars-Sinai Medical Center, Los Angeles, CA, USA, [4]Gilead Sciences, Inc., Foster City, CA, USA, [5]Department of Radiology, University of California San Diego, La Jolla, CA, USA, [6]Inova Fairfax Hospital, Falls Church, VA, USA, [7]Swedish Medical Center, Seattle, WA, USA, [8]Department of Gastroenterology, Yokohama City University Graduate School of Medicine, Yokohama, Japan, [9]Pinnacle Clinical Research, Austin, TX, USA, [10]Division of Gastroenterology and Hepatology, Center for Liver Health, The Chinese University of Hong Kong, Hong Kong, HK, [11] University Health Network, Toronto, Canada

Background: MRE is a quantitative imaging biomarker for the detection of advanced fibrosis due to NASH. Three single-center studies have reported the association between fibrosis stage and liver stiffness by MRE in patients with NAFLD. Our aim was to validate the performance of MRE for detection of advanced fibrosis using data from multiple clinical trials.
Methods: Baseline data were pooled on 296 subjects from seven randomized, phase 2 and 3 trials of subjects with NASH including the ATLAS and STELLAR-3/-4 trials. All subjects underwent 2D MRE and liver biopsy with centralized staging of fibrosis according to the NASH CRN classification. Associations between MRE-stiffness, fibrosis stage, noninvasive tests (NITs) of fibrosis (ELF, FibroTest, FIB-4, NAFLD Fibrosis Score [NFS]), and NASH activity (NAFLD Activity Score [NAS] ≥ 5 vs < 5) were determined. The discrimination of MRE for advanced fibrosis (F3-F4 vs F0-F2) and cirrhosis (F4 vs F0-F3) was evaluated using areas under receiver operating characteristic (AUROC) curves, and the operating characteristics of literature-based MRE thresholds (3.64 and 4.67 kPa, respectively) and optimal thresholds (defined by the maximal sum of sensitivity and specificity) were determined.
Results: Among the 296 subjects, fibrosis stages were F0-1 (6%), F2 (11%), F3 (44%), and F4 (40%); median MRE-stiffness was 4.71 kPa (IQR 3.52, 6.35); and 73% of subjects (n = 215) had MRE-stiffness $\geq$ 3.64 kPa. MRE was correlated with fibrosis stage (Spearman $\rho = 0.60$), and ELF, FibroTest, FIB-4, and NFS ($\rho = 0.47$–0.52; all $p < 0.05$). When stratified by fibrosis stage, MRE-stiffness was not influenced by NASH activity ($p = 0.89$). The AUROCs (95% CI) of MRE-stiffness for detecting advanced fibrosis and cirrhosis were 0.84 (0.79, 0.90) and 0.81 (0.76, 0.86), respectively. An MRE cutoff of 3.64 kPa was 82% sensitive and 73% specific for advanced fibrosis; the optimal cutoff (3.94 kPa) was 76% sensitive and 88% specific. For cirrhosis, a cutoff of 4.67 kPa was 78% sensitive and 65% specific, while the optimal cutoff (5.28 kPa) was 70% sensitive and 81% specific. Among subjects with F0-F2 fibrosis on biopsy, those with an MRE-stiffness $\geq$ 3.64 kPa (potential misclassifications [n = 13]) had higher ELF and FibroSure than those with a MRE $<$ 3.64 kPa (n = 36; both $p < 0.05$). Conversely, among subjects with F3-F4 fibrosis on biopsy, those with an MRE-stiffness < 3.64 kPa (n = 45) had lower ELF, FibroSure, FIB-4, and NFS compared with those with MRE-stiffness $\geq$ 3.64 kPa (n = 202; all $p < 0.05$).
Conclusions: This multi-center, multi-study validation demonstrates the clinical utility of 2D MRE for the detection of advanced fibrosis due to NASH.

Abstract #219

Fenofibrate mitigates increases in serum triglycerides due to the ACC inhibitor firsocostat in patients with advanced fibrosis due to NASH

Keyur Patel[1], Eric J. Lawitz[2], Guy Neff[3], Peter J. Ruane[4], Ziad H. Younes[5], Jie Zhang[6], Catherine Jia[6], Jay Chuang[6], Ryan S. Huss[6], Chuhan Chung[6], G. Mani Subramanian[6], Robert P. Myers[6], Michael S. Middleton[7], Rohit Loomba[7]

[1]University Health Network, Toronto, Canada, [2]Texas Liver Institute, University of Texas Health San Antonio, San Antonio, TX, USA, [3]Florida Digestive Health Specialists, Lakewood Ranch, FL, USA, [4]Ruane Clinical Research, Los Angeles, CA, USA, [5]GastroOne, Germantown, TN, USA, [6]Gilead Sciences, Inc., Foster City, CA, USA, [7]University of California at San Diego, San Diego, CA, USA

Background: Inhibition of acetyl-CoA carboxylase (ACC) may be associated with hypertriglyceridemia, which is responsive to PPAR-α agonism in pre-clinical models. Our objective was to evaluate the safety and efficacy of fenofibrate (FENO) to mitigate increases in serum triglycerides (TGs) in patients with advanced fibrosis due to NASH treated with the ACC inhibitor firsocostat (FIR).
Methods: Patients with advanced (F3-F4) fibrosis due to NASH (by biopsy or liver stiffness by MRE $\geq$ 3.64 kPa or FibroScan $\geq$ 9.9 kPa) and TGs $>$ 150 and $<$ 500 mg/dL were randomized to treatment with FENO 48 mg (n = 15) or 145 mg (n = 16) orally once daily for two weeks, followed by the combination of FENO + FIR 20 mg daily for 24 weeks. Serum lipids, liver biochemistry, markers of fibrosis, liver stiffness by FibroScan, and centrally-read MRI-PDFF and MRE were monitored.
Results: Overall, 71% of patients had diabetes, 87% were obese, and 35% had cirrhosis. At baseline (BL), median (IQR) fasting TGs in the FENO 48 mg and 145 mg groups were 218 mg/dL (166, 245) and 202 mg/dL (164, 354), respectively. After two weeks of FENO monotherapy, the median change in TGs was +2 mg/dL in the 48 mg group ($p = 0.93$ vs BL) and $-$ 42 mg/dL in the 145 mg group ($p = 0.02$; Figure). After 24 weeks of FENO + FIR combination therapy, TGs were not significantly different from BL (median [IQR] change from BL: +19 mg/dL [$-$ 27, 106] in 48 mg group [$p = 0.09$] and +6 mg/dL [$-$ 88, 90] in 145 mg group [$p = 0.99$]; Figure). One treatment-emergent Grade 3 TG elevation ($>$ 500 mg/dL) was observed in the FENO 48 mg group (405 mg/dL at BL and 974 mg/dL at week 24 of FENO + FIR). FENO and FENO + FIR were well tolerated; no grade 3 or 4 adverse events (AEs), treatment discontinuations due to AEs, or hepatotoxicity were observed. In the combined cohort, significant reductions from BL to week 24 were observed in serum ALT (median: 39 vs 27 U/L, $p < 0.001$), AST (36 vs 29; $p = 0.008$), GGT (50 vs 32 U/L; $p < 0.001$), bilirubin (0.5 vs 0.4 mg/dL; $p < 0.001$), liver stiffness by FibroScan (11.9 vs 8.3 kPa; $p < 0.001$), FibroTest (0.35 vs 0.25; $p = 0.001$), and hepatic PDFF (12.3% vs 9.5%; $p < 0.001$). At week 24, a $\geq$ 30% relative reduction in PDFF was observed in 43% of subjects (FIR 48 mg vs 145 mg: 40% vs 47%).
Conclusions: In patients with advanced fibrosis due to NASH, fenofibrate is safe and mitigates firsocostat-induced increases in serum triglycerides. The combination of firsocostat and fenofibrate

led to improvements in hepatic fat, liver biochemistry, and markers of fibrosis.

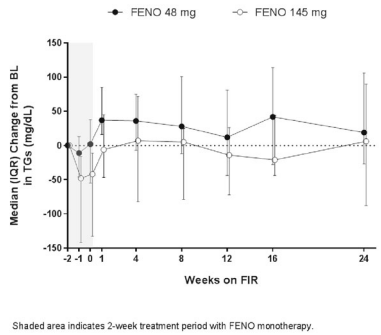


Figure: Serum triglycerides in patients treated with firsocostat and fenofibrate

Abstract #220

Race does not affect the performance of routinely available noninvasive tests for the discrimination of advanced fibrosis due to nonalcoholic steatohepatitis (NASH) in the phase 3 STELLAR trials of selonsertib

Vincent Wai-Sun Wong[1], Won Young Tak[2], George Boon Bee Goh[3], Pin-Nan Cheng[4], Eric J. Lawitz[5], Zobair M. Younossi[6], Raj Vuppalanchi[7], Natalie H. Bzowej[8], Ziad Younes[9], Naim Alkhouri[5], Ya Wang[10], Kathryn Kersey[10], Georgia Li[10], Marianne Camargo[10], Robert P. Myers[10], Stephen Djedjos[10], Stephen A. Harrison[11], Zachary Goodman[6], Michael H. Trauner[12], Manuel Romero-Gomez[13], Quentin M. Anstee[14], Shiv Sarin[15], Mindie H. Nguyen[16], Takeshi Okanoue[17]

[1]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, [2]Kyungpook National University Hospital, Daegu, South Korea, [3]Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore, [4]Department of Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan, [5]Texas Liver Institute, University of Texas Health San Antonio, San Antonio, TX, USA, [6]Inova Fairfax Hospital, Falls Church, VA, USA, [7]Indiana University Medical Center, Indianapolis, IN, USA, [8]Ochsner Medical Center, New Orleans, LA, USA, [9]Gastro One, Germantown, TN, [10]Gilead Sciences, Inc., Foster City, CA, USA, [11]Pinnacle Clinical Research, San Antonio, TX, USA, [12]Division of Gastroenterology and Hepatology, Medical University of Vienna, Vienna, Austria, [13]Hospital Universitario Virgen del Rocio, Sevilla, Spain, [14]Institute of Cellular Medicine, Newcastle University, Newcastle-upon-Tyne, UK, [15]Institute of Liver and Biliary Sciences, New Delhi, India, [16]Stanford University Medical Center, Palo Alto, CA, USA, [17]Department of Gastroenterology & Hepatology, Saiseikai Suita Hospital, Suita City, Osaka, Japan

Background: Routinely available noninvasive tests of fibrosis (NITs) can be used to identify patients with advanced fibrosis due to NASH, but their performance may vary by race. Our aim was to evaluate the effect of patient race on the diagnostic performance of NITs using data from the global phase 3 STELLAR studies of selonsertib.
Methods: The STELLAR studies (NCT03053050 and NCT03053063) enrolled patients with bridging fibrosis (F3) or compensated cirrhosis (F4) due to NASH (NAFLD Activity Score [NAS] $\geq$ 3). Baseline liver biopsies were centrally read using the NASH Clinical Research Network classification and NITs, including the NAFLD fibrosis score (NFS), Fibrosis-4 (FIB-4) index, Enhanced Liver Fibrosis (ELF) test, and liver stiffness by transient elastography (LS by TE) were measured. The performance of these tests to discriminate advanced (F3-F4) fibrosis by self-reported patient race was evaluated using areas under the receiver operating characteristics curves (AUROCs) with 5-fold cross-validation repeated 100x. Results for White and Asian patients are presented; data for other races (5% of patients screened) are excluded.
Results: Among 3202 patients screened for the STELLAR studies with evaluable liver histology, 24% were Asian and 71% were White. The median age was 58 years in both groups; 47% of Asians and 57% of Whites were female ($p < 0.0001$). The prevalence of F3-F4 fibrosis was 67% in Asians and 72% in Whites ($p = 0.01$). AUROCs for each of the NITS for the discrimination of advanced fibrosis were similar between Asian and White patients (**Table**). In general, literature-based thresholds for the NITs had similar sensitivity and specificity among the specific racial subgroups.
Conclusion: In these large, global phase 3 trials, the diagnostic performance of routinely available NITs for the discrimination of advanced fibrosis due to NASH was acceptable and similar between Asian and White patients.

Table: Diagnostic Performance of NITs to discriminate advanced fibrosis (F3-F4) in Asian and White patients screened for the STELLAR studies

NIT	AUROC (95% CI)*	Cutoff	% (95% CI)			
			Sensitivity	Specificity	PPV	NPV
NFS						
White (n=1710)	0.73 (0.73, 0.73)	>0.676	40 (37, 43)	87 (83, 91)	93 (91, 95)	25 (22, 28)
Asian (n=581)	0.75 (0.74, 0.75)		33 (29, 38)	92 (86, 96)	94 (89, 97)	28 (23, 32)
FIB-4						
White (n=2225)	0.78 (0.78, 0.78)	>2.67	33 (30, 35)	93 (91, 95)	93 (91, 95)	34 (32, 36)
Asian (n=732)	0.80 (0.79, 0.80)		48 (44, 53)	90 (85, 93)	91 (87, 94)	44 (39, 49)
ELF						
White (n=2259)	0.79 (0.79, 0.79)	>11.3	19 (17, 21)	98 (96, 99)	96 (93, 98)	31 (29, 34)
Asian (n=745)	0.81 (0.81, 0.81)		24 (20, 28)	96 (93, 98)	93 (87, 97)	37 (34, 41)
LS by TE						
White (n=1244)	0.79 (0.79, 0.80)	>11.4	77 (74, 79)	68 (60, 75)	94 (92, 96)	30 (26, 35)
Asian (n=427)	0.82 (0.81, 0.82)		73 (68, 78)	77 (67, 84)	91 (87, 94)	48 (40, 56)

* AUROC and 95% confidence interval (CI) were based on repeated 5-fold cross-validation (CV) 100x.

Abstract #264

Validation of histologic and noninvasive measures of fibrosis as surrogate endpoints of disease progression in patients with nonalcoholic steatohepatitis (NASH)

George Boon Bee Goh[1], Quentin M. Anstee[2], Michael Trauner[3], Eric J. Lawitz[4], Natalie Bzowej[5], Raj Vuppalanchi[6], Ziad Younes[7], Dora Ding[8], Georgia Li[8], Kathryn Kersey[8], Marianne Camargo[8], C. Stephen Djedjos[8], G. Mani Subramanian[8], Robert P. Myers[8], Vincent Wai-Sun Wong[9], Stephen A. Harrison[10], Takeshi Okanoue[11], Manuel Romero-Gomez[12], Zachary Goodman[13]

[1]Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore, [2]Institute of Cellular Medicine, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK, [3]Division of Gastroenterology and Hepatology, Medical University of Vienna, Austria, [4]Texas Liver Institute, University of Texas Health San Antonio, San Antonio, TX, USA [5]Oschner Medical Center, New Orleans, LA, USA, [6] Indiana University Medical Center, Indianapolis, IN, USA, [7]Gastro One, Germantown, TN, USA, [8]Gilead Sciences, Inc., Foster City, CA, USA, [9]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, [10]Pinnacle Clinical Research, San Antonio, TX, USA, [11]Saiseikai Suita Hospital, Suita City, Osaka, Japan, [12]Hospital Universitario Virgen del Rocio, Sevilla, Spain, [13]Inova Fairfax Hospital, Falls Church, VA, USA

Background: Surrogate endpoints that predict complications are necessary for approval of new therapies for NASH. We assessed associations between histologic and noninvasive fibrosis markers with disease progression in NASH.
Methods: Patients with advanced fibrosis (Ishak stages 3–6) due to NASH (NAS $\geq$ 3) were enrolled in two placebo-controlled trials of selonsertib. The trials were discontinued after 48 weeks due to lack of efficacy; hence treatment groups were combined for this analysis.

Liver fibrosis (baseline [BL] and W48) was staged according to the Ishak classification, hepatic collagen and α-SMA expression were quantified by morphometry, liver stiffness (LS) was measured by vibration-controlled transient elastography (VCTE), and ELF and NAFLD Fibrosis Score (NFS) were calculated. Cox regression determined associations between these parameters with disease progression (i.e. progression to cirrhosis in patients with bridging fibrosis and adjudicated clinical events [e.g. decompensation, transplantation, death] in those with cirrhosis), and discrimination was assessed using c-statistics.

Results: 1679 subjects with bridging fibrosis (n = 802) or cirrhosis (n = 877) were randomized (median age 59 yrs, 60% female, 74% with diabetes). During a median follow-up (FU) of 14.3 mos, 16% of subjects (117/748 with W48 biopsies) with bridging fibrosis progressed to cirrhosis. Risk of histological progression was greater with higher BL Ishak stage, hepatic collagen, α-SMA expression, ELF, NFS, and LS by VCTE, as well as greater increases in these markers over time (Table). BL ELF (c-statistic, 0.68) and LS by VCTE (0.70) more accurately discriminated progression to cirrhosis than BL Ishak stage (0.58) and hepatic collagen (0.56; all $p < 0.05$). During a median FU of 14.3 mos, 26 cirrhotic subjects (3%) had clinical events. BL factors associated with clinical events included higher Ishak stage, hepatic collagen, α-SMA, ELF, NFS, and LS by VCTE (Table). After adjustment for BL, increases in hepatic collagen, α-SMA, NFS, and VCTE were associated with an increased risk of events. Prediction of future clinical events was greatest for BL ELF (c-statistic, 0.84 vs. 0.66 for Ishak stage and 0.62 for hepatic collagen; both $p < 0.05$).

Conclusions: Clinical disease progression in patients with advanced fibrosis due to NASH is associated with greater fibrosis burden at baseline and larger increases over time, measured histologically or with noninvasive markers. These data support the utility of noninvasive fibrosis markers as endpoints in NASH clinical trials.

Variable *	Bridging Fibrosis (Progression to Cirrhosis)		Cirrhosis (Adjudicated Clinical Events)	
	HR (95% CI)	P-Value	HR (95% CI)	P-Value
Ishak stage				
BL 4 vs. 3	1.84 (1.29, 2.64)	0.0008	N/A	N/A
BL 6 vs. 5	N/A	N/A	7.76 (1.83, 32.83)	0.010
Hepatic collagen, %				
BL	1.24 (1.16, 1.32)	<0.0001	1.08 (1.03, 1.14)	0.004
Change from BL	1.20 (1.16, 1.23)	<0.0001	1.05 (1.01, 1.10)	0.020
α-SMA, %				
BL	1.10 (1.05-1.15)	< 0.0001	1.06 (1.01, 1.11)	0.011
Change	1.12 (1.10-1.15)	< 0.0001	1.04 (1.00, 1.09)	0.051
ELF				
BL	2.08 (1.74, 2.49)	<0.0001	3.79 (2.73, 5.26)	<0.001
Change from BL	1.42 (1.10, 1.84)	0.008	1.28 (0.75, 2.19)	0.36
NFS				
BL	1.54 (1.35, 1.74)	<0.0001	2.24 (1.64, 3.04)	<0.0001
Change from BL	1.78 (1.41, 2.24)	<0.0001	3.04 (1.90, 4.88)	<0.0001
LS by VCTE, kPa				
BL	1.07 (1.05, 1.08)	<0.0001	1.06 (1.04, 1.08)	<0.0001
Change from BL	1.04 (1.02, 1.06)	0.0005	1.04 (1.01, 1.07)	0.006

Abstract #307

Effects and optimal mode of physical exercise on liver enzymes and BMI in adult patients with nonalcoholic fatty liver disease: a meta-analysis

Shousheng Liu[1], Mengzhen Dong[1], Likun Zhuang[1], Yongning Xin[1,*]

Department of Infectious Disease, Qingdao Municipal Hospital, Qingdao 266011, China

Introduction: Accumulated evidences have shown the role of physical exercise in patients with nonalcoholic fatty liver disease (NAFLD), but the conclusions were not consistent.

Objectives: The aim of this study was to investigate the accurate effect of physical exercise and the optimal mode of physical exercise on liver enzymes and body mass index (BMI) in adults NAFLD patients.

Methods: PubMed, Embase database and Cochrane Library databases were searched for the relevant trials which were published up to August 2019. The analysis was restricted to the studies which examined the effect of supervised exercise intervention on liver enzymes (Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST)) and BMI. Fifteen randomized controlled trials (893 adults) were eligible for inclusion in this meta-analysis.

Results: The aerobic exercise could reduce the ALT levels markedly compared to the resistance exercise and the combined aerobic and resistance exercise. The combined aerobic and resistance exercise could reduce the AST levels significantly. The aerobic exercise could reduce the BMI markedly other than the resistance exercise and the combined aerobic and resistance exercise. The exercise duration times > 12 weeks and frequency > 3 times per week were tightly associated with the decreased ALT, AST and BMI.

Conclusion: physical exercise could reduce the serum levels of ALT, AST, and BMI in adult NAFLD patients effectively. Aerobic exercise more than 3 times per week and duration of more than 12 weeks may be the optimal mode of exercise for the improvement of NAFLD in adults.

Abstract #313

Efficacy, safety, and tolerability of lubiprostone for the treatment of non-alcoholic fatty liver disease: The LUBIPRONE, double-blind, randomized, placebo-controlled, phaseII study.

Takaomi Kessoku[1], Takashi Kobayashi[1], Annna Ozaki[1], Michihiro Iwaki[1], Yasushi Honda[1], Yuji Ogawa[1], Kento Imajo[1], Takuma Higurashi[1], Masato Yoneda[1], Kazumi Kubota[2], Masataka Taguri[2], Takeharu Yamanaka[2], Haruki Usuda[3], Koichiro Wada[3], Satoru Saito[1], Atsushi Nakajima[1]

[1]Department of Gastroenterology and Hepatology, Yokohama City University Graduate School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama 236-0004, Japan, [2]Department of Biostatistics, Yokohama City University Graduate School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama 236-0004, Japan, [3]Department of Pharmacology, Shimane University School of Medicine, 89-1, Enyacho, Izumo, Shimane 693-8501, Japan

Introduction: Nonalcoholic fatty liver disease (NAFLD) progression is associated with increased gut-permeability. We have previously reported that lubiprostone (LUB) ameliorated increased intestinal permeability.

Objectives: This study is a first proof of concept study that uses LUB to demonstrate improvement of NAFLD by controlling gut-permeability.

Methods: In this double-blind, placebo-controlled, randomized, phase II trial, 12 μg or 24 μg of LUB (LUB24 or LUB12) or placebo (PBO) were administered orally for 12 weeks. The primary and key secondary outcomes were the absolute change in ALT levels and lactulose-mannitol ratio (LMR), which is an indicator for intestinal permeability. LMR responder or nonresponder, which was defined as $LMR < 0$ or $LMR > 0$ (week 12–baseline). Other secondary outcomes were set as blood endotoxin, magnetic resonance imaging-proton density fat fraction (MRI-PDFF). Analyses were done by intention-to-treat.

Results: 150 patients were randomly assigned in LUB24 (n = 55), LUB12 (n = 50), or PBO (n = 45). We observed a significant decrease in ALT levels in LUB24 (p = 0.0007 vs PBO) and LUB12 (p = 0.002 vs PBO). Reduction of LMR, endotoxin and MRI-PDFF were significantly greater in LUB24 and LUB12 compared with PBO.

LMR-responders in LUB-treated groups observed significant reduction in ALT levels compared with LMR non-responder (LUB24; p = 0.002, LUB12; p = 0.0007). Adverse events were reported more frequently in LUB24 compared with LUB12 and PBO.
Conclusion: LUB was well tolerated and significantly reduced the liver enzyme and intestinal permeability of patients with NAFLD. In particular, the greater reduction in LMR-responder of both LUBs suggested that manipulating intestinal permeability may be a promising novel treatment target for NAFLD.

Abstract #372

Fibrinogen-like protein 2 exacerbates non-alcoholic steatohepatitis via interaction with TLR4 eliciting inflammation in macrophages and inducing hepatic lipid metabolism disorder

Junjian Hu[1*], Hongwu Wang[1], Xitang Li[1], Yonggang Liu[2], Yuqiang Mi[3], Hongyan Kong[1], Dong Xi[1], Weiming Yan[1], Xiaoping Luo[4], Qin Ning[1#]andXiaojing Wang[1#]

[1]Department and institute of infectious diseases, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China, [2]Department of pathology, Second People's Hospital, Nankai University, Tianjin, China, [3]Department of integrated traditional Chinese and western medicine, Second People's Hospital, Nankai University, Tianjin, China, [4]Department and institute of Pediatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China

Background: Fibrinogen-like protein 2 (fgl2) is an important regulator in immune-mediated liver injury.
Objectives: This study aims to investigate the role and mechanisms of fgl2 in the pathogenesis of NASH.
Methods: Hepatic fgl2 expression were tested by immunofluorescence staining in patients with NASH. The wild type and fgl2-/- C57BL/6 mice were subjected to methionine/choline-deficient (MCD) diet or high fat diet (HFD) for establishing NASH models. Bone marrow-derived macrophages (BMDMs) were stimulated with LPS or free fatty acids, and BMDMs-conditioned media (CM) was incubated with primary hepatocytes. The levels of proinflammatory cytokines in liver homogenate and cell supernatants were tested by ELISA. The NF-κB, p38-MAPK and NLRP3 inflammasome signaling pathways as well as lipid metabolism related genes were tested both in vivo and in vitro using western blotting or RT-PCR. The interaction between fgl2 and TLR4 was detected by immunocoprecipitation.
Results: Fgl2 was highly expressed in liver of NASH patients. Inflammatory liver injury and steatosis were attenuated in fgl2-/- NASH models. In both liver tissues and BMDMs, fgl2 deficiency resulted in reduced levels of proinflammatory cytokines including TNF-α, IL-1β, MCP-1, IL-6 and IL-18. Lipogenesis genes (Fasn, SREBP-2) were downregulated while lipolysis genes (PPARα, CPT1A) were upregulated in fgl2-/-groups. Meanwhile, activation of NF-κB p38-MAPK and NLRP3 inflammasome were decreased upon fgl2 disruption. Moreover, fgl2 was found to combine with TLR4 to activate these downstream inflammatory signaling pathways which further influence hepatic lipid metabolism and facilitate NASH progression.
Conclusion: Fgl2 interacts with TLR4 to activate multiple signaling pathways in macrophages to promote inflammation and steatosisin NASH.

Abstract #427

Analysis of clinical characteristics of different age stages, different body mass index and HBsAg positive patients with NAFLD

Zheng Xinchun[1], Huang Mingxing[1], Xia Jinyu[1]

[1]Department of Infectious Diseases, The Fifth Affiliated Hospital of Sun Yat-Sen University (SYSU), Zhuhai, Guangdong, China

Objective: To investigate the differences of liver function, renal function and metabolic indexes in different age, different BMI and HBsAg positive patients with nonalcoholic fatty liver disease (NAFLD).
Methods: Clinical data of 35039 NAFLD patients in the Fifth affiliated hospital of Sun Yat-sen university from March 2016 to December 2018 were collected and grouped according to age, BMI and HBsAg positivity, and differences in liver function, renal function and metabolic indicators between each group were analyzed.
Results In NAFLD patients, the proportion of fatty liver in women gradually increases over age, while the proportion of fatty liver in men gradually decreases, and finally the proportion of fatty liver in men and women converges. With the increase of age, ALT and AST in NAFLD patients tend to decrease, urea nitrogen (UA) and cystatin C increased gradually, triglyceride (TG) and total cholesterol (TCH) showed higher in the middle age stage, lower in the head and tail age stage, and no significant fluctuations in uric acid (UA) and creatinine (Cr). Compared with HBsAg negative patients with NAFLD, HBsAg positive patients showed ALT, AST, lactate dehydrogenase (LDH), total protein, albumin, direct bilirubin, total bile acid, Cr, UA increased significantly, and TG, TCH, high-density lipoprotein cholesterol (HDL-C) decreased obviously. Compared with NAFLD patients with normal BMI, ALT, AST, LDH, cholinesterase, UA and Cr were significantly increased in obese patients with NAFLD, while HDL-C was significantly decreased.
Conclusions: HBV infection and obesity could aggravate liver and renal function damage in patients with NAFLD.

Abstract #452

Nonalcoholic fatty liver promotes the progression of osteoporosis in HIV-infected patients receiving long-term TDF-based antiretroviral therapy

Zhijie Xu[1a], Pengyuan He[1a], Jianzhong Xian[2], Wuzhu Lu[2], Jingxian Shu[3], Wentao Luo[1], Chongjie Gan[1], Ruoman Ke[1], Jinyu xia[1*], Zongping Han[4*], Mingxing Huang[1,5]

[1]Department of Infectious Diseases, the Fifth Affiliated Hospital of Sun Yat-Sen University, Zhuhai, Guangdong, China, [2]Department of Ultrasonography, the Fifth Affiliated Hospital of Sun Yat-Sen University, Zhuhai, Guangdong, China, [3]Department of Pharmacy, the Fifth Affiliated Hospital of Sun Yat-Sen University, Zhuhai, Guangdong, China, [4]Department of Clinical Nutrition, the Fifth Affiliated Hospital of Sun Yat-Sen University, Zhuhai, Guangdong, China, [5]Guangdong Provincial Key Laboratory of Biomedical Imaging, the Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai, Guangdong, China

Introduction: Tenofovir (TDF) has a deleterious effect on bone mineral density (BMD), while nonalcoholic fatty liver disease (NAFLD) has been associated with a reduced BMD. Whether NAFLD aggravates the effect of TDF on BMD is not clear.

Objectives: The aim of this study was to analyze the BMD in HIV-infected patients with NAFLD receiving long-term TDF-based antiretroviral therapy (ART).
Methods: We conducted a cross-sectional study in HIV patients undergoing TDF-based ART for more than three years. The patients were divided into two groups equally by whether they had NAFLD. We measured BMD using an ultrasonic bone density apparatus, and liver ultrasonography was performed to determine the severity of fatty liver.
Results: A total of 84 patients were included in this study, with 35 belonging to the NAFLD group and 54 to the non-NAFLD group. Patients with NAFLD showed a worse BMD status than those without NAFLD. The incidence of osteopenia (42.9% versus 25.9%; $p < 0.01$) and osteoporosis (17.1% versus 3.7%; $p < 0.01$) was significantly higher in HIV-infected patients with NAFLD than in those without NAFLD.
Conclusion: Based on our results, the combination of NAFLD may promote the progression of osteoporosis in HIV-infected patients receiving long-term TDF-based ART. Furthermore, we may want to avoid using TDF for ART in HIV-infected patients with NAFLD.

Abstract #722

Analysis of the gut microbiomes in non-obese NAFLD

Michihiro Iwaki, Takaomi Kessoku, Anna Ozaki, Takashi Kobayashi, Yasushi Honda, Yuji Ogawa, Kento Imajo, Masato Yoneda, Satoru Saito, Atsushi Nakajima

Department of Gastroenterology and Hepatology, Yokohama City University Graduate School of Medicine, Yokohama, Japan

Background: NAFLD (nonalcoholic fatty liver disease) is a phenotype of the metabolic syndrome in the liver. Although obesity is considered to be the main cause of NAFLD, NAFLD can also occur in non-obese people, which has been referred to as non-obese NAFLD. Pathological conditions of non-obese NAFLD isn't well known. There was no article that examined the relationship between non-obese NAFLD and gut microbiomes in Japan. In this study, we examined profiles of non-obese NAFLD patients, including clinical features and gut microbiomes.
Methods: This study was a multicenter, cross-sectional observation. We evaluated laboratory biochemical parameters and gut microbiota profiles in 113 healthy control subjects, 51 non-obese (BMI < 25 kg/m^2) and 51 obese (BMI ≥ 30 kg/m^2) NAFLD patients who underwent liver biopsy between April 2005 and May 2016. We determined the gut microbiome characteristics, the diversity of gut microbiomes non-obese and the correlation between gut microbiomes and clinical parameters in non-obese NAFLD.
Results: In alpha diversity, no significant difference was observed between non-obese NAFLD and obese NAFLD. At the genus level we observed a significant decrease in the abundance of *Eubacterium* in non-obese NAFLD. We found that *Eubacterium* showed a negative correlation with the liver fibrosis in non-obese NAFLD patients
Conclusions: This study showed that *Eubacterium* was significantly decreased and negatively correlated with liver fibrosis in non-obese NAFLD. It was suggested that *Eubacterium* may be associated with the development of NAFLD. This was the first study showing the gut microbiome characteristic of biopsy-proven non-obese NAFLD in Japan.

Abstract #789

Roles of alcohol consumption in fatty liver in Japanese men and women: a longitudinal study

Moriya Akio[1], Iwasaki Yoshiaki[2], Ando Masaharu[1]

[1]Department of Gastroenterology, Mitoyo General Hospital, Kanonji, Japan, [2]Health Service Center, Okayama University, Okayama, Japan

Introduction: Several cross-sectional studies have reported an inverse association between moderate alcohol consumption and the prevalence of fatty liver; however, the number of longitudinal studies is limited.
Objectives: To confirm the longitudinal inverse association between alcohol consumption and the prevalence of fatty liver in another population.
Methods: We analyzed 2,709 men and 1,816 women (median age, 56 years old) with 15,640 observations who underwent systematic health checkups. Generalized estimating equation applied an exchangeable correlation structure for the within-individual correlation matrix was used to estimate any association between drinking pattern and fatty liver assessed by ultrasonography.
Results: The prevalence of fatty liver was 40% in men and 23% in women. While 67% of men and 26% of women reported habitual drinking. After a median follow-up period of 3 years, 265 of 1630 men (16%) and 103 of 1390 women (7%) had newly developed fatty liver; 266 of 1079 men (25%) and 123 of 426 women (29%) demonstrated remission of fatty liver. When drinking frequency was stratified into non-drinking or social drinking (reference), occasional drinking, and drinking daily in men, there was a significant inverse association with fatty liver in drinking daily (0.86 [0.76–0.97]), but not in occasional drinking (1.00 [0.88–1.13]). No drinking pattern was significantly associated with the prevalence of fatty liver in women.
Conclusion: Alcohol consumption may protect against fatty liver in a certain percentage of men who consume alcohol daily but not in women.

Abstract #836

Modeling quality-adjusted life years (QALYs) for patients with non-alcoholic fatty liver disease (NAFLD) in Hong Kong

Tampi, Radhika[1]; Wai-Sun Wong, Vincent[2]; Younossi, Issah[3]; Lai-Hung Wong, Grace[2]; Lik-Yuen Chan, Henry[2]; M. Younossi, Zobair[1,4]

[1]Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, VA, United States, [2]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, [3]Center for Outcomes Research in Liver Diseases, Washington DC, United States, [4]Department of Medicine, Center for Liver Diseases, Inova Fairfax Medical Campus, Falls Church, VA, United States

Introduction: NAFLD encompasses non-alcoholic steatohepatitis (NASH) and simple steatosis (NAFL). Given the epidemic of obesity, the burden of NAFLD is increasing globally. Along with clinical consequences, NAFLD has significant impact on economic and patient reported outcomes (PROs).
Objective: We aimed to calculate quality-adjusted life years (QALYs) accumulated by patients with NASH versus NAFL in Hong Kong.
Methods: We built a Markov model with 1-year cycles to calculate QALYs accumulated by adult patients with NAFL and NASH in Hong Kong over a lifetime horizon. Cohort size was determined by

population size, prevalence of NAFLD, and incidence of NASH (2017) in Hong Kong. Our model includes 11 health states—NAFL, NASH with fibrosis stages 0–3, compensated/decompensated cirrhosis, hepatocellular carcinoma, liver transplant, post liver transplant states, and 3 mortality states. Transition probabilities and utility values for each health state were age-stratified and derived from literature. Health utilities were assumed to be the same as in the United States. For NASH, utility values decreased by 0.2 with every 20-year increase in age. We discounted QALYs at 3% annually.

Results: Total QALYs accumulated for all NAFLD were 22 million over an average lifetime span of 50 years, or 0.529 per person-year. For NASH, total QALYs accumulated were 4.1 million, or 0.428 per person-year. Total QALYs accumulated for NAFL were 17.9 million, or 0.560 per person-year. Overall, average QALYs accumulated per person-year increased with age for NASH and NAFL.

Conclusion: This model estimates substantial clinical and economic impact of NASH in Hong Kong.

Age Group	NASH QALYs	NASH PY	NASH per PY	NAFL QALYs	NAFL PY	NAFL per PY	NAFLD QALYs	NAFLD PY	NAFLD per PY
18-29	490,853	1,465,703	0.335	2,413,797	5,102,095	0.473	2,904,650	6,567,798	0.442
30-39	729,992	1,969,728	0.371	3,311,140	6,628,014	0.500	4,041,132	8,597,742	0.470
40-49	792,420	1,968,005	0.403	3,740,652	6,852,827	0.546	4,533,072	8,820,832	0.514
50-59	974,674	2,173,665	0.448	4,191,872	7,007,212	0.598	5,166,546	9,180,877	0.563
60-69	545,558	1,069,629	0.510	2,997,316	4,616,293	0.649	3,542,875	5,685,922	0.623
70-79	465,195	798,238	0.583	961,336	1,369,351	0.702	1,426,532	2,167,589	0.658
80+	126,103	203,038	0.621	274,011	368,272	0.744	400,114	571,310	0.700
Total	**4,124,797**	**9,648,006**	**0.428**	**17,890,124**	**31,944,064**	**0.560**	**22,014,921**	**41,592,069**	**0.529**

Abstract #855

Non-invasive imaging modalities for assessment of fibrosis, inflammation and steatosis in a Japanese NASH population

Aslam, Filza[1], Mouchti, Sofia[2], Dennis, Andrea[2], Kelly, Matt[2], Banerjee, Rajarshi[2], Imajo, Kento[3], Nakajima, Atsushi[3]

[1]Perspectum Diagnostics, Singapore, Singapore, [2]Perspectum Diagnostics, Oxford, United Kingdom, [3]Department of Gastroenterology and Hepatology, Yokohama City University Graduate School of Medicine

Introduction: Current guidelines for non-alcoholic steatohepatitis (NASH) diagnosis rely on liver biopsy which is limited by its cost and invasiveness.

Objectives: This ongoing prospective study (UMIN000026145) aims to evaluate accuracy of multiparametric magnetic resonance imaging (mpMRI), magnetic resonance elastography (MRE) and transient elastography (TE) compared to biopsy for assessment of steatosis, fibrosis and inflammation in NASH.

Methods: Japanese patients suspected of NASH were screened with mpMRI-based iron-corrected T1 (cT1) and proton density fat fraction (PDFF), ultrasound-based controlled attenuation parameter (CAP), TE- and MRE-based liver stiffness measurement (TE-LSM, MRE-LSM). Biopsy was assessed using NAFLD Activity Score (NAS) and fibrosis staging using Kleiner-Brunt criteria. Diagnostic performances were assessed using area under receiver operating characteristics (AUROC).

Results: 97 patients have been screened. Median age 61.0 years; 80.4% BMI $\geq$ 25; 6.2% S0, 43.3% S1, 35.1% S2 and 15.5% S3 steatosis. 22.7% F1, 24.7% F2, 33.0% F3 and 16.5% F4 fibrosis; 55.7% NAS $\geq$ 4. Success rates for mpMRI, MRE and TE were 97.9%, 99.0% and 78.4%. For evaluation of steatosis (S $\geq$ 2), AUROCs for CAP and PDFF were 0.65 (0.52–0.78) vs 0.89 (0.83–0.95). For evaluation of fibrosis, AUROCs for TE-LSM, MRE-LSM and cT1 were 0.86 (0.78–0.95) vs 0.93 (0.88–98) vs 0.66 (0.54–0.77) for F $\geq$ 3 and 0.95 (0.89–0.99) vs 0.96 (0.92–0.99) vs 0.79 (0.67–0.91) for F $\geq$ 4. For detection of NAS $\geq$ 4, AUROCs for TE-LSM, MRE-LSM and cT1 were 0.60 (0.47–0.73) vs 0.58 (0.46–0.70) vs 0.77 (0.67–0.86).

Conclusion: mpMRI was the best-performing modality for evaluation of steatosis and NASH activity. MRE and TE had high diagnostic accuracy for assessment of fibrosis, albeit lower success rates with TE. Results highlight complementarity of techniques.

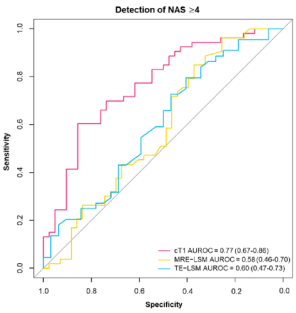


Figure: AUROC for detection of patients with NAS≥4 showed cT1 had best diagnostic accuracy.

Abstract #862

Comprehensive analysis of microRNAs associated with the effect of a sodium glucose co-transporter-2 inhibitor for the treatment of nonalcoholic steatohepatitis

Asahiro Morishita[1], Kei Takuma[1], Mai Nakahara[1], Kyoko Oura[1], Tomoko, Tadokoro[1], Koji Fujita[1], Joji Tani[1], Tsutomu Masaki[1]

[1]Department of Gastroenterology and Neurology, Faculty of Medicine, Kagawa University, Kagawa, Japan

Background/aim: SGLT2 inhibitors are a new type of glucose-lowering drugs for the treatment of type 2 diabetes mellitus. These mechanism of action is independent for pancreatic β-cell function and insulin resistance. Nonalcoholic steatohepatitis (NASH) is becoming an important public health concern and associated with insulin resistance and other metabolic risk factors such as type 2 diabetes mellitus, obesity, and dyslipidaemia. So far, various kinds of drugs have been used for the treatment of NASH, but these trials resulted in poor outcomes. The aim of this study is to determine therapeutic effects of SGLT2 inhibitors in NASH using Stelic Animal Model (STAM) mice, a validated animal model for NASH.

Methods: Eight-week-old male STAM mice were divided into 2 experimental groups and fed as follows: 1) high-fat diet (HFD) (control group); 2) HFD mixed with 16.7 μg/mouse/day of ipragliflozin, SGLT2 inhibitor (SGLT2I group). After 4 weeks, mice were sacrificed and blood samples and livers were collected. Livers were subjected to clinical parameters, histological study, mRNA and protein expressions for multiple genes, and microRNA analysis.

Result: SGLT2 inhibitor significantly decreased transaminases but not alkaline phosphatase. Histological examination revealed marked reduction of steatosis, ballooning, and inflammation in SGLT2I group. In addition, mice treated with SGLT2 inhibitor developed smaller area of liver fibrosis following fibrosis-related mRNA up-regulations. Furthermore, as for microRNA profiles, 15 microRNAs were up-regulated, and 16 microRNAs were down-regulated significantly in livers of SGLT2I group ($P < 0.05$). Unsupervised hierarchical clustering analysis showed that SGLT2I group clustered separately from control group.

Conclusion: SGLT2 inhibitor improved the clinical and histological development of NASH, and microRNAs might be a potential therapeutic target for the treatment of NASH.

Abstract #936

Impact of intermittent fasting on laboratory, radiological, and anthropometric parameters in non-alcoholic fatty liver disease (NAFLD)

Hanaa Badran[1], Maha Elsabaawy, Ahmed Sakr[1], Mahmoud Eltahawy[1]

[1]Department of Hepatology and Gastroenterology, National Liver Institute, Menoufia University, Shebin El-kom, Egypt

Background: NAFLD is representing the top of liver transplantation list in developed countries. Despite the ample flow of drugs in pipeline, lifestyle modifications are still the flawless solution of NAFLD.
Aim: to assess short term effects of intermittent fasting on various biochemical, radiological and anthropometric parameters in NAFLD patients.
Patients and methods: Ninety-eight NAFLD patients were prospectively recruited and voluntarily subjected to about 16 hours dry fasting with average 22–29 days without any special dietary recommendations. Anthropometric, laboratory and radiological selected parameters were measured before and after 30 days of intermittent fasting (Fasting phase). The same parameters were re-assessed before and after 30 days of non-fasting state (Non fasting phase). Changes if found will be compared between the 2 phases.
Results: recruited patients were mostly rural (76), hypertensive (34.7), diabetic (43.9), females (76.8%), with overt criteria of metabolic syndrome (67.3%). Liver transaminases (ALT&AST) were ameliorated significantly after fasting (p 0.003) with continued in the following month (p 0.000) especially in those with elevated ALT before fasting (46%). Of them eleven patients (24.4%) had experienced ALT normalization after one month fasting, which was furtherly increased to 15 (33.3%) one month later. Lipid profiles (cholesterol, triglycerides, HDL, LDL, cholesterol/HDL Risk ratio, were all significantly corrected following the intermittent fasting (p 0.000) and continuing in the next phase (p 0.000). Body mass index (BMI) was lessened only following the fasting (p 0.00), while no remarkable changes were noted regarding waist, hip, triceps skin fold thickness (p 0.07). Glycemic indices (HbA1C, postprandial, HOMA-IR) were significantly corrected. Fibrosis markers (FIB-4 and APRI) were significantly ameliorated (p 0.000), while inflammatory markers (c-reactive protein reduction did not last to the end of the study p 0.3).
Conclusion: Intermittent fasting had momentous improvements of many ultrasonographic and biochemical and anthropometric parameters of metabolic syndrome especially in early phases and prediabetics. Accordingly, regular fasting at least from 3 to 5 days monthly, along with diet planning are recommended for better control of NAFLD.

Abstract #948

Jiangzhi Granules improves liver injury through the role of TFF3 in regulating EGFR/AKT and NF-κB signaling pathway in NASH

Zhang Yifan[1], Li Yiping[1], Liu Yang[1], Yang Lili[1], Zheng Peiyong[1,2], Song Haiyan[1,2#]

[1]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, China, [2]China-Canada Centre of Research for Digestive Diseases, Shanghai, China

Objective: This study aims to explore the mechanism of traditional Chinese medicine formula Jiangzhi Granules (JZG) in improving liver injury in NASH mice, based on the effect of trefoil factor 3 (TFF3) against lipotoxicity to the liver.
Methods: C57BL/6 J mice were fed with a high-fat diet (HFD) to establish the NASH model. Since the 18th week, JZG was intragastrically administrated to the NASH mice simultaneously. At the end of the 22nd week, mice were sacrificed. Serum transaminase levels were measured and liver pathological changes were observed. The levels of TFF3, apoptosis and inflammation-related genes of liver tissues were detected. Additionally, the activation level of EGFR/AKT and NF-κB was investigated.
Results: NASH model mice had higher ALT levels, lower hepatic expression of TFF3, increased cleaved Caspase3, Bim, IL-1β, IL-6, TNF-α and p-NF-κB and decreased expression of p-EGFR and p-AKT in liver tissues than the control. Compared with the model group, mice with JZG treatment showed improved hepatosteatosis, inflammation and ballooning in liver tissues, reduced ALT, increased hepatic expression of TFF3, p-EGFR, and p-AKT. JZG also ameliorated hepatic expression of cleaved Caspase3, Bim, IL-1β, TNF-α and p-NF-κB.
Conclusions: JZG can promote the activation of EGFR/AKT and inhibit the activation of NF-κB through up-regulating TFF3 expression in the liver tissue of NASH mice, thereby reducing liver inflammation and apoptosis, which may contribute to the mechanism of JZG in improving liver injury in NASH.

Abstract #949

Comparative study on treatment outcome of Sitagliptin on histological activity and fibrosis score between diabetic and non-diabetic patients with biopsy proven nonalcoholic steatohepatitis.

Ghosh Jhumur[1,2*], Alam Shahinul[2], Mostafa Golam[2]

[1]*Assistant Professor, Department of Hepatology, M. H. Samorita Hospital and Medical College, Dhaka, Bangladesh. E-mail: [2]Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

Introduction: Hepatic Dipeptidylpeptidase-4 (DPP-4) expression in nonalcoholic fatty liver disease (NAFLD) is directly associated with hepatic lipogenesis and liver injury. Sitagliptin is an oral antihyperglycaemic agent that inhibits DPP-4 but there has few trial of Sitagliptin on human Nonalcholic steatohepatitis (NASH) to date.
Objective: To asses treatment outcome of Sitagliptin on NAFLD activity score (NAS) and fibrosis score between diabetic and non-diabetic patients with NASH.
Methods: In this open label case control study total 30 biopsy proven NASH patients with or without type 2 diabetes mellitus were included. 20 patients were treated with Sitagliptin plus life style modification (SL) and 10 patients were treated with only life style modification (L) for one year. Among SL group 11 patients were diabetic and 9 patients were non-diabetic. NAS improvement ≥ 2 and fibrosis score improvement ≥ 1 were defined as histological responder.
Results:The difference of NAS improvement between SL and L group was statistically significant ($P = 0.003$). Hepatocyte ballooning improvement was borderline significant ($P = 0.055$) in SL group. There was no improvement in the lobular inflammation and fibrosis score in both SL and L groups. The mean NAS was 1.8 ± 1.4 in diabetic group and 2.0 ± 1.5 in non-diabetic group. The mean fibrosis score was 0.2 ± 1.2 in diabetic group and 0.55 ± 1.23 in non-diabetic group. The difference of mean histological improvement was not statistically significant ($P < 0.5$) between the diabetic and non-diabetic NASH patients.

Conclusion: Sitagliptin may improve histological activity score without any deterioration of fibrosis score in NASH patients irrespective of diabetes mellitus.

Table: Mean histological improvement between diabetic and Nondiabetic NASH patients in SL group (N=20)

Liver biopsy	Diabetic patient (N=11)	Nondiabetic patient (N=9)	P value
NAFLD activity score	1.8±1.4	2.0±1.5	0.769[ns]
Steatosis	1.0±0.9	1.0±1.0	1.000 [ns]
Lobular inflammation	0.3±0.6	0.11±0.78	0.545 [ns]
Hepatocellular ballooning	0.3±0.7	0.33±0.78	0.928 [ns]
Fibrosis score	0.2±1.2	0.55±1.23	0.529 [ns]

Abstract #1010

Lipidomic signatures in patients with varying histological severity of non-alcoholic fatty liver disease

Muralidharan Sneha[1], Soon Gwyneth[2], Asim Shabbir [3], Binte Jumat Nur Halisah [1]Binte Abbas Sakinah [1], WJ Lee Jonathan [1,4], Muthiah Mark [4], Loo Wai Mun[4], Tan Eunice[4], Ji Shanshan[5], Burla Bo[5], WL Koh Hiromi[6], Choi Hyungwon[1], Wenk Markus[7], Torta Federico[7] and Yock Young Dan[1,4]

[1]Department of Medicine, National University of Singapore, Singapore, [2]Department of Pathology, National University Hospital, Singapore, [3]Department of Surgery, National University Hospital, Singapore, [4]Division of Gastroenterology & Hepatology, National University Hospital, Singapore, [5]Life Sciences Institute, National University of Singapore, Singapore, [6]Saw Swee Hock School of Public Health, National University of Singapore, Singapore, [7]Department of Biochemistry, National University of Singapore, Singapore

Introduction: Non-alcoholic fatty liver disease (NAFLD) represents a wide spectrum of pathology ranging from simple steatosis, steatohepatitis, fibrosis to cirrhosis. However, physicians are still reliant on liver biopsies, as there are no adequate non-invasive biomarkers for either NASH or fibrosis. Therefore, we aim to identify unique circulating lipidomic signatures for NASH and fibrosis in NAFLD patients.
Methods: Fasting serum samples collected from 163 Singaporean patients, were profiled, whereby the patients were either healthy controls (n = 36), simple steatosis (n = 35), incomplete NASH (n = 34), NASH with early fibrosis (n = 33), or NASH with late fibrosis (n = 25). 461 lipids were quantified and used for subsequent multivariate linear regression analysis, which included other clinical variables such as age, sex, and ethnicity.
Results: NAFLD patients with varying histological severity of NAFLD displayed distinctively altered patterns of many lipids. In particular, our results showed a stepwise change in the levels of triacylglycerides, polyunsaturated fatty acid containing phosphatidylethanolamines, free fatty acids and dihexosylceramides depending on the grade of steatosis, lobular inflammation, ballooning and fibrosis in NAFLD patients.
Conclusion: Patients with varying histological severity of NAFLD exhibit unique circulating lipidomic signatures, and may, therefore, be useful surrogate markers for NASH and NAFLD fibrosis.

Abstract #1012

Single doses of TERN-201, a novel selective semicarbazide-sensitive amine oxidase (SSAO) inhibitor, are safe, well-tolerated, and result in reduced plasma SSAO activity in healthy participants

M. Fenaux, Q. Zhang, Y. Wang, C. Jones, R. Halcomb and E. Quirk

Introduction: SSAO contributes to disease progression of non-alcoholic steatohepatitis (NASH) by 1) catalyzing oxidative deamination of primary amines to aldehyde, ammonium, and hydrogen peroxide (H_2O_2), causing oxidative and vascular damage, and 2) mediating binding and recruitment of inflammatory cells to the liver vascular endothelium to exacerbate liver inflammation. TERN-201 is a novel covalent SSAO inhibitor that improves NASH and fibrosis in rodent NASH models.
Objective: To assess the pharmacokinetic (PK) and pharmacodynamic (PD) responses of TERN-201 single doses in healthy human participants.
Methods: A double-blind, placebo-controlled, single ascending dose clinical trial was conducted in 4 groups of 8 healthy male and female participants randomized in sequential cohorts to receive 1 mg, 3 mg, 6 mg and 10 mg TERN-201 or matching placebo. PK was assessed for 48 hours after dosing. SSAO engagement was determined by measuring relative reductions in plasma H_2O_2 generation. Safety was assessed for 7 ($\pm$ 3) days after dosing.
Results: Half-life of TERN-201 in plasma was approximately 1 to 3 hours. In the placebo, 1, 3, 6 and 10 mg dose groups, mean decreases in plasma amine oxidase activity were 1.7%, 32%, 35%, 35% and 36% 6 hours postdose and 6.6%, 22%, 22%, 28% and 16% 24 hours postdose respectively. No clinically relevant adverse events or laboratory abnormalities were reported.
Conclusion: Despite a short plasma half-life, robust, prolonged decreases in plasma SSAO amine oxidase activity were observed following single doses of TERN-201, suggesting potent target engagement by TERN-201 and a slow multi-day SSAO protein regeneration cycle. All dose levels were well-tolerated in healthy subjects.

Abstract #1022

Silybin improves hepatic steatosis, inflammation and fibrosis by inhibiting NLRP3 inflammasome activation in mice with non-alcoholic steatohepatitis

Zhiyu Yang[1,2], Xiaoying Luo[1,2], Di Lu[1,2], Qiaoyun Xia[1], Yangqiu Bai[1], Xiaoke Jiang[1], Mingbo Cao[1], Xiuling Li[1], and Bingyong Zhang[1,2]

[1]Department of Gastroenterology, Henan Provincial People's Hospital, People's Hospital of Zhengzhou University, Zhengzhou, Henan, 450003, China, [2]Microbiome Laboratory, Henan Provincial People's Hospital, People's Hospital of Zhengzhou University, Zhengzhou, Henan, 450003, China

Introduction: Silybin is one of the effective, traditional Chinese medicines used as a hepatoprotective agent for liver diseases. Several human clinical trials have suggested that silybin may be useful for treatment of non-alcoholic steatohepatitis (NASH).
Objectives: Our aim was to investigate whether the therapeutic effect of Silybin on NASH was attributed to its inhibition effect on the NOD-like receptor family pyrin domain-containing 3 (NLRP3) inflammasome activation.

Methods: In our study, we used mice model of methionine-choline-deficient diet induced NASH. At different NASH stages, the activation of NLRP3 inflammasome was analyzed by means of immunohistochemistry, western blot, quantitative polymerase chain reaction, and Enzyme-linked immunosorbent assay respectively. After daily gavage of silybin (52.5 mg/kg) for 3 weeks, we evaluated the direct effect of silybin on hepatic steatosis, inflammation, and fibrosis in mice through assessing liver function and liver histology. After silybin treatment, the activation of NLRP3 inflammasome in liver tissues was also detected using the methods above and the nuclear factor kappa B (NF-κB) transactivities were analyzed in hepatoma cells using a gene reporter assay.
Results: NLRP3 inflammasome was activated in our NASH models, and Silybin improved NASH-related lesions and inhibited the transcriptional expression of some inflammatory and fibrosis-related factors in these mice. Associated with this, silybin suppressed the activation of NLRP3 inflammasome by inhibiting the transcriptional activity of NF-κB.
Conclusions: NLRP3 inflammasome could be activated and might have an essential role in NASH progression, and silybin treatment could have a potential therapeutic effect on NASH-associated lesions by inhibiting NLRP3 inflammasome activation.

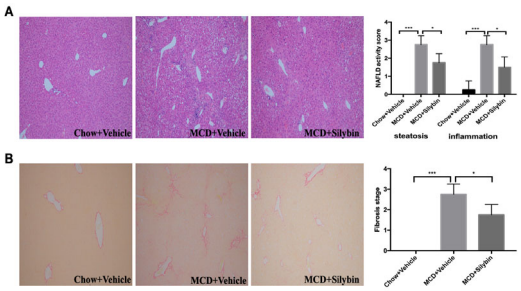


Figure 1. **Silybin improves NASH-related lesions in these mice NASH models.** In our study, mice were divided into three groups which including the Chow+Vehicle group, the MCD+Vehicle group, and the MCD+Silybin group. Steatosis and inflammation of the liver in mice of the three groups above were observed by HE staining (×100), and NAFLD activity score of the three mice groups was analyzed respectively (A). Liver fibrosis of the liver in mice of the three groups above was also observed by Sirius Red staining (×100), and the degree of liver fibrosis of the three mice groups was analyzed respectively (B). Data are presented as means ± SEM ($n = 5$). *$P < 0.05$, ***$P < 0.001$.

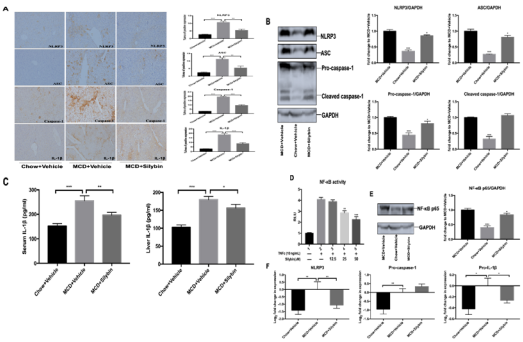


Figure 2. **Silybin suppressed the activation of NLRP3 inflammasome by inhibiting the transcriptional activity of NF-κB.** Liver tissues form mice of the three groups were used for immunohistochemistry to detect the expression of various components of NLRP3 inflammasome (×200) (A). The expression of NLRP3, ASC, and Caspase-1 (including Pro-caspase-1 and Cleaved caspase-1) in liver tissues from mice above, which were components of NLRP3 inflammasome, were detected by Western Blot. *$P < 0.05$, ***$P < 0.001$, both vs. MCD diet group ($n = 5$) (B). And the levels of IL-1β in serums and liver tissues from mice above were measured with an ELISA kit (C). Silybin repressed NF-κB transactivity in HepG2 cells. HepG2 cells were co-transfected with the NF-κB reporter plasmids and P65 expression plasmids for 24 h and pretreated with the control (DMSO), silybin (12.5, 25, 50 μM) for 18 h before treatment with TNF-α (10 ng/mL) for another 6 h. The RLU were measured by comparison to renilla luciferase activities. **$P < 0.01$, ***$P < 0.001$, both vs. TNF-α group (D). The expressions of NF-κB p65 in liver tissues from mice above were detected by Western Blot. *$P < 0.05$, ***$P < 0.001$, both vs. MCD diet group ($n = 5$) (E) Finally, the relative gene expressions of *NLRP3*, *Pro-caspase-1* and *Pro- IL-1β* in liver tissues from mice above were detected by RT-PCR. *Beta-actin* was used as an internal control for normalizing the mRNA levels (F). Data are presented as means ± SEM ($n = 5$). *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Abstract #1024

Pegbelfermin (PGBF) reduces serum levels of secondary bile acids (BAs) in patients with non-alcoholic steatohepatitis (NASH)

Luo, Yi[1], Charles, Edgar D.[1], Shipkova, Petia[1], Reily, Michael[1], Jarai, Gabor[1], Sanyal, Arun[2]

[1]Bristol-Myers Squibb, Princeton, NJ, USA; [2]Virginia Commonwealth University, Richmond, VA, USA

Introduction: Secondary BAs deoxycholic acid (DCA), glyco-DCA (GDCA), and tauro-DCA (TDCA) are elevated in patients with NASH relative to healthy adults. PGBF (PEGylated human fibroblast growth factor 21) improved steatosis and fibrosis biomarkers in a Phase 2, 16-week trial in patients with NASH without cirrhosis (NCT02413372).
Objective: Evaluate the effect of PGBF treatment on serum BAs in an exploratory post hoc analysis of NCT02413372.
Methods: Pre- and post-treatment BAs were measured in fasting serum with ultra high-performance liquid chromatography and mass spectrometry. A repeated measurement mean profile ANOVA model was applied. Holm's multiple testing adjustment was performed to assess treatment by day interaction effects. Dunnett's test (P value) was used to compare BA change from baseline in PGBF vs placebo groups.
Results: Baseline and Day 112 serum samples from 63 patients were analyzed (placebo: n = 24; PGBF QD: n = 21 and QW: n = 18). Primary BAs did not significantly change post-PGBF treatment. DCA, GDCA, and TDCA had median decreases from baseline from 61%–84%; all were significantly reduced in both PGBF groups vs placebo on Days 57 and 112 ($P < 0.01$). The ratio of total DCA:primary BAs was significantly reduced with PGBF QD vs placebo ($P = 0.0001$). Additionally, decreased secondary BAs contributed to a trend of lower total BAs in PGBF QD and QW groups vs placebo ($P = 0.036$ and $P = 0.165$, respectively).
Conclusions: PGBF treatment reduced secondary BAs and lowered the ratio of total DCA:primary BAs in patients with NASH without cirrhosis. Further investigation is needed to understand the mechanisms that mediate PGBF's effect on BAs.

Abstract #1025

Pharmacokinetics and safety of pegbelfermin (PGBF) administered in the abdomen and upper arm to normal, overweight, and obese healthy participants

Tirucherai, Giridhar S., Mora, Johanna, Revankar, Ratna, Charles, Edgar D.

Bristol-Myers Squibb, Princeton, New Jersey, USA

Introduction: PGBF, a PEGylated human fibroblast growth factor 21 (FGF21), improved steatosis and fibrosis biomarkers in a Phase 2 study in patients with non-alcoholic steatohepatitis (NASH).
Objective: Evaluate pharmacokinetics and safety of a single-dose, subcutaneous PGBF injection to the abdomen and upper arm in healthy normal weight, overweight, and obese participants.
Methods: MB130-070 was a Phase 1, open-label study. BMI (kg/m^2) cohorts: $18.0 \leq 25.0$ (normal), $> 25.0 \leq 30.0$ (overweight), and $> 30.0 \leq 40.0$ (obese). Treatment: 20 mg PGBF on Day 1 of successive treatment periods (1: abdomen; 2: arm). Serum for pharmacokinetic analysis and safety data were collected.

Results: In periods 1 and 2, 30 (n = 10/cohort) and 29 participants received PGBF, respectively. 90% were men; median age = 31 years. Arm vs abdomen: PGBF exposure was $\leq$ 30% higher in normal and overweight participants, and similar in obese participants. Exposure was $\leq$ 21% and $\leq$ 67% higher in normal vs overweight and obese participants, respectively. Adverse events (AEs): 6 occurred post-abdomen injection (overweight: n = 3; obese: n = 3); 18 occurred post-arm injection (normal: n = 6; overweight: n = 4; obese: n = 8). AEs were of mild/moderate intensity; no serious AEs or deaths occurred. One obese participant discontinued (non-treatment-related AE). One overweight participant had anti-FGF21 antibodies during period 2.
Conclusions: Subcutaneous abdominal and upper-arm injections of PGBF were generally well tolerated in healthy participants with a trend towards increased exposure with decreased BMI. Exposure was $\leq$ 30% higher in normal and overweight participants after administration to the arm vs abdomen. A dose-ranging study evaluating histological and biomarker responses to PGBF in patients with NASH is underway.

Abstract #1133

Prediction of long term outcome in lean NAFLD

Sripongpun Pimsiri, MD[1,2], Mannalithara Ajitha, PhD[1], Kim W. Ray, MD[1]

[1]Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Stanford, California, USA, [2]Gastroenterology and Hepatology Unit, Division of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Hat Yai, Thailand

Introduction: Non-alcoholic fatty liver disease (NAFLD) in lean individuals is an under-appreciated, poorly understood entity. Long-term outcome of those patients and its predictors are not well studied.
Objectives: To compare overall survival of lean individuals with and without NAFLD and to determine predictors of survival.
Methods: Using the National Health and Nutrition Examination Survey (NHANES) III and linked mortality data censored on December 31, 2015. Survey participants with age $\geq$ 18 years, body mass index (BMI) $<$ 25 kg/m^2 were included. Survey participants with NAFLD (definition: presence of hepatic steatosis on ultrasound) were categorized into low-risk, intermediate-risk, and high-risk of having significant fibrosis according to SAFE score (a score to predict fibrosis $\geq$ F2 in NAFLD patients incorporating FIB-4, BMI, albumin-globulin ratio, GGT, and diabetes). Kaplan-Meier method and Cox regression analyses were used to evaluate the survival.
Results: Of 3,529 eligible lean subjects. NAFLD was found in 24%. Among NAFLD subjects, 77.0% were low-risk, 17.7% intermediate-risk, and 5.2% were high-risk for having F $\geq$ 2. After a median of 22.7 years follow-up, survival curves of lean subjects with and without NAFLD are shown in Figure. In the multivariable analysis, mortality was increased significantly in lean NAFLD with intermediate-risk (aHR 1.29, 95% CI 1.03–1.61) and with high-risk (aHR 2.01, 95% CI 1.44–2.83) compared to that in subjects without NAFLD, which was not significantly different from that in lean NAFLD with low-risk subjects. Other significant variables in the model include: smoking status, and hypertension.
Conclusion: The SAFE score is an independent predictor of long-term outcome in lean subjects with NAFLD.

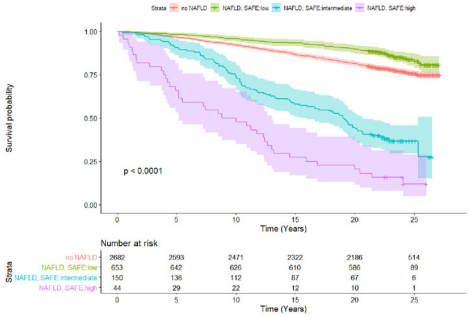


Figure. The Kaplan-Meier survival curves of lean survey participants without NAFLD and NAFLD with low-risk, intermediate-risk and high-risk of having significant fibrosis.

Abstract #1190

The effect of Oligonol® in non-alcoholic fatty liver disease (NAFLD) Patients

Techapaitoon S, M.D[1,2], Chutaputti A, M.D.[1,2]

[1]Bumrungrad International Hospital, Bangkok Thailand, [2]Vichaiyut Hospital, Bangkok Thailand

Introduction: The prevalence of Non-Alcoholic Fatty liver disease (NAFLD) is increasing all over the world. There are multifactorial mechanisms of NAFLD, Insulin resistance (IR) play a major role in pathophysiology of the disease. Previous reports of Oligonol®, an oligomerized polyphenol compound, extraction from Lychee fruit, showed effect of IR reduction.
Objective: The Primary objective of this study is to observe the IR level in NAFLD patient who under treatment with Oligonol® for 6 months. The secondary objective is the effect of Oligonol® on LFT and Liver Fat content (measurement by transient elastography)
Method: The NAFLD patients who have Fat content more than 250 db/m from Fibroscan with or without elevated LFT are include in the study. All patients receive Oligonol® 1 capsule 2 time/day (Total 200 mg.) for 6 months. The 3 months of follow up of IR (measurement by HOMA Score), BW, LFT, Lipid profile and Fibroscan at end of 6 months treatment.
Result: There are 19 cases, 13 (68.4%) male, 6 (31.5%) female, with mean age 48.38 years (range 21–76). The mean BMI is 29.18 kg/m^2, with 68% overweight and 32% obese. All patients tolerate treatment well with good compliance and have no side effect. 13/19 (68.42%) patients show decrease of IR HOMA from mean HOMA 5.18 to 3.47 in 6 months 12/13 patients with decrease IR HOMA score reveal significant improvement in AST from 62.91 to 35.83 U/L and ALT from 125.41 to 66 U/L. Moreover 6/13 (46.15%) who also lost about 5% of body weight have normalization of LFT. No weight gain in all 19 patients during the 6 months study period. 6 patients who have no decrease in HOMA score show no worsening of LFT, some with improvement.
Conclusion: 2/3 of NAFLD patients who take addition of Oligonol® 200 mg/day for 6 months show improvement in Insulin Resistance and hepatitis with no side effect.

Abstract #1259

The transcriptomal characteristics versus N-of-1 heterogeneity of human non-alcoholic fatty liver disease

Atsumasa Komori, Kugiyama Yuki, Bekki Shigemune, Suehiro Tomoyuki, Hashimoto Sator, Saeki Akira, Nagaoka Shinya, Abiru Seigo, Yamasaki Kazumi, Ito Masahiro, Yatsuhashi Hiroshi

Clinical Research Center, National Hospital Organization Nagasaki Medical Center, Omura 856-8562, Japan

Introduction and objectives: Due to emerging burden of non-alcoholic fatty liver disease (NAFLD), not only the pathogenesis but also the spectrum of disease phenotype are needed to be characterized. The aim of the study is to define the transcriptomal characteristics and heterogeneity of NAFLD liver, utilizing a cohort of patients and a N-of-1 longitudinal analysis.
Methods: Hepatic RNAs were extracted from biopsy samples of cohort 1 (N = 12) and of an atypical patient who obtained pathological remission by prednisolone, but had relapse after its cessation (longitudinal biopsies: In admission/stage 3; T1, in remission; T2, and in relapse/stage 2; T3). Microarray hybridization was performed on 3D-Gene Human Oligo chip 25 k (Toray Industries Inc., Japan). Commercially available hepatic RNA from 4 healthy volunteers were used as controls (CON). Normalized gene expression data were analyzed using GeneSpring (Agilent Technologies, U.S.A.). Differentially expressed genes in cohort 1 (NAFLD-DEGs) were defined those whose expression had FDR corrected $p < 0.05$ and a fold change ($\geqq 1.5$ or $\leqq 1/1.5$) in signal intensity, compared to CON. N-of-1 disease activity-associated genes (N-of-1 s) were defined those whose expression in T1 and T3 had a fold change ($\geqq 2$ or $\leqq 1/2$) in common, compared to T2. Pathway analysis were performed using IPA (QIAGEN, GmbH).
Result: Only 36 genes (upregulated;25, downregulated;11) were common in both NAFLD-DEGs (n = 1027) and N-of-1 s (n = 906). Significantly upregulated 49 canonical pathways (Z score > 2.0), including 30 immune-related ones, were identified in N-of-1 s, but not in NAFLD-DEGs.
Conclusion: The hepatic pathogenesis of NAFLD might be modulated by the personal disease activity-associated transcriptomes.

Abstract #1319

Correlation between lean nafld and andropause

Ishwar amalazari, Venkatesawaran, Premkumar

Institute of medical gastroenterology, MMC

Background: Lean NAFLD is special group of patients where etiology and risk factors for NAFLD debating. Many studies showed it's middle aged male predominant disease. Male menopause is known condition effects middle age men and it alters metabolic profile leads to increased cardiovascular risk factors.
Aim: To study the prevalence of andropause and its relation to Lean NAFLD.
Methods: we included 75 lean NAFLD patients and 75 age matched normal controls. The subjects screened for andropause using the St Louis Androgen Deficiency in the Adult Male (ADAM) questionnaire and aging male symptoms (AMS) score. Prevalence of andropause in both group calculated and compared. Considered significant if P value < 0.05.
Results: In 75 lean NAFLD patients 64 patient were clinically andropause and prevalence is 85%. In age matched normal controls 32 patients were clinically andropause and prevalence of 46%. After comparing between both groups prevalence of andropause significantly higher in lean NAFLD group with P value < 0.00028.
Conclusion: our study suggestive of andropause is clear predisposing risk factor implicating in development of lean NAFLD compared to age matched controls. It's known fact andropause is age related phenomenon in middle aged man but it's implications in development of metabolic syndrome including NAFLD not studied till. Lean NAFLD is known subgroup in NAFLD with low metabolic risk profile and slow progression but etiology and predisposing factors not clear. we consider andropause as risk factor for Lean NAFLD.

Abstract #1427

A prospective, multi-center, double-blind, randomized trial of Saroglitazar 4 mg compared to placebo in patients with non-alcoholic steatohepatitis

Shiv K Sarin[1], Manoj Sharma[2], Parshottam Koradia[2], Ajay Duseja[3], Shobna Bhatia[4], VinodKumar Dixit[5], Sandeep Nijhawan[6], Murugesh Mallaiyappan[7], Shrikant Mukewar[8], Sanjay Maroo[9], Manjunath Krishnappa[9], Payal Jain[9], Krupi Parmar[9], Pankaj Patel[9]

[1]Institute of Liver & Biliary Sciences, New Delhi, India, [2]BAPS Pramukh Swami Hospital, Surat, India, [3]Department of Hepatology, PGIMER, Chandigarh, India, [4]Department of Gastroenterology, Seth GS Medical College and KEM Hospital, Mumbai, India, [5]Department of Gastroenterology, Institute of Medical Science, Banaras Hindu University, Varanasi, India, [6]S.M.S Medical College and Attached Hospitals, Jaipur, India, [7]Kovai Diabetes Specialty Centre and Hospital, Coimbatore, India, [8]Midas Multispecialty Hospital Pvt. Ltd, Nagpur, India, [9]Zydus Research Centre, Cadila Healthcare Ltd, Ahmedabad, India.

Background: Pre-clinical and clinical studies suggest that Saroglitazar (a novel dual peroxisome proliferator activated receptor α/γ agonist) can be a potential treatment for non-alcoholic fatty liver disease (NAFLD)/ nonalcoholic steatohepatitis (NASH).
Objective: This phase-3, prospective, multi-center, double-blind, randomized trial of 52 weeks was conducted to determine efficacy and safety of Saroglitazar 4 mg compared to placebo in adult patients with NASH from July 2016 to October 2019 in India.
Methods: Total 102 adult patients with biopsy proven NASH without cirrhosis (fibrosis stage 1, 2, or 3) with a NAFLD activity score (NAS) of ≥ 4 with a score of at least 1 in each component (steatosis, lobular inflammation, and hepatocyte ballooning) were randomized in a ratio of 2:1 to Saroglitazar 4 mg and placebo at 10 centres in India.
Results: Baseline characteristics were balanced between Saroglitazar 4 mg and placebo groups. For the primary endpoint, there was a statistically significant reduction in proportion of patients with decrease in NAS ≥ 2 spread across at least 2 of the NAS components without worsening of fibrosis at week-52 in Saroglitazar 4 mg group (52.3%) compared to placebo group (23.5%) (*P-value*: 0.0427). For the secondary endpoints, Saroglitazar 4 mg significantly reduced mean score of hepatocyte ballooning, steatosis, lobular inflammation, and NAS from baseline to week-52 (p-value < 0.05). Saroglitazar 4 mg improved liver parameters and lipid parameters from baseline to week-52. Most of the AE's were mild to moderate in severity and Saroglitazar was well tolerated.
Conclusion: Saroglitazar 4 mg was found efficacious and safe in patients with NASH.

Table 1. Changes in efficacy outcomes in the per-protocol population of NASH population at week-52

Efficacy Outcomes	Treatment	Baseline (M±SD)	Week-52 (M±SD)	% Change From Baseline (M ± SD)	*p* value
NAS	Saroglitazar 4 mg	5.30±0.95	3.41±1.32	-34.66±26.03	<.0001
	Placebo	5.06±0.90	4.18±1.70	-17.55±28.57	0.0049
Steatosis	Saroglitazar 4 mg	1.93±0.70	1.02±0.70	-41.29±52.02	<.0001
	Placebo	1.82±0.73	1.35±0.86	-22.55±46.75	0.0478
Lobular Inflammation	Saroglitazar 4 mg	1.75±0.44	1.41±0.62	-12.50±47.16	0.0526
	Placebo	1.71±0.69	1.47±0.62	-5.88±49.98	0.5425
Hepatocyte Ballooning	Saroglitazar 4 mg	1.61±0.49	0.98±0.59	-35.23±42.56	<.0001
	Placebo	1.53±0.51	1.35±0.61	-2.94±48.32	0.7095
ALT (U/L)	Saroglitazar 4 mg	81.19±68.80	46.86±35.41	-27.79±36.41	<.0001
	Placebo	74.06±50.24	64.65±53.59	-12.32±28.16	<.0001
AST (U/L)	Saroglitazar 4 mg	47.37±33.33	32.16±16.16	-18.10±34.00	<.0001
	Placebo	45.25±26.55	38.00±18.39	-9.21±28.56	0.0004
ALP (U/L)	Saroglitazar 4 mg	100.37±24.78	68.98±29.28	-32.14±19.22	<.0001
	Placebo	96.69±28.25	100.59±30.17	8.48±33.12	<.0001
GGT (U/L)	Saroglitazar 4 mg	73.05±93.31	43.44±33.53	-29.27±37.13	<.0001
	Placebo	51.75±40.66	44.18±22.70	-3.46±26.75	0.0022
Triglyceride	Saroglitazar 4 mg	158.60±77.55	114.79±63.50	-24.51±31.93	<.0001
(mg/dL)	Placebo	128.06±52.82	133.24±47.00	5.74±28.98	<.0001
HDL (mg/dL)	Saroglitazar 4 mg	41.60±10.17	42.68±15.10	3.64±27.74	<.0001
	Placebo	42.06±8.27	41.35±8.42	-1.13±8.42	<.0001
LDL (mg/dL)	Saroglitazar 4 mg	120.63±36.74	108.30±36.92	-8.68±20.58	<.0001
	Placebo	123.88±25.60	140.06±45.53	6.24±10.35	<.0001
Sd-LDL (mg/dL)	Saroglitazar 4 mg	32.99±18.65	23.41±14.89	-22.02±40.19	<.0001
	Placebo	27.69±10.52	30.12±15.06	19.16±60.40	0.6021
VLDL (mg/dL)	Saroglitazar 4 mg	30.55±13.65	22.98±12.64	-24.39±32.01	<.0001
	Placebo	25.56±10.51	26.53±9.44	5.07±28.69	0.0367
Total cholesterol	Saroglitazar 4 mg	185.53±45.52	166.70±45.61	-9.27±15.77	<.0001
(mg/dL)	Placebo	184.13±30.19	199.06±51.93	3.14±10.34	<.0001
Non-HDL	Saroglitazar 4 mg	143.93±43.41	124.81±44.04	-11.92±20.88	<.0001
(mg/dL)	Placebo	142.50±28.47	157.71±51.59	4.30±13.21	<.0001

Abstract #1491 HSD17B13 **insertion variant confers protective effect on adverse liver outcomes in patients with non-alcoholic fatty liver disease**

Ting Yi-Wen[1], Kong Amanda SY[1], Zain Shamsul Mohd[2], Chan Wah-Kheong[3], Tan Hwa-Li[2], Mohamed Zahurin[2], Mohamed Rosmawati[3]

[1]Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, [2]The Pharmacogenomics Laboratory, Department of Pharmacology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, [3]Gastroenterology and Hepatology Unit, Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Introduction: An alarming rate of cardiovascular, malignancy and liver-related morbidity and mortality can be expected with the pandemic-level rise of non-alcoholic fatty liver disease (NAFLD). However, the relationship between NAFLD susceptibility genes and the long-term clinical outcomes remains unclear.
Objective: This study aimed to evaluate the clinical outcomes of patients with NAFLD and its association with the genetic determinants.
Methods: We followed 180 consecutive biopsy-proven NAFLD patients at the University Malaya Medical Centre (UMMC) from October 2009 until August 2019. Cardiovascular events, liver-related complications, malignancy and all-cause mortality were recorded. Genotyping for 17β-hydroxysteroid dehydrogenase 13 (*HSD17B13*), adiponutrin (*PNPLA3*), glucokinase regulatory (*GCKR*) and leptin receptor (*LEPR*) variants were done in 176 patients using rhAmp assays (IDT, USA).
Results: There were 140 (77.8%) patients with non-alcoholic steatohepatitis (NASH), of whom 64 (45.7%) had significant liver fibrosis (stage F $\geq$ 2) and 36 (25.7%) had advanced fibrosis or cirrhosis. During a median follow-up time of 78 months (range of 60–118 months), 36 (20%) patients experienced at least one clinical outcome. There were 24 (13.3%) cases of cardiovascular events, 8 (4.4%) liver-related complications, 6 (3.3%) extra-hepatic malignancies and 7 (3.9%) deaths recorded. On multivariate Cox regression analysis, the TA allele of *HSD17B13* rs72613567 was independently associated with reduced risk of liver-related complications (Hazard ratio [HR] = 0.003, 95% CI: 0–0.352, p = 0.017). *PNPLA3* rs738409, *GCKR* rs780094 and *LEPR* rs1137100 were not associated with any clinical outcomes.
Conclusion: A loss-of-function *HSD17B13* rs72613567 variant confers protective effect on adverse liver outcomes in patients with NAFLD.

Abstract #1539 **5-aminolevulinic acid attenuates palmitate-induced endoplasmic reticulum stress and hepatocyte lipoapoptosis via heme oxygenase-1 induction.**

Hashimoto Takaaki, Sugihara Takaaki, Kanda Tsutomu, Takata Tomoaki, Isomoto Hajime

Multidisciplinary Internal Medicine, Faculty of Medicine, Tottori University, Yonago, Tottori, Japan

Introduction: The endoplasmic reticulum (ER) stress plays a pivotal role in the progression of steatohepatitis. 5-aminolevulinic acid (5-ALA), a precursor in the heme biosynthetic pathway, has recently been reported to induce heme oxygenase (HO)-1. HO-1 exerts important cytoprotective actions.
Objective: In this study, we aimed to explore the therapeutic potential of ALA on palmitate-induced ER-stress and lipoapoptosis.
Methods: Huh-7 cells were treated with palmitic acid (PA) (800 mM) to induce steatosis for 8 hours. Steatosis was evaluated by Lipi-green staining. 5-ALA (200 mM) was also added with PA. The gene expression levels of the nuclear factor erythroid 2-related factor 2 (Nrf2), HO-1, Glucose-regulated protein 78 (GRP78), C/EBP homologous protein (CHOP) and B-cell lymphoma 2 (BCL-2) were evaluated by RT-PCR. Caspase-3/7 activity was evaluated by fluorescein active Caspase-3/7 staining. The cell death event was evaluated by Annexin V with sytox green staining.
Results: PA significantly induced steatosis and increased GRP78 expression in Huh-7 cells. 5-ALA significantly induced HO-1 and decreased GRP78 expression. However, Nrf2 and CHOP expression were not altered. Anti-apoptotic BCL-2 expression was significantly increased. Caspase 3/7 activity and cell death were significantly decreased by 5-ALA.
Conclusion: 5-ALA has a therapeutic potential on hepatic steatosis by suppressing ER stress and lipoapoptosis by HO-1 induction with upregulating BCL-2.

Abstract #1602

Are patients with non-alcoholic fatty liver disease (NAFLD) at risk of endothelial dysfunction?

Waleed Al-hamoudi[1,2], Amani Alsadoon[2], Mazen Hassanian[2,3], Hisham Alkhalidi[4], Ayman Abdo[1,2], Mohamed Nour[5], Rabea Halwani[6], Faisal Sanai[7], Abdulsalam Alsharaabi[3], Khalid Alswat[1,2], Ahmed Hersi[5], Ali Albenmous[8], Faisal Alsaif[2,3]

[1]Department of Medicine, college of Medicine, King Saud University. Riyadh, Saudi Arabia, [2]Liver Research Center, King Saud University. Riyadh, Saudi Arabia, [3]Department of Surgery, college of Medicine, King Saud University. Riyadh, Saudi Arabia, [4]Department of Pathology, college of Medicine, King Saud University. Riyadh, Saudi Arabia, [5]Department of Cardiac Science, college of Medicine, King Saud University. Riyadh, Saudi Arabia, [6]Immunology Research Laboratory and Asthma Research Chair, College of Medicine, King Saud University. Riyadh, Saudi Arabia, [7]Gastroenterology Unit, Department of Medicine, King Abdulaziz Medical City, Jeddah, Saudi Arabia, [8]Department of Liver Transplantation and Hepatobiliary Surgery, King Faisal Specialist Hospital and Research Center. Riyadh, Saudi Arabia

Introduction: Nonalcoholic fatty liver disease (NAFLD) is one of the most common liver diseases encountered worldwide. The relationship between NAFLD and cardiovascular disease has grown significantly in the past few years.
Objectives: to assess endothelial function through the evaluation of flow mediated dilatation (FMD) of the brachial artery.
Methods: Patients were recruited at the time of admission for laparoscopic cholecystectomy. Clinical, laboratory, and histological data were collected prospectively from the study population. Endothelial function was assessed through the evaluation of flow mediated dilatation (FMD) of the brachial artery.
Results: 139 patients were included in this prospective study (50 healthy controls, 47 NAFLD patients with steatosis, 42 NAFLD patients with steatohepatitis). All included individuals were nondiabetic (HBA1C < 6.4), furthermore patients with long standing hypertension or uncontrolled blood pressure, smokers, morbidly obese (BMI > 40) patients were excluded. The median and ranges for vascular FMD in the NASH, steatosis, and control groups were 6% (0–37.5%), 10.8% (0–40%) and 13.6% (0–50%), respectively. Control patients had a higher average FMD compared to patients with NAFLD (15.13 vs 10.46%) this difference reached statistical significance when comparing the control and steatohepatitis groups (13.6 vs 6, $p = 0.027$). Alanine aminotransferase was significantly higher in the steatohepatitis group compared to the steatosis and control groups (54 vs 31, $p = 0.008$). Cholesterol levels were similar in all groups.
Conclusion: In the absence of major cardiac risk factors we demonstrated a better endothelial function in healthy controls, manifested by a higher FMD of the brachial artery compared to NAFLD patients.

Abstract #1603

Prevalence of biopsy proven non alcoholic fatty liver among patients with gallstone disease

Sara H. Qahtani[1], Amani M. Alsadoon[2], Ayman A. Abdo[2], Mazen M. Hassainan[1], Abdulsalam B. Alsharabi[1], Ghadeer R. Aljuhani[1], Hisham MS. Alkhalidi[3], Mohammad S. Elsharkawy[4], Maram A. Alotaibi[3], Waleed K. Al-hamoudi[2,5], Faisal A. Alsaif[1]

[1]Department of Surgery, College of Medicine, King Saud University, Riyadh, Kingdom of Saudi Arabia, [2]Liver Disease Research Center, King Saud University Medical City, Riyadh, Kingdom of Saudi Arabia, [3]Department of Pathology, College of Medicine, Riyadh, Kingdom of Saudi Arabia, [4]Department of Radiology and Medical Imaging, King Saud University Medical City, Riyadh, Kingdom of Saudi Arabia, [5]Department of Liver Transplant, King Faisal Specialist & Research Hospital, Riyadh, Kingdom of Saudi Arabia

Introduction: Gallstone disease (GD) and non-alcoholic fatty liver disease (NAFLD) are associated with metabolic syndrome. Despite the benign nature of NAFLD, 10% of patients may develop advanced fibrosis and cirrhosis.
Objectives: to identify the prevalence and factors associated with NAFLD among GD patients in the Saudi population.
Methods: This is a single-center, observational cohort study that included patients seen in general surgery clinics at our institution from 2011–2017. All liver biopsies were taken at the time of cholecystectomy. Demographical and clinical data were prospectively collected from the study population.
Results: 301 GD patients were included in this study. The percentage of patients who were normal, overweight and obese, were 15%, 29% and 56%, respectively. 47.8% (143) of patients had NAFLD, of which 41.8% (125) showed steatosis, and 6% (18) had non-alcoholic steatohepatitis. A significant positive correlation between age and BMI and NAFLD was found. Obese patients with a BMI of 30–34.9 patients were 3.833 ($p = 0.028$) times more likely to have NAFLD compared to patients with normal BMI, and this value increased to 7.872 ($p = 0.019$) in patients with BMI exceeding 40. Additionally, patients with diabetes were 4.114 times ($p = 0.034$) more likely to have NAFLD compared with those who did not.
Conclusions: The prevalence of NAFLD among GD patients is high. High BMI and diabetes are independent factors associated with NAFLD in GD patients. This study would be useful in proposing the need for routine liver biopsy in selected patients during cholecystectomy.

Abstract #1637

Saroglitazar improves transaminases and transient elastography in patients with diabetic dyslipidemia and non-alcoholic fatty liver disease: a prospective observational cohort study

Goyal O[1], Goyal P[2], Chhina RS[1]

[1]Dept. of Gastroenterology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India, [2]R.G. Stone Hospital, Ludhiana, Punjab, India

Introduction: Saroglitazar is a dual Peroxisome Proliferator-Activated Receptors (PPAR) α and γ agonist approved for diabetic dyslipidemia and hypertriglyceridemia. PPAR-α action of Saroglitazar improves lipid parameters and PPAR-γ action improves insulin sensitivity. Non-alcoholic fatty liver disease (NAFLD) is closely associated with diabetic dyslipidemia and is one of the leading causes of chronic liver disease.
Objectives: We aimed to evaluate the efficacy and safety of saroglitazar in patients with diabetic dyslipidemia associated NAFLD.
Methods: This prospective observational study conducted in northern India included diabetic patients with baseline HbA1c $> 6.2\%$ and dyslipidemia (total cholesterol > 200 mg/dl, triglycerides > 150 mg/dl) who received Saroglitazar 4 mg once daily for at least 24 weeks. The laboratory parameters and transient elastography (Fibroscan, Echosens) at baseline and 24 weeks were compared using t test. Trial was registered with CTRI, India (Registration No. CTRI/2019/05/019199)
Results: Total 92 patients were enrolled (age 49.4 ± 13.4 years; 79.3% (n = 73) males; mean BMI-28.7). Of these, 82.6% (n = 76) patients had alanine aminotransferase (ALT) $>$ ULN and/or fatty liver on ultrasonography. After 24 weeks of treatment, serum triglycerides significantly reduced from 328 ± 82 mg/dl to 139 ± 69 mg/dl ($P < 0.0001$), HbA1c from $7.7 \pm 0.8\%$ to $6.3 \pm 0.7\%$ ($P < 0.0001$), ALT from 96 ± 47 IU/L to 39 ± 15 IU/L ($P < 0.0001$), and transient elastography from 11.1 ± 6.7 Kpa to 9.6 ± 5.1 Kpa (p value = 0.04). Saroglitazar was found to be safe and well tolerated.
Conclusions: Saroglitazar leads to significant improvement in serum transaminases and transient elastography in patients with diabetic dyslipidemia and NAFLD. Therefore, it can be a potential therapeutic option for the treatment of NAFLD associated with metabolic syndrome.

Abstract #1658

Myeloid-specific TL1A overexpression exacerbates hepatic steatosis and inflammation through up-regulating NF-κB signaling pathway in NASH

Luo Yuxin, Guo Jinbo, Zhang Xiaolan

Department of Gastroenterology, The Second Hospital of Hebei Medical University, Hebei Key Laboratory of Gastroenterology, Shijiazhuang, China

Introdution: Macrophages play an important role in Non-alcoholic steatohepatitis (NASH) by regulating inflammatory responses. TNF-like ligand 1 aberrance (TL1A) increased in macrophages of many inflammatory diseases. The *TL1A*$^{-/-}$ mice showed weight reduced, abdominal adipose tissue and leptin decreased. And TL1A could activate the nuclear factor κB (NF-κB) and then promotes macrophages' activation and recruitment into liver.
Objective: To investigate the role of myeloid-specific TL1A overexpression in NASH.
Methods: FMS-TL1A-GFP-transgenic (Tg) and wild type (WT) mice were fed with high fructose high fat (HFHF) diets and methionine-choline deficiency (MCD) diets to induce two NASH models. TL1A in liver and liver macrophages was measured. Lipid droplet and the level of cholesterol and triglyceride were observed. TNF-α, IL-1β and IL-6 in serum and hepatic tissue were measured by ELISA and real-time qPCR. The apoptotic hepatocytes were detected by flow cytometry and Western blot. NF-κB p65 and IκBα in liver tissue, bone marrow-derived macrophages and Kuffer cells were measured by western blot.
Results: The expression of TL1A in liver tissue and macrophages was increased in the two NASH models. Hepatic steatosis, inflammatory responses and hepatocyte apoptotis were exacerbated in myeloid-specific TL1A overexpressed mice. The expression of NF-κB p65 protein showed a significantly higher level in Tg mice fed with HFHF or MCD than that in WT mice and in macrophages with TL1A overexpression of than that in WT macrophages. And the result of IκBα was opposite ($P < 0.05$).
Conclusion: Myeloid-specific TL1A overexpression may exacerbate hepatic steatosis and inflammation through up-regulating the NF-κB signaling pathway in NASH.

Abstract #1738

Steatosis vs fibrosis as forerunner of coronary artery disease in NAFLD

Jijo Varghese

Background and objectives: Non-alcoholic fatty liver disease (NAFLD) is emerging as an important chronic liver disease, the leading cause of mortality in which is coronary artery disease (CAD). Risk stratification for liver related outcomes in NAFLD are available whereas measures to stratify risk for cardiovascular outcomes in NAFLD patients are sparse. The objective of the study was to study NAFLD as a risk factor for CAD, to assess whether steatosis or fibrosis has correlation with CAD in NAFLD and to use Carotid intima media thickness (CIMT) as a noninvasive tool to predict the risk of CAD in NAFLD.
Methods: Case control study.125 cases with angiographically proven coronary artery disease and 125 controls with normal angiogram were enrolled after informed consent and subjected to sonography and blood investigations.
Results: The prevalence of NAFLD in CAD patients was 46.4% and was an independent risk factor for CAD (OR = 10.614, p = 0.027). Subgroup analysis of NAFLD patients with CAD and without CAD revealed that male gender, T2DM, systemic hypertension, low HDL, elevated triglycerides, elevated ALT levels and steatosis (grades of fatty liver) were independent risk factors for CAD in NAFLD patients. Liver fibrosis measured by liver stiffness measurement did not correlate with CAD (p = 0.483). The mean CIMT value of 0.55 mm had a sensitivity of 81% and specificity of 68% (AUROC = 0.696, p = 0.0001) to predict CAD in NAFLD patients.
Conclusions: NAFLD is an independent risk factor for CAD. Hepatic steatosis not fibrosis is the forerunner of CAD in NAFLD. The mean CIMT value of 0.55 mm is a sensitive tool to predict CAD in NAFLD patients.

Abstract #1889

Both alcoholic and non-alcoholic steatohepatitis (BASH): a preliminary study from eastern India.

Meher Dinesh, Mishra Debakanta, Khatua Chitta Ranjan, Panigrahi Subhendu, Barik Rakesh Kumar, Sahu Saroj Kanta, Pradhan Subhasis, Nath Gautam, Khandelwal Reshu, Anirvan Prajna, Gogoi Mrinal, Bharali Pankaj, Singh Shivaram Prasad

Department of Gastroenterology, S.C.B Medical College and Hospital, Cuttack, India

Introduction: Both alcoholic and non-alcoholic steatohepatitis (BASH) has emerged as a new entity. There is scanty data available on BASH from India.
Objectives: To study the biophysical and biochemical characteristics of steatotic patients with BASH.
Methods: We studied 5039 out patients diagnosed with steatosis / fatty liver on ultrasonography from 2010–2019. On the basis of obesity (BMI $\geq$ 25) and alcohol intake they were classified into four groups i.e. Idiopathic Steatosis (A), Steatosis with Obesity (B), Steatosis with Alcohol (C) and Both Alcoholic and Non-alcoholic Steatohepatitis /BASH (D). Anthropometric and biochemical data were analyzed and differences studied between the groups.
Results: BASH patients were significantly of lower age as compared to lean NAFLD (A) and obese NAFLD (B) group. BMI was significantly higher in BASH group in comparison to lean NAFLD and alcoholic steatohepatitis/ASH (C). Waist-hip ratio was significantly higher in BASH group in comparison to others. Significantly higher total cholesterol and triglycerides levels were observed in BASH group in comparison to lean and obese NAFLD. BASH group had lower serum albumin but higher alanine aminotransferase (ALT) and gamma glutamyl transferase (GGT) levels. Transient elastography (TE) value was significantly higher in BASH group in comparison to others. Parameters like platelet counts, fasting blood sugar, aspartate aminotransferase (AST), insulin, HOMA-IR were not statistically different in BASH patients compared to others.
Conclusion: BASH patients appeared to be more obese with higher BMI and W/H ratio. BASH patients had higher serum triglycerides, cholesterol, ALT and GGT levels but lower serum albumin levels. BASH patients had higher Transient elastography values compared to ASH and NAFLD subjects.

Abstract #1895

Prebiotics' plus probiotics' effect on the patients with nonalcoholic fatty liver disease

Khutsishvili N.[1,2]

[1]David Tvildiani Medical University, [2]Curatio Clinic

Introduction: Non-alcoholic fatty liver disease (NAFLD) is a very common disorder caused by a build-up of fat in the liver, often affecting overweight or obese people. Intestinal microbiota has been proved to play a role in the pathogenesis and development of obesity and NAFLD.

Aim: The aim of the study was to explore the impact of probiotics' plus prebiotics' (synbiotics) on the patients with NAFLD.
Methods: We studied 79 patients in total. Control group with placebo was included. A mixture of 6 probiotic agents (*Bifidobacterium bifidum, Bifidobacterium longum, Lactobacillus fermentum, Lactobacillus plantarum, Lactobacillus acidophilus, E-Coli M-17)* and an auxiliary prebiotic component: *fructoligosaccharide 50 mg.* was prescribed to 41 patients (*I group*) with elevated aminotransferase and serum triglyceride (TGs) levels for 16 weeks versus 38 patients (*II group*) who were given placebo. Overall, in the patients alcohol consumption accounted for less than 30 g/day. Lifestyle modification was advised for both groups. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), TGs, Body Mass Index (BMI), ultrasonographic grades of fatty liver were assessed in the end of the trial.
Results: Totally, 73 patients completed the study (6 dropped out in the I group). In the first group there was a significant reduction in the serum aminotransferase levels ($p = 0.001$) and TGs levels ($p = 1.0$) comparing the placebo group. ($p = 0.998$ and $p = 0.993$, respectively). BMI reduction and improvement in ultrasonographic grading was more remarkable in synbiotics' group.
Conclusions: Synbiotics showed good results in 16 weeks in the treatment of NAFLD along with lifestyle modificitanion.

Abstract #1912

A study on the association between severity of fibrosis in non alcoholic fatty liver disease and visceral fat volume

George Bony, Devadas Krishnadas, N premalatha, Nahaz Nibin, Krishna Anju, L Simna, Varghese Jijo, P Arun

Medical Gastroenterology, Medical College Trivandrum, India

Introduction: Various studies have shown that visceral fat was closely associated to the components of Inflammation and Fibrosis in NAFLD. Computerized Tomography (CT) scan is an effective method to measure Visceral fat volume.
Objective: Measure visceral fat volume and to find out it's association with liver fibrosis (as assessed by Vibration controlled Transient Elastography (VCTE)).
Methods: All patients with newly diagnosed NAFLD (after excluding other causes of hepatic steatosis) who were undergoing Cross-Sectional abdominal Imaging were taken up for the study. Transient elastography was done to assess hepatic fibrosis.
Results: 64 patients were taken up for the study. There were 36 males and 28 females. AUROC curve for visceral fat in predicting advanced fibrosis was plotted. AUROC was 0.733 and at a cut off of 167.5 cm^3, visceral fat had a sensitivity of 77.4% and a specificity of 51.5% in predicting advanced fibrosis. In subgroup analysis, females and those with BMI $\leq$ 25 Kg/M^2, Visceral fat was not a predictor of advanced fibrosis whereas in males and those with BMI $>$ 25, Visceral fat was a predictor of advanced fibrosis. When females with BMI $>$ 25Kg/M^2 were analyzed it was found that in females with BMI $>$ 25 Kg/M^2 visceral fat was not a predictor of advanced fibrosis.
Conclusions: Visceral fat measured at L3-L4 level with a cut off of 167.5cm^3had sensitivity of 77.4% and specificity of 51.5% in predicting advanced fibrosis. Visceral fat was a predictor of advanced fibrosis in males with BMI $>$ 25 Kg/M^2.

Abstract #1925

Presence and significance of hepatic steatosis and steatohepatitis in chronic non-fatty liver disease

Urzua, Alvaro M[1], Contreras, Felipe[2], Leiva, Jose Miguel[2], Moreno, Nicolas[2], Jimenez, Ana[2], Ordenes, Kevin[2], Vera, Daniela[1], Henriquez, Victor[1], Cattaneo, Maximo[1], Poniachik, Jaime[1]

[1]Seccion Gastroenterologia, Hospital Clinico Universidad de Chile, Santiago, Chile, [2]Alumno medicina, Facultad de Medicina, Universidad de Chile, Santiago, Chile

Introduction: Non-alcoholic (NAFLD) and alcoholic fatty liver disease (ALD) are very common conditions. Disease severity is determined by the presence of stetatosis, steatohepatitis and significant fibrosis (SF). There is little information on the role of NAFLD and ALD as co-factor in the progression to SF in chronic non-fatty liver diseases (CNFLD).
Objective: Describe frequency and impact on fibrosis of steatosis and steatohepatits in liver biopsies of CNFLD.
Methods: Observational, retrospective study with biopsies performed between 2015–2018 in one hospital. Presence of steatosis, steatohepatitis and fibrosis were recorded; METAVIR for fibrosis (F3-F4 is SF).
Results: 268 liver biopsies analyzed; 93 patients with NAFLD and ALD excluded. 175 included: 53% autoimmune hepatitis (AIH), 27% primary biliary cholangitis (PBC), 7% viral hepatitis (VH) and 13% other etiologies; 74% women; age 52 (18–82) years. Steatosis was present in 58%, steatohepatitis in 46% and fibrosis in 67% (SF in 61%). The presence of SF according to the presence of steatosis or steatohepatitis was 36% of SF in those with steatosis vs. 48% in those without (NS); 65% of SF in those with steatohepatitis vs 36% in those without (p 0.004). The grade of SF, according to etiology of liver disease and the presence of SH was: In AIH 92% vs 38% (p 0.001); in PBC 20% vs 24% (NS) and in VH 50% vs 22% (NS).
Conclusions: Steatosis and steatohepatitis are frequent in biopsies of CNFLD in our population. Presence of SH is associated with a higher degree of fibrosis, especially in those with AIH.

Abstract #1926

Liver stiffness measured by Fibroscan is associated with microvascular complications in Filipinos with Diabetes Mellitus

Sawadjaan Leila B., Ong Janus P.

The Medical City Section of Gastroenterology, Pasig, Philippines

Introduction: There is increasing evidence that suggest that patients with diabetes mellitus (DM) are at a particularly high risk for non-alcoholic steatohepatitis (NASH) and is related to its complications. Guidelines have recommended that there is no evidence of cost-effectiveness to support a non- alcoholic fatty liver disease (NAFLD) screening in adults even if they have DM.
Objectives: This study examines whether liver fibrosis, diagnosed by transient elastography by Fibroscan, correlates with chronic microvascular complications in patients with DM.
Methods: This retrospective cross- sectional study included Filipino patients with diabetes mellitus from a diabetes center at The Medical City Hospital who underwent liver stiffness measurement (LSM) by transient elastography using Fibroscan from January 2019 to December 2019. Patients included had data of Hba1c, body mass index (BMI), presence of chronic kidney disease, diabetic retinopathy or diabetic neuropathy, and liver stiffness measurement by Fibroscan

collected through chart review. Significant LSM was established at > 9.6 kPa.

Results: 84 patients were included in the study. There were 45 (53%) in the no fibrosis group and 39 (34%) in the advanced fibrosis group. The mean age of the subjects was 56 years old, with a range of 31 to 85 years old. Males comprised 58.9% (n = 49) and females 41% (n = 35). The average BMI of the subjects was 29 kg/m^2, with 79% being obese. Using Fisher exact test, the association of advanced fibrosis and presence of microvascular complication is significant at 0.0003, $p < 0.5$. Among those in the F0 category, 3 had at least one microvascular complication; while there were 17 in the F4 category. An LSM of ≥ 9.6 kPa was found to be associated with the presence of a microvascular complication in DM patients ($X^2 = 1$, N = 84) = 20.17, $p = 0.000156$. The higher the level of advanced fibrosis, the more likely will there be a number of microvascular complications.

Conclusion: This study suggests that Filipino patients with microvascular complications of diabetes mellitus were more likely to have advanced fibrosis on Fibroscan. However, a bigger sample population and control of confounding variables are needed to confirm these findings.

Table 3. Patient Characteristics All Subjects

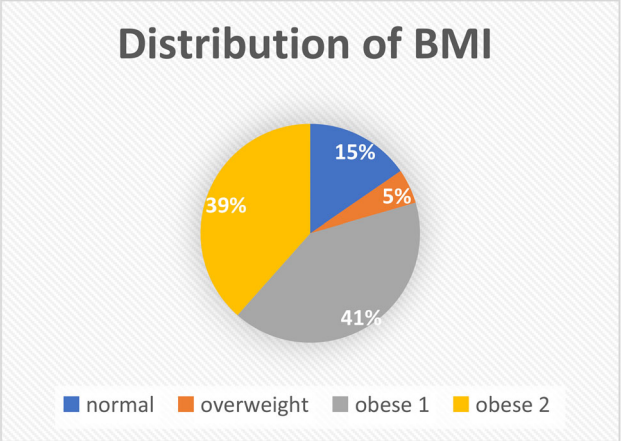
Characteristic	N= 84 (%)
Age (mean)	56.12 (SD = 13.04; variance 170.27)
BMI (mean)	29.01 (SD = 5.88; variance 34.6)
Male sex n (%)	49 (58.9)
HbA1c >7%	23 (28)
No microvascular complication	52 (53)
At least 1 microvascular complication	32 (38)

Table 4. Outcomes by Two Groups

Characteristic	No Fibrosis (n=45)	Advanced Fibrosis (n=39)	p- value
No microvascular complication	36	16	0.00024
Presence of nephropathy	6	14	0.0601
Presence of retinopathy	2	5	0.16
Presence of neuropathy	1	4	0.12
Presence of composite	9	23	.00024

Table 5. Subgroup analysis: by LSM

Liver Stiffness Measurement	Frequency of Patients with Complications
F0- F1	3 (6.6%)
F2	6 (13.3%)
F3	7 (18%)
F4	17 (43%)



Abstract #1932

Relationship of post-prandial lipaemia and inflammatory markers in cases of non-alcoholic fatty liver disease (NAFLD)

Nath Gautam[1], Singh Shivaram Prasad[1], Avasthi Rajnish[2]

[1]Department of Gastroenterology, S.C.B Medical College and Hospital, Cuttack, India, [2]Department of Medicine, UCMS & GTB Hospital, New Delhi, India

Introduction: NAFLD is one of the commonest hepatic disorder, worldwide. Clinically, it encompasses a broad spectrum of derangements from fat accumulation (steatosis) to severe inflammation and fibrosis (NASH, non-alcoholic steatohepatitis) that can lead to cirrhosis. Postprandial lipid storage contributes substantially to the liver triglyceride (TG) pool in NAFLD and the magnitude of postprandial lipaemia predicts liver steatosis. However, there is paucity of information on the mechanistic relationship between postprandial lipaemia and NAFLD.

Objectives: To study the association between post prandial lipaemia and inflammatory markers in NAFLD.

Method: We evaluted the postprandial lipaemic response to standardised fat challenge, in 20 NAFLD cases and compared it with 20 matched healthy controls; serial serum samples were estimated for TG level from zero to 8hour at 2hr interval. We also measured baseline serum lipids and inflammatory markers (TNFα and IL-6).

Results: The Area under curve (AUC) for triglyceridemia was calculated for the two groups using trapezoid rule, which showed a statistically significant difference ($p < 0.001$) between the two groups (1814.20 ± 166.46 vs 1341.25 ± 153.36). As expected, the two groups showed a significant difference in baseline TG, HDL and serum cholesterol. Both TNF-α and IL-6 were found statistically higher in NAFLD.

Conclusions: Postprandial hyperlipaemic state present in NAFLD cases may have promoted a pro-inflammatory environment characterized by constantly higher TNF-α and IL-6 levels. This might in turn perpetuate a vicious cycle of insulin resistance and hepatic fat accumulation.

Abstract #2017

Heme oxygenase-1 prevents mitochondrial dysfunction via modulating mfn-2 in non-alcoholic steatohepatitis

Li Dongdong[1,2], Dong Shiming[1,2], Zhao Dandan[1,2], Du Jinghua[1,2], Yuan Xiwei[1,2], Zaid[1,2], Zhao Wen[1,2], Liu Lingdi [1,2], Cui Luyao [1,2], Nan Yuemin[1,2]

[1]Department of Traditional and Western Medical Hepatology, Third Hospital of Hebei Medical University, 050051 Shijiazhuang, China, [2]Director of Hebei Provincial Key Laboratory of liver fibrosis in chronic liver diseases

Background and aims: Non-alcoholic steatohepatitis (NASH) is the progressive stage of non-alcoholic fatty liver disease (NAFLD) and there are no approved effective therapies. Oxidative stress underlies the pathogenesis of NASH and mitochondrial dysfunction participates in oxidative stress process. Heme oxygenase-1 (HO-1) plays a pivotal role in defending the liver against oxidative stress and inflammation. The aim of this study is to investigate whether HO-1 displays its protective role via modulation mitochondrial function to attenuate steatohepatitis in the pathogenesis of NASH.

Methods: Hepatocyte-specific HO-1 knockout (HO-$1^{-/-}$) mice were generated. The male HO-$1^{-/-}$ mice and age/sex matched wild-type (HO-$1^{+/+}$) C57BL/6 J mice were fed with two different diets-high fat diet (HFD) for 16 weeks and methionine and choline deficient (MCD) diet for 4 weeks to induce steatohepatitis (6 mice per group). Normal chow or corresponding control diet supplemented with DL-methionine were fed to control group. HO-1 inducer (Hemin) and inhibitor (ZnPP-IX) were administrated to the HO-$1^{+/+}$ and HO-$1^{-/-}$ mice. H&E staining, Oil Red O and blood biochemistry were performed for observation of hepatic steatosis and inflammation. The *p*EX-HO-1 and HO-1 sh-RNA plasmid were transfected to LO-2 hepatocytes. The changes of mitochondrial ultrastructure were assessed by Transmission electron microscope (TEM). The mRNA and protein expressions of HO-1, mitochondrial related genes were detected by RT-PCR, Western blot and IHC. Mitochondrial PCR array were used to screen the crucial genes of mitochondrial injury in nutritional steatohepatitis. Mitochondrial fragmentation was assessed by Mito-Tracker stanning in palmitic acid (PA) treated LO-2 cells. Mitochondrial function was determined by assessing membrane potential, reactive oxygen species (ROS), ATP content and mitochondrial DNA (mtDNA) damage.

Results: As compared to HO-$1^{+/+}$ mice, HO-1 genetic knockout significantly aggravated liver injury, and these changes were associated with dysregulated expressions of mitochondria-related genes in two different diet-induced NASH mice. Mitochondrial ultrastructure was deteriorated by genetic depletion of HO-1 by TEM analysis. In agreement with this, HO-1 knockdown in vitro promoted mitochondrial dysfunction, which was evidenced by decreasing membrane potential and ATP content as well as exacerbating ROS content and mtDNA damage. In contrast, HO-1 overexpression reversed these changes in PA induced steatosis. Mechanistically, HO-1 induced the expression of Mfn-2, led to mitochondrial dysfunction, and thereby caused steatohepatitis in the pathogenesis of NASH. Serum HO-1 levels were negatively correlated with mitofusin-2 (Mfn-2) levels in NASH patients. In addition, the hepatic steatosis and necroinflammation were significantly ameliorated by administration of Hemin, which companied improvement of mitochondrial function.

Conclusions: Taken together, our study demonstrates, for the first time, that HO-1 attenuates diet-induced steatohepatitis via preventing mitochondrial dysfunction and these findings implicate HO-1 as a potential therapeutic strategy for NASH.

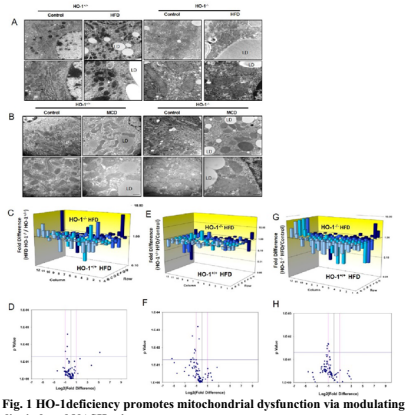


Fig. 1 HO-1deficiency promotes mitochondrial dysfunction via modulating mitochondrial related protein Mfn-2 in diet induced NASH mice

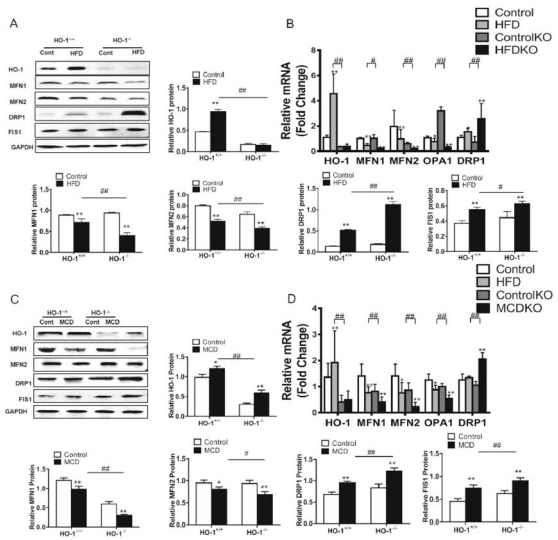


Fig. 2 HO-1 deficiency promotes mitochondrial dysfunction in mice liver

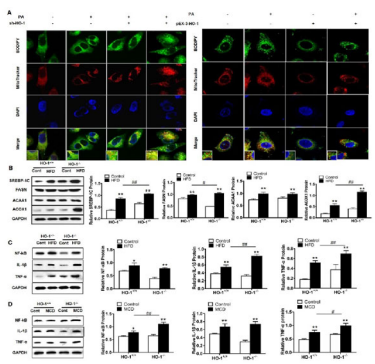


Fig. 3 HO-1 abolishes lipid accumulation and metabolism in PA induced steatosis and induces inflammation in diet-induced mice

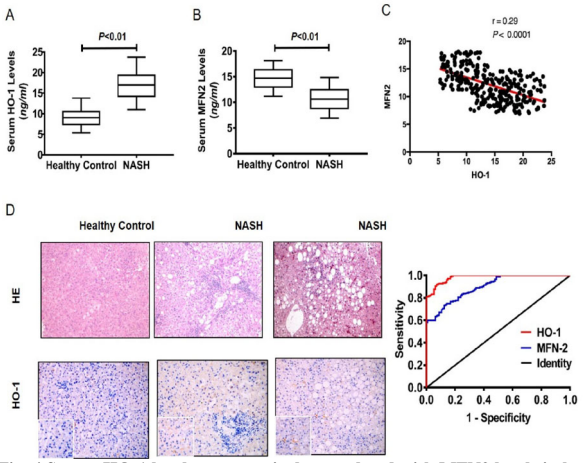


Fig. 4 Serum HO-1 levels are negatively correlated with MFN2 levels in human

Abstract #2030

The deficiency of decorin exacerbates hepatic steatosis via downregulation of Erk1/2

Dong Shi Min

Introduction: Non-alcoholic fatty liver disease (NAFLD) is one of common chronic liver diseases. Decorin plays a protective role in cirrhosis and liver cancer. However, there is little evidence on its expression and significance in NAFLD.
Objective: Our study is to investigate the level change, distribution and molecular mechanism of decorin in NAFLD.
Methods: The plasma decorin levels of 60 NASH patients and 30 healthy controls were tested by ELISA. HE staining and immunohistochemistry were performed in human liver sections. Western blot was used to evaluate hepatic proteins in wild-type mice fed high fat diet for 16 weeks. Moreover, LO-2 cells were transfected with decorin-specific siRNA (siDCN) followed by 200 μM palmitic acid (PA) treatment. Hepatic proteins and lipid droplets were evaluated by western blot and immunofluorescence.
Results: Plasma decorin was elevated in NASH patients (44.72 *vs* 56.12, $p < 0.0001$). Decorin was located in the nuclei of hepatocytes and the area of inflammatory cell infiltration of the liver in NASH patients. Hepatic decorin, SREBP, FAS, MAPKp38, NF-κB and TNF-α were upregulated in NASH mice. Immunofluorescence indicated inhibited decorin and increased lipid droplets in siDCN + PA hepatocytes. Western blot demonstrated upregulated decorin in hepatocytes treated with PA and reduced decorin, Erk1/2 and the phosphorylation of Erk1/2 in siDCN + PA hepatocytes.
Conclusion: Plasma and hepatic decorin levels are significantly elevated in NAFLD patients. The decorin plays a protective role in NAFLD by modulating Erk1/2.

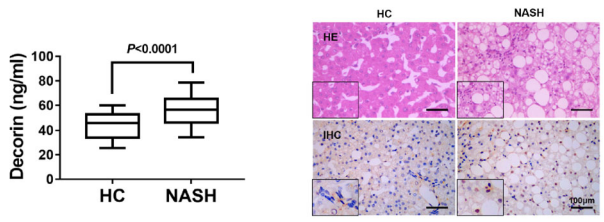


Fig 1. Decorin protein was significantly increased in the plasma and liver of NASH patients.

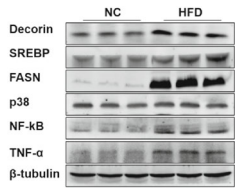


Fig 2. Hepatic decorin was promoted in NASH mice in accord with lipid synthesis and proinflammatory cytokines.

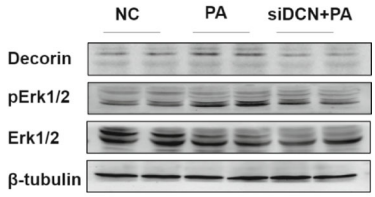


Fig 3. The deficiency of decorin exacerbates hepatic steatosis via downregulation of Erk1/2

Abstract #2031

Anti-oxidant properties of Phyllanthus *niruri* are responsible for improving serum biochemistry and expression of NFKβ/PI3K/AKT pathway in an animal model of Non alcoholic Fatty Liver Disease (NAFLD)

Mehta Manu[1], Gupta Sarika[2], Duseja Ajay[1]

[1]Department of Hepatology, PGIMER, Chandigarh, [2]Department of Biosciences and biotechnology, Banasthali vidyapith, Jaipur

Introduction and objective: Herbal medicines are potential therapeutic agents for treatment of patients with liver diseases. Objective of present study was to evaluate antioxidant properties of *Phyllanthus niruri*; study its affect on the serum biochemistry and expression of NFKβ/PI3K/AKT pathway in animal model of NAFLD..
Methods: Plant extract of Phyllanthus *niruri* was prepared by Soxhlet method. Antioxidant properties were studied by SOD, Hydrogen Peroxide, DPPH and FRAP; effect on liver function tests, lipid profile and expression of NFKβ/PI3K/AKT pathway (RT- PCR) was studied in four groups of C57BL/6 male mice [Group A—Control mice (n = 6), Group B methionine-choline deficient diet (MCDD) mice (n = 6), Group C (n = 6) and Group D (n = 6)—Control and MCDD mice given *Phyllanthus niruri* (200 mg/kg).
Results: Plant extract of Phyllanthus *niruri* showed increasing antioxidant properties with increasing concentration [SOD activity (% inhibition) 27.93 at 20 μg/ml, 89.65 at 100 μg/ml, DPPH scavenging (% inhibition) 27.63 at 20 μg/ml and 91.64 at 100 μg/ml]. Treatment with crude extract significantly improved serum bilirubin (0.69 ± 0.14 vs. 1.19 ± 0.18; $p = 0.004$) serum ALT (29.40 ± 14.39 vs.71.19 ± 9.13; $p = 0.001$), serum triglycerides (129.73 ± 15.63 vs 155.83 ± 11.32; $p = 0.031$) and serum HDL (49.92 ± 6.25 vs 23.00 ± 7.16; $p = 0.01$) in group D. *P niruri* plant extract also significantly down regulated the expression of AKT (0.90 ± 0.17 vs. 5.89 ± 2.63; $P < 0.0001$), NF-KB (0.84 ± 0.29 vs. 4.78 ± 2.04;

$P < 0.0001$), PI3K (0.69 ± 0.25 vs. 2.20 ± 1.07; $P < 0.0001$) and IRS (1.41 ± 1.08 vs. 4.63 ± 2.36; $P = 0.003$) in group D.
Conclusion: Phyllanthus *niruri* has significant anti-oxidant properties which in an animal model could be responsible for improving serum biochemistry and in regulating the NFKβ/PI3K/AKT pathway.

Abstract #2041

Urinary neutrophil gelatinase associated lipocalin (NGAL); a new biomarker for predicting chronic kidney disease (CKD) in patients with nonalcoholic fatty liver disease (NAFLD)

Navadurong Huttakan, MD.[1], Phathong Chonlada, B.Sc.[2], Srisawat Nattachai, MD.[3], Treeprasertsuk Sombat, MD., Ph.D.[2,4]

[1]Department of Medicine, Faculty of Medicine, Chulalongkorn University, and Thai Red Cross, Bangkok 10330, Thailand, [2]Department of Medicine, Division of Gastroenterology, Faculty of Medicine, Chulalongkorn University, and Thai Red Cross, Bangkok 10330, Thailand, [3]Department of Medicine, Division of Nephrology Critical Care Medicine, Faculty of Medicine, Chulalongkorn University, and Thai Red Cross, Bangkok 10330, Thailand,[4]Liver Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand

Introduction: There were reports of high prevalence of CKD in nonalcoholic fatty liver disease (NAFLD) patients. Urinary neutrophil gelatinase associated lipocalin (urine NGAL) is a reliable biomarker of renal dysfunction but no evidences for predicting CKD in NAFLD patients.
Objective: To determine prevalence of CKD and to identify predictors of CKD in NAFLD patients.
Methods: This was a cross-sectional study conducted in NAFLD patients diagnosed by Transient elastography (TE) or liver biopsy at university hospital. Cut off values for fibrosis staging by TE (KPa) were $F2 \geq 7$, $F3 \geq 8.7$, $F4 \geq 10.3$. Advanced liver fibrosis means F3-4. CKD means eGFR < 60 ml/min/1.73 m^2.
Results: We enrolled 99 patients with mean age of 54 ± 15 years old (15.3% diagnosed by liver biopsy and 84.7% by TE). Prevalence of CKD in NAFLD patients was 8%. About 39% were advanced liver fibrosis. CKD was identified in 15.4% with F3-4 and 3.4% with F1-2 ($P = 0.056$). Median (IQR) of urine NGAL (ng/ml) in non-CKD and CKD were 15 (9.6–25.2) and 48.6 (18.22–89.12) respectively, which was significantly different in univariate analysis ($P = 0.01$), but was not significantly different in each fibrosis stage (F0 = 18.3 (9.1–35.15), F1-2 = 17.5 (11.17–2.05), F3-4 = 13.8 (9.5–25.2); $P = 0.28$). By ROC curve, cut off level of urine NGAL of 36.75 ng/ml (95%CI 0.54–0.95) for predicting CKD with sensitivity of 75% and specificity of 85%. By multivariate analysis, urine NGAL > 36.75 ng/ml (OR 1.02[1.00–1.04], $P = 0.023$) was significant predictor for CKD.
Conclusion: Prevalence of CKD in NAFLD patients was 8% similar to the previous studies (4.8–5%). Urine NGAL cut-off > 36.75 ng/ml is a predictor for CKD in NAFLD patients.

Factors	Total (N=99)	No CKD eGFR >60 (N=91)	CKD eGFR <60 (N=8)	P value
Age (mean±S.D.)	54±15	53±15	67±11	0.012
Sex				0.715
Male	41 (41.4%)	37 (40.7%)	4 (50%)	
Female	58 (58.6%)	54 (59.3%)	4 (50%)	
BMI	31.35±9.43	31.83±9.59	26.08±5.56	0.099
DM	45 (45.5%)	41 (45.1%)	4 (50%)	1
HT	67 (67.7%)	61 (67.0%)	6 (75%)	1
DLP	56 (56.6%)	53 (58.2%)	5 (62.5%)	1
eGFR (N)	99	91	8	<0.001
mean±S.D.	91.72±22.10	95.61±18.26	47.43±10.65	
median (IQR)	93.16 (77.78-106.28)	93.96 (82.20-107.49)	49.24 (40.99-55.86)	
UACR (N)	75	70	5	0.007
mean±S.D.	167.60±593.44	101.94±470.62	1086.82±1250.16	
median (IQR)	16.8 (8.61-37.46)	14.10 (8.17-32.8)	519.28 (28.66-2428.75)	
<30	53 (70.7%)	52 (74.3%)	1 (20%)	0.024
≥30	22 (29.3%)	18 (25.7%)	4 (80%)	
CAP (dB/m) (N)	98	90	8	0.018
mean±S.D.	299.65±59.50	304.28±57.27	247.63±63.17	
median (IQR)	309.5 (268.25-337.5)	312 (276-339.25)	248.5 (186.5-305)	
<296	41 (41.8%)	35 (38.9%)	6 (75%)	0.065
≥296	57 (58.2%)	55 (61.1%)	2 (25%)	
TE (KPa) (N)	98	90	8	0.063
mean±S.D.	10.48±10.62	9.49±8.34	21.66±21.45	
median (IQR)	7.55 (5.1-11.77)	7.35 (5.1-10.4)	17.05 (5.87-30.12)	
<10	69 (70.4%)	66 (73.3%)	3 (37.5%)	0.047
≥10	29 (29.6%)	24 (26.7%)	5 (62.5%)	
Fibrosis staging				0.056
0 to 2	59 (60.2%)	57 (63.3%)	2 (25%)	
3 to 4	39 (39.8%)	33 (36.7%)	6 (75%)	

Factors	Total (N=99)	No CKD eGFR >60 (N=91)	CKD eGFR <60 (N=8)	P value
Liver biopsy proven NAFLD	15 (15.3%)	14 (15.4%)	1 (12.5%)	1
AST/ALT (N)	99	91	8	0.074
mean±S.D.	0.93±0.35	0.90±0.32	1.22±0.52	
median (IQR)	0.87 (0.68-1.10)	0.86 (0.67-1.07)	1.09 (0.78-1.67)	
<0.8	38 (38.4%)	36 (39.6%)	2 (25%)	0.707
>0.8	61 (61.6%)	55 (60.4%)	6 (75%)	
FIB4 score (N)	99	91	8	0.004
mean±S.D.	0.13±0.10	0.12±0.09	0.26±0.17	
median (IQR)	0.10 (0.06-0.16)	0.09 (0.06-0.15)	0.23 (0.12-0.37)	
<1.45	99 (100%)	91 (100%)	8 (100%)	
>1.45	0	0	0	
APRI base (N)	99	91	8	0.09
mean±S.D.	0.42±0.36	0.39±0.32	0.68±0.61	
median (IQR)	0.30 (0.22-0.46)	0.30 (0.21-0.42)	0.45 (0.26-0.91)	
<0.5	77 (77.8%)	72 (79.1%)	5 (62.5%)	0.146
>0.5	20 (20.2%)	18 (19.8%)	2 (25%)	
>1.5	2 (2%)	1 (1.1%)	1 (12.5%)	
NFS score (N)	95	87	8	0.017
mean±S.D.	-1.68±2.85	-1.82±2.91	-0.13±1.63	
median (IQR)	-1.42 (-2.40 - -0.57)	-1.51 (-2.62 - -0.78)	-0.39 (-1.26-0.87)	
< 0.625	89 (93.7%)	83 (95.4%)	6 (75%)	0.079
> 0.625	6 (6.3%)	4 (4.6%)	2 (25%)	
Urine NGAL (N)	99	91	8	0.019
mean±S.D.	30.02±41.73	26.84±37.17	66.25±63.42	
median (IQR)	15.6 (9.9-30.6)	15 (9.6-25.2)	48.6 (18.22-89.12)	
NAS score (N)	14	13	1	0.61
mean±S.D.	4.36±1.39	4.38±1.45	4	
median (IQR)	4.5 (3.75-5.25)	5 (3.5-5.5)	4 (4-4)	

Abstract #2045

Liver sinusoidal endothelial cell-specific knockdown of RUNX1 reduces hepatic inflammation and immune cell infiltration in mice models of non-alcoholic steatohepatitis

Savneet Kaur[1], Dinesh M Tripathi[1], Impreet Kaur[1], Sumati Rohilla[2], Abhishak Gupta[1], Vikash Kumar[3], Vegi Naidu[4], Subham Banerjee[4], Shiv K Sarin[1]

[1]Institute of Liver and Biliary Sciences, New Delhi, India, [2]Gautam Buddha University, Greater Noida, India, [3]National Institute of Immunology, New Delhi, India, [4]National Institute of Pharmaceutical Education and Research, Guwahati, India.

Background and aims: Our recent studies have reported an increased expression of Runt-related transcription factor (RUNX1) in liver sinusoidal endothelial cells in patients with non-alcoholic steatohepatitis (NASH). Here, we further dissected the role of RUNX1 in NASH by in vitro and in vivo studies.
Methods: In vitro, RUNX1 gene expression was downregulated in LSECs using RUNX1-siRNA followed by analysis of their angiogenic gene expression and functions by RT-PCR, and matrigel assays. In vivo, RUNX1 was silenced in LSECs in methionine choline deficient (MCD) diet-induced NASH mice by using a nanodelivery system consisting of nanolipocarrier encapsulated RUNX1-siRNA (RUNX1-NLC). After characterization of the RUNX1-NLC (both in vitro and in vivo), liver cells and liver infiltrating lymphocytes (LILs) were analyzed to study expression of RUNX1 and other angiogenic/adhesion molecules by RT-PCRs and flow cytometry. MCD mice treated only with nanolipocarrierswithout RUNX1 siRNA served as vehicle.
Results: An in vitro knock-down of RUNX1 gene in LSECs (> 50%) resulted in substantial downregulation of their angiogenic and adhesion gene expression and also angiogenic properties. In vivo, a knockdown of about 40% was achieved in the expression of RUNX1 gene in CD31 + liver endothelial cells of RUNX1-NLC treated mice, which showed a reduced expression of adhesion molecules, VCAM1 and ICAM1 in comparison to the vehicle mice. RUNX1-NLC treated mice showed marked reduction of $CD45^+CD3^+$ T cells in the liver as compared to vehicle (25.8 ± 1.8 vs $39.6 \pm 2.5\%$). Also, percentages of $CD11b^+F4/80^+$ inflammatory monocytes/macrophages were significantly lower in RUNX1-NLC mice as compared to that seen in vehicle mice (5.9 ± 1.1 vs $21.9 \pm 2.6\%$). A decrease in inflammatory cells in liver was also well evident in the H & E liver sections of

the RUNX1-NLC mice versus vehicle animals. Hepatic TNF-α and CCL2 levels showed significant reduction in RUNX1-NLC mice in comparison to that of the vehicle mice ($p < 0.05$).

Conclusion: A decrease in RUNX1 expression in LSECs reduces their expression of adhesion molecules, causing decreased infiltration of myeloid and T cells in liver, decreasing inflammation in NASH liver. The study highlights the significance of a nanodelivery system for in vivo cell-specific gene silencing and proposes it as a strategy to target LSEC-associated inflammation in NASH.

Abstract #2106

Expanding the potential benefits of vitamin e in nafld patients: a meta-analysis of randomized controlled trials

Rahadini, A[1], Prabaswari, NP[1], Effendi, GB[1], Widodo, B[2]

[1]Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia, [2]Gastroenterology and Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Introduction: Non-alcoholic fatty liver disease (NAFLD) is characterized by lipid deposition in the liver parenchyma without significant history of alcohol consumption or other secondary causes. Disease presentation of NAFLD ranges from asymptomatic disease to cirrhosis with the complication of liver failure and hepatocellular carcinoma. Insulin resistance and oxidative stress play a vital role in the progression towards NAFLD in all age groups. Currently, there is no established treatment for this disease. Several pilot studies have provided evidence that antioxidants such as vitamin E improve clinical and histologic features of NAFLD. Vitamin E is considered a chain-breaking antioxidant in free radical reactions such as lipid peroxidation.

Objective: To evaluate the potential benefits of vitamin E in NAFLD patients.

Method: We searched PUBMED and EMBASE from their inception to November 2019. The outcomes were as follows; ALT, AST, GGT, ALP, BMI, steatosis score, lobular inflammation, ballooning, and fibrosis. Using random-effects meta-regression model, data were pooled to determine the weighted mean difference (WMD) of the outcomes. The meta-analysis was conducted using Revman 5.3 software.

Result: A total of 8 randomized controlled trials involving 539 NAFLD patients were included in the analysis. The pooled analysis showed that, comparing with the control group, patients treated with vitamin E had significant improvement in ALP of − 9.42 U/L, fibrosis of − 0.43, lobular inflammation of − 0.18, and steatosis of − 0.62.

Conclusion: Vitamin E as adjuvant therapy has potential benefits in NAFLD patients by significantly improving biochemical and histological changes.

Abstract #2183

The interactive effect between non-alcoholic fatty liver disease and chronic hepatitis B in biochemistry levels and liver biopsy

Zhang Siyu

Department of Traditional and Western Medical Hepatology, The Third Hospital of Hebei Medical University, Shijiazhuang, 050051, China

Introduction: Chronic hepatitis B (CHB) and Non-alcoholic fatty liver disease (NAFLD) is two significant causes of chronic liver disease worldwide. However, the interaction between NAFLD and CHB is controversial.

Objective: To investigate the interactive effect between NAFLD and chronic hepatitis B (CHB) in biochemistry levels and liver biopsy.

Methods: A total of 668 patients were enrolled in this cross-sectional study who were performed by liver biopsy from March 2007 to October 2019. Patients had either CHB (n = 438), CHB complicated with non-alcoholic hepatic steatosis (CHB/NAFLD, n = 173), or NAFLD (n = 73). The demographic, biochemistry and biopsy characteristics of each patient were collected.

Results: Aminotransferase (ALT), glutamyl transpeptidase (GGT) and blood platelet levels were higher in patients with CHB/NAFLD than patients with CHB, and lower than patients with NAFLD. Prothrombin time (PT) is highest in CHB patients than the levels in the other groups ($p < 0.01$). Metabolic syndrome is most prevalent in patients with NAFLD, followed by patients with CHB/NAFLD (24.7% vs 7.6%, $p < 0.01$). Liver steatosis $F \geq 2$ was observed in 49 (31.2%) patients with CHB/NAFLD,55 (75.3%) patients in NAFLD ($p = 0.000$). Grade of inflammation $(G) \geq 2$ in Metavir scoring system was detected in 211 (48.2%) patients with CHB, while 76 (48.4%) patients with CHB/NAFLD and 19 (26.0%) patients with NAFLD ($p < 0.01$). Stage of fibrosis $(S) \geq 3$ in 99 (22.6%) patients with CHB,24 (15.3%) patients with CHB/NAFLD, and 6 (8.2%) patients with NAFLD. Besides, Age, gender and HBV DNA levels did not show any significant differences between patents with CHB and CHB/NAFLD.

Conclusion: Patients with NAFLD may develop more serious liver inflammation and less severity of liver steatosis when complicated with CHB. Besides, liver steatosis may protect patients with CHB from advanced liver fibrosis.

Variable	CHB(n=438)	CHB/NAFLD(n=157)	*P* value	NAFLD(n=73)	*P* value
Age, y	35.0(27.0,44.0)	37.0(30.0,47.0)	0.019	37.0(27.5,49.5)	0.724
Male patient, n (%)	299(68.0)	121(77.1)	0.029	49(67.1)	0.110
BMI, Kg/m^2	22.6(20.5,25.4)	26.0(23.9,28.3)	0.000	27.0(25.4,28.6)	0.046
Hypertension, n (%)	46(10.5)	15(9.6)	0.737	12(16.4)	0.131
Hypertriglyceridemia, n (%)	28(6.4)	32(20.4)	0.000	40(54.8)	0.000
Hypohigh-density Lipoproteinemia, n (%)	60(13.7)	34(21.7)	0.019	24(32.8)	0.068
Hyperglycemia, n (%)	46(10.5)	30(19.1)	0.006	27(37.0)	0.003
Mets, n(%)	11(2.5)	12(7.6)	0.002	18(24.7)	0.001
NA treatment, n(%)	123(28.0)	38(24.2)	0.348	-	-
HBeAg-negative, n(%)	200(45.7)	63(40.1)	0.231	-	
HBV DNA×10^4,IU/ml	12.9(0.2,1340.0)	48.0(0.1,3930.0)	0.126	-	-
WBC(×10^9/L)	5.5(4.6,6.7)	5.9(5.0,7.1)	0.006	6.5(5.4,7.3)	0.077
Hb(g/L)	146.9(133.0,157.9)	154.0(142.0,162.4)	0.000	155.0(138.0,164.0)	0.702
PLT(×10^9/L)	191.0(150.0,234.0)	205.0(167.3,251.8)	0.011	230.0(189.0,277.0)	0.031
ALT(U/L)	39.0(22.0,77.3)	32.0(22.0,52.0)	0.015	99.0(44.0,152.0)	0.000
GGT(U/L)	24.0(16.0,45.0)	32.0(22.0,52.0)	0.000	62.0(37.8,99.3)	0.000
UREA	4.6(3.7,5.5)	4.5(3.7,5.5)	0.654	4.5(3.7,5.5)	0.821
PT(s)	11.8(11.0,13.0)	11.3(10.9,12.0)	0.000	11.3(10.3,12.0)	0.089
Grade in Metavir ≥2,n(%)	211(48.2)	76(48.4)	0.960	19(26.0)	0.001
Stage in Metavir ≥3,n(%)	99(22.6)	24(15.3)	0.052	6(8.2)	0.139
Hepatic steatosis ≥2,n(%)	-	49(31.2)	-	55(75.3)	0.000

Table 1. Characteristics of 668 patients with either CHB, CHB/NAFLD, or NAFL

Abstract #2187

The efficacy of non-invasive tests (NIT) FiB-4, NAFLD Score, liver stiffness measurement (LSM) and FAST score to determine the fibrotic stage of liver on liver biopsies

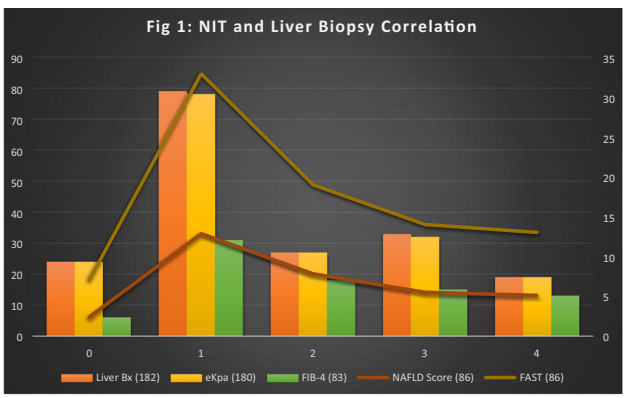
Mubarak, Abdullah, MD, Talati, Tapan, MD Aronowitz, Alexandria, Zachary Mubarak

Department Hepatology, Institution Liver Center of Texas, City, Dallas, Country, USA

Introduction: Liver biopsy, an invasive procedure, is considered the gold standard test to assess liver inflammation and fibrosis. NIT tests such as Fibrosis-4 (FIB-4), Nonalcoholic Fatty Liver Disease (NAFLD) score and Fibroscan with FAST score is an alternative method to evaluate chronic liver disease.
Objective: The NIT tests are cost-effective and safer to assess liver fibrosis on the NAFLD population.
Method: Five hundred and Seventy-Six patients who had a Fibroscan from April 2015–October 2019 were included in the analysis. Demographics, clinical history & lab data (< 6 months prior to Fibroscan) and who underwent a liver biopsy were analyzed. FIB-4, NAFLD Score, FAST Scores were calculated from publicly available online calculators.
Results: Patients mean age was 53.48, 215 were males and 362 females as outlined in Table 1: 122 patients had Diabetes Mellitus (DM); 167 patients had hyperlipidemia and 223 patients had a BMI > 30. Patients had missing clinical or lab data were excluded from analysis. 182 patients had a liver biopsy for further assessment of NASH. 180 patients had LSM and 86 patients had FAST scores and 83 patients had FIB-4 calculated. 86 patients also had the data to calculate NAFLD Scores. Figure 1 shows an excellent correlation of the NIT and liver biopsy data. NIT's performed as well as liver biopsy in determining mild liver fibrosis (Stage 0–1) as well as moderate to severe liver fibrosis (Stage 2–4). Higher liver fibrosis has an increased overall and liver related mortality.
Conclusion: NIT's are an excellent option for initial diagnosis of fibrotic NASH as well as monitoring of clinical changes with time. Larger cohort of patient populations can be studied to determine if our results are similar in other populations.

Table 1

Demographics		**Liver Biopsy & NIT (n)**	
Age (Mean)	53.48	Liver Biopsy	182
Males	215	LSM (Fibroscan)	180
Females	362	NAFLD Score	86
DM*	122	FIB-4	83
BMI > 30	223	FAST Score	86
Hyperlipidemia*	167		* Available Data



Poster Presentations

Abstract #30

Non-alcoholic fatty liver disease patients without metabolic syndrome had higher levels of hemoglobin: a single center experience

Eda Kaya[1], Yusuf Yilmaz[1,2]

[1]Institute of Gastroenterology, Marmara University, Istanbul, Turkey, [2]Department of Gastroenterology, Marmara University School of Medicine, Istanbul, Turkey

Introduction: Higher hemoglobin level is associated with both metabolic syndrome (MetS) and non-alcoholic fatty liver disease (NAFLD). Moreover, increased hemoglobin is related to severer liver histology. In this study, we aimed to compare hemoglobin levels of NAFLD patients with and without MetS.
Methods: We analyzed clinical and histological data of 641 NAFLD patients, who were followed-up in our tertiary care center between 2009 and 2019. MetS was determined using the National Cholesterol Education Program-Adult Treatment Panel III criteria to include 3 or more of the following: increased waist circumference, elevated triglycerides, reduced high-density lipoprotein cholesterol, hypertension and elevated fasting blood glucose.
Results: The study population consisted of mostly obese patients (60.5%) with MetS (63%) as depicted in Table 1. Patients without MetS had significantly higher levels of hemoglobin (15.0 [7.1–18.9] mg/dL vs 14.2 [8.6–18.2] mg/dL, $P < 0.001$), iron (96.5 [10.5–412] mcg/dL vs 83 [13–400] mcg/dL, $P = 0.009$) and ferritin (106 [7.8–667] ng/mL vs 89 [3.8–821.2] ng/mL, $P = 0.004$) compared to those with MetS. Histologically, patients with MetS had significantly severer disease considering higher significant (39.4% to 20%) and advanced fibrosis (19.6% to 13.1%), ($P = 0.012$ and $P = 0.036$, respectively). Regarding presence of non-alcoholic steatohepatitis there was no significant difference ($P = 0.298$).
Conclusion: Although both NAFLD and MetS were reported to be associated with higher hemoglobin levels in the literature, we found that NAFLD patients without MetS had higher hemoglobin levels. However, patients with MetS showed a severer liver histology.

Table 1. General characteristics of the biopsy-proven NAFLD patients with and without metabolic syndrome.

	Total (n=641)	With metabolic syndrome (n=404)	Without metabolic syndrome (n=237)	p
Age, median [minimum-maximum] (years)	47 [18-71]	49 [21-71]	44 [18-71]	**<0.001**‡
Gender (male/female)	348/293	182/22	166/71	**<0.001**†
Body mass index, median [minimum-maximum] (kg/m^2)	31.2 [18.3-56.0]	32.1 [23.7-56.0]	29.3 [18.3-51.8]	**<0.001**‡
Lean / overweight / obese	41/212/388	13/104/287	28/108/101	**0.001**†
Type 2 diabetes mellitus	235	196	39	**<0.001**†
Hypertension	217	186	31	**<0.001**†
Waist circumference, median [minimum-maximum] (cm)	104 [70-147]	106 [79-147]	100 [70-135]	**<0.001**‡
AST, median [minimum-maximum] (U/L)	42 [11-302]	41 [11-302]	43 [12-147]	0.077‡
ALT, median [minimum-maximum] (U/L)	66 [12-343]	61.5 [12-343]	75 [12-296]	**0.001**‡
Total cholesterol, median [minimum-maximum] (mg/dL)	210 [74-419]	211.5 [74-419]	207 [83-417]	0.057‡
Triglycerides, median [minimum-maximum] (mg/dL)	163 [37-1107]	189.5 [39-1107]	121 [37-1107]	**<0.001**‡
HDL cholesterol, median [minimum-maximum] (mg/dL)	44 [18-96]	42 [18-84]	47 [19-96]	**<0.001**‡
Platelets, median [minimum-maximum] × 10^3 per microliter	240 [77-543]	240 [77-435]	240.5 [106-543]	0.471‡
Hemoglobin, median [minimum-maximum] (mg/dL)	14.5 [7.1-18.9]	14.2 [8.6-18.2]	15.0 [7.1-18.9]	**<0.001**‡
Iron, median [minimum-maximum], mcg/dL	87 [10.5-412]	83 [13-400]	96.5 [10.5-412]	**0.009**‡
Ferritin, median [minimum-maximum], ng/mL	95 [3.8-821.2]	89 [3.8-821.2]	106 [7.8-667]	**0.004**‡
Total iron binding capacity, median [minimum-maximum], mcg/dL	373 [130-534]	375 [130-534]	369.5 [140-511]	0.206‡
Uric acid, mean±SD (mg/dL)	6.2±1.5	6.2±1.5	6.3±1.4	0.372*
Glucose, median [minimum-maximum] (mg/dL)	100 [66-307]	105 [73-307]	94 [66-300]	**<0.001**‡
HbA1c, median [minimum-maximum] (%)	5.8 [3.5-11.1]	6.0 [4.5-11.1]	5.6 [3.5-11.1]	**<0.001**‡
HOMA-IR median [minimum-maximum]	4.0 [0.3-28.8]	4.4 [1.0-28.8]	3.4 [0.3-21.8]	**<0.001**‡
SAF algorithm classification, NASH / NAFL, (n)	553/78	359/45	204/33	0.298†
Classification according to NASH-CRN, non-NASH/borderline NASH/ definite NASH (n)	36/191/414	16/122/266	20/69/148	0.059†
Grade of steatosis (S) according to the SAF score: S1 / S2 / S3 (n)	162/259//220	101/163/140	61/96/80	0.966†
Stage of activity (A) according to the SAF score: A0 / A1 / A2/ A3 / A4, (n)	13/57/146/208/217	3/38/94/128/141	10/19/52/80/76	**0.042**†
Stage of fibrosis (F) according to the SAF score: F0 / F1/ F2 / F3 / F4, (n)	208/204/119/86/24	111/134/80/63/16	97/70/39/23/8	**0.008**†
Mild disease/severe disease (n)	65/576	38/366	27/210	0.421†
NAS score (NASH CRN), median [minimum-maximum]	5 [1-8]	5 [1-8]	5 [1-8]	0.442‡
Significant fibrosis (F≥2), (n)	229	159	70	**0.012**†
Advanced fibrosis (F≥3), (n)	110	79	31	**0.036**†
Cirrhosis (F=4), (n)	24	16	8	0.707†

Abstract #31

Comparison of clinical and histological characteristics of biopsy-proven non-alcoholic fatty liver patients with and without type 2 diabetes mellitus: 10 years of experience from a single tertiary care center

Yusuf Yilmaz[1,2]

[1]Institute of Gastroenterology, Marmara University, Istanbul, Turkey, [2]Department of Gastroenterology, Marmara University School of Medicine, Istanbul, Turkey

Introduction: Non-alcoholic fatty liver disease (NAFLD) has a severer clinical and histological presentation in patients with type 2 diabetes mellitus (T2DM). Here, we aimed to compare general characteristics of NAFLD patients with and without T2DM.

Methods: We included biopsy-proven NAFLD patients, who were diagnosed in our tertiary care center. Histological evaluation of the liver specimens was performed by single pathologist according to Non-alcoholic Steatohepatitis-Clinical Research Network scoring system and Steatosis, Activity and Fibrosis/Fatty Liver Inhibition of Progression algorithm. A fibrosis stage of F $\geq$ 2 was considered significant, F $\geq$ 3 advanced fibrosis and F = 4 cirrhosis.

Results: The study cohort consisted of 231 diabetic and 403 nondiabetic biopsy-proven NAFLD patients (median age: 47 [18–71] years, 347 males and 287 females). The prevalence of clinical comorbidities including metabolic syndrome and obesity were significantly higher among diabetic patients compared to nondiabetics ($P < 0.001$ and $P = 0.001$, respectively). On the other hand, significantly higher alanine transaminase levels were found in patients without T2DM (69 [12–343] U/L) in comparison of those with T2DM (57 [12–268] U/L, $P < 0.001$). Regarding liver histology, significant fibrosis, advanced fibrosis and cirrhosis were present in 53.7%, 31.6% and 8.7% of the patients with T2DM, respectively and 25.3%, 8.7% and 1% of the patients without T2DM, respectively ($P < 0.001$ for each). Accordingly, patients with T2DM were more likely to have non-alcoholic steatohepatitis (NASH) (91.3% to 85.9%, $P = 0.042$).

Conclusion: Considering a higher prevalence of severer liver histology in terms of fibrosis stage and NASH among patients with T2DM, screening and follow-up for NAFLD can be considered in clinical routine.

Table 1. General characteristics of the biopsy-proven NAFLD patients with and without type 2 diabetes.

	Total (n=634)	With type 2 diabetes (n=231)	Without type 2 diabetes (n=403)	p
Age, median [minimum-maximum] (years)	47 [18-71]	51 [28-71]	44 [18-71]	**<0.001**‡
Gender (male/female)	347/287	99/132	248/155	**<0.001**†
Body mass index, median [minimum-maximum] (kg/m^2)	31.2 [18.3-56.0]	32.5 [22.4-56.0]	30.5 [18.3-52.0]	**<0.001**‡
Lean / overweight / obese	41/207/368	11/57/163	30/150/223	**0.001**†
Metabolic syndrome	398/236	191/40	207/196	**<0.001**†
Systolic blood pressure, median [minimum-maximum] (mmHg)	120 [90-190]	129 [100-190]	120 [90-190]	**<0.001**‡
Diastolic blood pressure, median [minimum-maximum] (mmHg)	80 [51-120]	80 [51-120]	80 [60-120]	**0.007**‡
Waist circumference, median [minimum-maximum] (cm)	104 [70-147]	107 [79-147]	103 [70-146]	**<0.001**‡
AST, median [minimum-maximum] (U/L)	41.5 [11-302]	41 [11-302]	42 [12-278]	0.578‡
ALT, median [minimum-maximum] (U/L)	66 [12-343]	57 [12-268]	69 [12-343]	**<0.001**‡
Total cholesterol, median [minimum-maximum] (mg/dL)	210 [74-419]	206 [74-370]	211 [79-419]	0.557‡
Triglycerides, median [minimum-maximum] (mg/dL)	163.5 [37-1107]	175 [46-584]	159 [37-1107]	0.123‡
HDL cholesterol, median [minimum-maximum] (mg/dL)	44 [18-96]	45 [25-84]	43 [18-96]	0.068‡
Platelets, median [minimum-maximum] × 10^3 per microliter	240 [77-543]	236 [77-471]	241 [89-543]	0.121‡
Hemoglobin, median [minimum-maximum] (mg/dL)	14.5 [7.1-18.9]	14.0 [8.5-18.9]	14.8 [7.1-17.9]	**<0.001**‡
Uric acid, mean±SD (mg/dL)	6.2±1.5	6.0±1.6	6.4±1.3	**0.027***
Glucose, median [minimum-maximum] (mg/dL)	100 [66-307]	123 [77-307]	96 [66-132]	**<0.001**‡
HbA1c, median [minimum-maximum] (%)	5.8 [3.5-11.1]	6.6 [4.5-11.1]	5.6 [3.5-7.8]	**<0.001**‡
HOMA-IR median [minimum-maximum]	4.0 [0.3-28.8]	4.9 [0.4-28.8]	3.4 [0.3-16.0]	**<0.001**‡
SAF algorithm classification, NASH / NAFL, (n)	557/77	211/20	346/57	**0.042**†
Classification according to NASH-CRN, non-NASH/borderline NASH/ definite NASH (n)	36/190/408	8/63/160	28/127/248	0.068†
Grade of steatosis (S) according to the SAF score: S1 / S2 / S3 (n)	162/254/218	50/95/86	112/159/132	0.209†
Stage of activity (A) according to the SAF score: A0 / A1 / A2/ A3 / A4, (n)	13/57/145/205/214	4/15/49/73/90	9/42/96/132/124	0.191†
Stage of fibrosis (F) according to the SAF score: F0 / F1/ F2 / F3 / F4, (n)	206/202/118/84/24	44/63/51/53/20	162/139/67/31/4	**<0.001**†
Mild disease/severe disease (n)	65/569	17/214	48/355	0.069†
NAS score (NASH CRN), median [minimum-maximum]	5 [1-8]	5 [1-8]	5 [1-8]	**0.008**‡
Significant fibrosis (F≥2), (n)	226/35.6%	124/53.7%	102/25.3 %	**<0.001**†
Advanced fibrosis (F≥3), (n)	108/17%	73/31.6%	35/8.7%	**<0.001**†
Cirrhosis (F=4), (n)	24/3.8%	20/8.7%	4/1%	**<0.001**†

Abstract #32

Liver stiffness measurement by Fibroscan increases diagnostic accuracy in non-alcoholic fatty liver disease patients classified as indeterminate risk for advanced fibrosis according noninvasive scores

Yusuf Yilmaz[1,2]

[1]Institute of Gastroenterology, Marmara University, Istanbul, Turkey, [2]Department of Gastroenterology, Marmara University School of Medicine, Istanbul, Turkey

Background/aim: Non-alcoholic fattyliver disease fibrosis score (NFS) and Fibrosis-4 (FIB-4) score for estimating the advanced liver

fibrosis in non-alcoholic fatty liver disease (NAFLD) are used confidently in eliminating advanced fibrosis, rather than detecting it. Therefore, paired combination with liver stiffness measurement (LSM) by transient elastography is recommended. Here, we aimed to validate this algorithm in our study population.

Methods: A total of 141 biopsy-proven NAFLD patients were included to the study. We calculated FIB-4 and NFS scores and performed LSM in each patient. We investigated diagnostic performances and accuracies in single and combined use of those tests.

Results: The general characteristics of the patients are depicted in Table 1. The best cut-off point for LSM for our study population was detected as 11.85 kPa (AUROC: 0.810). Using FIB-4 (< 1.3 for low risk of advanced fibrosis and > 2.67 for high risk of advanced fibrosis) combined with LSM by Baveno VI, we detected the best agreement with the reference standard in our population (Kappa = 0.599). This combination had the positive predictive value of 0.762 at a sensitivity of 67%, the negative predictive value of 0.861 present at a specificity of 91%. Moreover, it also showed the lowest misclassification (n = 13, 9.25%) and lowest discordance rate (n = 12, 8.5%) (Table 2).

Conclusion: A combined use of FIB-4 with LSM (< 10 kPa for exclusion of advanced fibrosis, ≥ 15 kPa for inclusion of advanced fibrosis) was able to diagnose the patients with advanced fibrosis with highest diagnostic accuracy.

Table 1. General characteristics of the study patients

Age, year	48.13±11.59
Gender, male/female	76/65
BMI, kg/m^2	32.89 [49.12-23.71]
Lean/overweight/obese	4.3%/24.1%/71.6%
Metabolic syndrome	78%
Type 2 diabetes mellitus	62.4%
Hypertension	54.6%
Waist circumference, cm	107.88 ± 11.588
AST, U/l / increased AST %	40 [247.0-15.0]/51.1%
ALT, U/l / increased ALT %	54 [483.0-12.0]/67.4%
Total cholesterol, mg/dl	212.42 ± 47.72
Triglycerides, mg/dl	169.0 [584.0-37.0]
HDL cholesterol, mg/dl	44.0 [84.0-19.0]
Platelets, × 10^3 per microliter	222.0 [543.0-88.5]
Hemoglobin, mg/dL	14.40 [8.6-18.2]
Uric acid, mg/dL	6.37 ± 1.53
Glucose, mg/dL	110.0 ± 37.11
HbA1c, %	5.9 [11.1-4.1]
HOMA-IR	4.51 [28.76-1.0]
HOMA-IR > 2.7	85%
SAF algorithm classification, NASH/NAFL	95%/5%
Stage of fibrosis (F) according to the SAF score: F0 / F1/ F2 / F3 / F4	11.3%/29.8%/22.7%/26.2%/9.9%
NAS score (NASH CRN)	5.56±1.49
NAFLD activity score (NAS), <3/3-4/≥5 (n, %)	2, 1.4%/ 35, 24.8%/104, 73.8%
Significant fibrosis (≥F2)/advanced fibrosis (≥F3)/Cirrhosis (F4)	58.8%/36.1%/9.9%
NASH+NAS≥4+F≥2	56.7%

Table 2. Comparison of diagnostic tests in single and combined use (n=141)

Diagnostic tool	Sensitivity (%)	Specificity (%)	False negative	False positive	Positive predictive value	Negative predictive value	Positive likelihood ratio	Negative likelihood ratio	Misclassification (n/%)	Indetermine (n/%)	Discordance (n/%)	Kappa
FIB-4*	18%	97%	0.818	0.027	0.750	0.730	6.818	0.841	29/20.6%	33/23.4%	-	0.234
FIB-4*+LSM[1]	72%	80%	0.276	0.203	0.618	0.864	3.565	0.346	21/14.9%	-	48/34%	0.498
FIB-4*+LSM[2]	61%	88%	0.387	0.120	0.679	0.846	5.108	0.440	21/14.9%	-	35/24.8%	0.507
FIB-4*+LSM[3]	62%	91%	0.381	0.089	0.722	0.864	6.933	0.418	13/9.2%	49/34.8%	15/10.6%	0.555
FIB-4**	32%	96%	0.680	0.044	0.727	0.793	7.253	0.711	20/14.2%	48/34%	-	0.299
FIB-4+LSM[1]**	79%	75%	0.211	0.250	0.638	0.864	3.158	0.281	25/17.7%	-	35//24.8%	0.513
FIB-4+LSM[2]**	72%	85%	0.282	0.154	0.700	0.857	4.667	0.333	23/16.3%	-	24/17%	0.561
FIB-4+LSM[3]**	67%	91%	0.333	0.089	0.762	0.864	7.467	0.366	13/9.2%	49/34.8%	12/8.5%	0.599
NFS	21%	93%	0.788	0.068	0.583	0.723	3.097	0.846	31/22.0%	35/24.8%	-	0.195
NFS+LSM[1]	71%	80%	0.290	0.197	0.647	0.845	3.608	0.361	21/14.9%	-	49/34.8%	0.501
NFS+LSM[2]	64%	88%	0.364	0.123	0.700	0.842	5.162	0.415	13/9.2%	-	35/24.8%	0.526
NFS+LSM[3]	61%	93%	0.391	0.075	0.778	0.845	8.065	0.423	13/9.2%	49/34.8%	16/11.3%	0.568

Abstract #33

Clinical and histological characteristics of biopsy-proven non-alcoholic fatty liver disease patients: a single tertiary care center experience from Turkey

Yusuf Yilmaz[1,2]

[1]Institute of Gastroenterology, Marmara University, Istanbul, Turkey, [2]Department of Gastroenterology, Marmara University School of Medicine, Istanbul, Turkey

Introduction: Non-alcoholic fatty liver disease (NAFLD) represents a growing burden worldwide with an estimated prevalence of 25%. Despite of usually benign nature of NAFLD, non-alcoholic steatohepatitis (NASH), more progressive subtype of NAFLD, is more likely to cause liver related morbidity and mortality, which made them target population for consideration in clinical trials. Here, we sought to present clinical and histological characteristics of a sample of Turkish patients with biopsy-proven NAFLD.

Methods: This is retrospective analysis of prospectively collected data collected over 10-year period. The study consisted of consecutive patients with biopsy-proven NAFLD who were followed-up in our tertiary care center between 2009 and 2019. Histological classification of biopsies was performed according to the Steatosis, Activity, Fibrosis/Fatty Liver Inhibition of Progression (SAF/FLIP) algorithm and the NASH-Clinical Research Network (NASH-CRN) scoring system.

Results: A total of 644 consecutive patients (median age: 47 [18–71], 294 male and 350 female) were included in the study. According to SAF/FLIP algorithm, 87.9% of the patients had NASH. Based on NASH-CRN scoring 5.6%, 29.7% and 64.7% of the patients were classified as non-NASH, borderline and definite NASH, respectively. Significant and advanced fibrosis were present in 36% and 17.4% of the study cohort, respectively (Table 1). With regards to clinical picture patients with NASH had significantly more comorbidities and severer histological presentation (Table 2).

Conclusion: In terms of high prevalence of NASH and liver fibrosis, NAFLD is a growing public health problem. Expediting the progress in conducted clinical trials is essential for slowing down NASH progression.

Table 1. Clinical and histological characteristics of the study patients (n=644).

Characteristics	
Age, median [minimum-maximum], year	47 [18-71]
Gender, male/female (n)	294 (45.7%)/350 (54.3%)
BMI, median [minimum-maximum], kg/m^2	31.2 [18.3-56.0]
Lean/overweight/obese (n)	41 (6.4%)/213 (33.1%)/390 (60.5%)
Metabolic syndrome (yes/no)	404 (62.7%)/240 (37.3%)
Type 2 diabetes mellitus (yes/no)	407 (63.2%)/237 (36.8%)
Hypertension (yes/no)	219 (34%)/425 (66%)
Systolic blood pressure, median [minimum-maximum], mmHg	120 [90-190]
Diastolic blood pressure, median [minimum-maximum], mmHg	80 [51-120]
Hyperlipidemia (yes/no)	360 (60%)/284 (40%)
Waist circumference, median [minimum-maximum], cm	104 [70-147]
Hip circumference, median [minimum-maximum], cm	108 [63-155]
Albumin, median [minimum-maximum], mg/dl	4.7 [3.4-5.9]
AST, median [minimum-maximum], U/l	42 [11-302]
ALT, median [minimum-maximum], U/l	66 [12-343]
ALP, median [minimum-maximum], U/l	89 [25-625]
GGT, median [minimum-maximum], U/l	49 [9-559]
LDH, median [minimum-maximum], U/L	215 [19-969]
Total bilirubin, median [minimum-maximum], mg/dl	0.67 [0.05-7.6]
Direct bilirubin, median [minimum-maximum], mg/dl	0.17 [0.01-1.83]
Total protein, median [minimum-maximum], g/dl	7.8 [6.4-9.1]
Total cholesterol, median [minimum-maximum], mg/dl	210 [74-419]
Triglycerides, median [minimum-maximum], mg/dl	163 [37-1107]
HDL cholesterol, median [minimum-maximum], mg/dl	44 [18-96]
LDL cholesterol, median [minimum-maximum], mg/dl	134 [28-400]
Leucocytes, median [minimum-maximum], per mL	7000 [2400-14900]
Platelets, median [minimum-maximum], × 10^3 per microliter	240 [77-543]
Hemoglobin, median [minimum-maximum], mg/dl	14.5 [7.1-18.9]
Glucose, median [minimum-maximum], mg/dl	100 [66-307]
Creatinine, median [minimum-maximum], mg/dl	0.82 [0.41-2.13]
BUN, median [minimum-maximum], mg/dl	16 [6-51]
Uric acid, mean±SD, mg/dl	6.2±1.5
HbA1c, median [minimum-maximum], %	5.8 [3.52-11.1]
HOMA-IR, median [minimum-maximum]	4.0 [0.32-28.76]
Prothrombin time, median [minimum-maximum], seconds	12.9 [7.5-16.5]
International normalized ratio, median [minimum-maximum], seconds	1.01 [0.19-1.9]
Activated partial thromboplastin time, median [minimum-maximum], seconds	29.4 [18.5-40.9]
SAF algorithm classification, NASH / NAFL, (n)	566 (87.9%)/78 (12.1%)
Classification according to NASH-CRN, non-NASH/borderline NASH/ definite NASH (n)	36 (5.6%)/191 (29.7%)/417 (64.7%)
Grade of steatosis (S) according to the SAF score: S0 / S1 / S2 / S3 (n)	0 (0%)/162 (25.2%)/262 (40.7%)/220 (34.1%)
Stage of activity (A) according to the SAF score: A0 / A1 / A2/ A3 / A4, (n)	13 (2%)/57 (8.9%)/146 (22.7%)/210 (32.5%)/218 (33.9%)
Stage of fibrosis (F) according to the SAF score: F0 / F1/ F2 / F3 / F4, (n)	208 (32.3%)/204 (31.7%)/120 (18.6%)/87 (13.5%)/25 (3.9%)
Mild disease/severe disease (n)	65 (10.1%)/579 (89.9%)
NAS score (NASH CRN), median [minimum-maximum]	5 [1-8]
Significant fibrosis (F≥2), (n)	232 (36%)
Advanced fibrosis (F≥3), (n)	112 (17.4%)
Cirrhosis (F=4), (n)	25 (3.8%)

Table 2. Comparison of patients with NAFL and NASH in terms of comorbidities and histological severity

	Patients with NAFL (n=78)	Patients with NASH (n=566)	P
Type 2 diabetes mellitus (yes/no)	58 (74.4%)/20 (25.6%)	349 (61.7%)/217 (38.3%)	**0.029**
Hypertension (yes/no)	13 (16.7%)/65 (83.3%)	206 (36.4%)/360 (63.6%)	**0.001**
Hyperlipidemia (yes/no)	28 (35.9%)/50 (64.1%)	332 (58.7%)/ 234 (41.3%)	**<0.001**
Metabolic syndrome (yes/no)	45 (57.7%)/33 (42.3%)	359 (63.4%)/207 (36.6%)	0.326
Significant fibrosis (yes/no)	2 (2.6%)/76 (97.4%)	110 (19.4%)/456 (80.6%)	**<0.001**
Advanced fibrosis (yes/no)	0 (0%)/78 (100%)	25 (4.4%)/541 (96.1%)	**<0.001**
Stage of activity (A) according to the SAF score: A0 / A1 / A2/ A3 / A4	13 (16.7%)/57 (73%)/ 7 (9%)/ 1 (1.3%)/ 0 (0%)	0 (0%)/ 0 (0%)/139 (24.6%)/ 209 (36.9%)/ 218 (38.5%)	**<0.001**

Abstract #77

New diagnostic method for mild hepatic steatosis using magnetic resonance imaging-protein density fat fraction

Koizumi Y[1], Hirooka M[1], Tanaka T[1], Sunago K[1], Yukimoto A[1], Nakamura Y[1], Watanabe T[1], Yoshida O[1], Tokumoto Y[1], Abe M[1], Hiasa Y[1]

[1]Departments of Gastroenterology and Metabology, Ehime University Graduate School of Medicine, Toon City, Ehime, Japan

Introduction: Hepatic steatosis is defined as the abnormal accumulation of fat in $\geq$ 5% of hepatocytes. Hepatic steatosis can be measured using controlled attenuation parameter (CAP). However, it is difficult to measure mild fatty changes (fat in $<$ 5% of hepatocytes) using CAP. Recently, magnetic resonance imaging-proton density fat fraction (MRI-PDFF) can reportedly diagnose mild hepatic steatosis.
Objective: To compare the diagnostic performance of CAP and MRI-PDFF when diagnosing hepatic steatosis.
Methods: All 51 participants underwent MRI-PDFF and CAP measurements to detect hepatic steatosis between April 2018 and June 2019. We compared the correlation between the MRI-PDFF and CAP values and their ability to diagnose liver steatosis.
Results: The number of cases by steatosis grade was S0: 7, S1: 9, S2: 7, and S3: 14. There was a positive correlation between the MRI-PDFF and CAP values ($R^2 = 0.543$, $P < 0.0001$). The area under the receiver operating characteristic curve (AUC-ROC) for MRI-PDFF and CAP for each steatosis grade was $\geq$ S1, 0.94 and 0.83; $\geq$ S2, 0.96 and 0.94; S3, 0.97 and 0.92, respectively. The significant difference between the AUC-ROCs was examined by the DeLong test. The diagnosis comparison for $\geq$ S1 between MRI-PDFF and CAP was P = 0.047; $\geq$ S2, P = 0.565; S3, P = 0.396.
Conclusions: MRI-PDFF is comparable with CAP, but MRI-PDFF is more effective at diagnosing mild liver steatosis. MRI-PDFF is a useful modality with a high diagnostic ability and can detect mild liver steatosis that is challenging to diagnose with CAP.

Abstract #82

Is higher BMI associated with worse overall mortality in hepatocellular carcinoma patients? An evidence based case report

Alessa Fahira[1], Ratu Shafira Hanifah[1], Mohamad Prasetio Wardoyo[1]Amirah Deandra Diba[1], Rahadian Ramadhan[1], Julie Dewi Barliana[2]

[1]Faculty of Medicine, Universitas Indonesia, [2]Department of Ophthalmology, Faculty of Medicine, Universitas Indonesia

Introduction: Liver cancer is currently the second deadliest cancer in the world with hepatocelullar carcinoma (HCC) being the commonest form—accounting 90% of all its cases. With the current global alarming increase of obesity, there is hence an increase of fatty liver disease cases, which is one of the major non-viral etiology of cirrhosis in the world. The objective of this study is to evaluate whether obese HCC patients have worse survival outcome.
Method: PubMed, Cochrane, Scopus, ProQuest, and EBSCOhost were comprehensively searched for systematic review and cohort prognostic researches studying overall survival of HCC patients who are underweight and obesity according to their BMI. Three studies were selected and critically appraised. Data were then summarized descriptively.
Results: The three studies included consist of one meta-analysis and two cohort studies. Meta-analysis study stated no association between overweight and obesity status with higher mortality rate in Asian race HCC patients (aHR, 1.10; 95% CI, 0.63–1.92). A cohort study from Japan reported while there was a significant difference of mortality rate in obese HCC patients in bivariate analysis, adjustment with other important prognostic factors with multivariate analysis found no significant correlation between obesity and HCC-related mortality rate (aHR, 1.00; 95% CI, 0.83–1.22). Another cohort study from China reported that HCC-related mortality rate in patients with higher BMI was lower than in patients with lower BMI (aHR, 0.347; 95% CI, 0.239–0.302).
Conclusion: There is no association between higher BMI with HCC-related mortality in Asian race patients.

Abstract #97

Non-alcoholic fatty liver disease among patients with inflammatory bowel disease in qatar: prevalence and risk factors

Al Mohannadi M[1], Chandra P[2], Varughese B[1], Darweesh A[3], Hamid A[1], Badi A[1], Al Kaabi S[1], Yakoob R[1], Al Ejji K[1], Sultan K[1], Abunahia N[1], Shah M[3], Derbala M[1]

[1]Gastroenterology and Hepatology, Hamad Medical Corporation, Doha, Qatar, [2]Research Affairs, Hamad Medical Corporation, Doha, Qatar, [3]Radiology Department, Hamad Medical Corporation, Doha, Qatar

Introduction: Non-alcoholic fatty liver disease has been progressively identified in inflammatory bowel disease patients in Qatar, though metabolic risk factors for NAFLD are less frequent in patients with IBD.
Objectives: We aimed to characterize NAFLD in IBD patients and to determine factors associated with its severity.
Methods: A retrospective observational study was conducted between January 2008 and December 2017 at Hamad Hospital, Doha, Qatar.
Results: Of 913 IBD patients with a mean age of 36.9 $\pm$ 13.2 years and BMI 26.9 $\pm$ 6.1; 550 (60.2%) were males, 383 (41.9%) with Crohn's disease and 530 (58.1%) with Ulcerative colitis. 24 (22.2%) patients had severe steatosis. The overall prevalence of NAFLD was 11.8% and does not differ significantly between CD and UC patients. Multivariate analysis showed age $>$ 40 to 50 years, age $>$ 50 years, BMI $>$ 30 kg/m2 and diabetes mellitus significantly associated with an increased risk of NAFLD. Females were less likely having risk of NAFLD in comparison to males. The treatment with biologic does not increase the risk of steatosis. The predicted cutoff NAFLD score $\geq$ -1.67 had good predictive ability for significant steatosis in IBD cases.
Conclusions: The prevalence of NAFLD is not uncommon among IBD patients in Qatar. Older age, high BMI and diabetes mellitus increase risk and high-risk patients need to be closely monitored and considered for early interventions that may limit the use of more hepatotoxic drugs. Non-invasive NAFLD screening using NAFLD Score could assist in early disease diagnosis and can be easily implemented in any setting of IBD clinics.

Abstract #105

Novel strategies to optimize animal models of human nonalcoholic steatohepatitis for drug development

Briand François[1] and Sulpice Thierry[1]

[1]Physiogenex, Escalquens, France

Introduction: Preclinical animal models are needed to develop therapies targeting nonalcoholic steatohepatitis (NASH), but they miss the concept that NASH-related deaths are linked to cardiovascular diseases, and their limited predictivity and/or long duration of induction represent clear limitations for drug development.
Objectives/Methods: To optimize animal models, we have developed a rapid 3-week NASH mouse model fed a high-fat/cholesterol/cholic acid/cyclodextrin diet (HFCC/CDX), a Diet-Induced Obese NASH (DIO-NASH) mouse model housed at thermoneutrality (30 °C), and a DIO-NASH hamster model, for better evaluation of drugs targeting NASH.
Results: Mice fed a HFCC/CDX for only 3 weeks induced liver steatosis, insulin resistance, oxidative stress, inflammation and fibrosis, all improved by the clinical benchmarks liraglutide and elafibranor. Housing DIO-NASH mice for 16 weeks at thermoneutrality resulted in obesity, insulin resistance, NASH and portal/bridging fibrosis. Additionally, mice developed diastolic and systolic dysfunction as measured by echocardiography. With a more similar lipids and bile acids metabolism as compared to humans, DIO-NASH hamsters develop obesity, insulin resistance, dyslipidemia, advanced NASH and bridging fibrosis, with severe diastolic dysfunction but preserved ejection fraction. Unlike mouse and rat, hamsters show human-like histopathological features of hepatocyte ballooning (confirmed with cytokeratin-18 and Sonic Hedgehog immunostaining). While it could not be detected in mouse and rat, the clinical side-effects of the benchmark obeticholic acid (e.g. higher LDL-cholesterol and lower HDL-cholesterol) are observed in DIO-NASH hamsters, further suggesting better predictivity.
Conclusion: These optimized NASH animal models with more human-like conditions, including cardiovascular complications, will help to better develop novel therapies targeting NASH.

Abstract #109

Association between metformin administration and degrees of fibrosis in type 2 diabetes patients with non-alcoholic liver disease

Prasetya-Ignatius Bima[1], Kurniawan-Andree[1], Atmodjo-Wahyuni Lukita[2], Lugito-Nata Pratama Hardjo[1], Aprilyanri-Iegreat[2], Virliani-Cindy[2], Charles-Stefanny[2]

[1]Internal Medicine, Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia, [2]Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia

Introduction: Non-Alcoholic Fatty Liver Disease (NAFLD) is known to be prevalent among patients with type 2 diabetes. NAFLD will increase the patient's risk of mortality and morbidity. This risk is known to be related to the degree of fibrosis. Metformin has been proposed as one of the medications that might be related to degree of fibrosis in NAFLD due to its property as inhibitor of insulin resistance.
Objectives: To understand the association between administration of metformin and degree of fibrosis in type 2 diabetes patients with NAFLD.
Methods: This study was a cross sectional study on adult type 2 diabetes patients treated in the outpatient clinic of Siloam General Hospital. Presence of NAFLD was determined using abdominal ultrasonography. Patients with NAFLD were further evaluated using NAFLD fibrosis score to assess their degree of liver fibrosis. Administration of metformin for the last 3 months were noted from the medical record.
Results: We analysed 85 patients with diabetes. NAFLD were diagnosed in 59 patients (69,4%). There was non-significant association between metformin administration with NAFLD occurrence on Chi square (PR 1,805; 95% CI 0,600–5,432; p = 0,289). Fibrosis classification using NAFLD Fibrosis Score was able to be carried out in 40 NAFLD patients, with advanced fibrosis detected in only 3 (7,5%) patients. No statistically significant association were found between metformin administration and advanced fibrosis using Fischer-Exact test (p = 0,394).
Conclusion: There were no statistically significant associations between metformin administration with the occurrence of NAFLD or with Fibrosis Degree in NAFLD.

Abstract #136

Pathologic findings of patients with nonalcoholic fatty liver disease and the impact of concurrent hepatitis B virus infection in Taiwan

Su Hau-Jyun

Department of Internal Medicine, National Taiwan University College of Medicine and Hospital, Taipei City, Taiwan

Background and aims: Pathologic data of non-alcoholic fatty liver disease (NAFLD) was limited and the association between NAFLD and chronic hepatitis B remained unclear in Taiwan. This study aimed to determine the pathological manifestations of NAFLD and the impact of concurrent hepatitis B virus (HBV) infection in a medical center.
Methods: Retrospective review of 104 consecutive random liver biopsies with the histologic diagnosis of NAFLD or cryptogenic cirrhosis from 2009 to 2018 was conducted. Clinical, biochemical and histological data were compared among various stages of NAFLD and between those with or without concurrent HBV infection.
Results: Advanced fibrosis was documented in 42% of Taiwanese patients with NAFLD according to METAVIR scoring system and was associated with aging (odds ratio, 1.06; 95% CI, 1.03–1.10), hypertension (odds ratio, 2.97; 95% CI, 1.31–6.74), diabetes mellitus (odds ratio, 4.36; 95% CI, 1.78–10.70) and concurrent HBV infection (odds ratio, 3.55; 95% CI, 1.46–8.58) by multivariate analyses. Concurrent HBV was found in 28.57% of the NAFLD patients. Patients with concurrent HBV had lower platelet counts, longer prothrombin time/INR and higher fibrosis stage than those without HBV infection.
Conclusions: Advanced fibrosis in patients with NAFLD was common in the biopsy series, and was related to aging, hypertension, diabetes mellitus and concurrent HBV infection.

Abstract #139

The development and validation of a novel general liver fibrosis score (GLFS) for nash-associated advanced fibrosis based on centaur clinical trial data

Alkhouri Naim[1], Lawitz Eric[1], Kayali Zeid[2], Agollah Germaine[3], Rodriguez Gerardo[3], Seyedkazemi Star[3], Martins, Eduardo Bruno[3], Noureddin Mazen[4]

[1]Texas Liver Institute, University of Texas Health, San Antonio, TX, USA, [2]Inland Empire Liver Foundation, Rialto, CA, USA, [3]Clinical Development, Allergan Plc, South San Francisco, CA, USA, [4]Cedars Sinai, Comprehensive Transplant Center, Los Angeles, CA, USA

Introduction: Liver fibrosis is an independent predictor of long-term clinical outcomes and mortality in nonalcoholic steatohepatitis (NASH).
Objectives: A validated general liver fibrosis score (GLFS) was developed to predict probability of advanced liver fibrosis associated with NASH.
Methods: CENTAUR (NCT02217475) was a randomized, controlled study in adults with biopsy-diagnosed
NASH and liver fibrosis (CRN-stage F1–F3) receiving cenicriviroc or placebo. To develop the GLFS, baseline dataset was randomly split into training (n = 239) and holdout test (n = 50) datasets. Logistic regression analysis was performed using backward elimination process on training dataset, with fibrosis stage as dependent variable (F1–2 vs. advanced F3) and baseline factors and covariates, including clinical measures, biomarkers, and comorbidities, used to predict fibrosis stage. Accuracy was defined as 1-(FalsePositiveRate + FalseNegativeRate).
Results: 289 participants, 52.6% females, median age 56 years, 52.6% had Type2 Diabetes Mellitus (T2DM), 72.3% were obese (BMI > 30 kg/m2). In the model, presence of T2DM was the most impactful factor that increased risk (Odds Ratio: 3.4[1.6, 7.4]95%CI). Logistic model McFadden goodness-of-fit score (0–100) for GLFS was 0.26, with excellent pseudo R2 of 0.6 in cross-validation. The training model had 88.5% accuracy in prediction of test dataset fibrosis cases (F1–2 vs. advanced F3), corresponding to a cut-off value of 0.597 (NPV = 0.837; PPV = 0.889; specificity = 0.923; sensitivity = 0.774). Performance (Area Under the Receiver Operating Characteristics) for GLFS 0.82[0.77,0.87]95%CI, FIB-4 0.72[0.64,0.79]95%CI, AST/ALT 0.75[0.68,0.82]95%CI, and NFS 0.73[0.67,0.79]95%CI.
Conclusion: GLFS is a novel noninvasive score that predicted the probability of advanced liver fibrosis (F3) due to NASH with good accuracy. In the CENTAUR study, GLFS outperformed other commonly used fibrosis indices.

Abstract #157

Measurement of liver stiffness by transient elastography as a non invasive method for diagnosis of non alcoholic fatty liver disease

Mahmoud Elkadeem

Introduction: Nonalcoholic fatty liver disease is an important cause of chronic-liver disease. It is often asymptomatic and incidentally diagnosed. Liver biopsy is the gold standard diagnostic test. There is no established non-invasive test to determine fibrosis accurately in non-alcoholic steatohepatitis. This study aimed to evaluate transient elastography as a noninvasive method for diagnosis of non alcoholic fatty liver disease in comparison to other non invasive methods as indicators of fibrosis. **Methods**: This study included 200 patients with bright liver shown by abdominal ultrasound after exclusion of other causes of chronic liver disease. Transient elastography was done to calculate fibrosis score and controlled attenuation parameter (CAP) score. Subjects were grouped according fibrosis score (F0–2, and F3–4). FIB4 index, APRI, BARD, NAFLD and BAAT scores were calculated.
Results: There were 47 of the patients had advanced fibrosis while 153 of them had mild fibrosis. Patients with advanced fibrosis significantly differed from the others as regards age, platelets, liver functions, and other non invasive scores. The cut-off value of elastography score was found to be 6.7 (sensitivity 80%, specificity 58.3%), and 291.5 for CAP score (sensitivity 80%, specificity 42.9%). Receiver operating curve analysis revealed high sensitivity of APRI, BAARD, and FIB4, and moderate to high specificity.
Conclusion: Many of the non invasive scores are helpful in exclusion more than prediction of fibrosis. Transient elastography and controlled attenuation parameter were found to be accurate non invasive methods with a very good performance in diagnosing stages of steatosis and fibrosis in NAFLD patients.

Abstract #174

Ultrasound-guided attenuation parameter (UGAP) for detection of hepatic steatosis with chronic liver diseases

Yudai Fujiwara), Hidekatsu Kuroda), Tamami Abe[1], Yuriko Mikami[1], Takuma Oguri), Sachiyo Noguchi[2], Naohisa Kamiyama) and Yasuhiro Takikawa[1]

[1]Division of Hepatology, Department of Internal Medicine, Iwate Medical University, [2]Ultrasound General Imaging, GE Healthcare

Introduction and objectives: Nonalcoholic fatty liver disease is a main cause of chronic liver disease (CLD) worldwide. However, a quantitative, non-invasive modality for the follow-up of hepatic steatosis has not been established. We investigated the diagnostic performance of ultrasound-guided attenuation parameter (UGAP) and quantification for assessing hepatic steatosis by a liver biopsy (LB).
Methods: We prospectively analyzed 242 consecutive CLD patients who underwent UGAP, CAP, and a LB on the same day. UGAP was performed using the LOGIQ E9. We acquired a B-mode image of the liver parenchyma. RF signals corresponding to the images were compensated by the reference signal previously measured from the uniform phantom with known attenuation (0.5 dB/cm/MHz). The attenuation coefficient (AC) was calculated from the signals' decay slope. Steatosis was categorized as S0, < 5%; S1, 5–33%; S2, 34–66% or S3, ≥ 67%.
Results: The success rate of UGAP and CAP was 100% and 94.8%, respectively. The median AC values in patients with S0 (n = 92), S1 (n = 103), S2 (n = 32) and S3 grade (n = 15) were 0.44, 0.51, 0.62 and 0.73 dB/cm/MHz, respectively, demonstrating a stepwise increase with increasing severity of steatosis ($P < 0.0001$). A significant correlation between the AC and the percentage steatosis and CAP values was found ($P < 0.001$). The area under the receiver operating curve of UGAP for identifying ≥ S1/≥ S2/≥ S3 was 0.838/0.945/0.945, respectively.
Conclusion: UGAP showed high diagnostic accuracy for detecting hepatic steatosis in patients with CLD.

Abstract #193

High prevalence of advanced fibrosis at time of nonalcoholic fatty liver disease diagnosis reflects under-diagnosis and lack of awareness

Brian Mendoza[1], Kabiru Ohikere[2], Robert J. Wong[3]

Division of Gastroenterology and Hepatology, Alameda Health System, Highland Hospital, Oakland, CA, USA

Introduction: Lack of awareness and under-diagnosis of nonalcoholic fatty liver disease (NAFLD) contributes to advanced disease at diagnosis.
Objectives: We prospectively evaluated sex- and age-specific trends in disease severity at time of NAFLD diagnosis using non-invasive assessment of fibrosis among a community-based cohort.
Methods: Consecutive adults with NAFLD at a single-center safety-net health system from August 2017 to September 2019 were prospectively evaluated using transient elastography (TE). Hepatic fibrosis was categorized using TE liver stiffness measurements: stage > 2 (F2): > 7.2 kPa; stage > 3 (F3): > 9.9 kPa; cirrhosis (F4): > 14.0 kPa. Comparisons of > F3 prevalence between groups used chi-square testing and adjusted multivariate logistic regression models.
Results: Among 921 consecutive NAFLD patients (49.8% women, mean age 53.5 ± 12.1), 56.9% were stage F0–1, 16.4% F2, 26.7% > F3. Older age at diagnosis was associated with significantly higher prevalence of > F3 (33.9% (age > 65) vs. 29.7% (age 50–65) vs. 19.3% (age < 50), p = 0.01), and there was a trend towards higher prevalence of > F3 in men compared to women (28.8% vs. 25.0%, p = 0.20). On multivariate regression, age > 65 at time of NAFLD diagnosis was associated with significantly higher odds of > F3 (OR 2.24, 95% CI 1.34–3.74, p < 0.01), and there remained a trend towards higher odds of > F3 in men vs. women (OR 1.35, 0.95–1.91, p = 0.09).
Conclusion: Among a community-based NAFLD cohort, 26.7% had > F3 and 16.6% had cirrhosis at diagnosis; older age and male sex were associated with higher odds of > F3. Greater NAFLD awareness is needed to improve early diagnosis and treatment to prevent continued disease progression.

Abstract #195

Predictors for incidence and remission of nonalcoholic fatty liver disease in obese children

Lin, Yu-Cheng[1], Chang, Pi-Feng[1], Chang, Mei-Hwei[2], Ni, Yen-Hsuan[2]

[1]Department of Pediatrics, Far Eastern Memorial Hospital, New Taipei City, Taiwan, [2]Departments of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan

Introduction: The status of non-alcoholic fatty liver disease (NAFLD) changes over time dynamically. Factors associated with NAFLD incidence and remission in obese children are not clear.
Objective: We aimed to investigate the incidence, remission and predicting factors in a prospective cohort of obese children.
Methods: Obese children aged 9–10 and 12–13 years were recruited from schools and followed up annually for 2 years. Ultrasonographic evidence of NAFLD was performed at baseline and Year 1. Alanine aminotransferase (ALT) levels were measured at baseline, Year 1 and Year 2. Elevated ALT was defined as above 26 U/L for boys and 22 U/L for girls. The genes responsible for NAFLD susceptibility, including *PNPLA3*, *GCKR*, *TM6SF2* and *MBOAT7*, were genotyped.
Results: At baseline, 86 of 422 (20.3%) subjects had ultrasonography-diagnosed NAFLD. At Year 1, of the 249 subjects without NAFLD at baseline, 20 (8.0%) developed NAFLD. The baseline body mass index (BMI) z-score and increment in BMI z-score independently predicted incident NAFLD. Of the 68 subjects with NAFLD at baseline, 36 (52.9%) had NAFLD remission. Decrement in BMI z-score independently predicted NAFLD remission. The four studied NAFLD susceptible genes were not significantly associated either the incidence or remission of NAFLD. Similarly, changes in BMI z-score predicted the incidence and remission of elevated ALT at Year 2.
Conclusion: In this obese children study, the increment/decrement in BMI z-score independently predicted the incidence and remission of pediatric NAFLD. As a result, weight management may have beneficial effects on the natural history of NALFD in obese children.

Abstract #196

A traditional Chinese medicinal formula containing geniposide, chlorogenic acid and polydatin inhibits de novo lipogenesis initiated by XBP1s in mouse of non-alcoholic fatty liver disease induced by high-fructose diet

Tian-HuaJie[1], Leng-Jing[1], Fang-Yi[1], Zhao-Jianan[1], Hu-Yiyang[2], Peng-Jinghua[1]*

[1]Institute of Liver diseases, Shuguang Hospital affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, China, [2]Institute of Clinical Pharmacology, Shuguang Hospital affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, China.

Introduction: Qushi Huayu decoction (QHD) is a traditional Chinese medicine for non-alcoholic fatty liver disease (NAFLD). De novo lipogenesis (DNL), controlled by spliced x-box binding protein 1 (XBP1s) is the important source of fatty acid (FA), bypass of carbohydrate response element-binding protein (ChREBP) and sterol regulatory element-binding protein (SREBP) 1.
Objective: Effect of QHD on DNL initiated by XBP1s was evaluated in vitro and in vivo to disclose the mechanism of QHD inhibiting steatosis and the responsible components.
Methods: (1) Mice were fed with high-fructose diet (HFD) for 2 weeks to induce hepatic DNL and administrated with QHD intragastrically simultaneously. Hepatic histology, triglyceride (TG), key enzymes of DNL, inositol-requiring enzyme (IRE) 1α, phospho-IRE1α and XBP1s were evaluated, as well as nuclear ChREBP, SREBP1 and XBP1s. (2) HepG2 cell stimulated with tunicamycin for 24 h to activate XBP1s was administrated with identified seven components of QHD respectively. Cellular TG, FA, IRE1α, phospho-IRE1α, XBP1s and the target genes of XBP1s including acetyl-coenzyme A carboxylase (ACC) 2 and stearoyl-CoA desaturase (SCD)1, were evaluated.
Results: QHD ameliorated hepatic steatosis, increased hepatic TG, FA, and protein expression of key enzymes of DNL, IRE1α, phospho-IRE1α, XBP1s, nuclear ChREBP and XBP1s, but not SREBP1 in NAFLD mice. In HepG2 cells, geniposide, chlorogenic acid and polydatin respectively inhibited protein expression of IRE1α, phospho-IRE1α, XBP1s, ACC2 and SCD1, and concentration of TG and FA induced by tunicamycin.
Conclusion: QHD inhibited hepatic DNL associated with IRE1α—XBP1s pathway closely, in which, geniposide, chlorogenic acid and polydatin was the effective component.

Abstract #203

Choline-deficient high fat diet-induced nonalcoholic steatohepatitis in BALB/c mice

Saut Horas H Nababan[1], Seruni Khaerunisa[1], Ening Krisnuhoni[2], Erni Erfan[3], Nafrialdi[4], Irsan Hasan[1], Rino A Gani[1]

[1]Hepatobiliary Division, Internal Medicine Department, Faculty of Medicine, Universitas Indonesia, Indonesia, [2]Department of Anatomy Pathology, Faculty of Medicine, Universitas Indonesia, Indonesia, [3]Department of Oral Biology, Faculty of Dentistry, Universitas Trisakti, Indonesia, [4]Department of Pharmacology and Therapeutics, Faculty of Medicine, Universitas Indonesia, Indonesia.

Background: This study was designed to investigate the effect of choline-deficient L-amino acid-defined high-fat diet (CDAHFD) in inducing nonalcoholic steatohepatitis (NASH) in BALB/c mice.
Methods: Six-week-old BALB/c mice were fed standard diet or CDAHFD (n = 6/group) for six weeks. Liver histology was assessed by hematoxylin-eosin (H&E). The liver mRNA expression levels of TNFα, TGFβ1, COL1α1, GPx1, and UCP2 were analyzed using reverse transcription-polymerase chain reaction. Liver fatty acids contents were analyzed using gas chromatography with a flame ionization detector (GC-FID).
Results: After 6 weeks of being fed CDAHFD, BALB/c mice maintained weight gain. Plasma levels of alanine aminotransferase were significantly increased. CDAHFD-fed BALB/c mice developed an enlarged liver and histologically the livers showed steatosis and lobular inflammation. Significant elevations in mRNA expression levels of TNFα, TGFβ1, COL1α1, GPx1, and UCP2 were observed in BALB/c mice fed CDAHFD. Hepatic free fatty acid compositions in CDAHFD-fed BALB/c mice were characterized by significant increase of both saturated fatty acids and ratio of long-chain n-6/n-3 polyunsaturated fatty acids (PUFAs).
Conclusions: We demonstrated that CDAHFD feeding induced alteration of liver free fatty acids and could cause the progression of NASH in BALB/c mice.

Abstract #239

Association between depression and nonalcoholic fatty liver disease: contributions of insulin resistance and inflammation

Seung Ha Park and Joo won Lee

Department of Internal Medicine, Inje University Haeundae Paik-Hospital, Inje University College of Medicine, Busan, Kore

Background: It is unclear whether depression is linked to nonalcoholic fatty liver disease (NAFLD). The purpose of this study was to examine the association between depression and NAFLD and whether the association is partly explained by insulin resistance or inflammation.
Methods: Subjects consisted of 4,688 adults who participated in the 2016 Korea National Health and Nutrition Examination Survey. Depression was defined by Patient Health Questionnaire-9 score $\geq$ 10 or a previous diagnosis of depression. NAFLD was defined by hepatic steatosis index $>$ 36. Insulin resistance was assessed by triglycerides and glucose (TyG) index. Inflammation was measured with C-reactive protein (CRP).
Results: Depression had a significant association with TyG index (p = 0.005), but not with CRP. Depression was a significant predictor of NAFLD (OR = 1.63; 95% CI, 1.26–2.10; p $<$ 0.001). Adjustment for sociodemographic features and waist circumference did not substantially affect the results. Further adjustment for comorbidities reduced the estimate for depression by 23% (OR = 1.56; 95% CI, 1.18–2.06; p = 0.002). Inclusion of CRP in a fully adjusted model did not affect the results. Addition of the TyG index decreased the estimate for depression by 28% (OR = 1.39; 95% CI, 0.88–2.19; p = 0.161), and the resulting estimate became no longer significant. The TyG index remained the independent predictor of outcome.
Conclusions: These data support an association of depression with NAFLD. Insulin resistance seems to play a major role in modulating the association between depression and NAFLD risk.

Abstract # 245

Comparison of elderly and non-elderly patients with cirrhosis

Akane Kurosugi

Introduction: In Japan, aging is progressing in patients with cirrhosis.
Objectives: We examined the backgrounds and prognoses of elderly and non-elderly patients with cirrhosis.
Methods: We retrospectively analyzed 233 patients with cirrhosis who were hospitalized for the first time between April 2014 and March 2019. Cirrhosis was defined as FIB-4 index $>$ 3.25 or diagnosis of portal hypertension. Patients were divided into two groups: elderly ($\geq$ 75 years) and non-elderly ($<$ 75 years).
Results: There were 88 elderly patients (37.8%) and 145 non-elderly patients (62.2%). Comparing elderly and non-elderly patients, the male:female ratio was significantly higher in the non-elderly (43:45 vs. 103:42, p = 0.001). Regarding background liver conditions (viral:non-viral), the proportion of non-viral conditions was significantly higher in the non-elderly (46:42 vs. 48:97, p = 0.005). The proportion of patients who received follow-up services focused on liver diesase before hospitalization was significantly lower in the non-elderly (61:27 vs 80:65, p = 0.032). The median Child Pugh score was higher in the non-elderly (8 vs. 9 points, p = 0.079). The rate of HCC complications at first hospital admission was significantly lower in the non-elderly (48.9% vs. 32.4%, p = 0.018). The cumulative elderly survival rate was 68.2%, 50.9%, and 38.6%, and 33.1% for 1, 2, 3, and 4 years, respectively. In the non-elderly, the cumulative survival was 68.9%, 63.1%, 51.2%, and 44.1% for 1, 2, 3, and 4 years, respectively. These differences were non-significant (p = 0.32).
Conclusion: Early detection of nonalcoholic steatohepatitis (NASH) and alcoholic cirrhosis in young males with limited access to medical services is important.

Abstract #266

Readiness to change in self-management of chinese patients with nafld: a national cross-sectional survey

Huang Rui

Introduction: Self-management is an important intervention in non-alcoholic fatty liver disease (NAFLD) management. The University of Rhode Island Change Assessment (URICA) Scale was widely used to assess the readiness to change of various health-related behaviors.
Objective: Our study aimed to examine the association between characteristics and readiness to change in Chinese NAFLD patients.
Methods: In this national cross-sectional survey, NAFLD patients were identified. URICA were used.
Results: 5181 NAFLD patients among China were included (figure). The mean age was 43.79 $\pm$ 13.29 years and 55% were males. 46% were obese. 4%, 0.5% patients had NASH or cirrhosis. The mean AST and triglyceride (TG) were 39.9 $\pm$ 37.9U/L and 2.44 $\pm$ 2.14 mmol/L. 4832 (93.3%) patients were in the pre-

contemplation (PC) stage. Only 341 (6.6%) and 8 (0.2%) patients were in contemplation (C) or preparation (P) stages, while no one was in maintenance (M) stage. Comparing patients in PC and C/P stages, females, the old, those with lower education level, those in the country or with higher income, those without cardiovascular diseases were apt to seriously consider the possibility of behavioral change or commit to change when facing to their NAFLD. Patients with higher BMI, AST and TG were unaware there is a problem that must be faced. Logistic regression indicated a positive correlation between cardiovascular disease and C/P stages, while a negative correlation between obesity, TG and C/P stages.

Conclusions: Patient education of self-management is badly in need in China, as obesity and TG emerged as a negative correlation with readiness to change.

Abstract #268

The mechanism of naringin, a main active ingredient of Ganshuang (a Chinese herbal complex) on cell protection in a novel tissue-engineered fatty liver model

Xiaohui zhang[1,2], Yizhi Zhang[1,2], Wen Gao[3], Shuang Liu[1,2], Qiao Wu[4], Yu Chen[1,2*], Zhongping Duan[1,2*]

[1]Artificial Liver Center, Beijing Youan Hospital, Capital Medical University, Beijing 100069, China, [2]Beijing Municipal Key Laboratory of Liver Failure and Artificial Liver Treatment Research, Beijing 100069, China, [3]Department of Hepatology and Endocrinology, Beijing Youan Hospital, Capital Medical University, Beijing 100069, China, [4]Department of infectious diseases, Beijing Tiantan Hospital, Capital Medical University, Beijing, 100070, China

Background: Oxidative stress plays an important role in Nonalcoholic fatty liver disease (NAFLD). Naringin ($C_{27}H_{32}O_{14}$, a flavonone), is a main active ingredient of Ganshuang, (a popular Chinese herbal complex in China and Asia). We recently established a novel tissue-engineered fatty liver model (TEF, a NAFLD model; DOI: 10.1021/acsbiomaterials.8b00652). The present study was aimed to use this unique NAFLD model to assess the effects and mechanisms of naringin on fatty liver.

Methods: Triglycerides (TGs) kits were used to assess the TG accumulation. Reactive oxygen species (ROS), superoxide dismutase (SOD), glutathione (GSH), and malondialdehyde (MDA) were measured by commercial kits. Relative gene and protein were detected via q-PCR/western blot. Mitochondrial membrane potential (MMP) was detected by JC-1 fluorescence-labeled microprobe. TUNEL staining was for apoptosis.

Results: Compared to TEF liver, naringin treatment resulted in 47% reduction of intracellular TG ($P < 0.01$) and down-regulated pyruvate dehydrogenase kinase-4, a biomarker of insulin-resistance. Carnitine palmitoyltransferase-I (CPT-1), the crucial enzyme in β-oxidation of fatty acid, was up-regulated after naringin treatment. Naringin significantly reversed the MMP (17%, $P < 0.05$), and reduced cell apoptosis in TEF liver. Meanwhile, naringin increased GSH and SOD levels ($P < 0.05$), decreased intracellular ROS level (46.2%, $P < 0.05$), and MDA level (48%, $P < 0.01$), indicating naringin reduced the apoptosis by enhancing anti-oxidant effect.

Conclusion: Naringin could decrease TG accumulation and protect cell from ROS injury. The possible mechanism is naringin enhanced CPT-1 expression, and reduced ROS production and increased SOD and GSH, which decreased the injury of MDA to mitochondrial, and consequently reduced apoptosis.

Abstract #303

Independent association of physical activity with nonalcoholic fatty liver disease and alanine aminotransferase levels

Jun Kyu Lee

Abstract: The aim of the current study was to examine the independent association of physical activity with nonalcoholic fatty liver disease (NAFLD) and aminotransferases while adjusting for obesity and diet. A data from 32,391 participants aged ≥ 20 years in the Korea National Health and Nutrition Examination Surveys (KNHANES) was analyzed by logistic regression models and general linear models. Physical activity was assessed from the questionnaire by health-enhancing physical activity (HEPA). The physical activity was negatively associated with NAFLD after adjustment for multiple factors with an odds ratio of 0.66 (95% CI, 0.57–0.76) comparing the most active (HEPA active) and the least active (inactive) participants. Among the participants with NAFLD, physical activity also showed an independent negative association with alanine aminotransferase (ALT) levels but not with aspartate aminotransferase levels. These independent associations were not observed when comparing the minimally active and inactive participants. Physical activity is independently associated with the degree of hepatocellular injury in patients with NAFLD as well as the risk of NAFLD in the general population. Sufficiently active physical activity greater than a minimally active level may be needed to lower the risk of NAFLD and ALT levels.

Abstract #332

Prevalence, incidence, and risk factors of tamoxifen-related nonalcoholic fatty liver disease: a systematic review and meta-analysis

Bora Lee[1*], Eun-Ae Jung[2*], Jeong-Ju Yoo[3§], Sang Gyune Kim[3§], Cheon-Beom Lee[3], Young Seok Kim[3], Soung Won Jeong[4], Jae Young Jang[4], Sae Hwan Lee[5], Hong Soo Kim[5], Baek-Gyu Jun[6], Young Don Kim[6], Gab Jin Cheon[6]

Backgroud/aims: Tamoxifen is known to be associated with an increased risk of developing fatty liver. The aim of this systematic review and meta-analysis was to evaluate the prevalence and incidence of fatty liver developed after tamoxifen treatment in breast cancer patients.

Methods: A systematic search of the PubMed (Medline), EMBASE, OVID Medline, Cochrane Library, and other databases for this review was performed. Abstracts from the search were reviewed by two investigators to choose manuscripts for full text review. Event rates were calculated with a random-effects model.

Results: The search yielded 165 references. Of these, 25 were included in the quantitative summary. We analyzed data of a total of 9,662 patients treated with tamoxifen and 3,683 patients not treated with tamoxifen. The prevalence of fatty liver among patients with breast cancer taking tamoxifen was 52.7%. The incidence of fatty liver was much higher in the tamoxifen group than in the control group [98.4/1000 person-year vs. 15.5/1000 person-year; incidence rate ratio: 2.86, 95% CI (confidence interval): 1.98–4.13, $I^2 = 59\%$] regardless of countries. The main risk factors were body mass index (BMI) [Hazard ratio (HR): 1.16, 95% CI: 1.09–1.24] and hypercholesterolemia (HR: 1.01, 95% CI: 1.00–1.02).

Conclusions: The use of tamoxifen is associated with increased risk of incidence and prevalence of fatty liver, especially in patients with high BMI and hypercholesterolemia.

Abstract #337

Arrhythmia as extrahepatic complication in patients with non-alcoholic fatty liver disaese: a systematic review and meta-analysis

Putra, Boby Pratama; Putra, Felix Nugraha

Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Introduction: Non-alcoholic fatty liver disease (NAFLD) is world-wide health problems whose global prevalence about 24%. NAFLD is related with cardiovascular complications which contributes to 40–45% of NAFLD's total deaths. Previous studies showed association between NAFLD and arrhythmia yet the result is inconsistent.
Objectives: This study aims to measure association between NAFLD and arrhythmia risk.
Methods: We did comprehensive searching with predefined keywords in online databases of Pubmed, EMBASE, and Cochrane Library. We included all relevant observational studies until November 17, 2019. We used The Newcastle-Ottawa Scale for assessing bias risks. Analysis of studies was performed to provide pooled Odds Ratio (OR) for cross-sectional studies and pooled Hazard Ratio (HR) for cohort studies with 95% Confidence Interval (CI) with random effect models.
Result: We included 9 of 108 observational studies about atrial fibrillation (AF). Analysis of 4 cross-sectional studies showed significant association between NAFLD and AF with pooled OR 2.90 (95% CI 1.51–5.57, p = 0.001, heterogeneity I^2 = 69%), while pooled HR of 5 AF cohort studies is 1.72 (95% CI 1.23–2.42, p = 0.002, I^2 = 69%). We did sub-analysis 3 of 66 cross sectional studies about Right Bundle Branch Blocks (RBBB) with pooled OR 3.09 (95% CI 0.42–22.59, p = 0.27, I^2 = 92%) and blocks other than RBBB with pooled OR 1.62 (95% CI 0.70–3.74, p = 0.27, I^2 = 67%). There is no significant association between NAFLD and conduction blocks with pooled OR 2.35 (95% CI 0.67–8.22, p = 0.56, I^2 = 96%).
Conclusion: NAFLD has significant association with AF and no significant association with conduction blocks. Further studies are needed to determine direct causality.

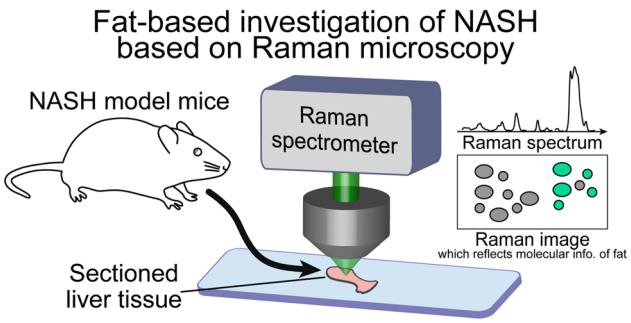
Abstract #339

Molecular imaging analysis of accumulated fats in non-alcoholic steatohepatitis by Raman microscopy

Minamikawa Takeo[1,2,3], Ichimura-Shimizu Mayuko[4], Takanari Hiroki[5], Shiomi Ryosuke[2], Kusaka Hiroki[2], Tanioka Hiroki[2], Hase Eiji[1], Yasui Takeshi[1,2], Tsuneyama Koichi[4,5]

[1]Department of Post-LED Photonics Research, Institute of Post-LED Photonics, Tokushima University, Tokushima 770-0804, Japan, [2]Graduate School of Technology, Industrial and Social Sciences, Tokushima University, Tokushima, Tokushima 770-8506, Japan, [3]PRESTO, Japan Science and Technology Agency (JST), Tokushima, Tokushima 770-8506, Japan, [4]Department of Pathology and Laboratory Medicine, Graduate School of Medical Sciences, Tokushima University, Tokushima, Tokushima 770-8503, Japan, [5]Department of Interdisciplinary Researches for Medicine and Photonics, Institute of Post-LED Photonics, Tokushima University, Tokushima 770-0804, Japan.

Introduction: Non-alcoholic steatohepatitis (NASH) is a common liver disease associated with obesity. Although the predominant evidence of NASH is the accumulation of excess fat, the pathological role of the fat on the progression of NASH has not been clearly understood due to lack of fat-based investigation of the pathogenesis of NASH. Raman microscopy has the potential to characterize molecular structures of fat based on molecular vibrations.
Objectives: We sought to visualize and characterize the accumulated fats in the liver of NASH model mice by Raman microscopy for the investigation of NASH in terms of fat.
Methods: Frozen-sectioned liver tissues of NASH model mice induced by high-fat/cholesterol/cholate diet were subjected to Raman analysis. A home-made laser-scanning Raman microscope with the excitation laser operating at 532 nm was employed.
Results: By applying the Raman microscopy to the liver of the NASH model mice, we succeeded to visualize the distribution of lipid droplets in hepatocytes. The detailed analysis of Raman spectra revealed the difference of molecular structures of the lipid droplets, such as the degree of saturation of triglycerides in the lipid droplets. We also found that the inhomogeneous distribution of cholesterol and triglyceride in the lipid droplets depending on the histology of fat accumulation.
Conclusion: We visualized and characterized the fat of NASH model mice by Raman microscopy at the cellular level. Our findings demonstrated that the Raman imaging analysis was feasible to characterize the NASH model mice in terms of the molecular structures of fat.



Abstract #396

Implication of exosomal miRNA to classify severity of NAFLD with biopsy-proven

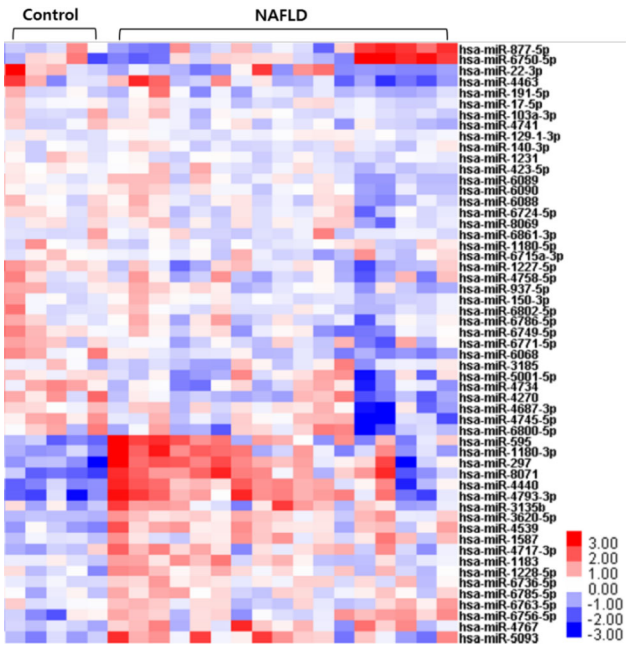
Kwan Soo Byun[1], Young-Sun Lee[1], Min-jin Lee[1], Sehwa Kim[1], Ji Hoon Kim[1], Yeon Seok Seo[1], Hyung Joon Yim[1], Jong Eun Yeon[1]

[1]Department of Internal Medicine, Korea University College of Medicine

Introduction: Nonalcoholic fatty liver disease (NAFLD) is becoming leading cause of chronic liver disease. Although determining the exact mechanisms that lead to NAFLD and NASH is important for disease identification, factors that regulate disease progression are largely unknown.
Objectives: In this study, we analyzed serum exosomal miRNA from biopsy-proven NAFLD patients and compared miRNA expression according to disease severity.
Method: Sera were collected from 5 healthy volunteers and 21 patients with biopsy-proven NAFLD without other chronic liver disease from November 2016 to January 2018. Sera were stored at –20 °C and thawed for isolation of the exosomes. Exosomes were isolated from sera using an exosome isolation kit. Total RNA was extracted from exosomes and microarray analysis for miRNA was performed.
Results: Mean age and BMI were 53.5 ± 12.3 years and 29.9 ± 4.6 kg/m^2, respectively. Female was dominant (n = 17, 80.1%). In microarray analysis, total 2,578 miRNAs were identified. When we compared miRNA expression between healthy controls (n = 5) and NAFLD patients (n = 21), 21 miRNAs significantly

increased in NAFLD patients comparing with controls and 34 miRNAs significantly increased in controls. (Figure) When patients were classified into NASH group (n = 9) and non-NASH group (n = 12), 5 miRNAs showed higher expression comparing with NAFL group including miRNA 122 and 185, whereas 3 miRNAs showed lower expression in NASH group comparing with NAFL group. Next, we classified patients into non-significant fibrosis group (F0–2, n = 12) and significant fibrosis group (F3–4, n = 9). 40 miRNAs expression increased in advanced fibrosis group comparing with non-advanced fibrosis group.

Conclusion: Exosomal miRNA expression analysis showed significant differences according to status of NAFLD, NASH, and fibrosis. These results mean exosomal miRNA expression might be important factor for disease progression in NALFD patients. Further validation studies are needed to identify the role of exosomal miRNA in disease progression of NAFLD.



Abstract #446

Albumin binding function as a diagnostic biomarker for nonalcoholic fatty liver disease

Sun Lejia[1], Liu Meixi[1], Wang Qing[2], Xu Gang[1], Yin Huanhuan[1], Yang Huayu[1], Zhou Junying[3], Mao Yilei[1]

[1]Department of Liver Surgery, Peking Union Medical College (PUMC) Hospital, PUMC & Chinese Academy of Medical Sciences, Beijing, 100730, China, [2]Department of Medical Examination Center, Hebei General Hospital, Shijiazhuang, 050051, China, [3]Department of Infectious Disease, The Third Hospital of Hebei Medical University, Shijiazhuang, 050051, China

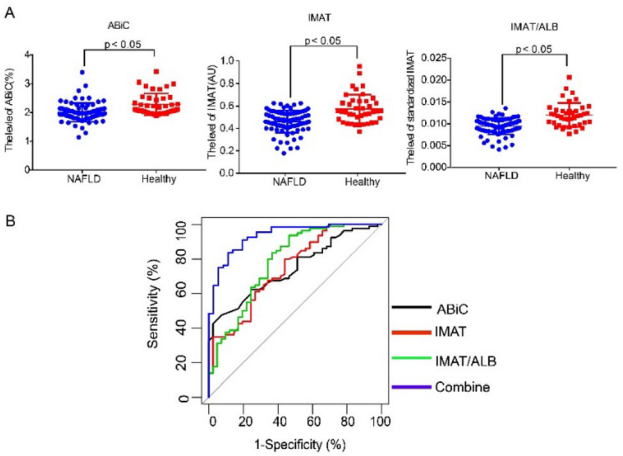
Introduction: A diagnostic indicator for non-alcoholic fatty liver disease (NAFLD) is lacking. Albumin binding function has been reported to be of great diagnostic and prognostic value in liver cirrhosis. However, its role in NAFLD patients is unknown.

Objectives: To investigate the role of albumin binding function in NAFLD patients.

Methods: An age/sex-matched, case-control study was performed. Albumin-binding capacity (ABiC) and albumin metal ion binding ability, assessed by ischemia modified albumin (IMA), were measured. Binary logistic regression and receiver operating characteristic (ROC) curves were performed.

Results: 80 NAFLD patients and 41 healthy controls were included. Albumin binding function was significantly lower in NAFLD (ABiC: 196.00%, $P < 0.001$; IMA transformed (IMAT): 0.461, $P < 0.001$; and IMAT/albumin: 0.947×10^{-2}, $P < 0.001$) than controls (ABiC: 211.00%; IMAT: 0.575; and IMAT/albumin: 1.206×10^{-2}). The frequency of NAFLD increased as albumin binding function decreased. Multivariate logistic regression analysis showed that ABiC and IMAT could serve as independent risk factors for NAFLD [ABiC: odds ratio (OR) = 3.015, P = 0.030; IMAT/albumin: OR = 3.900, P = 0.011]. Lastly, the ROC curve suggested that albumin binding function may predict the presence of NAFLD (ABiC: area under ROC (AUROC) = 0.745, $P < 0.001$; IMAT: AUROC = 0.743, $P < 0.001$; IMAT/albumin: AUROC = 0.784, $P < 0.001$). When albumin binding function, body mass index (BMI), and triglyceride were combined, diagnostic capacity was enhanced (AUROC = 0.935, $P < 0.001$).

Conclusions: This is the first study to explore the alterations of albumin binding function and its clinical significance in NAFLD. Our findings suggest albumin binding function as a novel, potential biomarker for diagnosing NAFLD.



Abstract #470

Outcomes of liver transplantation for non-alcoholic steatohepatitis at New Zealand liver Transplant unit over last 20 years

Hassan Ibrahim[1], Gane Edward[2]

[1]Hepatology registrar, New Zealand Liver Transplant unit (NZLTU), Auckland City Hospital, Auckland, New Zealand, [2]Hepatologist and transplant physician, New Zealand Liver Transplant unit (NZLTU), Auckland City Hospital, Auckland, New Zealand

Introduction: Non-alcoholic steatohepatitis (NASH) is the most rapidly growing indication for liver transplantation globally and is anticipated to become the leading cause in New Zealand within the next decade due to the growing epidemics of obesity and diabetes.

Objectives: To determine the outcomes following liver transplantation.

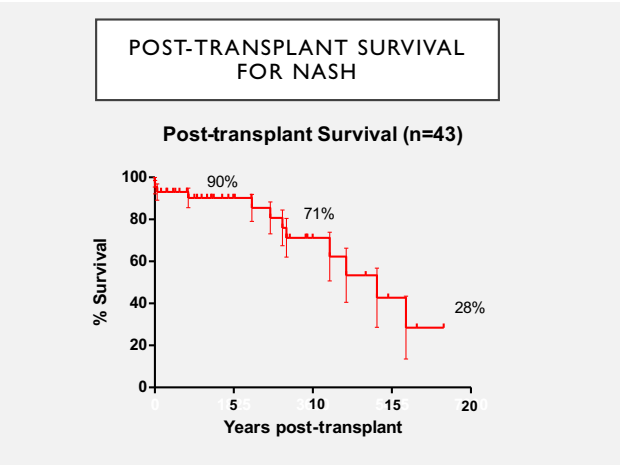
Methods: All NASH cases underwent liver transplantation at NZLTU between 1999 and 2019 were included.

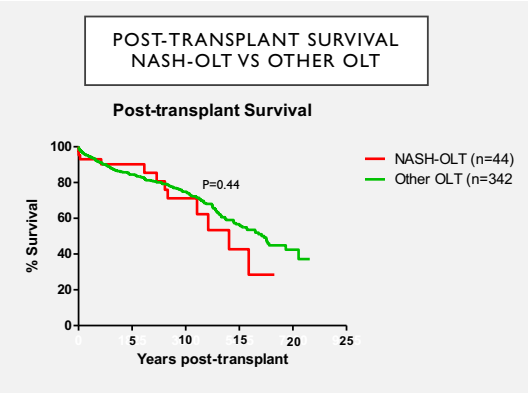
Results: 43 patients underwent liver transplantation for NASH during the study period, of which two third were performed for decompensated liver cirrhosis (DLC) and one third for hepatocellular carcinoma (HCC). Patients were predominantly male 70% with a median age of

58 years. 84% were obese with a median body mass index of 35, 60% were diabetics, 49% were hypertensive, and 14% had dyslipidaemia. Number of liver transplants for NASH increased from 12 patients in the first decade compared to 31 patients in the second decade, an increment by 250%. 32.5% patients had treated rejection post-transplantation. Three patients died in the early post-operative period. Out of 9 late deaths, three died of renal failure, and one of recurrent DLC, one of non-HCC solid organ cancer. Overall survival was 90% at 5 years and 71% at 10 years (similar to non-NASH transplants, P 0.47)

Conclusion: The number of liver transplants for NASH increased significantly during the study period. Half of late deaths were related to complications of metabolic syndrome (55%). Management of metabolic complications following transplantation for NASH will be a major challenge in the future.

Keywords: NASH, Liver transplantation, Cirrhosis and HCC





Abstract #576

The clinical and patient-reported outcomes (pro) profile of patients with chronic liver disease (cld) in asian countries: data from real-world practices varies across the world

Younossi, Zobair M.[1,2], Yu, Ming-Lung[3], Yilmaz, Yusuf[4,5], Wong, Vincent Wai-Sun[6], Duseja, Ajay K.[7], Chan, Wah Kheong[8], Fan, Jian-Gao[9], Eguchi, Yuichiro[10], Hamid, Saeed S.[11], Ong, Janus[12], Younossi, Issah[13], Nader, Fatema[13], Racila, Andrei[13], Ziayee, Mariam[13], Stepanova, Maria[13], on behalf of the Global NASH Council

[1]Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, VA, United States, [2]Center for Liver Diseases and Department of Medicine, Inova Fairfax Hospital, Falls Church, VA, United States, [3]Hepatitis Research Center, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [4]Institute of Gastroenterology, Marmara University, Istanbul, Turkey, [5]Department of Gastroenterology, School of Medicine, Marmara University, Istanbul, Turkey, [6]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, [7]Department of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh, India, [8]Gastroenterology and Hepatology Unit, Gastrointestinal Endoscopy Unit, Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, [9]Xinhua Hospital, Shanghai Jiatong University School of Medicine, Shanghai, China, [10]Liver Center, Saga University Hospital, Saga, [11]Medicine, Aga Khan University, Karachi, Pakistan, [12]University of the Philippines, College of Medicine, Manila, Philippines, [13]Center for Outcomes Research in Liver Diseases, Washington, DC, United States

Background: At least one in five CLD patients live in Asia. The aim was to assess clinical profile and PROs of CLD patients enrolled into the Global-Liver-Registry (GLR) from several Asian countries.

Methods: GLR is prospectively enrolling subjects (NAFLD/NASH, HBV or HCV) from real-world practices worldwide. Clinical and PRO data (FACIT-F, CLDQ, WPAI) are being collected. For this analysis, we selected CLD patients enrolled from 9 Asian countries (N = 2364: N = 581 HBV, N = 497 HCV, N = 1268 NAFLD/NASH) and used patients enrolled from non-Asian countries for comparison (N = 5303).

Results: Compared to HBV and NAFLD/NASH, Asian HCV patients were older, less likely male and less employed ($p < 0.05$). On the other hand, Asian patients with NAFLD/NASH had higher BMI, more sleep apnea, diabetes, hypertension and hyperlipidemia ($p < 0.05$). The rate of lean NAFLD (Adjusted for Asian-specific BMI) was 10%. Across CLD etiologies, the rates of cirrhosis were similar (6–8%, $p > 0.05$); while ALT, AST, and liver stiffness by transient elastography were the highest in NAFLD/NASH ($p < 0.0001$). PRO scores were lowest in Asian NAFLD/NASH patients: mean total FACIT-F 115 ± 27 (range 0–160) vs. 124 ± 25 (HBV) and 130 ± 23 (HCV), and mean total CLDQ 5.2 ± 1.1 (range 1–7) vs. 5.7 ± 1.1 and 5.9 ± 0.8, respectively. Similar to GLR subjects from other regions, NAFLD/NASH was the most common CLD in Asia (54% vs. 55%, p = 0.62).

Conclusions: Of all subjects enrolled from Asia into the GLR, NAFLD/NASH was the most common cause of CLD. Since these patients tend to have more comorbidities and lower PRO scores, NAFLD/NASH potentially poses substantial public health burden in that region.

Abstract #600

NAFLD disease burden—Hong Kong, Singapore, South Korea, and Taiwan, 2020–2035

Homie Razavi[1], George Goh Boon Bee[2,3], Henry Lik Yuen Chan[4,5], Rong Nan Chien[6,7], Wan-Long Chuang[8], Chris Estes[1], James Fung[5,9], Tsung Hui Hu[10], Jee-Fu Huang[11,12], Byoung Kuk Jang[13], Dae Won Jun[14], Jia Horng Kao[15], Jin-Woo Lee[16], Kathryn Razavi-Shearer[1], Wai-Kay Seto[9], Grace Lai-Hung Wong[4,5], Vincent Wai-Sun Wong[4,5], Han-Chieh Lin[17,18]

[1]Center for Disease Analysis Foundation, Lafayette, Colorado, US, [2]Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore, [3]Duke-National University of Singapore Medical School, Singapore, [4]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, [5]State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong, [6]Department of Gastroenterology and Hepatology, Chang-Gung Memorial Hospital and University at Keelung, Keelung, Taiwan, [7]Community Medicine Research Center, Chang-Gung Memorial Hospital, Keelung, Taiwan, [8]Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [9]Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, China, [10]Division of Hepatogastroenterology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, [11]Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, [12]Faculty of Internal Medicine and Hepatitis Research Center, School of Medicine, College of Medicine, and Center for Cancer Research and Liquid Biopsy, Kaohsiung Medical University, Kaohsiung, Taiwan, [13]Department of Internal Medicine, Keimyung University School of Medicine, Daegu, Korea, [14]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Republic of Korea, [15]National Taiwan University College of Medicine, and National Taiwan, University Hospital, Taipei, Taiwan, [16]Department of Internal Medicine, Inha University School of Medicine, Incheon, Korea, [17]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, [18]Faculty of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan

Nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) present a growing burden of liver disease in the Asia-Pacific region. Epidemic levels of obesity among young people, and susceptibility to develop metabolic syndrome at lower BMI and at younger ages means that the region's population is at risk of developing complications in the coming decades. A model was constructed to estimate changes in the burden of NAFLD-related morbidity and mortality in four areas (Hong Kong, Singapore, South Korea, and Taiwan).

The disease progression model tracked all NAFLD cases in each area with longitudinal changes in prevalence based on long term trends for adult obesity. Fibrosis progression was tracked over time among NAFLD populations and the number of advanced cases and liver-related deaths were estimated. Prevalent NAFLD cases were projected to increase 6% (South Korea) to 25% (Singapore) during 2020–2035, and NASH cases increase 25–45% during the time period. Incident cases of NAFLD-related liver cancer are expected to increase by 90–100%, and incident decompensated cirrhosis increase by 90–155%. Similarly, NAFLD-related liver deaths are projected to increase between 100–160% in each area in the time period from 2020 to 2035. NAFLD disease burden is projected to continue increasing among populations in the region who are experiencing historically unprecedented levels of obesity, and rapid aging. Continued increases in the number of advanced liver disease cases and associated mortality are expected. Halting the growth of metabolic syndrome will be crucial for preventing continued increases in disease burden in the Asia-Pacific region.

Abstract # 691

Simple anthropometric measurements model for predicting liver steatosis of non-alcoholic fatty liver disease screening: a preliminary report

Eka Surya Nugraha, M. Begawan Bestari, Dolvy Girawan, Nenny Agustanti, Yudi Wahyudi, Siti Aminah Abdurahman

Division of Gastroenterology and Hepatology, Department of Internal Medicine, Hasan Sadikin General Hospital, Universitas Padjadjaran, Bandung, Indonesia

Introduction: Fatty liver (FL) is highly prevalence, estimated 25% in normal population. Ultrasound Attenuated Parameter (UAP) are novel feature to identify FL severity. However, high cost and limited access to this device in Indonesia, boundaries the physicians. Therefore, simple method was needed for assessing the FL.
Objective: The aim of this study is to construct algorithm model from simple anthropometric measurements to the UAP for mass screening of FL.
Methods: This was a cross-sectional, observational study. Subjects between 18 and 65 years old with or without comorbid diseases were included. Subjects were fasting 6 to 8 hours before examinations. Independent variables were age, sex, body weight, height, Body Mass Index (BMI), waist circumference, and diabetes status. Dependent variable was the UAP, obtained by Fibrotouch® device. Variables were tested for normality, correlation for univariate, then multiple regression for multivariate analyses and identify collinearity. The backward method multiple regression constructed the equation models to predict UAP.
Results: Fourty two subjects had been enrolled. Mean age 46,88 (SD 11,02) years old, 61,9% were male, 33,3% were diabetes. UAP score were normal distribution. Univariate analysis showed body weight, BMI, and waist circumference had correlation to UAP ($p < 0.001$). In multivariate, the BMI was only significant ($p = 0.01$). Constructed regression model to predict UAP was BMI × 7,386 + Waist Circumference:0.875–8.507 (adjusted $R^2 = 51.8\%$).
Conclusion: BMI and waist circumference can be modelled to predict UAP for FL screening and severity. This study remains in progress to recruit more subjects to finalized the algorithm model and validation.

Abstract #695

Clinicopathological characteristics leading to fibrous progression of the liver in nonalcoholic fatty liver disease

Suda Takeshi, Kanefuji Tsutomu[1], Abe Atsushi[2], Hoshi Takahiro, Abe Satoshi, Morita Shinichi, Yagi Kazuyoshi, Hatakeyama Shigeaki[3], Terai Shuji[4]

Department of Gastroenterology and Hepatology, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Minami-Uonuma, Japan, [1]Division of Gastroenterology and Hepatology, Niigata Tokamachi Hospital, Tokamachi, Japan, [2]Joetsu-Area General Health Care Center, Joetsu, Japan, [3]Hatakeyama Medical Clinic, Joetsu, Japan, [4]Division of Gastroenterology and Hepatology, Graduate School of Medical and Dental Sciences, Niigata University, Niigata, Japan.

Introduction: Given pandemic of nonalcoholic fatty liver disease (NAFLD), effective managements request selection of risky cases.
Objectives: To define the clinicopathological characteristics of risky NAFLD.
Methods: Two-dimensional shear wave elastography (2dSWE) was measured more than twice in 229 NAFLD cases with an interval of 508 ± 251 days. A region-of-interest was placed at 3 sites in each

segment, and a median value was calculated. Energy intake was quantified using brief-type self-administered diet history questionnaire. No specific medicine was administrated for metabolic syndrome.

Results: The cases were 61.9 ± 9.3 years old consisting of 157 males and 72 females with body mass index (BMI) of 24.1 ± 2.3 kg/m^2. The median of 2dSWE on the first measurement was 1.33 m/sec (IQR, 1.28–1.39). The energy intake was 1902 ± 540 kcal/day. In 117 and 65 cases (***Improved***), 2dSWE was continuously or intermittently decreased at the rate of 0.040 or 0.022 m/sec/year, respectively, while consistent increase was observed in the rest of 47 cases (***Progressed***) at the rate of 0.022 m/sec/year. BMI tended to be higher in ***Progressed*** ($p = 0.082$). Although white blood cell count was not different between two groups ($p = 0.56$), the proportion of neutrophil was significantly higher in ***Progressed*** ($p = 0.0051$). Among various nutrients, saturated fatty acids consisting of 4 or 6 carbohydrates were taken less in ***Progressed*** ($p = 0.040$ and $p = 0.034$, respectively).

Conclusion: The cases with higher BMI and percentage of neutrophil eating less amount of short- and medium-chain fatty acids may cause progression of liver fibrosis in NAFLD.

Abstract #700

Simple anthropometric indices are useful for predicting non-alcoholic fatty liver disease in rural bangladeshi population

Mohammad Izazul Hoque

Introduction: NAFLD is the most common liver disease worldwide. The screening of general population for the presence of NAFLD with abdominal ultrasound may not be a cost effective approach. Alternative non-invasive markers for prediction of NAFLD are needed. Aim of the study was to assess whether the simple anthropometric indices are useful for predicting non-alcoholic fatty liver disease in rural Bangladeshi population.

Method: This cross-sectional study was performed in a village of Cumilla, Bangladesh during a 6-month period in a randomly selected sample of adult general population. All inhabitants older than 18 years were invited to participate in the study. Those who were agreed to take part in this study was made an appointment with the study team for detailed history and physical examination and laboratory testing. The diagnosis of NAFLD was made on the basis of ultrasonography. Statistical analyses were performed using the SPSS software, version 16.0.

Result: Baseline clinical and anthropometric parameters of NAFLD patients were mean age 42.98 ± 13.03 years, mean BMI 25.66 ± 3.15, mean waist circumference 88.62 ± 8.20, mean height 151.18 ± 10.61, mean weight 58.78 ± 9.24, mean liver size 13.71 ± 1.65, mean systolic blood pressure 125.48 ± 16.26, mean diastolic blood pressure 81.79 ± 9.22. The AUROC values in both genders were 0.832 for BMI, 0.763 for waist circumference, 0.771 for the waist/height ratio. The Cut-off values in both genders were 24.4 for BMI, 75.40 for waist circumference and 0.54 for the waist/height ratio. Sensitivity in both genders were 80.24% for BMI, 82.34% for waist circumference, 79.56%for the waist/height ratio. Specificity in both genders were 79.12% for BMI, 80.45% for waist circumference, 78.98% for the waist/height ratio.

Conclusion: The simple anthropometric parameters, such as BMI, waist circumference, waist height ratio is useful for predicting NAFLD. Besides, our study also clearly demonstrated that a simple assessment of BMI is as efficacious as other anthropometry parameters in predicting NAFLD.

Abstract #705

Exercise effect on liver fibrosis of nonalcoholic steatohepatitis in mice

Kenichi Tanaka[1], Hirokazu Takahashi[1], Keizo Anzai[1], Yuichiro Eguchi[2]

[1]Division of Metabolism and Endocrinology, Facility of Medicine, Saga University, Saga, Japan, [2]Liver Center, Saga Medical School, Saga, Japan

Introduction: Development of liver fibrosis is most important prognosis factors. Exercise training is a robust treatment of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH). It is also well known that exercise has pleiotropic effect on various tissues and organs including liver. However, exercise effects on liver fibrosis has not been well elucidated.

Objectives: We investigated the effect of exercise training on liver fibrosis of NASH mice model.

Methods: 6-week-old male mice started to be fed choline-deficient, L-amino-acid-defined and high-fat diet with 0.1% methionine (CDA-HFD). Mice were housed in normal cage (sedentary group; CDA-control) or wheel cage (wheel cage running group; CDA-WCR) for 8 weeks. All mice were sacrificed at 14-week-old. Finally, body weight, glucose tolerance test (GTT), NAFLD activity score (NAS), liver fibrosis stage and mRNA levels were evaluated.

Results: There was no difference in body weight, glucose level and food intake. The GTT showed no significance of glucose AUC, HOMA-R and insulinogenic index. Pathologically, azan staining showed that WCR tended to prevent development of liver fibrosis, and NAS was ameliorated in WCR group compared to control (NAS, 6 ± 0.27 vs 4 ± 0.27, $p < 0.01$). mRNA expression of CD36, CPT1a, ACC1, SCD1, Col1a, Pdgfrb, Tgfbr1, Timp1, Timp2 and MMP2 were significantly decreased in CDA-WCR ($p < 0.01$).

Conclusion: Exercise training might prevent the progression of steatohepatitis and liver fibrosis in mice

Abstract #708

Non-alcoholic fatty liver disease potentiates inhibitory checkpoints expression on antiviral effector cells following murine hepatitis virus infection

Wu Ting[1], Wang Hongwu[1], Wang Xiaojing[1], Yan Weiming[1], Xi Dong[1], Luo Xiaoping[2] and Ning Qin[1]

[1]Department and Institution of Infectious Diseases, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, [2]Department of Pediatrics, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Introduction: In view of the uptrend of concurrence of non-alcoholic fatty liver disease (NAFLD) and viral hepatitis, the impact of NAFLD on viral hepatitis has aroused general concern. Here, we found higher expression of inhibitory checkpoints on antiviral effector cells in NAFLD mice infected with hepatitis virus.

Objectives: To investigate the influence of NAFLD on the induction of programmed cell death protein 1 (PD-1) and NKG2A, important inhibitory checkpoints responsible for exhaustion of $CD8^+PD\text{-}1^+$T cells and $NKG2A^+$ NK cells, in viral hepatitis.

Methods: Sixty 6-week-old female C3H/HeN mice had received HFD or standard chow diet (SCD) for 12 weeks randomly, and were injected with 10 plaque forming units of murine hepatitis virus strain 3 (MHV-3) intraperitoneally. Intrahepatic $CD8^+PD\text{-}1^+$T cells and

$NKG2A^+$ NK cells were detected by flow cytometer on day 8 post infection.
Results: Following HFD-induced steatosis established, there was no difference in the expression of PD-1 or NKG2A between two dietary groups. The frequencies of $CD8^+$ $PD\text{-}1^+$T cells (6.923 ± 2.348% vs. 14.775 ± 1.889%, $P < 0.001$) and $NKG2A^+$ NK cells (6.704 ± 1.094% vs. 11.240 ± 1.350%, $P = 0.002$) elevated more profoundly in NAFLD mice compared to SCD fed mice post viral infection.
Conclusions: In MHV-3 infection, more inhibitory checkpoints express on $CD8^+$ $PD\text{-}1^+$T cells and $NKG2A^+$ NK cells in NAFLD mice. NAFLD could potentiate exhaustion of antiviral effector cells and impair viral eradication

Abstract #737

Assessment of liver fibrosis with transient elastography in NAFLD patients

Butt N[1], Rai L[1], Channa RH[1], Khemani H [1], Soomro SA[1] Abbasi A[2]

[1]Gastroenterology Department, Jinnah Postgraduate Medical Centre, Karachi, Pakistan, [2]Medical Unit II, Dow University of Health Sciences, Ojha Campus, Karachi, Pakistan.

Introduction: Transient Elastography (TE) is a non-invasive technique for estimating liver fibrosis. There is a limited data about the performance of TE in Pakistani patients with non-alcoholic fatty liver disease (NAFLD). An overall prevalence of NAFLD in Pakistan is 47%. In the present study, we have evaluated the diagnostic accuracy of TE in identifying different degrees of fibrosis in NAFLD patients
Methodology: A Cross-sectional study was undertaken at the Department of Gastroenterology, Jinnah Postgraduate Medical, Karachi, Pakistan. All patients above the age of 18 years, with diagnosis of NAFLD were included in the study. All patients with hepatitis, hepatic malignancies, hepatobiliary infections, and biliary tract disease were excluded from the study. Fibrosis score was calculated through Elastography as: F0–F1 (5.3–7.1 kPa, Normal); F2 (7.5–8.5 kPa, Mild/Grade-I); F3 (9.5–13.0 kPa, Moderate/Grade-II); and F4 (13.1–18.8 kPa, Severe/Grade-III). This study is an ongoing study.
Results: A total of 162 patients were enrolled in the study, from which 41 (25%) were male and 121 (75%) were female, with a mean age of 39.60 ± 9.74 years. Out of these, 108 (67%) belonged to the lower socioeconomic class. One hundred and twenty one (75%) patients had fatty liver on ultrasound and 41 (16%) had hepatomegaly with fatty changes. TE revealed 64 (40%) patients had a score of F0-F1, 61 (38%) F2, 28 (17%) F3, and only 9 (6%) had a score of F4.
Conclusion: The detection of liver fibrosis at early stages is crucial in preventing its progression to cirrhosis which is the irreversible process. Reversal of fibrosis is only possible if it is diagnosed as early as possible and managed with appropriate treatment.

Abstract #757

A survey on perceptions of non-alcoholic fatty liver disease: a real life experience from Pakistan

Butt N[1], Rai L[1], Channa RH[1], Khemani H [1], Soomro SA[1] Abbasi A[2]

[1]Gastroenterology Department, Jinnah Postgraduate Medical Centre, Karachi, Pakistan, [2]Medical Unit II, Dow University of Health Sciences, Ojha Campus, Karachi, Pakistan.

Background and aims: Non-alcoholic fatty liver disease (NAFLD) is associated with metabolic syndrome, an overall prevalence of 47% was found in a previous study from Pakistan, however there is no community based study from Pakistan about perception and awareness of NAFLD in patients who are actually suffering from it. Here we aim to explore the awareness and perceptions of patients with NAFLD
Method: A Cross-sectional study was undertaken at the Department of Gastroenterology, Jinnah Postgraduate Medical Centre, Karachi, Pakistan. All patients > 18 years, with a suspected diagnosis of NAFLD were included. Patients with, hepatitis, hepatic malignancies, hepato-biliary infections, and biliary tract disease were excluded from the study. Perceptions of NAFLD were assessed using a self-administered survey questionnaire.
Results: A total of 162 patients with NAFLD were enrolled in the study with a mean age of 39.60 ± 9.74 years. One hundred & eight (67%) belonged to the lower socioeconomic class. Out of which 41 (25%) were male and 121 (75%) were female. Forty-two patients (26%) knew about their disease while only 26 (16%) knew what fatty liver is. The majority 100 (62%) considered themselves overweight while 113 (70%) were called upon by others as overweight. Almost half of the population 82 (51%) thought of the weight as having edema and most of them 127 (78%) felt they need to lose weight. Around 108 (67%) believed they exercise enough while 90 (56%) considered it as the chores of the house. 82 (51%) of them believed that they overeat while 70 (43%) thought that they eat inappropriate food. Moreover, only 23 (14%) knew about the co-morbids of NAFLD. When inquired about alternative medications, 40 (25%) were taking it while 32 (20%) considered those harmful.
Conclusion: According to our results, the majority of subjects had no idea about NAFLD. Enhanced public education is warranted to improve understanding and knowledge about common disorders, especially in our country. Moreover, further exploration into the awareness and attitudes of NAFLD is needed to develop strategies for combating this disease.

Abstract #783

Characterization of fibrosis in non-alcoholic steatohepatitis by use of second-harmonic-generation microscopy

Eiji Hase[1], Hiroki Takanari[2], Mayuko Ichimura-Shimizu[3], Yuri Hayashi[2], Takeo Minamikawa[1,4,5], Takeshi Yasui[1,4], Koichi Tsuneyama[2,4].

[1]Department of Post-LED Photonics Research, Institute of Post-LED Photonics, Tokushima University, Tokushima 770-0804, Japan, [2]Department of Interdisciplinary Researches for Medicine and Photonics, Institute of Post-LED Photonics, Tokushima University, Tokushima 770-0804, Japan, [3]Department of Pathology and Laboratory Medicine, Graduate School of Medical Sciences, Tokushima University, Tokushima, Tokushima 770-8503, Japan, [4]Graduate School of Technology, Industrial and Social Sciences, Tokushima University, Tokushima, Tokushima 770-8506, Japan, [5]PRESTO, Japan Science and Technology Agency (JST), Tokushima, Tokushima 770-8506, Japan

Introduction: Second-harmonic-generation (SHG) microscopy is a promising tool for the observation of collagen fiber in tissues without staining. Considering that the SHG light intensity depends on the structural maturity, density, and aggregates of collagen molecules, SHG microscopy may be a promising probe for visualizing the degree

of fibrosis. In this paper, we applied SHG microscopy to non-alcoholic steatohepatitis (NASH) tissues in order to confirm the possibility of the technique for the characterization of fibrosis.
Objectives: To compare the difference of fibrosis between NASH and other liver fibrosis for the characterization of fibrosis in NASH by use of SHG microscopy.
Methods: Thin-sectioned liver tissues in animal model of NASH was prepared to confirm the feasibility of SHG imaging. Human tissues were examined followed by animal tissues. NASH, alcoholic steatohepatitis (ASH), and viral hepatitis model were prepared. A home-built SHG microscope equipped with infrared femtosecond laser was used.
Results: From the SHG images, structural differences of fibrosis between NASH and other liver fibrosis were observed due to the different maturity of collagen fiber in each tissue. The structure of collagen fiber visualized on SHG images in ASH was dot-like structure, whereas that in NASH was more fibrous structure. Furthermore, the result of SHG intensity-based image analysis showed that the possibility of the quantitative evaluation of NASH in terms of fibrosis.
Conclusion: Our results indicate that SHG microscopy may be a potential tool for the characterization of fibrosis in NASH.

Abstract #802

A novel 3-step approach for predicting advanced fibrosis in non-alcoholic fatty liver disease

Kobayashi Takashi, Ogawa Yuji, Nakajima Atsushi

Department of Gastroenterology and Hepatology, Yokohama City University Graduate School of Medicine 3-9, Fukuura, Kanazawa-ku, Yokohama, Kanagawa, Japan, 236-0004

Introduction: It has been reported that the 2-step approach, in which Fibrosis-4 (Fib-4) index is used first and followed by enhanced liver fibrosis (ELF) test or vibration-controlled transient elastography (VCTE), can improve prediction of advanced fibrosis in non-alcoholic fatty liver disease (NAFLD) patients. However, the low positive predictive value (PPV) and high misclassification rate are problems.
Objectives: We aimed to evaluate the 3-step approach combining scoring systems, liver fibrosis markers, and VCTE as a novel algorithm.
Methods: We performed a retrospective analysis of data from 183 NAFLD patients as a training cohort and 166 NAFLD patients as a validation cohort, who underwent liver biopsy from January 2014 to July 2019. We assessed several types of 2-step approaches and 3-step approaches.
Results: The misclassification rates of 2-step approach A (using ELF score for patients with indeterminate Fib-4 index), 3-step approach A (using VCTE for intermediate group in 2-step approach A), 2-step approach B (using type 4 collagen 7 s for patients with indeterminate Fib-4 index), and 3-step approach B (using VCTE for intermediate group in 2-step approach B) were 29.0, 21.3, 24.0, and 20.8%, respectively. The PPVs of them were 55.5, 65.5, 61.1, and 65.9%. The negative predictive values of them were 91.1, 90.2, 92.0, and 90.8%, respectively. Similar trends were seen in the validation cohort.
Conclusion: The 3-step approach improved misclassification rate and PPV in predicting advanced fibrosis in NAFLD patients compared to 2-step approach. Also, it may be helpful to use type 4 collagen 7 s instead of ELF score.

Abstract #804

Efficacy of vitamin B6 in the treatment of nonalcoholic fatty liver disease: an open-label, single-arm, single-center study

Kobayashi Takashi, Ogawa Yuji, Nakajima Atsushi

Department of Gastroenterology and Hepatology, Yokohama City University Graduate School of Medicine, 3-9, Fukuura, Kanazawa-ku, Yokohama, Kanagawa, Japan, 236-0004

Introduction: Vitamin B6 (VitB6) functions as co-factor for various enzyme reactions involved in amino acid, glucose, and fat metabolism. VitB6 deficiency causes hepatic lipid accumulation; its supplementation ameliorates fatty liver in mice.
Objectives: This is the first study examining the therapeutic effects of VitB6 administration in nonalcoholic fatty liver disease (NAFLD) patients.
Methods: This was an open label, single-arm, single-center study. Twenty-three NAFLD patients received VitB6 (90 mg/day) orally for 12 weeks. We evaluated their clinical parameters before and after VitB6 treatment. We also quantified liver fat and fibrosis using magnetic resonance imaging (MRI)-based proton density fat fraction (PDFF) and magnetic resonance elastography (MRE). The primary endpoint was the change in alanine aminotransferase (ALT) levels. Secondary endpoints were the changes in MRI-PDFF, MRE, serum VitB6, metabolic and hepatic function-related parameters.
Results: Twenty-two patients finished the protocol. MRI-PDFF, a parameter of hepatic lipid accumulation, reduced significantly after 12 weeks (from $18.7 \pm 6.1\%$ to $16.4 \pm 6.4\%$, $p < 0.001$). ALT did not change significantly after VitB6 treatment. When divided into MRI-PDFF responders (MRI-PDFF reduction $> 8\%$) and MRI-PDFF non-responders (MRI-PDFF reduction $< 8\%$), the fibrosis-4 (Fib-4) index of the responders at baseline was significantly lower (responders: 1.18 ± 0.85, non-responders: 2.09 ± 0.97, $p = 0.03$).
Conclusion: VitB6 administration can ameliorate hepatic fat accumulation in NAFLD patients.

Abstract #844

Fibrosis regression benefit more from weight loss (≥ 5%) in obese NAFLD patients than non-obese

Yiwen Shi

Aims: Weight loss is the most effective on fibrosis regression of non-alcoholic fatty liver disease (NAFLD). This study is aimed to estimate the difference of fibrosis regression between non-obese and obese patients.
Methods: Patients diagnosed as NAFLD by liver biopsy according to NASH CRN scoring system were consequentially enrolled and followed-up in this study. Obese was defined as BMI ≥ 25 kg/m^2. Fibrosis regression was defined as LSM decreased more than 15% compared to baseline.
Results: A total of 71 NAFLD patients (aged 52.7 ± 11.2 years, male 23.9%) with median follow-up 3.1 (1.3, 5.6) years were included. The advanced fibrosis (F3/4) was detected in 50.0% non-obese group and in 47.6% obese group. Long-term liver-related events (ascites, variceal bleeding or HCC, n = 5) only occurred in obese group but not non-obese group (P = 0.117). None of these patients achieved weight loss more than 5%. The LSM decrease was significantly associated with the percent of weight loss (r = 0.300, P = 0.036), especially in obese patients (r = 0.424, P = 0.022) but not in non-obese group (r = 0.140, P = 0.056). In patients achieved successful weight loss (more than 5%), obese groups had a trend toward higher rate of LSM decrease. In obese group, cox regression analysis showed the weight

loss (P = 0.009) was independently associated with LSM decrease, while in non-obese group, fibrosis stage (P = 0.008) but not weight loss (P = 0.053) was associated with LSM decrease.
Conclusion: Obese patients benefit more from weight loss to achieve fibrosis regression. Therefore, non-obese patients urgently need additional treatment to prevent the progression of fibrosis.

Abstract #853

A double-blind, randomized, placebo-controlled, phase II study to assess the efficacy and safety of insulin sensitizer in patients with nonalcoholic steatohepatitis in Asia– an interim report

Jee-Fu Huang[1,2,3,4], Ming-Lun Yeh[1,2,3], Chung-Feng Huang[1,2,3], Ching-I Huang[1,2,3], Chia-Yen Dai[1,2,3], Shinn-Chern Chen[1,3], Ming-Lung Yu[1,2,3,4], Wan-Long Chuang[1,2,3]

[1]Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [2]Graduate Institute of Clinical Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, [3]Faculty of Internal Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, [4]Centre for Liquid Biopsy and Cancer Research Centre, Kaohsiung Medical University, Kaohsiung, Taiwan.

Background and aim: Non-alcoholic steatohepatitis (NASH) is the leading liver disease globally. Insulin sensitizer has been demonstrated the efficacy in lowering liver fat and inflammation of NASH patients. We conducted the randomized trial aiming to investigate the efficacy and safety of insulin sensitizer in Asian NASH patients.
Methods: A total of 90 biopsy-proved NASH patients was consecutively randomized into receiving either oral Pioglitazone 40 mg/day or placebo for 24 weeks and another 12 weeks post-treatment follow up. Biochemistry profiles, liver biopsy and magnetic resonance imaging (MRI) were collected before and after the intervention, respectively. The histological severity of NASH was evaluated and the primary endpoint was the efficacy of pioglitazone in liver biochemistry and fat accumulation.
Results: among the 90 NASH patients recruited, 66 (73.3%) were male and the mean age was 44.1 ± 12.7 years old. Diabetes, dyslipidemia, and metabolic syndrome were found in 21 (23.3%), 55 (61.1%), and 52 (57.8%) of the patients. The mean body mass index (BMI) was 28.9 ± 3.9 kg/m^2 and 29 (32.2%) patients of obesity. The mean AST, ALT, glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglyceride, and uric acid were 52 ± 23 U/L, 90 ± 39 U/L, 103.8 ± 16.2 mg/dl, 215.1 ± 33.7 mg/dl, 44.0 ± 10.6 mg/dL, 141.1 ± 35.2 mg/dL, 165.6 ± 116.0 mg/dL, and 6.8 ± 1.4 mg/dL, respectively. The mean HOMA-IR was 2.82 ± 2.74. The 2nd MRI at 6 months after first dosing showed a significantly decreased liver fat content from 19.6 ± 8.9% to 15.7 ± 7.6%. (p = 0.001). More than half (52.4%) of the patients had improvement of liver fat content and only 19.0% of the patients had worsening liver fat content on the 2nd MRI. Further analysis demonstrated initial higher liver fat content as the only independent factor associated with improvement of liver fat content at 2nd MRI (OR 1.22, 95% CI 1.082–1.369, p = 0.001). For histology changes, most of the patients showed none change or improvement in steatosis, NASH grade and stage. Only a few patients (< 10%) showed a worsening change in histology.
Conclusions: The preliminary results of the randomized trial demonstrated insulin sensitizer improved liver fat on MRI and NASH severity on histopathology. Further analysis upon the study deblinding is mandatory to evaluate the efficacy and safety.

Abstract #885

Phellodendron bark and its component berberine prevent nonalcoholic steatohepatitis-related fibrosis in mice

Shimizu-Ichimura Mayuko, Ph.D, Koichi Tsuneyama, M.D., Ph.D.

Department of Pathology and Laboratory Medicine, Institute of Biomedical Sciences, Tokushima University Graduate School, 3-18-15 Kuramoto-cho, Tokushima 770-8503, Japan

Introduction: Phellodendron bark (PB) grows naturally in the northeastern part of Asia. Berberine (Ber), which is the main component of PB, has suppressive effects against fat accumulation and inflammation in the liver.
Objectives: The aim of this study was to examine the effects of Ber and its complex PB against nonalcoholic steatohepatitis and hepatic fibrosis in the experimental mouse model.
Methods: Male C57Bl6/J mice were fed a high-fat and high-cholesterol (HFC) diet which was containing 5% PB or 0.06% Ber for 9 weeks.
Results: Histological steatohepatitis including steatosis, lobular inflammation and fibrosis (stage 1 or 2) were seen in mice fed the HFC diet. Some of the blue-stained fibers by Azan-Mallory staining were surrounding bright and multinuclear giant cells in the HFC diet-fed mice. These cells were positively stained by mac-2, suggesting that they were macrophages. We called these histological findings "ring-like fibrosis" and "macrophage balls", respectively. Adding the PB and Ber to HFC diet attenuated steatosis and fibrosis with less observation of "macrophage balls". Hepatic cholesterol content was lower in the Ber diet-fed mice than the HFC diet-fed mice. Increased expression of microsomal triglyceride transfer protein in the liver could explain the low cholesterol content in the Ber diet-fed mice.
Conclusion: Growing evidence has suggested that cholesterol promoted hepatic inflammation and fibrosis. Feeding PB and Ber prevented NASH-related fibrosis through suppression of cholesterol accumulation and macrophage aggregation.

Abstract #916

Liver incytes: assessment of fibrosis and steatosis in patients and healthy volunteers

Tam, Edward[1], Curry, Michael[2], Schneider, Caitlin[3], Barakat, Fatma[4], Hassanein, Tarek[4], Afdhal, Nezam[2]

[1]LAIR Centre, Vancouver, Canada, [2]Beth Israel Deaconess Medical Center, Boston, United States, [3]Sonic Incytes, Vancouver, Canada, [4]Southern California Research Center, Coronado, United States

Background: Non-invasive liver fibrosis and steatosis measurements have shown better disease staging and clinical management.
Purpose: To evaluate the ability of Liver Incytes to discriminate between healthy volunteers (HV) and those with non-alcoholic fatty liver disease (NALFD) or Hepatitis C virus post Sustained viral response (SVR).
Method: Liver Incytes is a steatosis and elasticity measurement system (Sonic Incytes, BC, Canada) comprising an ultrasound transducer and a vibration device to generate multi-frequency (40–70 Hz), steady state shear waves in the patient. The elasticity and attenuation are measured over a volume, using an intercostal approach. HV had no history of liver disease. Patients were enrolled with either NALFD or HVC post SVR. A FibroScan® (FS) stiffness threshold of > 8 kPa and Controlled Attenuation Parameter (CAP) > 238 dB/m

determined advanced fibrosis and steatosis. FS was used to compare to Liver Incytes results.

Results: A total of 50 HV and 48 patients were recruited. 27 patients had clinically diagnosed NAFLD and 21 had HCV post SVR. Median [IQR] stiffness for the HV was 4.8 [1.1] and 7.5 [1.7] kPa for patients on Liver Incytes and 4.4 [1.3] and 12.5 [9.0] kPa with FS. Mean attenuation for the HV and patients was 200 [61] and 298 [98] respectively on Liver Incytes and CAP score was 210 [59] and 295 [96] on FS respectively. The Area Under the Receiver Operating Curve (AUROC) for Liver Incytes was 0.964 for fibrosis and 0.985 for steatosis, using historical FS as the reference.

Conclusion: Initial results show that Liver Incytes is able to discriminate HV from patients with advanced fibrosis and steatosis.

Abstract #929

The circulating micro-RNAs (-122, -34a and -99a) as predictive biomarkers for non-alcoholic fatty liver diseases

Olfat M. Hendy[1], Hatem Rabie[1], Amr El Fouly[3], Mohamed Abdel-Samiee[2], Nashwa Abdelmotelb[1], Amr Aly Elshormilisy[4], Mahmoud Allam[2], Samia Taher Ali[5], Nessren Mohamed Bahaa EL-Deen[6], Shimaa Abdelsattar[7], Somia Mokabel Mohamed[8]

[1]Department of Clinical Pathology, National Liver Institute, Menoufia University, Menoufia, Egypt, [2]Department of Hepatology and Gastroenterology, National Liver Institute, Menoufia University, Menoufia, Egypt, [3]Department of Endemic Medicine, Faculty of Medicine, Helwan University, Cairo, Egypt, [4]Department of Internal Medicine, Faculty of Medicine, Helwan University, Cairo, Egypt, [5]Department of Internal Medicine, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt, [6]Department of Tropical Medicine, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt, [7]Department of Clinical Biochemistry, National Liver Institute, Menoufia University, Menoufia, Egypt, [8]Department of Physiology, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt

Introduction: It remains essential for patient safety to develop non-invasive diagnostic tools to diagnose non alcoholic fatty liver rather than invasive techniques.

Objectives: Our case-control study was to address the circulating miRNAs value as potential non invasive biomarker for the diagnosis of NAFLD and monitoring of disease progression.

Methods: Routine clinical assessment, laboratory tests, anthropometric study and liver biopsy results reported for 210 patients with NAFLD (124 patients of simple steatosis (SS) and 86 of NASH). Apparently matched for age and gender healthy participants (n = 90) were enrolled as a control group. Serum sample were tested for mirco-RNAs (-122, -34a and -99a) by quantitative-PCR.

Results: By histopathology, 124 of NAFLD group were of SS and 86 patients were of NASH. Compared with the control subjects, both mi-RNA-122 and -34a level were increased in NAFLD ($p < 001$) and at a cut-off = 1.261, mi-RNA-122 had 92%-sensitivity, 85%-specificity to differentiate between NAFLD from healthy controls. While mi-RNA-99a were significantly decreased in NAFLD patients with observed decrease in disease severity, and at a cut-off = 0.46, the miR-99a had 94%-sensitivity and 96%-specificity to discriminate between SS from NASH.

Conclusion: The integration of circulating mi-RNA panel achieved to diagnose NAFLD cases and to discriminate between SS and NASH. Large scale study is still needed to verify the other miRNAs profile and their role in NAFLD pathogenesis and targeting therapy.

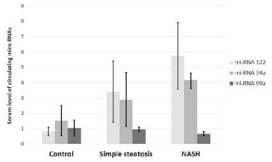


Figure (1): comparing the different mean levels of circulating mi-RNAs (-122, -99a and -34a) among the main studied groups [healthy controls vs NAFLD and the simple steatosisvs NASH patients].

Parameters	Control Group	NAFLD	P-value	Simple Steatosis	NASH	P-value
	N = 90 Mean ± SD	n = 210 Mean ± SD		n = 124 Mean ± SD	n = 86 Mean ± SD	
mi-RNA 122	0.82 ± 0.27	4.15 ± 2.94	**<0.001**	3.41 ± 1.98	5.74 ± 2.16	**<0.005**
mi-RNA 34a	1.53 ± 0.98	2.96 ± 1.62	**<0.05**	2.89 ± 1.75	4.12 ± 0.48	**<0.001**
mi-RNA 99a	1.04 ± 0.52	0.85 ± 0.23	**<0.05**	0.95 ± 0.14	0.67 ± 0.12	**<0.001**

Table (1) Comparison of anthropometric measurements and biochemical tests in simple steatosis and NASH patients.

Parameters	Simple Steatosis (n=124) M±SD	NASH (n=86) M ±SD	p value
BMI (kg/m²)	29.1 ±3.8	32.4 ±4.5	>0.05
Waist (cm)	87.9 ±3.6	94.3 ±8.7	>0.05
Triglycerides (mg/dl)	152.1 ±25.9	177.4 ±36.3	>0.05
T. cholesterol (mg/dl)	198.4 ±22.5	210.5 ±39.2	>0.05
HDL-c (mg/dl)	35.2 ±4.3	37.2 ±6.5	>0.05
LDL-c (mg/dl)	131.7 ±21.4	139.1 ±28.9	>0.05
Fasting Glucose(mg/dl)	98.2 ±9.3	101.2 ±10.2	>0.05
Fasting Insulin (uIU/ml)	9.2 ±1.2	10.6 ±1.9	>0.05
HOMA-IR	4.1 ±1.1	4.7 ±0.9	>0.05
AST (IU/L)	49.2 ±11.6	55.2 ±14.2	>0.05
ALT (IU/L)	58.2 ±9.6	65.2 ±8.3	>0.05
GGT (IU/L)	62.3 ±10.2.	67.8 ±17.3	>0.05
ALP (IU/L)	67.2 ±14.1	70.2 ±12.5	>0.05
S. Albumin (g/dl)	3.8 ±0.12	3.5 ±0.31	>0.05

Table (2): Circulating mi-RNAs expression studied in correlation to clinical, biochemical and histopathological parameters among NAFLD patients (n=210).

Parameters	mi-RNA-122		mi-RNA-34a		mi-RNA-99a	
	r	p	r	p	r	p
Gender	0.121	>0.05	0.013	>0.05	0.172	>0.05
Triglycerides (mg/dl)	0.42	**<0.05**	0.52	**<0.01**	-0.32	**<0.05**
LDL-c (mg/dl)	0.37	**<0.05**	0.32	**<0.05**	-0.51	**<0.01**
HOMA index	0.40	**<0.05**	0.38	**<0.05**	0.072	>0.05
AST (U/L)	0.49	**<0.01**	0.47	**<0.05**	-0.21	>0.05
ALT (U/L)	0.51	**<0.01**	0.54	**<0.01**	-0.39	**<0.05**
Histological findings:						
Steatosis	0.38	**<0.05**	0.40	**<0.05**	-0.24	>0.05
Activity	0.43	**<0.05**	0.59	**<0.01**	-0.61	**<0.01**
Inflammation	0.32	**<0.05**	0.52	**<0.01**	-0.58	**<0.01**
Ballooning	0.51	**<0.01**	0.35	**<0.05**	-0.41	**<0.05**
Fibrosis	0.61	**<0.01**	0.37	**<0.05**	-0.35	**<0.05**

Abstract #946

NAFLD as a metabolic syndrome

Manri Kawakami, M.D., Ph.D., Fusao Ikeda M.D., Ph.D. and Shin-ichi Fujioka, M.D., Ph.D.

Okayama Saiseikai General Hospital

Aim: Non alcoholic fatty liver disease (NASH) is not independent disease, but one of the metabolic syndrome and often have metabolic comorbidities. We investigated the metabolic comorbidities of NAFLD to check the characteristic and care point of NAFLD.

Methods: We investigated 893 patients diagnosed as NAFLD in our hospital in 3 years (2013–2015).

Results: Among 93 patients consulted to our hospital and diagnosed as NASH, about 80% of the patients have metabolic comorbidities. 56 patients accompanied by obesity (60%), 56 patients by

hyperlipidemia (60%), 37 patients by hypertension (40%), 19 patients by diabetes (20%) and 19 patients by hyperuricemia (20%). The prevalence rate of hypertension or diabetes in obesity (BMI > 25 kg/m^2) were significantly higher than the other ($\chi^2 = 4.107$, $\chi^2 = 4.121$).
Among 177 patients consulted by other clinics and diagnosed NAFLD, 46 patients were diagnosed diabetes (26%), which was 10% higher than 29 patients pre-diagnosed diabetes (16%). Among 107 patients consulted by Health check-up systems and diagnosed NAFLD, 29 patients were diagnosed diabetes (27%), which was 10% higher than 24 patients pre-diagnosed as diabetes (16%).
Conclusion: The patients with NAFLD have metabolic comorbidities in high rate, especially diabetes.

Abstract #967

Nonalcoholic fatty liver disease (NAFLD) and the risk of atrial fibrillation

Sherief Abd-Elsalam[1], Mahmoud A. Abou Omar[2], Mohamed Yousef[1]

[1]Department of Tropical Medicine, Tanta University, Tanta, Egypt, [2]Department of Cardiology, Tanta University, Tanta, Egypt

Background and aims: Nonalcoholic fatty liver disease (NAFLD) is now the factor behind the development of liver cirrhosis, liver cell failure, and liver transplantation in many cases. However, its relation to atrial fibrillation (AF) could not be cleared up. The purpose of the study was to evaluate prevalence of AF in the setting of NAFLD; the association between them, and to evaluate risk factors of AF in this category of patients.
Methods: This cross-sectional study was performed on 400 patients between January 2018 and June 2019. These patients were analyzed for the presence of NAFLD and presence of persistent or chronic AF.
Results: There were 138 patients with NAFLD, and 20 patients with persistent or permanent AF. Factors associated with AF were old age, male gender, and high values of AST, ALT, GGT, and serum uric acid. The participants with AF had a significantly greater prevalence of NAFLD than those without AF
Conclusion: Incidence and Prevalence of AF in NAFLD patients was high. Severity of liver disease was an important predictor of new-onset AF.

Abstract #974

Relationship between Helicobacter pylori infection and nonalcoholic fatty liver disease (NAFLD) in a developing country: a cross-sectional study

Sherief Abd-Elsalam[1], Yousry Esam-Eldin Abo-Amer[2], Aisha Sabal[3], Rehab Ahmed[3]

[1]Tropical Medicine Department, Tanta University, Tanta, Egypt, [2]Hepatology, Gastroenterology and Infectious Diseases Department, Mahala Hepatology Teaching Hospital, Gharbia, Egypt, [3]Hepatology, Tropical Medicine and Infectious diseases departments, National Hepatology and Tropical Medicine Research Institue, Cairo, Egypt

Background: Non-alcoholic fatty liver disease (NAFLD) is a very common disease that affects 25–30% of the population in western countries. Many studies have observed the importance of H. pylori infection in the development of insulin resistance, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, and liver fibrosis and cirrhosis. However, the evidence from different studies was controversial. The present study, aimed to investigate the relationship between H. pylori infection and NAFLD in a developing country.
Patients and methods: This cross-sectional study included all the attending outpatient clinics at four Major University hospitals and two research and clinical institutes in a developing country in the period between June and October, 2019. Patients were assessed for the diagnosis of H. pylori infection as detected by H. pylori antigen in stool; they were also assessed for the diagnosis of NAFLD by ultrasound, fibroscan and CAP.
Results: The study was conducted on 646 patients; H. pylori infection was found to be present in 538 patients (83.3%). NAFLD (diagnosed by both U/S and Fibroscan with CAP), ALT, AST, hepatomegaly, hypertension, fasting blood sugar were significantly higher in H. pylori +ve group than H. pylori −ve group. After performing Linear regression of independent risk factors of NAFLD to prove or to refute the role of Helicobacter; H. pylori positivity, total cholesterol, degree of fatty liver by ultrasound, fasting blood sugar and diastolic blood pressure were independent risk factors for NAFLD.
Conclusions: Helicobacter pylori infection was independent risk factors for NAFLD and correlated with increased degree of steatosis.

Abstract #982

Study the prevalence of non alcoholic fatty liver disease among Banha university employees

Reda Elbadawy

Gastroenterology, Hepatology Department and Infectious Disese Banha University, Egypt

Background: An emerging concern is the apparent onset of significant for Non Alcohoic Fatty Disease (NAFLD) in early life at age of 20th even earlier.
Aim: of the study to evaluate the prevalence of NAFLD among Banha University employees, its complications and associated risk factors.
Methodology: This is cross sectional study at Banha University Hospital among employees, age of the subjects from 20–60 years old both males and females All investigations done. Liver FattyAcid Binding protein (LFABP) is unique novel biomarker for fatty liver, its complications was done by ELIZA.
Results: Prevalence of NAFLD was 56%, Carotid Intimal thickness > 1.1 cm (CIMT) that mean early sign of atherosclerosis. Fatty pancreas was present in 70%. Risk factors was 7 risk factors and was of statistically significant ranged from (< 0.036 to < 0.001) correlated with this high prevalence of fatty liver. LFABP level was ranged (0.29–6 ng/ml) and of statistical significant with BMI, ALT, AST. ALP, GGT and LDL/HDL ratio.
Conclusion and solution: Treatment of the risk factors to prevent and delay the development and progress of NAFLD and its complications especially fatty pancreas that lead to DM. Also this will decrease CVS mortality and Morbidity. Use of L-FABP as biomarker in the work up of NAFLD diagnosis, its complications.

Abstract #1004

From the general practice to the transplant room: greater rise in liver transplant candidacy due to NAFLD-associated HCC

Metin Basaranoglu

Division of Gastroenterology, Department of Internal Medicine, Bezmialem Vakif University Turkey

Excessive accumulation of fat in hepatocytes in the absence of significant alcohol consumption occurs in up to 30% of adults [1–5]. This condition, termed non-alcoholic fatty liver disease (NAFLD), predisposes to non-alcoholic steatohepatitis (NASH), which progresses to cirrhosis and its complications, including hepatocellular carcinoma (HCC) [6–9]. Currently, it is estimated that NAFLD is the third leading cause of HCC. Relative to other Europeans, the Turkish population exhibits a higher rate of obesity that is comparable to that in the United States. Overall, 56% of the Turkish population is overweight, especially preobese (body-mass index: 25–29.9 kg/m^2). The prevalence of NASH as a precursor of NAFLD-associated cirrhosis is 3% and 20% in non-obese and obese subjects, respectively [1–3]. The global obesity epidemic has been associated with the increasing burden of NAFLD. It has been estimated that the rising prevalence of NAFLD will soon lead to large cohorts of patients with HCC. Case-1: A 63 years-old man presented with abdominal pain at the out patient clinic. He did very well 2 weeks ago. His condition and exams were within the normal levels and abdominal ultrasound every 6 months. He has mild type 2 diabetes and under the control by metformin. His mother was diabetic and dead due to NASH-associated cirrhosis with HCC. His physical exam showed over-weight. Lab exam showed mildly increased AST and GGT. Blood α-FP level was greater than 10.000. His liver MRI showed a large tumoral mass larger than 7 cm in diameter in the right lobe with cirrhotic liver. Further examination showed that he has NASH-associated cirrhosis with HCC. Case-2: A 58 years-old gentleman has been diagnosed as NASH-associated cirrhosis 5 years ago. Every six months, blood tests and liver ultrasound were performed and all normal. Two-years ago, abdominal MRI showed 3 nodules with the largest one 11 mm in diameter on segment 7. In 2019, in addition to the ultrasound, liver MRI repeated and showed that high grade dysplastic nodules with the highest size 13 mm on segment 2, 6 and 7. Liver transplantation was performed. Resected whole liver showed hcc within the nodules. In this regard, I would like to drawn attention for that greater rise in liver transplant candidacy due to NAFLD-associated HCC. Our study group recently published that of the 258 patients with decompensated cirrhosis [10]. HCC was detected in 38 patients (14.7%). The incidence rate of HCC was 5.0% in patients with NAFLD, 26.7% in patients with hepatitis B, 34.5% in patients with hepatitis C, and 5.7% in other diseases ($P < 0.0001$). Of the 38 patients with HCC, 13% had PVT. Moreover, HCC increased the mortality rate in almost all the groups. The mortality rate in hepatitis B group increased from 31% (17/55) in patients without HCC to 75% (15/20) in patients with HCC ($P = 0.001$). In the group with hepatitis C, the mortality rate increased from 32% (6/19) in patients without HCC to 90% (9/10) in patients with HCC ($P = 0.005$). The mortality rate in NAFLD patients increased from 47.5% during follow-up to 80% after HCC developed. Although NAFLD is a risk factor for HCC, the prevalence rate of HCC in cirrhotic NAFLD has not been well established, despite its reported range of 2.4% to 12.8%. Our results with 5.0% NAFLD-related HCC with cirrhosis was lower than previously reported with 2.4%-12.8% in patients with NAFLD. In conclusion; as a hepatologist, never do not forget that the mortality rate of patients with NAFLD-associated HCC did differ from that in patients without HCC (from 47.5% to 80%).

Abstract #1068

Effect of liraglutide therapy on hepatic steatosis and liver stiffness in patients with nonalcoholic fatty liver disease

Alam Shahinul[1], Khan Asma Helen, Islam Saiful, Anam Kamrul

Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Introduction: Approximately one-third of the adult population of Bangladesh is affected by Non-alcoholic fatty liver disease (NAFLD). There are no universally accepted pharmacological therapies for NAFLD.

Objective: We have designed this study to observe the efectiveness of liraglutide on hepatic steatosis and liver stiffness in obese diabetic NAFLD patients.

Methods: We have included 32 diabetic patients with BMI > 25 (kg/m^2), evidence of fatty liver by CAP and ultrasonography and raised SGPT after excluding the other causes of NAFLD. They were divided in 2 groups: 16 patients in each group liraglutide in one group (L) and control (C) group. For the treatment group liraglutide were started with an initial dose of 0.6 mg/day for seven days followed by 1.2 mg/day for rest of the period a total duration of 24 weeks. For both the group advice for life style modification by diet and exercise was given.

Results: In control group improvement of CAP was (from 297.00 $\pm$ 53.59 to 296.19 $\pm$ 51.53 dB/M; P = 0.95), stiffness (from 7.80 $\pm$ 5.20 to 7.88 $\pm$ 9.16 Kpa; p = 0.95), weight (from 71.75 $\pm$ 9.6 to 71.19 $\pm$ 10.32 kg; p = 0.615), BMI (from 29.25 $\pm$ 4.97 to 29.04 $\pm$ 4.28 kg/m^2; p = 0.643), ALT (from 48.00 $\pm$ 15.90 to 48.60 $\pm$ 1.70 iu/l; p = 0.94), AST (from 45.07 $\pm$ 21.90 to 54.47 $\pm$ 73.90 iu/l; p = 0.59). None of these were significantly improved. In liraglutide group CAP was improved (from 335.62 $\pm$ 50.22 to 202.98 $\pm$ 117.67 dB/m; p = 0.002), liver stiffness (from 80.48 $\pm$ 28.88 to 9.32 $\pm$ 5.57 Kpa; p = 0.026), weight (from 82.93 $\pm$ 13.08 to 81.50 $\pm$ 15.33 kg; p = 0.17), BMI (from 34.01 $\pm$ 5.31 to 33.09 $\pm$ 6.41 kg/m^2; p = 0.17), ALT (from 84.53 $\pm$ 42.01 to 49.53 $\pm$ 23.13 iu/l; p = 0.005), AST (from 57.45 $\pm$ 14.87 to 32.27 $\pm$ 11.97 iu/l p = 0.001).

Conclusion: There is clear benefit of 6 months liraglutide therapy in NAFLD with improvement of steatosis, stiffness and transaminases.

Abstract #1102

Vitamin D deficiency: an independent predictor of nonalcoholic steatohepatitis

Hui Beom Hwang

Introduction: Previous studies have suggested a role for vitamin D deficiency in the pathogenesis of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH), but they have been yet controversial. The aim of this study is to assess the role of 25-hydroxyvitamin D (25-OH D) levels in predicting the probability of the presence of NASH in patients with NAFLD.

Method: The patients who underwent liver biopsy due to clinically suspected NAFLD were included. Subjects were divided into 3 groups according to their plasma 25-OH D levels (normal, > 30 ng/ml; insufficiency, 20–30 ng/ml; deficiency, < 20 ng/ml). NASH was defined as the presence of hepatic steatosis and lobular inflammation with ballooning degeneration, based on the EASL guideline.

Result: Among the total of 792 subjects, 581 (73.4%) and 149 (18.8%) subjects were classified as 25-OH D deficiency and insufficiency groups, respectively. The prevalence of NASH in subjects with 25-OH D deficiency, with 25-OH D insufficiency, and with normal 25-OH D level were 80.2%, 66.4%, and 59.1% ($p < 0.001$). A crude analysis showed that 25-OH D deficiency was associated with NASH (odds ratio [OR] = 2.04, 95% confidence interval [CI] = 1.38–3.04, p value < 0.001, *vs.* insufficiency group; OR = 2.81, 95% CI = 1.49–5.29, p value = 0.001, *vs.* normal group), while 25-OH D insufficiency was not related with NASH (OR = 1.37, 95% CI = 0.69–2.73, p value = 0.371, *vs.* normal group). This association persisted after adjustment for gender and HbA1c (OR = 2.14, 95%

CI = 1.43–3.19, p value < 0.001, *vs.* insufficiency group; OR = 3.57, 95% CI = 1.84–6.90, p value < 0.001, *vs.* normal group).
Conclusion: Patients with vitamin D deficiency more likely to have NASH compared to those with insufficiency or normal vitamin D levels.

Abstract #1103

Association between non-alcoholic fatty liver disease and extrahepatic malignancy risk and mortality: a systematic review

Lirendra M*, Simanihuruk V, Raharjo M, Permana SL, Purnama W, Lesmana CRA

Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Non-alcoholic fatty liver disease (NAFLD) affects a third of the world's population. It is estimated that the prevalence of NAFLD worldwide is 24–30% and still increasing. Previous studies found that NAFLD is associated with extrahepatic malignancy development; however, relationship between the two is still not clear.
Objective: The aim of this study is to summarize studies regarding the association between NAFLD and extrahepatic malignancy.
Methods: Studies were collected by looking up the keywords "NAFLD" and "extrahepatic malignancy" in PubMed, Cochrane, and Elsevier. We included all original manuscripts published in between 2013–2019. Review articles were excluded. Studies with subjects less than 18 years old, primary liver cancer, hepatitis virus infection, autoimmune disease, and other primary cancers were also excluded. Six reviewers independently reviewed and summarized full articles of the collected studies.
Results: 15 out of 30 studies (12 cohorts, 2 cross-sectionals, and 1 case control study) were eligible for analysis. This systematic review found that NAFLD is associated with higher risk of extrahepatic malignancy, such as colorectal cancer, breast cancer, pancreatic cancer, gastric cancer, and uterine cancer. The most common extrahepatic malignancy was found in the gastrointestinal tract. Patients with extrahepatic malignancy and NAFLD had poorer survival. A possible mechanism for development of extrahepatic malignancy in NAFLD patients is the paracrine effect of insulin resistance, metabolic disease, visceral adipose tissue, and ectopic fat on the liver and adjacent organs.
Conclusion: NAFLD is associated with increased extrahepatic malignancy risk and mortality.

Abstract #1123

Dithizone protects against non-alcoholic fatty liver disease in a Paneth cells-oriented gut microbiota-associated mechanism

Saisai Zhang[1], Fung-Yu Huang[1], Hau Tak Chau[1], Danny Ka-Ho Wong[1,2], Lung-Yi Mak[1], Man-Fung Yuen[1,2], Wai-Kay Seto[1,2]

[1]Department of Medicine, The University of Hong Kong, Hong Kong SAR, [2]State Key Laboratory for Liver Research, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR

Introduction: Paneth cells secrete antimicrobial peptides regulating the gut microbiota, but its role in the pathogenesis of non-alcoholic fatty liver disease (NAFLD) remains poorly understood.
Objectives: To determine the role of Paneth cells in maintaining homeostasis in a NAFLD mouse model.
Methods: Eight-week old C57Bl/6 J male mice (n = 28) were given a high-fat diet (HFD, 60% kcal fat, Research Diets, New Brunswick, NJ) or low-fat diet (LFD, 10% kcal fat) for 12 weeks. Paneth cell granules were pharmacologically depleted by intravenous injection of dithizone (10 mg/kg) every three weeks. Metagenomic DNA were extracted from fecal samples for Pacbio Single Molecule Real-Time (SMRT) sequencing to identify changes in microbial composition and structure.
Results: Dithizone-treated HFD mice, when compared to non-dithizone-treated HFD mice, had a significant reduction in liver mass gain (1.94 ± 0.02 g vs. 1.2 ± 0.14 g, $p = 0.0007$), hepatic triglyceride content (53.52 ± 5.93 mg/g vs. 28.98 ± 7.40 mg/g, $p = 0.0419$), plasma insulin level (5.80 ± 0.68 ng/ml vs. 2.95 ± 0.46 ng/ml, $p = 0.0255$), and a significantly improved glucose tolerance ($p = 0.0323$). Altogether 247,277 reads were obtained from Pacbio SMRT sequencing. PCoA based on unweighted-unifrac and weighted-unifrac distance demonstrated a significant difference between non-dithizone-treated and dithizone-treated LFD mice ($p = 0.017$ and 0.045 respectively), but not in HFD mice ($p > 0.05$). In terms of bacterial taxonomic profiling at the phylum level, non-dithizone-treated HFD mice, when compared to dithizone-treated HFD mice, had significantly lower Firmicutes/Bacteroidetes ratio (2.64 ± 0.58 vs. 1.15 ± 0.20, $p = 0.0306$) and significantly higher abundance of Proteobacteria (64.86 ± 28.88 vs. 251.40 ± 71.35, $p = 0.0321$).
Conclusion: Depletion of Paneth cell granules by dithizone can ameliorate the severity of NAFLD, possibly through a gut microbiota-dependent mechanism.

Abstract #1144

Association of atrial fibrillation and advanced liver fibrosis in patients with non-alcoholic fatty liver disease

Kang Min Kyu[1], Park Jung Gil[1], Park Soo Young[2], Tak Won Young[2], Kweon Young Oh[2], Jang Se Young[2], Lee Yu rim[3], Hur Keun[3]

[1]Department of Internal Medicine, College of Medicine, Yeungnam University, Daegu, Republic of Korea, [2]Department of Internal Medicine, School of Medicine, Kyungpook National University, Daegu, Republic of Korea, [3]Department of Biochemistry and Cell Biology, School of Medicine, Kyungpook National University, Daegu, Republic of Korea

Introduction: Although non-alcoholic fatty liver disease (NAFLD) has been reported to be independently associated with increased incidence of atrial fibrillation (AF), the association of advanced liver fibrosis with AF in NAFLD patients has not been established. Advanced liver fibrosis in patients with NAFLD is related to all-cause, cardiovascular, and liver-related mortality.
Objectives: We aimed to investigate the association between atrial fibrillation and advanced liver fibrosis in patients with NAFLD.
Methods: From January 2010 to December 2017, 6293 NAFLD patients aged 35 years and older were enrolled. All electrocardiograms were diagnosed after a review by a skilled cardiologist. The stage of liver fibrosis is assessed by new adjusted, non-invasive scoring model including NAFLD fibrosis score (NFS) and Fibrosis-4 (FIB-4) index, which was determined as the both low and high cut-off value (COV).
Results: Of 6293 patients with NAFLD, 59 (0.9%) were diagnosed with AF. In NAFLD patients, AF was strongly associated with advanced liver fibrosis, assessed by both COVs of NFS (adjusted for obesity, hypertension, high sensitivity C reactive protein, lipid profile, and sex, ORs = 12.29 to 14.55, $P < 0.01$ in the high-COV group, respectively). In addition, AF was significantly associated with

advanced liver fibrosis, assessed by both COVs of FIB-4 (adjusted for obesity, hypertension, albumin, gamma-glutamyl transferase, high sensitivity C reactive protein, lipid profile, and sex, ORs = 3.84 to 5.97, $P < 0.05$ in the high-COV group, respectively).
Conclusion: AF may be associated with advanced liver fibrosis in patients with NAFLD.

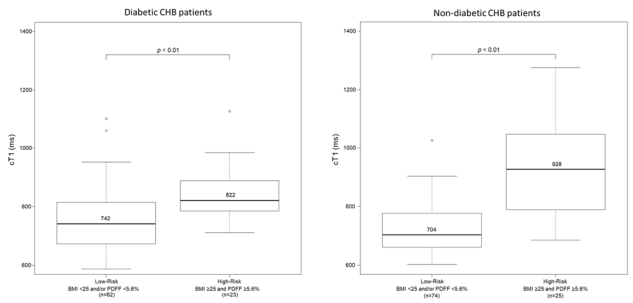
Abstract #1145

Prevalence of concurrent non-alcoholic fatty liver disease in chronic hepatitis B patients using non-invasive multiparametric MRI

Seto, Wai-Kay[1]; Chiu, Keith[2]; Mak, Lung-Yi[1]; Aslam, Filza[3]; Kin, Stella[3]; Kelly, Matt[4]; Banerjee, Rajarshi[4]; Yuen, Man-Fung[1]

[1]Department of Medicine, The University of Hong Kong, Hong Kong, [2]Department of Diagnostic Radiology, The University of Hong Kong, Hong Kong, [3]Perspectum Diagnostics, Singapore, [4]Perspectum Diagnostics, Oxford, United Kingdom

Introduction: Non-alcoholic fatty liver disease (NAFLD) is strongly associated with type 2 diabetes (T2D). In recent years, an increasing number of patients with concurrent chronic hepatitis B (CHB)-NAFLD is observed. However, risk of NAFLD among CHB patients is not fully known. Liver *MultiScan* is a non-invasive multiparametric MRI (mpMRI)-based tool measuring proton density fat fraction (PDFF) and iron-corrected T1-relaxation time (cT1), correlating with hepatic steatosis and fibro-inflammation respectively.
Objectives: In this study, we use mpMRI to determine the prevalence of NAFLD among CHB patients with and without T2D.
Methods: Clinically-stable diabetic and non-diabetic CHB patients recruited consecutively from a specialist liver clinic in Hong Kong underwent Liver *MultiScan*. High-risk individuals for NAFLD were identified by including those with BMI $\geq$ 25 kg/m^2 and PDFF $\geq$ 5.6%.
Results: 184 CHB patients were recruited (mean age 58.5 $\pm$ 8.2 years, mean BMI 25.7 $\pm$ 4.2 kg/m^2, 76% male, 46% T2D). No significant difference observed in median cT1 and PDFF between diabetics (cT1 731 ms, PDFF 4.3%) and non-diabetics (cT1 767 ms, PDFF 4.9%). 48 (26%) were identified as high-risk for NAFLD (23 diabetic, 25 non-diabetic). Median cT1 values were significantly higher ($p < 0.01$) for high-risk vs low-risk individuals within both groups (high-risk vs low-risk: diabetic 822 ms vs 742 ms; non-diabetic 928 ms vs 704 ms). However, no significant difference observed in median cT1 values between high-risk diabetics and non-diabetics.
Conclusion: Results consistent with previous studies where higher BMI is linked with fatty liver in CHB patients. Prevalence of individuals at high-risk for NAFLD with elevated cT1 values highlights the relevance of Liver*MultiScan* in identifying patients with concurrent disease.



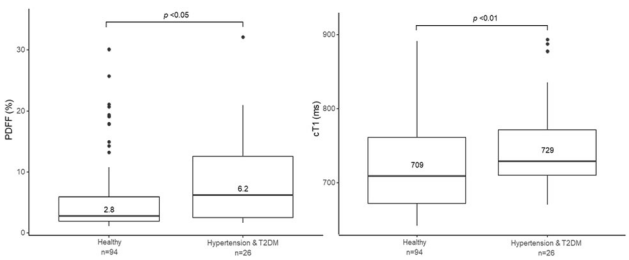
Abstract #1146

Prevalence of NAFLD in Singaporean hypertension patients using non-invasive multiparametric MRI

Aslam, Filza[1], Kin, Stella[1], Kelly, Matt[2], Banerjee, Rajarshi[2], Bryant, Jennifer[3], Chin, Calvin[3]

[1]Perspectum Diagnostics, Singapore, [2]Perspectum Diagnostics, Oxford, UK, [3]National Heart Centre, Singapore

Introduction: Hypertension (HTN) is associated with insulin resistance, type 2 diabetes (T2D) and linked to development of non-alcoholic fatty liver disease (NAFLD). Liver*MultiScan* is a non-invasive multiparametric MRI (mpMRI)-based tool measuring proton density fat fraction (PDFF) and iron-corrected T1-relaxation time (cT1) which correlate with hepatic steatosis and fibro-inflammation, respectively.
Objectives: The purpose of this study is to compare prevalence of NAFLD amongst hypertensive and healthy individuals using Liver *MultiScan*.
Methods: Patients with HTN and self-declared healthy volunteers with no history of T2D and HTN prospectively recruited from a single centre in Singapore underwent an mpMRI scan. PDFF and cT1 values were calculated from the MR data.
Results: 26 HTN patients (mean age 61.2 years, mean BMI 24.7%, 81% T2D) and 94 healthy volunteers (mean age 47.4 years, mean BMI 23.7%) were recruited. Median (IQR) cT1 and PDFF values were significantly higher (cT1: $p < 0.01$; PDFF: $p < 0.05$) in the hypertensive group [(cT1: 729 ms (710 ms–772 ms); PDFF: 6.2% (2.6%–12.5%)] versus healthy volunteers [cT1: 709 ms (673 ms–762 ms); PDFF: 2.8%, (2.0%–5.9%)]. Amongst hypertensive and healthy volunteers respectively, 53.8% (14/26) and 27.7% (26/94) had hepatic steatosis (PDFF $\geq$ 5.6%) while 11.5% (3/26) and 7.4% (7/94) had both high fibro-inflammation (cT1 $\geq$ 800 ms) and steatosis.
Conclusion: Prevalence of hepatic steatosis and fibro-inflammation is higher amongst hypertensive patients versus healthy volunteers, potentially explained by link between T2D and HTN. Previous studies demonstrated that high cT1 values correlate with liver-related outcomes. Elevated cT1 values highlights utility of Liver*MultiScan* to non-invasively identify those who may benefit most from early intervention.



Abstract #1164

Effect of L-carnitine on fatty liver induced by high fructose diet

Bahçecioğlu IH[1], Ispiroğlu M[1], Tuzcu M[2], Özercan IH[3]

[1]Division of Gastroenterology, Firat Üniversity, Elazig-TURKEY, [2]Faculty of Medicine, Department of Biology, Faculty of Scienes, Firat Üniversity, Elazig-TURKEY, [3]Department of Pathology, Firat Üniversity, Elazig-Turkey

Key Words: Fructose, L-Carrnitine, Fatty liver

Introduction: In this study, we aimed to investigate the preventive effect of L-carnitine in fatty liver induced by high fructose (30%).

Methods: A total of 28 male Sprague-Dawley rats were used in the study. The rats were divided into four equal groups: Group 1 (n = 7): a normal diet for 16 weeks; Group 2 (n = 7): n = normal diet for 16 weeks + i.p L-carnitine 50 mg/kg 2 days in a week). Group 3 (n = 7): High fructose diet (30% fructose) for 16 weeks, *i. p* serum saline; Group 4 (n = 7): 16 weeks high fructose diet (30% fructose) + i.p L-carnitine 50 mg/kg was administered 2 days in a week. At the end of 16 weeks, rats were killed by decapitation. Liver samples were taken for biochemical and histopathological examination. Histopathological examination and tissue MDA levels, NFkB, TNF α, TGF β1 levels were studied.
Results: Liver tissue MDA levels were higher in the fructose-fed group; Fructose + L-Carnitine was significantly lower in the group ($p < 0.05$). Liver tissue NFkB, TNF-α, TGF-β1 levels were higher in the fructose group compared to the control group. L-Carnitine and fructose were significantly lower in the group ($p < 0.05$, $p < 0.05$, $p < 0.001$, respectively). Steatosis and inflammation were significantly lower in the group administered L-Carnitine with fructose ($p < 0.05$).
Conclusion: As a result, L-Carnitine is effective against steatosis and inflammation in experimental NAFLD induced by fructose. Further studies with longer duration are needed for its effect on fibrosis.

Abstract #1169

Clinical spectrum of non-alcoholic fatty liver disease in patients with diabetes mellitus—cross-sectional study

Kaina Chen[1,5], Wei Kwan Sng[2], Joanne Hui Min Quah[2,5], Jin Liu[5], Bee Yen Chong[2], Hwee Khim Lee[2], Xue Fei Wang[2], Nur Fadhilah Binte Rasid[2], Ngiap Chuan Tan[2,5], Pik-Eu Chang[1,5], Hong Chang Tan[3], Yong Mong Bee[3], Woon Puay Koh[4,5], George Boon Bee Goh[1,5]

[1]Department of Gastroenterology and Hepatology, Singapore General Hospital, [2]SingHealth Polyclinics, Singapore, [3]Department of Endocrinology, Singapore General Hospital, [4]Saw Swee Hock School of Public Health, National University of Singapore, Singapore, [5]Duke NUS Medical School, Singapore

Background: Non-alcoholic fatty liver disease (NAFLD) is increasingly widespread and Type 2 diabetes Mellitus (T2DM) is a key contributor to NAFLD progression and predicts liver fibrosis and mortality. Existing guideline do not actively recommend NAFLD screening among diabetic patients, and the clinical spectrum of NAFLD among T2DM patients remains to be fully clarified.
Objectives: We explored the prevalence, clinical spectrum, and risk factors of NAFLD and liver fibrosis among T2DM patients.
Methods: This is a cross-sectional study that enrolled T2DM subjects from a primary care clinic and a diabetes centre in Singapore. All subjects underwent transient elastography for hepatic steatosis and fibrosis assessment.
Results: Overall, 78.72% (344/436) of the T2DM subjects had NAFLD, of which 13.08% (45/344) had advanced fibrosis. Higher ALT level (OR = 1.04; 95% CI: 1.00–1.08; p = 0.029) and obesity (BMI $\geq$ 27.5 kg/m^2, OR = 3.15; 95% CI: 1.90–5.23; $p < 0.001$) were independent factors associated with NAFLD. Higher AST level (OR = 1.06; 95% CI: 1.02–1.11; p = 0.008), CAP value (OR = 1.02; 95% CI: 1.00–1.03; p = 0.003), lower platelet count (OR = 0.99; 95% CI: 0.98–1.00; p = 0.009) and concomitant hypertension (OR = 4.56; 95% CI: 1.18–17.62; p = 0.028) were independent factors associated with advanced liver fibrosis.
Conclusions: Our study demonstrated a high prevalence of NAFLD among T2DM patients, and a much higher proportion of advanced liver fibrosis compared to the sgeneral population. Increased awareness and vigilance for identifying NAFLD and advanced fibrosis among T2DM patients should be advocated.

Abstract #1213

Characteristics of concurrent cardiovascular diseases in patients with NAFLD

Alexander Nersesov[1], Amina Rakisheva[2], Aisulu Mussagaliyeva[2], Nurzhan Temenov[2], Damen Akhmetova[2], Rubanov Ivan[1], Rubanova Anastasiya[1], Amirbekkyzy Zhadyra[1], Puzankova Yelizaveta[1]

[1]Department of Gastroenterology, Asfendiyarov National Medical University, Almaty, Kazakhstan, [2]Unit of Internal Diseases Nr2, Institute of Cardiology and Internal Diseases, Almaty, Kazakhstan

Introduction: Non-alcoholic fatty liver disease (NAFLD) is associated with metabolic syndrome including hypertension (Ht), but associations with other cardiovascular diseases (CVD) need further evaluation.
Objectives: To characterize CVD spectrum in patients with NAFLD.
Methods: Retrospective single center study (2016–2018) of 416 patients with NAFLD and CVD, diagnosed by abdominal US, FIB-4, APRI scores, BP, ECG, coronary angiography and laboratory tests.
Results: The majority pf patients were Asians (64%), males (59.4%) with mean age of 63.09 ± 9.04. BMI $\geq$ 30 kg/m^2 had 64% of males and 71.9% of females (p = 0.09). The mean cholesterol was 4.67 ± 1.26 (LDL 3.0 ± 1.68, HDL 1.06 ± 0.35), triglycerides—1.98 ± 1.24. FIB-4 lower 1.45 was revealed in 36.8% of males and 29.9% of females, over 3.25—in 1.2% and 0.5%, respectively and the rest 20.5% and 11.1% belonged to grey zone. APRI of 0.7 and higher was in 1% of males and 0.8% of females, 1.0 and higher—in 0.5% and 0.3%, respectively. Coronary artery disease (51%), previous myocardial infarction (32.7%) were more common for males ($p < 0.001$ and p = 0.003, respectively), whereas Ht (95%) and atrial fibrillation (AF) (43%) for females (p = 0.05 and $p < 0.001$, respectively). Of 416 patients, 32.2% had AF (48.9% were Caucasians, 23.2%—Asians, $p < 0.001$). Obesity was more prevalent in AF patients (74.8%, p = 0.04), and FIB-4 over 1.45 were characteristic of Asians (42.1%) compare to Caucasians (23.3%, p = 0.03).
Conclusion: The majority of patients had mild to moderate NAFLD, obesity, dyslipidemia and Ht. Despite of high prevalence of AF among Caucasians, the liver fibrosis was more relevant for Asians with AF.

Abstract #1221

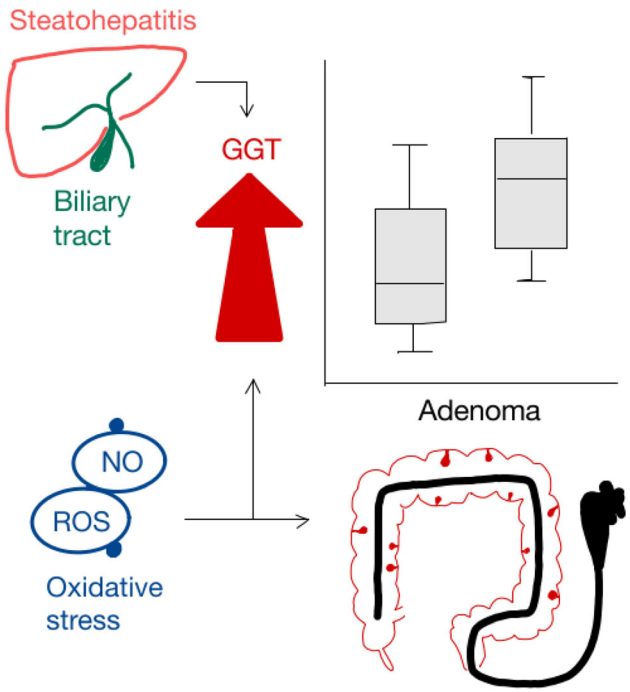
Relationship between serum gamma-glutamyl transferase level, colorectal adenoma and steatohepatitis

Tzu-Chan Hong, M.D.[1], Hung-Chih Yang, M.D., Ph.D.[1,2], Chi-Ling Chen, Ph.D.[2], Jia-Horng Kao, M.D., Ph.D.[1,2], Chun-Jen Liu, M.D., Ph.D.[1,2], Ming-Jen Chen, M.D., M.S[3], Horng-Yuan Wang, M.D., Ph.D.[3], Yang-Che Kuo, M.D., Ph.D.[3,4], Lo-Yip Yu, M.D., Ph.D.[3,4], Kuang-Chun Hu, M.D., Ph.D.[3,4]

[1]Department of Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei 10051, Taiwan, [2]Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei 10048, Taiwan, [3]Division of Gastroenterology, Department of Internal Medicine, MacKay Memorial Hospital, Taipei 10449, Taiwan, [4]Health

Evaluation Center, MacKay Memorial Hospital, Taipei 10449, Taiwan

Introduction: Cost-effective serology tests may increase the predictive accuracy of colonoscopy for colorectal cancer screening. Reportedly, gamma-glutamyl transferase (GGT) is associated with oxidative stress and carcinogenesis and has been found to be elevated in the serum of cancer patients and colorectal adenoma tissue.
Objectives: We aimed to investigate the association between serum GGT levels and colorectal adenoma.
Methods: This single-center, health examination-based cohort enrolled 4669 subjects from 2006 to 2015. Baseline characteristics, laboratory data, bidirectional gastrointestinal endoscopy, and transabdominal ultrasonography were used to evaluate the severity of fatty liver.
Results: We found an elevated median GGT level in subjects with tubular adenoma compared with those without (23 IU/L and 20 IU/L, $p < 0.001$). A GGT cutoff of $\geq$ 20 IU/L reached a maximal Youden index in receiver operating curve (ROC) analyses. Subsequent regression analyses showed an odds ratio of 1.46 (95% CI 1.17–1.82, $p < 0.001$) for age, body mass index, diabetes diagnosis, total cholesterol, triglycerides, low-density lipoprotein cholesterol, and positive Helicobacter pylori urease test, all being associated with an increased incidence of colon adenoma. Subgroup analysis showed that the odds ratio (OR 1.27, 95% CI 1.15–1.68, $p < 0.001$) is only significant and highest in patients with a negative or mild fatty liver and an ALT level of $\leq$ 40 IU/L.
Conclusion: The results suggested a positive correlation of GGT with colon adenoma incidence and a predictive value with a cutoff point of > 20 IU/L, which is within the normal range. The effect may be most prominent for those without steatohepatitis.



Abstract #1266

Lifestyle habits and nonalcoholic fatty liver disease in the multicenter cap-asia study

Zhang XR[1,2], Goh GB[3], Wong GL[1,2], Chan WK[4], Fan JG[5], Seto WK[6], Lee HW[7], Kim SU[7], Huang YH[8], Lin HC[8], Lee IC[8], Kim YJ[9], Jang JY[10], Jeong SW[10], Kim YS[11], Kim SG[11], Chow WC[3], Wong VW[1,2]

[1]Department of Medicine and Therapeutics and [2]State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong, [3]Singapore General Hospital, Singapore, [4]University of Malaya, Malaysia, [5]Shanghai Jiao Tong University, P.R. China, [6]University of Hong Kong, Hong Kong, [7]Yonsei Medical University, South Korea; [8]Taipei Veterans General Hospital, Taiwan, [9]Seoul National University College of Medicine, South Korea, [10]Seoul SoonChunHyang University Hospital, South Korea, [11]Bucheon SoonChunHyang University Hospital, South Korea

Introduction: Unhealthy diet and physical inactivity are strong risk factors for nonalcoholic fatty liver disease (NAFLD). Data on the lifestyle habits of Asian NAFLD patients are scarce.
Objectives: We aimed to compare lifestyle habits of NAFLD patients in different Asian regions.
Methods: In this multicenter prospective cohort study, we collected clinical data and lifestyle data of NAFLD patients from Singapore, mainland China, Hong Kong SAR, Taiwan and Malaysia. Exercise habits were assessed using the International Physical Activity Questionnaire.
Results: 555 NAFLD patients were included in the final analysis (mean age 54.5 ± 11.2 years, 52.3% male, body mass index 28.5 ± 4.9 kg/m^2, median liver stiffness 6.7 kPa). Compared with other regions, more patients from mainland China (27.4%) and Taipei (25.1%) were smokers. Binge drinking was rare and was only seen in 6 (3.5%) patients from Singapore and 1 (1.6%) patient from mainland China. Majority of patients drank coffee (355/555, 64.0%) and tea (445/555, 80.2%), with varying amounts and durations in different regions. Soft drink consumption was most common in Singapore (62.2%) and Malaysia (57.7%). Only 29.7% of patients met the Physical Activity Guidelines Recommendations, with no major differences across regions. The median (interquartile range) total MET minutes per week was 1173.0 (462.0–2217.0).
Conclusion: There is considerable difference in the lifestyle habits of NAFLD patients across Asian regions. However, physical inactivity is common in all regions. Healthcare providers may use the comparative data to identify areas of deficiency.

Abstract #1325

The role of non-invasive tests in the diagnosis of fatty liver disease in PCOS patients

Fehmi Ates[1], Dervis Akkurd[2], Osman Ozdogan[1], Serkan Yaras[1], Mustafa Zanyar Akkuzu[1], Orhan Sezgin[1], Engin Altintas[1]

[1]Mersin University Faculty of Medicine Gastroenterology Department, [2]Mersin University Faculty of Medicine İnternal Medicine Department

Objectıve: The aim of this study was to investigate the presence of fatty liver in patients with polycystic ovary syndrome (PCOS) by ultrasonography and hepatic non-invasive indices and to investigate the relationship between metabolic and biochemical parameters.
Materıal and method: The study included 33 newly diagnosed PCOS patients and 29 healthy controls. Anthropometric and blood pressure measurements of all the participants were performed. Biochemical and hematological tests were investigated in venous blood samples of the participants. Ultrasonography was used as the radiological method in the evaluation of hepatosteatosis and fibrosis. In addition, three non-invasive hepatic steatosis index [NAFLD liver fat score, lipid accumulation production (LAP), and hepatic steatosis index (HIS)] were used to evaluate the hepatic steatosis. Moreover,

two non-invasive liver fibrosis indices [FIB-4 and aspartate aminotransferase (AST)-platelet ratio index (APRI)] were used to evaluate hepatic fibrosis.

Results: In our study, the incidence of hepatosteatosis in PCOS patients was significantly higher than in the control group (69.7% vs 34.5% $p \leq 0.05$). LAP and HIS scores, which are non-invasive indices of hepatosteatosis, were significantly higher in PCOS patients compared to the control group (LAP: 40.5 ± 35.1 and 21.2 ± 17.4, $p = 0.016$; HIS score: 35.9 ± 6.6 and 31.8 ± 5.9, $p = 0.017$). There was no significant difference between patients with PCOS with and without metabolic syndrome in terms of liver steatosis (81.8% vs. 63.6 $p = 0.430$). There was no significant difference between the groups in terms of NAFLD liver fat score, FIB 4 and APRI fibrosis scores.

Conclusıon: Fatty liver disease may cause serious clinical consequences if not diagnosed and treated early in the patients with polycystic ovary syndrome. PCOS is a risk factor for nonalcoholic fatty liver disease independent of metabolic syndrome. Abdominal ultrasonography and two non-invasive liver indices: LAP and HIS are easy and effective diagnostic methods to determine fatty liver disease in PCOS patients.

Abstract #1394

Utility of noninvasive scoring systems of fibrosis for detecting advanced fibrosis in patients with leaner nonalcoholic fatty liver disease (NAFLD)

Singh Shivaram Prasad, Khatua Chitta Ranjan, Sahu Saroj Kanta, Meher Dinesh, Nath Gautam, Khandelwal Resu, Nath Preetam, Mishra Debakanta, Panigrahi Subhendu, Barika Rakesha Kumar, Pradhan Subhasis, Singh Ayaskant, Narayan Jimmy, Parida Prasant

Srirama Chandra Bhanja Medical College, Cuttack, Odisha, India

Introduction: In patients with Nonalcoholic fatty liver disease (NAFLD), AST to Platelet Ratio Index (APRI), NAFLD Fibrosis score (NFS), Fibrosis 4 score (FIB 4) are endorsed by international guidelines as noninvasive markers of fibrosis.

Objective: To explore the relationship between advanced fibrosis with APRI, NFS and FIB4

Methods: 240 biopsy proven-NAFLD patients with anthropometric and biochemical data were included. The efficacy and cut-off point of the NFS, FIB4 and APRI to detect advanced fibrosis was evaluated by area under receiver operating curve (AUROC) and maximum Youden index analysis respectively. Besides correlation was also done for each scoring system with presence of advanced fibrosis. P value ≤ 0.05 was taken as significant.

Results: Male to female ratio was 3.63. Mean age and BMI were 39.33 ± 9.59 years and 26.64 ± 3.68 kg/m^2 respectively. 68% patients had liver fibrosis. Most patients had grade 1 or 2 fibrosis. 9 (4%) patients had grade 3 fibrosis while none had grade 4 fibrosis. AUROC of NFS, FIB4 and APRI for diagnosing $\geq$ F3 fibrosis were 0.656, 0.557 and 0.572 respectively. No significant correlation was noted between $\geq$ F3 fibrosis with APRI ($r = 0.121$, $p = 0.396$), FIB4 ($r = 0.093$, $p = 0.517$) and NFS ($r = 0.219$, $p = 0.123$).

Conclusion: Most NAFLD patients did not have advanced liver fibrosis. NFS had the highest accuracy for detecting advanced liver fibrosis in patients. None of the scoring systems significantly correlated with advanced liver fibrosis. The algorithm of NFS and FIB4 for detecting advanced fibrosis may not be appropriate in our leaner NAFLD patients.

Table: Sensitivity, specificity, positive predictive value and negative predictive value of various noninvasive scoring systems for detecting advanced fibrosis in patients with NAFLD

Noninvasive score	Score	Sensitivity	Specificity	PPV	NPV
APRI	1.09	17%	88%	42%	68%
FIB4	2.02	26%	91%	39%	67%
NFS	0.243	38%	97%	66%	94%

Abstract #1407

A retrospective study of the demographic composition of a diverse patient population with a diagnosis of NAFLD/ NASH in a single urban centre in Toronto, Ontario, Canada

Jammu A[1], Dallali H[1], Lee J[1], Mahmood M K[1], Kausar S[1], Magnes M[1], Elkhashab M[1]

[1]Research, Toronto Liver Centre, Toronto, Canada

Background: Given the increased prevalence of NAFLD/NASH, it is important to gain better understanding of defining characteristics of affected populations.

Objective: A retrospective analysis of a diverse population with a NAFLD and/or NASH diagnosis receiving care through a single centre in Toronto, Ontario, Canada.

Methods: Retrospective review of charts at Toronto Liver Centre was conducted to identify NAFLD and/or NASH cases (n = 2764). Patient demographics, medical history, and Fibroscan® results were analyzed through descriptive statistics.

Results: Of 2764 charts, 2585 pure NAFLD and 142 pure NASH diagnoses identified. Ethnicity spans five continents: Asia (57.3%), Commonwealth of Independent States (4.5%), Eastern Europe (3.2%), Latin America & Caribbean Islands (6.4%), Near East (5.9%), Northern Africa (9.5%), Northern America (1.8%), Sub-Saharan Africa (7.3%), Western Europe (4.1%). Of the cases: 58.0% male (1602 patients), 42.0% female (1162 patients); age distribution: < 30–1.7%, 30–39–8.4%, 40–49–19.6%, 50–59–29.6%, 60–69—23.2%, 70–79–11.8%, < 80–5.3%.

Major comorbid conditions reported: obesity (42.0%), dyslipidemia (38.9%), hypertension (32.9%), diabetes (22.4%), GERD (15.1%), hypothyroidism (8.2%), depression (7.5%), IBS (5.3%), CAD (4.3%). Of this cohort, elevated LFTs (22.0%), chronic HBV infection (8.5%), chronic HCV infection (6.0%), hepatomegaly (17.9%), splenomegaly (5.4%), focal liver lesion mass (4.9%), cirrhosis (4.4%). Major cancer history observed for: breast cancer (1.6%), prostate cancer (0.6%), thyroid cancer (0.5%) and liver cancer (0.5%). Fibroscan® results were registered in 1946 cases and relative proportion of initial fibrosis staging was: F0—35.7%, F0 to F1—20.9%, F1—15.8%, F1–F2—8.2%, F2—8.4%, F2–F3—3.3%, F3—2.1%, F3–F4—1.6%, F4—5.2%. Steatosis results were available in 1385 of the 1946 Fibroscan® results: S0—11.8%, S0–S1—2.2%, S1—16.1%, S1–S2—2.2%, S2—23.9%, S2–S3—6.4%, S3—37.4%.

Conclusion: Majority of patients were between 40 to 70, male (58%) and had one or more components of metabolic syndrome: obesity (42%), dyslipidemia (38.9%), hypertension (32.9%) and type 2 diabetes mellitus (22.4%). 20.6% had initial liver stiffness compatible with moderate to severe fibrosis. 4.3% of the cohort had established cirrhosis.

Abstract #1451

Treatment of non-alcoholic steatohepatitis: own experience

B. S. Ilyassova, B. S. Abzhaparova, B. B. Baymakhanov

The A.N. Syzganov's National Scientific Center of Surgery, Almaty, Kazakhstan

Introduction: Aldivia is a new hepatoprotective drug, the active substance of which is biphenyldimethyldicarboxylate (BDD), which is a synthetic analogue of Schisandrin (Schisandrin C.), one of the components of Chinese magnolia vine, used for thousands of years in China and Japan to treat diseases of the gastrointestinal tract. ALDIVIA® contains 7.5 mg of the patented instant form BDD, in a soft capsule. The mechanism of action of Aldivia is increasing of the level and activity of microsomal liver enzymes P450, increasing of the activity of antioxidant enzymes such as glutathione peroxidase, glutathione reductase and glutathione S-transferase.
The aim of study: To evaluate the effectiveness of the herbal preparation Aldivia with non-alcoholic steatohepatitis. The study included 30 patients. Inclusion Criteria were patients of both sexes aged 18–75 years; the diagnosis of NAFLD, steatohepatitis was established on the basis of the analysis of the clinical picture (presence of excess weight, elevation of transaminases, determination of cholestasis according to biochemical studies, negative results of the study on markers of viral hepatitis and AMA, ANA, lack of history of alcohol consumption at a dose of more than 30 ml per day for men and above 20 ml for women), written informed consent for the study provided by the patient. Exclusion Criteria were Cirrhosis of the liver, mental illness; oncological diseases; liver disease of viral etiology; alcoholic liver disease; diseases of accumulation; pregnancy or lactation; age less than 18 years; severe concomitant diseases in the stage of decompensation; other liver diseases. The drug was given with a dose of 1 tab 3 times a day. The course of therapy was 90 days. The effectiveness of treatment with the drug « Aldivia » was evaluated by the dynamics of the levels of ALT, AST, bilirubin, γ-GTP, alkaline phosphatase and by the results of a study of the quality of life using the SF-36 questionnaire. The use of the drug "Aldivia" in the treatment of patients with non-alcoholic steatohepatitis is accompanied by a statistically significant decrease in the levels ALT from 78.1 ± 5.9 to 38.1 ± 7.4 UI (P = 0.017), AST from 74.5 ± 6.7 to 39.5 ± 4.8 UI (P = 0.004), alkaline phosphatase from 128.0 ± 14.7 to 87.5 ± 11.8 UI (P = 0.007), γGTP 118.1 ± 12.5 to 57.1 ± 9.0 UI (P = 0.006), improvement of the emotional, psychological and physical state of patients. Good tolerability of the drug, the absence of undesirable phenomena, are of great importance for the formation of adherence to patients taking the drug and achieving a sustainable response to therapy.
Conclusion: The results of the study showed that the drug Aldivia is an effective drug for the treatment of non-alcoholic steatohepatitis, since its use normalizes the levels of transaminases, γGTP, alkaline phosphatase and significantly improves the quality of life of patients with non-alcoholic steatohepatitis

Abstract #1483

Accuracy of fibrosis-4 (FIB-4) score compare NAFLD fibrosis score (NFS) for advance fibrosis in nonalcoholic fatty liver disease (NAFLD)

Ayu Fitriani, Fardah Akil, Nu'man AS Daud, Andi Muhammad Luthfi Parewangi, Rini Rachmawarni Bachtiar, Susanto H Kusuma, Amelia Rifai

Centre of Gastroenterology-Hepatology HAM Akil/DR. Wahidin Sudirohusodo General Hospital Division of Gastroenterology-Hepatology,*Department of Internal Medicine, University of Hasanuddin, Makassar-Indonesia

Introduction: Transient elastography (Fibroscan), Fibrosis-4 (FIB-4) score, NAFLD Fibrosis score (NFS) are a noninvasive tool for diagnosis of liver fibrosis. Transient elastography had superior performance to other noninvasive biochemical tests in diagnosing advanced fibrosis and cirrhosis and validated tool to assess the stage of fibrosis in NAFLD patients. The accuracy of noninvasive tools for the diagnosis of severe fibrosis in patient with nonalcoholic fatty liver disease (NAFLD) is still limited in clinical practice.
Objective: To compare FIB-4 and NFS with LSM for assess liver fibrosis in NAFLD patients.
Methods: This cross-sectional analysis study enrolled 89 NAFLD patients diagnosis by ultrasound and performed transient elastography (Fibroscan) for liver stiffness measurement. FIB score and NFS were calculated and assess the suitability with LSM using Kappa test. Their diagnostic accuracy were assessed based on area under the receiver operating characteristic (AUROC) curve, sensitivity and specificity.
Results: We found 48 (53.9%) male and 41 (46.1%) female, median age of 47.2 years and mostly with obesity 57 (60%). The advanced fibrosis (≥ F3) for LSM/FIB-4/NFS were 20 (22.5%)/6 (6.7%)/4 (4.5%) respectively. Suitability of FIB-4 compare to NFS for LSM are 25.2% vs 16.5% ($p < 0.001$). AUROC for advanced fibrosis was higher for FIB-4 (AUROC: 0.75 ± 0.59; p = 0.001) compared with NFS (AUROC: 0.70 ± 0.67; p = 0.006) Sensitivity/specificity of FIB-4 and NFS were 80%/71% and 75%/60% respectively.
Conclusion: FIB-4 have superiority for diagnosis advance fibrosis stages compare to NFS in NAFLD patients.

Abstract #1523

Lipid profile in grading of fatty liver and liver fibrosis

Abdul Mubdi Ardiansar*, Fardah Akil, Muhammad Luthfi Parewangi, Nu'man AS Daud Rini Rahmawarni Bacthiar, Susanto H Kusuma, Amelia Rifai

Centre of Gastroenterology-Hepatology HAM Akil/DR. Wahidin Sudirohusodo General Hospital, Division of Gastroenterology-Hepatology,*Department of Internal Medicine, University of Hasanuddin, Makassar-Indonesia

Introduction: In non-alcoholic fatty liver disease (NAFLD), liver overproduces several atherogenic factors such as lipoproteins where's fatty liver is associated with increased serum low-density lipoproteins (LDL) and triglycerides (TG), combined with decreased high-density lipoproteins (HDL). In several studies, number of NAFLD cases can progress to fibrosis with abnormal lipid profile.
Objectives: To detect and compare lipid profile with grading of fatty liver and degree of liver fibrosis.
Methods: This retrospective analysis using 89 NAFLD patients diagnosed by ultrasound. Lipid profile was collected and grade of fatty liver based on the sonography was categorized into 3: 1 (mild)/ 2 (moderate)/3 (severe). Liver fibrosis grading are measured by Fibroscan TE: F0F1 no/mild fibrosis, F2F3 significant fibrosis, and > F3 advance fibrosis/cirrhosis. Analysis data using one-way ANOVA with $p < 0.05$ was considered as statistically significant.
Result: Lipid abnormalities was found in 82 (92.1%) with raised TG/cholesterol/LDL levels in 49 (55.1%)/ 55 (61.8%)/54 (60.7%) respectively and decreased in HDL 38 (42.7%); mean of TG/cholesterol/ LDL/HDL were 175.8 ± 79.5/213.4 ± 41.9/ 144.4 ± 40.8/42.9 ± 12.9 mg/dl. Based on fatty liver grade, mean TG 174.02 ± 69.263/cholesterol 216.09 ± 40/LDL 148.13 ± 41.9 were found to be markedly higher but lower HDL 41.15 ± 12.1 mg/dl in grade 2 compare grade 1/3; in liver fibrosis grade, mean TG/cholesterol/LDL: 189.67 ± 74.9/218.5 ± 48.8/147.9 ± 43.9 mg/dl respectively were higher in grade F0F1 compare F2F3/> F3 and lower HDL level 38.8 ± 15 mg/dl found only in grade > F3. These level of lipid abnormalities were not significantly associated with increasing grades of fatty liver and liver fibrosis ($p > 0.05$).

Conclusion: Lipid profile abnormality was observed in moderate grading of fatty liver and in early or advance degree of liver fibrosis.

Abstract #1596

Hepatic R2* reflects liver inflammation and hepatocellular ballooning in patients with nonalcoholic fatty liver disease

Imajo Kent, Kessoku Takaomi, Honda Yasushi, Ogawa Yuji, Yoneda Masato, Kirikoshi Hiroyuki, Saito Satoru, Nakajima Atsushi

Department of Gastroenterology, Yokohama City University Graduate School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama, 236-0004, Japan.

Introduction: Although hepatic iron accumulation is associated with liver inflammation in chronic liver disease, it is unclear whether it is associated with nonalcoholic fatty liver disease (NAFLD) pathogenesis. MRI-R2* map is a tool to evaluate liver-specific iron deposition noninvasively. However, R2* was reported previously to be influenced by proton density fat fraction (PDFF). Therefore, we assessed the association between R2* and PDFF/pathological findings in patients with NAFLD.
Methods: We undertook a retrospective study of 202 patients and a prospective study of 122 patients with liver biopsy proven NAFLD. The concentration and deposition pattern of hepatic iron were evaluated in 122 patients prospectively by atomic absorption spectrometry and iron staining.
Results: R2* values correlated positively with ALT levels and reflected the grade of liver inflammation and hepatocyte ballooning. In contrast, serum ferritin levels correlated positively with AST levels and insulin resistance (IR), and reflected the grade of steatosis. Although R2* values had a significant correlation with PDFF when the values were < 60 Hz, there was no correlation between R2* values and PDFF when the values were > 60 Hz. In addition, R2* values reflected severe hepatic inflammation plus hepatocyte ballooning grade in patients with R2* values > 60 Hz who had high hepatic iron concentration compared with R2* values < 60 Hz.
Conclusion: Liver-specific iron deposition-induced liver injury might be predictable by measuring R2* values noninvasively especially in patients with R2* values > 60 Hz, rather than measuring serum ferritin levels, which might predict IR and steatosis grade due to systemic iron overload.

Abstract #1604

Long term outcome of patients transplanted for non alcoholic steatohepatitis related cirrhosis

Dr. Isam Salih[1], Dr Sarra Yousif[1], Dr. Khalid Bzeizi[1], Dr Saad Alghamdi[1], Dr. Ali Albenmousa[1], Dr. Salih Alqahtani[1] and Dr. Waleed Al Hamoudi[1,2]

[1]Liver Transplant, King Faisal Specialist Hospital and Research Center, [2]Department of Medicine, King Saud University

Introduction: Cirrhosis secondary to Nonalcoholic Steatohepatitis (NASH) is projected to become the leading indication for liver transplantation (LT) worldwide.
Objectives: to evaluate the prevalence of metabolic syndrome and long term outcome of patients transplanted for NASH related cirrhosis.
Methods: All patients transplanted for NASH related cirrhosis at our institution from 2001 to 2016 were included in this study. Patients data were collected from our prospectively collected database.
Results: 108 patients were transplanted for NASH related cirrhosis at our institution. Sixteen (15%) patients had pretransplant hepatocellular carcinoma. Pretransplant obesity (BMI > 30), diabetes, hyperlipidemia and hypertension were present in 43 (40%), 57 (53%), 20 (19%), and 30 (28%) patients, respectively. Following LT patients were followed for an average of 103 months (range 54–203 months). Post-transplant diabetes, hyperlipidemia and hypertension were present in 62 (57%), 25 (23%) and 48 (44%) patients, respectively. Fifty (46%) patients developed disease recurrence with significant fatty infiltration on various imaging modalities. Additionally, 48 (44%) patients developed renal impairment (GFR < 60). Sixteen patients were treated for mild rejection and only one patient developed ductopenic rejection resulting in graft loss. Sixteen (15%) patients developed severe cardiovascular complications. Overall survival during the follow period was 83%. One and 3 year survivals were 92.5% and 87% respectively. Sepsis was the commonest cause of death in our patient population. Three patients died secondary to acute cardiovascular events.
Conclusion: Disease recurrence in our patient population was common; however, post-transplant cirrhosis remains rare. The prevalent metabolic syndrome negatively impacted renal function and resulted in cardiovascular complications.

Abstract #1643

Optimal dose of obeticholic acid in the management of non-alcoholic steatohepatitis-related fibrosis: a systematic review

Setiawan SI[1], Zhang E[1]; Sari MSG[1], Jorisca[1], Tendean M[2]; Soetedjo N[3], Angelia F[4]; Ndraha S[5]

[1]General Practitioner, Bhakti Asih General Hospital, Banten, Indonesia, [2]Department of Internal Medicine, UKRIDA Faculty of Medicine and Health Science, Jakarta, Indonesia, [3]Endocrinology and Metabolic Division, Department of Internal Medicine, Padjajaran University—Hasan Sadikin General Hospital Bandung, Indonesia, [4]Department of Pharmacology, UKRIDA Faculty of Medicine and Health Science, Jakarta, Indonesia, [5]Department of Internal Medicine, UKRIDA Faculty of Medicine and Health Science, Jakarta, Indonesia

Introduction: Non-alcoholic fatty liver disease (NAFLD) is the most common chronic progressive liver disease. NAFLD may progress to non-alcoholic steatohepatitis (NASH) further resulting in cirrhosis and hepatocellular carcinoma. Studies have shown that obeticholic acid, a bile acid derivate of potent activator of Farnesoid X nuclear receptor, can improve fibrosis in NASH.
Objective: To evaluate the optimal dose of obeticholic acid in managing NASH related fibrosis.
Methods: Systematic literature search was conducted in multiple databases (PubMed, Cochrane, Lancet, Springer Link, Science Direct, ProQuest, EBSCO, and Jstor) using specific MESH terms ("obeticolic" AND ("NASH" OR "NAFLD" OR "steatohepatitis") AND "fibrosis"). The inclusion criteria were randomized controlled trials (RCTs) or meta-analysis including obeticholic acid in NASH or NAFLD patients evaluated for at least 72 weeks. Eligible studies then appraised using evidence-based toolkit.
Results: Two RCTs involving 1988 patients were analyzed. Obeticholic acid 25 mg group showed greater improvement in fibrosis compared to placebo (RR 2.2; 95% CI 1.4–3.2; $p < 0.0001$), which is superior compared to 10 mg group (RR 1.6; 95% CI 1.1–2.5; $p = 0.025$). However, significant NASH resolution at 72 weeks did not occur (RR 1.5; 95% CI 0.9–2.6; $p = 0.08$). In addition, early

treatment with obeticholic acid would improve liver enzyme level after 3 months of administration.
Conclusion: Treatment with 25 mg obeticholic acid was superior compared to 10 mg and placebo in improving NASH-related fibrosis, but no significant resolution of NASH noted.

Abstract #1677

Lipids profile, gamma-glutamyl transferase and hyperferritinemia in patients with NAFLD/NASH

Sargsynats Narina *[1]

[1]Infectious Diseases, Elit-Med Medical Centre, Yerevan, Armenia

Introduction: Non-alcoholic fatty liver disease (NAFLD) is currently the world's most common liver disease, that affecting 25% of the adult population, can lead to liver cirrhosis and cancer.
Objectives: The aim of the study is evaluation of correlation BMI, liver function tests, and lipid profile with NAFLD in small Armenian cohort.
Methods: 50 patients with ultrasound-diagnosed NAFLD were involved in the study (62% male), 27–76 years old (50.6±11.5), BMI 32.4±6.0 kg/m^2. We evaluated following biochemical and lipids profile parameters: AST, ALT, GGT, ferritin (FERR), glucose, triglycerides (TG), cholesterol (CHOL), high density lipoprotein (HDL), low density lipoprotein (LDL). Atherosclerosis risk also was part of report. Statistical analysis was done by SPSS11.0 with regression analysis.
Results: F4 had 12% of patients, 62% had obesity, 36% had diabetes. Range and mean ± SD or SE of evaluated parameters in Tab.1. Interestingly in six patients with high level of FERR (more than 500 ng/mL) we checked mutation in HFE and revealed 187C > G (rs1799945) heterozygous in three and homozygous in 1patient. Atherosclerosis risk 9.0–33.8 (17.1±6.0). Using atherosclerosis risk, LDL, CHOL, HDL, TG predictors simultaneously 87% (adjusted $R^2 = 0.875$) of the variance in GGT can be predicted from TG and atherosclerosis risk combined. The ANOVA table shows that the combination of the predictors significantly predict GGT ($p = 0.0001$). The coefficients table shows significance of TG and atherosclerosis risk to the prediction of GGT.
Conclusion: NAFLD characterized with high level of enzymes, ferritin, high risky level of LDL, HDL and TG. According to regression analysis TG and atherosclerosis risk have influence on GGT level in NAFLD patients.

Descriptive Statistics of patients with NAFLD/NASH (n=50)

	Normal range	Unit	Range	Minimum	Maximum	Mean	Std. Error	Std. Deviation
GLUC	3.89-5.83 >60 y. 4.44-6.38	mmol/L	18.0	4.4	22.3	6.907	.458	3.0717
CHOL	Desirable <5.18 Borderline5.18 - 6.19 High: > 6.22	mmol/L	16.70	2.85	19.55	6.1852	.3546	2.50712
HDL	High risk <1.04 Min. risk >1.55	mmol/L	1.36	.43	1.79	1.0083	.0385	.26653
LDL	Optimal < 2.59 Near or above optimal 2.59-3.35 Borderline high 3.36-4.12 High 4.13-4.89	mmol/L	8.48	.59	9.07	3.9452	.2313	1.60232
	Very high > 4.9							
TG	Normal < 1.70 1.70-2.25 Borderline high High 2.26-5.64 Very high > 5.65	mmol/L	56.25	.75	57.00	3.7444	1.1102	7.85006
Athero-sclerosis risk	Low 27-40 Middle 18-27 High 12-18 Dangerous 0-12		24.8	9.0	33.8	17.070	.742	5.0308
ALT	<55	U/L	325	14	339	67.94	8.02	54.979
AST	5 - 34	U/L	180	12	192	43.93	5.15	34.919
GGT	9 - 36	U/L	942	18	960	88.12	20.47	141.799
FERR	4.63-204.00	ng/mL	1887	60	1947	481.84	99.18	543.229

Abstract #1702

Predictors of clinically significant fibrosis among patients with non-alcoholic fatty liver disease (NAFLD)

Sy, Marianne Linley; and Cervantes, JG

[1]Institute of Digestive and Liver Diseases, St. Luke's Medical Center—Global City, Philippines, [2]Institute of Digestive and Liver Diseases, St. Luke's Medical Center-Global City, Philippines.

Introduction: Nonalcoholic fatty liver disease (NAFLD) is observed worldwide, with increasing prevalence. NAFLD may lead to cirrhosis that carries poor clinical outcome. Early diagnosis of clinically significant fibrosis in NAFLD patients is crucial as it is one of the major predictors of liver disease-specific morbidity and mortality.
Objective: We aim to determine the predictors associated with clinically significant liver fibrosis among adult patients with NAFLD.
Methods: This is a multicenter, analytical, cross-sectional study utilizing a retrospective review of records in the liver databank of St. Luke's Medical Center Quezon City and Global City, from January 2018 to June 2019. Adult patients diagnosed with non alcoholic fatty liver disease who underwent liver elastography were included. Clinically significant fibrosis is defined as F2, F3, and F4 on liver elastography.
Results: A total of 1092 patients were included. Binary logistic regression showed that for every unit increase in age in years, the odds of having clinically significant fibrosis increases by about 1.6% (aOR 1.016, 95% CI 1.003 to 1.03). Males are twice as likely to have clinically significant fibrosis (aOR 2.041, 95% CI 1.45 to 2.88). Compared to mild fatty liver, patients who had severe fatty liver were nearly twice as likely to have clinically significant fibrosis (aOR 1.691, 95% CI 1.13 to 2.53).
Conclusion: Increasing age, male gender, obesity, diabetes mellitus are clinical predictors of development of clinically significant fibrosis among patients with NAFLD. NAFLD patients with clinically significant fibrosis also tend to have higher AST, higher ALT, and higher bilirubin level.

Abstract #1704

Overview of NAFLD in patients with metabolic syndrome at prof. Dr. R. D. Kandou hospital in manado

Dwi Argo W[1], Waleleng B J[2], Rotty L[2], Tendean N [2], Gosal F[2], Winarta J[2], Waleleng A[2]

[1]Department of Internal Medicine, Faculty of Medicine, Sam Ratulangi University, Manado, Indonesia, [2]Division of Gastroentero-Hepatology, Department of Internal Medicine, Faculty of Medicine Sam Ratulangi University/Prof. Dr. R. D. Kandou Hospital, Manado, Indonesia

Background: Growing prevalence of metabolic syndrome is accompanied with increasing incidence of Non Alcoholic Fatty Liver Disease (NAFLD), which is a common manifestation of liver abnormalities in metabolic syndrome.
Objective: This study aims to determine the clinical profile of NAFLD patients with metabolic syndrome at Prof. Dr. R. D. Kandou Hospital, Manado
Methods: This study used descriptive method with retrospective approach. Research subjects were all adult with metabolic syndrome who came for treatment at Prof. Dr. R. D. Kandou Hospital, Manado between November 2018 to October 2019. Data collected included demographic data, clinical parameters, laboratory and radiological result of patients.

Results: Total of 102 patients were included; 55 (53.9%) of them were men, ranging from 20 to 80 years. Most of the patients were aged under 65 years old (n = 91 [89.2%]). There were 38 patients (37.3%) had body mass index > 30 kg/m^2; 78 patients (76.5%) diagnosed having hypertension (blood pressure ≥ 130/85 mmHg); as many as 92 patients (90.2%) had abdominal circumference in men ≥ 90 cm and women ≥ 80 cm. Impaired fasting blood sugar was found in 66 patients (64.7%), while there were 74 patients (72.5%) with HDL < 40 mg/dL in men and < 50 mg/dL in women; There were 77 patients (75.5%) with triglycerides > 150 mg/dL.
Conclusion: In metabolic syndrome patients with NAFLD, we found three main findings which are central obesity, high triglyceride levels, and low HDL levels.

Abstract #1713

The correlation between type 2 diabetes melitus and non alcoholic steato hepatic measured by controlled attenuation parameter (CAP) in Prof dr Kandou Hospital Manado Indonesia

Kurniawan M[1], Tendean N[2], Waleleng B J[2], Gosal F[2], Rotty L[2], Winarta J[2], Waleleng A[2]

[1]Resident of Internal Medicine in Sam Ratulangi University Faculty of Medicine Manado, [2]Gastroentero-Hepatology Division of Internal Medicine Sam Ratulangi University Faculty of Medicine/Prof. Dr. R.D. Kandou Hospital Manado, North Sulawesi, Indonesia

Introduction: Non Alcoholic Fatty Liver Disease (NAFLD) is a disease with multifactorial causes and it's considered to progress severe into Non Alcoholic Steato Hepatic (NASH). Nowadays, NASH prevalence increased worldwide. It is known that patient with type 2 diabetes melitus (T2DM) are at high risk in developing NASH and they are more likely worsening insulin resistance. CAP is a noninvasive tool that reliable to measure NASH.
Objectives: The purpose of this study is to determine the correlation of NASH in T2DM compared to normal individuals using CAP Fibroscan®.
Methods: Subjects who underwent to this cross sectional study were divided into T2DM and control, undergoing CAP Fibroscan®. Values of CAP 250 dB/m were the cutoffs for the presence of Steato Hepatic. All subjects who met the exclusion criteria (hepatitis, obesity, dyslipidemia, impaired liver function, and history of alcoholic) were excluded from the study and processed with SPSS. Distribution of data was tested with *Kolgomorov-Smirnov*. The correlation between NASH and T2DM was tested using bivariate analysis.
Results: Population were 30 patients (T2DM, n = 15; control, n = 15), 17 women and 13 men. Average age of population is 53.23 ± 11.11 years. The mean CAP value was significantly higher in subjects with T2DM (295 dB/m) than in those control (219.1 dB/m). The results of the analysis test with fisher's exact test are p value = 0.001 and odds ratio = 17.875. These results showed correlation of NASH in T2DM subjects and T2DM are 17 fold higher risks to have NASH.
Conclusion: There was a correlation between T2DM and NASH measured by CAP fibroscan®.

Abstract #1778

Benefits of low-carbohydrate diet in non-alcoholic fatty liver disease

Chyntia Olivia Maurine Jasirwan[1], Gerald Abraham Harianja[2]

Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, University of Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine, University of Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Backgrounds: Non-alcoholic liver disease is strongly associated with obesity and dietary habits. The degree of liver inflammation shows a positive correlation with the percent amount of carbohydrate energy consumed.
Aim: To identify the benefits of a low-carbohydrate and low-fat diet on changes in hepatic fat in NAFLD (non-alcoholic fatty liver disease) population.
Methods: Literature searching was conducted by using databases PubMed, EBSCOhost, ScienceDirect. The keywords, inclusion, and exclusion criteria were also applied. The articles were appraised to discuss validity, importance, and applicability.
Result: Browning, et al found that intrahepatic fat decreased significantly in the low-carbohydrate diet group (-55% ± 14 vs. -28% ± 23, P = 0.008). Kirk, et al found that patients on a low-carbohydrate diet show faster intrahepatic fat reduction than patients on a high carbohydrate diet (29.6% ± 4.8 vs. 8.9% ± 1.4, P < 0.05). Haufe, et al found that there was no significant difference between the low-carbohydrate diet group (25% carbohydrate, 45% fat, 1600 kcal/day) and the low-fat diet group (52% carbohydrate, 27% fat, 1600 kcal/day). Jang, et al found that calorie restriction is more a factor that improves fatty liver than macronutrient composition. Bian, et al found that there was no difference in intrahepatic fat between a group of carbohydrate restriction < 20 grams for 6 days with a group of total calorie consumption of 1000 kcal/day for 7 months.
Conclusion: There is still a lack of evidence to show the role of a low-carbohydrate diet in NAFLD (non-alcoholic fatty liver disease) patients.

Abstract #1779

Colonoscopy as screening for colorectal adenoma or colorectal cancer in patients with non-alcoholic fatty liver disease

Chyntia Olivia Maurine Jasirwan[1], Bertin Tanggap Tirtana[2]

Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2] Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: After cardiovascular disease, extrahepatic cancer is a major cause of death in patients with non-alcoholic fatty liver disease (NAFLD). NAFLD increases the risk of colorectal cancer (CRC). Colonoscopy screening of adenoma and CRC in patients with NAFLD is still controversial.
Objectives: This study was done to determine the role of colonoscopy screening in patients with NAFLD.
Methods: An online search of PubMed, Cochrane Library, and Scopus led to two relevant articles. Only articles involving human subjects and published within the last 3 years were included in this study. Review articles, case reports, and case series were excluded. Critical appraisal was done to assess validity, importance, and applicability using the Appraisal Tool for Cross-Sectional Studies (AXIS) and Critical Appraisal Skills Programme.
Results: All NAFLD patients in these two studies underwent colonoscopy screening. Mantovani et al found that NALFD increases the prevalence and incidence of colorectal adenoma and CRC. Kim et al found that NAFLD is associated with an increased prevalence of colorectal adenoma, advanced adenoma, and multiple adenoma.

Patients with significant fibrosis have an increased risk of colorectal complications compared to those without fibrosis.
Conclusion: Colonoscopy screening for colorectal adenoma or CRC may be considered in patients with NAFLD, especially those with significant fibrosis.

Abstract #1780

Effect of probiotics and synbiotics on fibrosis stage and fatty liver index in patients with non-alcoholic fatty liver disease

Chyntia Olivia Maurine Jasirwan[1], Ahmad Nur Aulia[2]

Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2] Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: There are currently no recommended pharmacologic treatments or procedures for non-alcoholic fatty liver disease (NAFLD). The administration of probiotics can decrease the fibrosis stage in choline-methionine-deficient mice NAFLD models.
Objectives: This study assesses the effectiveness of probiotics and synbiotics to improve the fibrosis stage and fatty liver index of patients with NAFLD.
Methods: An online search of PubMed, Cochrane Library, and Google Scholar found two articles. Inclusion criteria were clinical studies published within the last 5 years written in English involving human subjects. Exclusion criteria were review articles, case reports, studies involving pediatric subjects, or studies involving animal subjects. Critical appraisal was done to assess validity, importance, and applicability using the Centre of Evidence-Based Medicine questionnaire.
Results: Mofidi et al found that administration of synbiotics for 28 weeks was associated with significant improvements in fibrosis and steatosis compared to placebo (transient elastography—1.71 kPa SE 0.25 vs. -0.71 kPa SE 0.18, $p < 0.001$ and controlled attenuation parameter -59.89 SE 6.14 vs -14.14 SE 1.04, $p < 0.001$). Kobyliak et al found that administration of probiotics for 8 weeks was associated with significant improvement in fatty liver index compared to placebo (84.33 ± 2.23 to 78.73 ± 2.58, $p < 0.001$) but not with significant improvement in liver stiffness measured by shear wave elastography compared to placebo (7.16 ± 0.2 to 6.76 ± 0.22, $p = 0.052$ vs. 7.28 ± 0.22 to 7.14 ± 0.26, $p = 0.396$).
Conclusion: Administration of synbiotics may improve fibrosis and steatosis in patients with NAFLD. Administration of probiotics may improve fatty liver index in patients with NAFLD.

Abstract #1793

Waist circumference as a screening tool for non-alcoholic fatty liver disease in patients with normal body mass index

Khairunissa, Seruni Tyas Khairunissa; Aprilicia, Gita; Nababan, Saut Horas H.

Hepatobiliary Division, Internal Medicine Department, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia.

Introduction: Non-alcoholic fatty liver disease (NAFLD) is characterized by liver steatosis and commonly associated with metabolic syndrome, including obesity. NAFLD has also been reported in patient with normal body mass index (BMI).
Objective: The aim of this study was to evaluate the role of waist circumference as a screening tool for NAFLD in patients with normal BMI.
Methods: A cross sectional study of 260 adult patients with normal BMI (18.5–22.9 kg/m^2) was performed. Data on AST, ALT, fasting glucose levels, lipid profile, and waist circumference were collected. Fatty liver was diagnosed using ultrasonography (USG).
Results: Based on USG, 25/260 (9.6%) patients had fatty liver. Normal BMI patients with NAFLD had significantly higher ALT ($p < 0.01$), fasting glucose level ($p < 0.01$), triglycerides level ($p < 0.01$) and waist circumference ($p < 0.05$) when compared with non-NAFLD patients. Average waist circumference in NAFLD patients was 83.24 ± 4.06 cm. For NAFLD screening in normal BMI patients, waist circumference with cut-off value ≥ 79.5 cm had sensitivity 88%, specificity 60.4% with negative predictive value 97.9%
Conclusion: Waist circumference measurement can be used as a screening tool for NAFLD in patients with normal BMI.

Abstract #1806

Non alcoholic fatty liver disease in Inflammatory bowel disease—tend to be lean?

Anju Krishna Krishnakumar

Background: Non alcoholic fatty liver disease (NAFLD) is being increasingly described in inflammatory bowel disease (IBD). Conventional risk factors for NAFLD may not be seen in patients with NAFLD in IBD, hence may be under detected. Lean NAFLD is defined as NAFLD that developed in patients with body mass index < 23 kg/m2. We compared the clinical and metabolic profiles of NAFLD in patients with or without IBD.
Methods: 60 NAFLD patients with IBD were compared with 120 NAFLD patients without IBD. Anthropometric measurements, fasting lipid profile, liver function tests, 2D shear wave elastography of all patients were done. The presence of metabolic syndrome was defined by International Diabetes Federation.
Results: Lean NAFLD was observed more in those with IBD than in those without IBD (75% vs35%). Body mass index was lower in NAFLD patients with IBD (20.7 ± 3.43 vs 24.5 ± 3.49). Weight, waist circumference, Waist/Hip ratio, triceps skin fold thickness, Mid arm circumference and metabolic parameters like total cholesterol, triglycerides, LDL were also significantly lower in patients with NAFLD with IBD (table). Metabolic syndrome is found to be more prevalent in NAFLD without IBD than NAFLD with IBD, even though it did not reach statistical significance (20% Vs 33.3%). Liver fibrosis was significantly higher in the IBD with NAFLD group.
Conclusion: Most of the patients with NAFLD in IBD were Lean without having many of the conventional risk factors. However liver fibrosis was higher in this group. Hence they may need surveillance for early detection of liver morbidity and possible intervention.

Parameters(mean±SD/proportions)	NAFLD with IBD(n=60)	NAFLD without IBD (n=120)	P value (significance level≤.05)
Age	42.45±15.9	40.05±11.37	.247
Sex (male gender)	65%	52.5%	.151
BMI	20.71±3.43	24.5±3.49	.000*
Waist circumference(cm)	83.4±12.9	88.5±8.7	.000*
Mid arm circumference(cm)	25.57±3.92	27.73±3.3	.000*
Waist-hip ratio	0.92±0.08	1±0.00	.000*
Triceps fold thickness	19.95±7.3	22.4±7.2	.034*
Total cholesterol	155.5±35.7	205.4±37.69	.000*
Triglycerides	93.17±42.24	129.71±31.5	.000*
LDL	88.93±24.25	108.47±27.47	.000*
Lean NAFLD (BMI<23kg/m2)	**75%**	**35%**	**.000***
Metabolic syndrome	**20%**	**33.3%**	.081
ALT	28.55±35.8	35±18.5	.113
2D Shear wave elastography	6.46±1.91	5.29±1.42	.000*

Abstract #1834

Nutritional intake amongst patients with NAFLD: findings from a pilot study within a single tertiary institute

Binte Abbas Sakinah[1], Whitton Clare[2], Binte Jumat Nur Halisah[1], Lee Wei Jie Jonathan[1,3], Yock Young Dan[1,3]

Yong Loo Lin School of Medicine, National University of Singapore, Singapore, [2] Saw Swee Hock School of Public Health, National University of Singapore, Singapore, [3] Division of Gastroenterology & Hepatology, National University Hospital, Singapore

Background: For equivalent levels of over-nutrition, Asians are more prone to metabolic syndrome, insulin resistance and non-alcoholic fatty liver disease (NAFLD). The role of specific macronutrients, such as saturated fatty acids or sugars (e.g. fructose) have been deemed critical to the onset and progression of NAFLD.

Objective: We thus aim to compare the nutritional intake between non-NAFLD and NAFLD patients, as well as amongst NAFLD patients, obese (BMI $\geq$ 25 kg/m^2) and non-obese (BMI $<$ 25 kg/m^2) NAFLD patients.

Methods: Eighty-three sequential patients undergoing screening colonoscopy were recruited to undertake a 163-item validated semi-quantitative food frequency questionnaire. Each food or beverage item surveyed was tagged, and its data subsequently aggregated to generate a patient's total daily energy and key nutrient profiles. Patients were diagnosed with NAFLD either through screening ultrasonography or transient elastography. Statistical analysis was conducted using binary logistic regression and calculated using SPSS v25.

Results: 53 patients (63.9%) had NAFLD, of which 16 patients (30.2%) are not obese. There were no significant differences in total energy intake between patients with and without NAFLD, after adjusting for age, gender and BMI (p = 0.84). Sugar intake increased with the presence of NAFLD (p = 0.02). Amongst NAFLD patients, sugar intake decreased with increasing BMI (p = 0.01).

Conclusion: Results suggest that NAFLD development, particularly amongst non-obese Asian population, may not be result of simply general overnutrition, but rather an overnutrition of specific macronutrients, such as a diet rich in sugar. Further studies to better the understanding of specific nutritional components on NAFLD pathogenesis may translate to moderate focused dietary interventions for NAFLD.

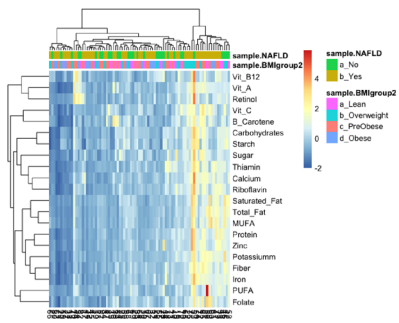


Figure 1: Unsupervised clustered heatmap of representative total nutrients intake per day (per1000kcal/day) of all 83 participants in the study. All features were plotted in terms of z-normalized values (rows). Presence of NAFLD (1st row) and BMI status defnied by Asian BMI cut-off are shown on the top of the graph (2nd row).

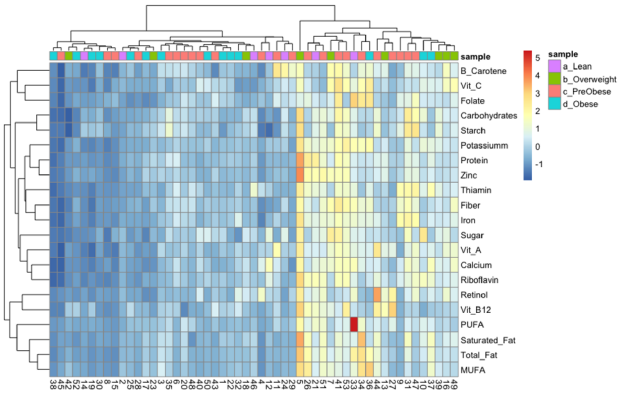


Figure 2: Unsupervised heatmap of participants with NAFLD.

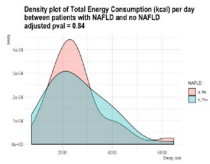


Figure 3: Density plot demonstrating no difference in total energy intake between participants with NAFLD and those without.

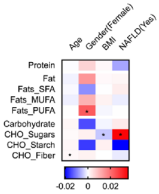


*Figure 4: Heatmap plotting the co-efficient values from a multivariant linear regression model performed for each nutrient (row) against the variables (Age, Gender, BMI and presence of NAFLD). Significant association (p<0.05)s are highlighted with *. Each nutritional component was treated as compositional data, whereby the relative abundance (% of total energy intake) was square-root and then fitted into the linear regression model.*

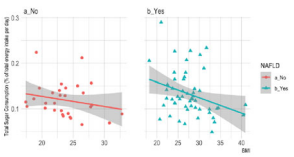


Figure 5: Scatterplot of participants total sugar intake (represented as relative % of total energy intake) against BMI. Participants with NAFLD are in green and those without are in red, whereby (1) patients with NAFLD have significantly higher relative proportions of sugar intake compared to non NAFLD patients, and in both subsets (2) there is a negative correlation between increasing BMI and relative sugar intake.

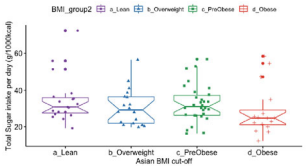


Figure 6: Boxplot of only participants with NAFLD, binned into the Asian BMI cut-off categories, against their total sugar intake per day (g/1000kcal). Obese NAFLD patients have lower total sugar intake, although all NAFLD patients are still taking much more than recommended total sugar intake of 5% (ie 12.5g/1000kcal) per day.

Abstract #1837

Relationship between abdominal circumference and BMI with controlled attenuation parameter in NAFLD patients

Tumewu N[1], Waleleng B J[2], Tendean N[2], Gosal F[2], Rotty L[2], Winarta J[2], Waleleng A[2]

[1]Department of Internal Medicine, Faculty of Medicine Sam Ratulangi University, Manado, Indonesia, [2]Division of Gastroentero-Hepatology, Department of Internal Medicine, Faculty of Medicine Sam Ratulangi University/Prof. Dr. R.D.Kandou Hospital, Manado, Indonesia

Introduction: Nonalcoholic Fatty Liver Disease (NAFLD) condition can develop into advanced chronic liver disease. One of NAFLD risk factor is overweight due to high proportion of body fat. The proportion of body fat can be assessed with Body Mass Index (BMI) and Abdominal Circumference (AC). Controlled Attenuation Parameter (CAP) is a non-invasive method for detecting hepatic stetosis. Previous studies showed CAP score may related with BMI and AC.
Objective: This study aims to analyze the relationship between CAP and BMI and also the relationship between CAP and AC.
Methods: The population in this study were NAFLD patients at Prof. Dr. dr. R.D. Kandou Manado. 44 samples were taken from patients under the age of 60 years old. The results of data collection were analyzed using the Spearman method with SPSS software version 25.
Results: This study found among 44 NAFLD patients, with median age 52 years old (interquartile range [IQR] 10.0) had median CAP score of 297 (IQR 59.25), median BMI of 21.43 kg/m^2 (IQR 4.17), and median AC of 95 cm (IQR 9.0). We found significant relationship between CAP and BMI with significance value 0.001 and correlation value of 0.497, which indicating moderate level of correlation. On the other hand, this study also found significant relationship between CAP and AC with significance value 0.000 and correlation value of 0.579 which indicating moderate level of correlation.
Conclusion: There is significant relationship between CAP and BMI and also a significant relationship between CAP and AC.

Abstract #1839

Correlation between controlled attenuation parameters score using fibroscan with lipid profile in non-alcoholic fatty liver patients

Hadinata E[1], Waleleng B J[2], Tendean N[2], Gosal F[2], Rotty L[2], Winarta J[2], Waleleng A[2]

[1]Department of Internal Medicine, Faculty of Medicine, Sam Ratulangi University, Manado, Indonesia, [2]Division of Gastroentero-Hepatology, Department of Internal Medicine, Faculty of Medicine Sam Ratulangi University/Prof. Dr. R. D. Kandou Hospital, Manado, Indonesia

Introduction: Non -Alcoholic Fatty liver (NAFLD) is a potentially progressive disease that may lead to cirrhosis and liver cancer but is frequently underrecognized. Diagnosis of nonalcoholic fatty liver disease (NAFLD) remains a challenge, as liver biopsy is needed to accurately detect steatosis and fibrosis. Therefore, an accurate non-invasive method is needed. Controlled attenuation parameter (CAP) is a reliable method for non-invasive quantification of liver fat.
Objective: We aimed to investigate the rate of NAFLD as estimated by CAP and correlate findings with lipid profile in screening setting.
Methods: The population in this study were diagnosed NAFLD by ultrasonography at Prof. Dr. dr. R.D. Kandou during November–December 2019. Subjects were examined for transient elastography (Fibroscan) and lipid profile. Exclusion criteria were clinical and laboratory sign of hepatitis B and hepatitis C, history of alcohol consumption, diabetes, history of taking drugs that cause hepatic steatosis and/or lipid lowering drugs, and presence of cholestatic liver disease. Correlation was analyzed using the Pearson method with SPSS software.
Results: Total of 50 NAFLD patients had mean age 48.5 ± 6.8 years old and 24 patients (48%) were men. We found mean CAP score of 286.38 ± 43.42, LDL 116.66 ± 39 mg/dl, HDL 38.42 ± 8.88 mg/dl, triglyceride 186.30 ± 85.36 mg/dl. There was no correlation between CAP and LDL (p = 0.884), HDL (p = 0.339), and total cholesterol (p = 0.92). There was significant correlation between CAP and triglyceride (p = 0.001).
Conclusion: CAP and triglyceride level were significantly correlated. Increased triglyceride levels are directly proportional to the rate of NAFLD. This is indicated by increased CAP scores in patients with high triglyceride levels. These parameters may be used as noninvasive method for detection of NAFLD.

Abstract #1840

The effect of ursodeoxycholic acid on fibrosis change in patients with nonalcoholic fatty liver disease after 3 months of treatment

Irawaty A[1], Waleleng B J[2], Tendean N[2], Gosal F[2], Rotty L[2], Winarta J[2], Waleleng A[2]

[1]Department of Internal Medicine, Faculty of Medicine Sam Ratulangi University, Manado, Indonesia, [2]Division of Gastroentero-Hepatology, Department of Internal Medicine, Faculty of Medicine Sam Ratulangi University/Prof. Dr. R.D.Kandou Hospital, Manado, Indonesia

Introduction: Nonalcoholic fatty liver disease (NAFLD) has emerged as the most common chronic liver condition in the world. Effective therapy for NAFLD is still lacking. We investigated the effects of Ursodeoxycholic acid (UDCA) in the treatment of fibrosis in NAFLD.
Objective: This study was aimed to evaluate the effect of UDCA on fibrosis improvement.
Method: A before and after study was performed on NAFLD patients from October 2018 until October 2019 in Prof. R.D. Kandou Hospital. Demographic and laboratory data were retrieved from the patient's medical record. Diagnosis of NAFLD was established by abdominal ultrasound while fibrosis stage was assessed using transient elastography (FibroScan, Echosens, Paris) with M-probe. Changes of liver stiffness measurement (LSM) values were tested using a paired t test. Patients might or might not follow the advice given regarding dietary pattern and exercise.
Results: A total of 42 cases were retrieved during the study period; 26 (61.9%) of them were men. Patients' mean age was 51.7 ± 14.7 years. There were 28 (66.7%) patients with obesity, 11 (26.2%) with dyslipidemia, 10 (23.8%) with diabetes mellitus. After 3 month therapy, there were significant reduction of LSM ($p = 0.004$) and body mass index ($p < 0.005$).

Conclusion: 3 months of treatment with UDCA improved liver stiffness. Life style modification including exercise and diet also play a role in decreasing liver stiffness.

Abstract #1892

Prevalence and severity of nonalcoholic fatty liver disease (NAFLD) among patients with coronary artery disease

Kannan M[1], Duseja Ajay[2], Bahl Ajay[3], Gupta Ankur[3], Panda Prashant[3], Taneja Sunil[2], Dhiman Radha Krishan[2]

Departments of Internal Medicine[1], Hepatology[2], and Cardiology[3] Postgraduate Institute of Medical Education and Research, Chandigarh, India, 160012

Introduction and Objective: Even though enough literature exists regarding the prevalence of CAD in patients with NAFLD, the literature on the prevalence and severity of NAFLD in patients with CAD is sparse. Objective of the present study was to assess the prevalence of NAFLD and its severity in patients with CAD.
Methods: In a prospective study, consecutive adult patients with CAD were screened for the presence and severity of NAFLD after an informed consent. The study had the approval of Institute's Ethics Committee. CAD was diagnosed on coronary angiography and severity assessed by number of vessels involved and SYNTAX score.
Results: Of 256 patients screened over one and half years, 100 patients (males 71, mean age 56.7 $\pm$ 9.6yrs) meeting the criteria were included. Prevalence of NAFLD on USG and CAP was 48% and 42% respectively and 38 patients (38%) had evidence of steatosis on both modalities. Severity of hepatic steatosis as assessed on CAP (n = 42) was S1 (248 to $\leq$ 268 dB/m) in 26.2%, S2 (268 to 288 dB/m) in 31% and S3 (> 288 dB/m) in 42.8% patients respectively. Seven (18.4%) patients had abnormal ALT (> 40 IU/L); significant hepatic fibrosis (LSM $\geq$ 8 kPa) was observed in 6 (15.8%) among 38 patients with hepatic steatosis on both USG and CAP. Severity of CAD did not affect the prevalence or severity of NAFLD; severity of NAFLD did not affect the severity of CAD.
Conclusion: NAFLD is common in patients with CAD; majority of them have mild disease without significant necro-inflammation and hepatic fibrosis.

Abstract #1900

Moderate alcohol consumption and its effect on fibrosis stage in patients with non-alcoholic fatty liver disease

Simanjuntak-Cindya Klarisa [1], Lesmana-Cosmas Rinaldi A.[2]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Heavy alcohol consumption is a risk factor for chronic liver disease and should be avoided in patients with non-alcoholic fatty liver disease (NAFLD). Interestingly, a few epidemiological studies showed that prevalence of metabolic syndrome is lower in individuals consuming moderate alcohol compared to no alcohol. Another study showed that alcohol consumption < 1 drink per day is beneficial for NAFLD patients. There is currently no recommendation regarding alcohol consumption for patients with NAFLD.
Objectives: To compare the effect of moderate alcohol consumption compared to no alcohol on fibrosis stage of patients with NAFLD.
Methods: Online search of PubMed, Cochrane Library, and EBSCO led to five relevant articles. Critical appraisal was done to assess validity, importance, and applicability using the Centre of Evidence Based Medicine questionnaire.
Results: Yamada et al found that hepatocellular ballooning score and fibrosis score were significantly lower in patients consuming moderate alcohol compared to no alcohol. Hagstrom et al found that fibrosis stage was lower in patients consuming moderate alcohol (OR 0.23, 95% CI 0.08–0.66, p = 0.006) compared to no alcohol. Ajmera et al found no significant difference in fibrosis stage between patients consuming moderate alcohol and no alcohol. Mitchell et al found that moderate alcohol consumption was associated with improvement in advanced fibrosis (OR 0.33, CI 95% 0.14–078, p = 0.01). Chang et al found that consuming moderate alcohol was associated with worsening fibrosis markers.
Conclusion: The effect of moderate alcohol consumption on fibrosis stage of patients with NAFLD is still debatable.

Abstract #1928

Reliability of ultrasound attenuation parameter using fibrotouch and its correlation with body mass index

C. Rinaldi A. Lesmana[1,2], Levina S. Pakasi[2], L. A. Lesmana[1,2]

Department of Internal Medicine, Hepatobiliary Division, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Digestive Disease and GI Oncology Center, Medistra Hospital, Jakarta, Indonesia

Background: A new generation of transient elastography (TE) with two-dimensional image integration guiding system and higher frequency than previous TE has been recently introduced, which simultaneously calculates liver stiffness and ultrasound attenuation parameter (UAP). The reliability of the algorithm used in the device has not been largely studied, especially in obese people.
Objective: To evaluate the reliability of UAP and its correlation with body mass index (BMI).
Method: This was a cross-sectional study between October 2018 and September 2019 in Medistra Hospital, Jakarta. Subjects were adult patients who need liver stiffness assessment (Fibro Touch®, Wuxi Hisky Medical Technology Co. Ltd., Wuxi, China). The grading of fatty liver based on UAP was: none (UAP < 345 dB/m), mild (UAP 245–264 dB/m), moderate (UAP 265–294 dB/m), and severe (UAP $\geq$ 295 dB/m). Ten valid measurements are required for reliable results, with a success rate > 60% and an interquartile range/median (IQR/M) of $\leq$ 30%. The Asian criteria for BMI were applied: underweight (< 18.5 kg/m^2), normal (18.5–22.9 kg/m^2), overweight (23.0–24.9 kg/m^2), obese class I (25.0–29.9 kg/m^2), and obese class II ($\geq$ 30 kg/m^2). Kappa statistic (κ) was calculated for agreement between UAP and conventional ultrasonography in patients who had abdominal ultrasonogram. Mean differences for ordinal data were tested using one-way ANOVA.
Results: Three hundred patients were enrolled consecutively during the study period; 161 (53.7%) among them were men. Patients' mean age was 47.2 $\pm$ 13.73 years old. The overall success rate was 99.85% and the overall IQR/M for UAP were 5.358%. Fatty liver was none in 100 (33.3%), mild in 44 (14.7%), moderate in 65 (21.7%), and severe in 91 (30.3%) subjects. Median UAP was increased with higher BMI, i.e. 212.2 dB/m (underweight) vs. 236.8 dB/m (normal) vs. 258.5 (overweight) vs. 280.5 dB/m (obese class I) vs. 321.2 dB/m (obese class II); $p < 0.001$. Conversely, the IQR/M were significantly lower in subjects with higher BMI: 8.43% (underweight), 7.14% (normal), 5.05% (overweight), 4.64% (obese class I), 3.11% (obese class II); $p < 0.001$. There was a strong positive correlation between BMI and

UAP (r = 0.701; r^2 = 0.491; $p < 0.001$). There were 159 patients who had abdominal ultrasound results. UAP and ultrasound showed a moderate agreement (κ = 0.576).
Conclusion: The overall success rate and reliability of UAP measurement using Fibro Touch is very high. The reliability is significantly higher in obese than non-obese subjects. The UAP and BMI showed significant association; however, its agreement with conventional ultrasonography is only moderate.

Abstract #1930

Clinical use of fibro touch to assess hepatic steatosis and fibrosis simultaneously in adult obese patients and their associations with the non-alcoholic fatty liver disease scoring system: a preliminary study

C. Rinaldi A. Lesmana,[1,2] Ayu Diandra Sari, [3,4] Levina S. Pakasi,[2] Rina Agustina,[3,4] L. A. Lesmana[1,2]

[1]Department of Internal Medicine, Hepatobiliary Division, Faculty of Medicine, Universitas Indonesia-Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Digestive Disease and GI Oncology Center, Medistra Hospital, Jakarta, Indonesia, [3]Department of Nutrition, Faculty of Medicine, Universitas Indonesia-Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia, [4]Human Nutrition Research Center, Indonesian Medical Education and Research Institute, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

Background: A new generation of transient elastography (TE) with high frequency has been recently introduced, which simultaneously calculates fat attenuation parameter (FAP) and liver stiffness measurement (LSM). Previously, we have developed and validated a scoring system to detect non-alcoholic fatty liver disease (NAFLD) in adult population non-invasively with good diagnostic performance. There is no study yet to evaluate simultaneous hepatic steatosis and fibrosis with scoring system in adult obese people.
Objective: To evaluate hepatic steatosis and fibrosis using new generation TE and their association with NAFLD scoring system in adult, and obese people.
Method: This was a community-based, cross-sectional study among adults with body mass index (BMI) > 25 kg/m^2 between June and December 2018 in Jakarta who were part in a larger study in the Human Nutrition Research Center (HNRC), the Indonesian Medical Education and Research Institute (IMERI), Faculty of Medicine, Universitas Indonesia. Eligible subjects were invited to undergo liver ultrasound and LSM (Fibro Touch®, Wuxi Hisky Medical Technology Co. Ltd., Wuxi, China) in Medistra Hospital, Jakarta. Diagnosis of fatty liver is established if FAP $\geq$ 240 dB/m whereas significant fibrosis (F2) was defined if LSM was $\geq$ 7.3 kPa. The NAFLD scoring system consisted of six risk factors, i.e. BMI > 25 kg/m^2, male sex, age > 35 years, triglycerides > 150 mg/dL, high density lipoprotein cholesterol levels of < 40 mg/dL for men or < 50 mg/dL for women, and alanine aminotransferase (ALT) levels > 35 U/L. Based on the total score, the probability of fatty liver presence was then calculated and expressed as percentage.
Results: Forty-three subjects whom agreed to join the measurement consisted of 28 (65.1%) women and 15 (34.9%) men. All subjects showed fatty liver on ultrasound; 14 (32.6%) subjects were diagnosed with mild fatty liver; 9 (20.9%) subjects with moderate fatty liver; and 20 (46.5%) subjects with severe fatty liver based on the FAP criteria. Significant hepatic fibrosis was found in 19 (44.2%) subjects, consisted of 18 (41.9%) subjects with F2 and 1 (2.3%) subject with F4. Both FAP and LSM were significantly higher in subjects with high NAFLD probability. FAP has a moderate correlation with NAFLD probability (Spearman's *rho* = 0.501; p = 0.001) and ALT level (*rho* = 0.503; p = 0.001) and a weak correlation with BMI, waist circumference, and visceral fat. LSM only had a weak correlation with NAFLD probability, visceral fat, and ALT level.
Conclusion: Both FAP and LSM showed significant association with NAFLD probability derived from a validated NAFLD scoring system. This new generation TE could potentially be used routinely to evaluate hepatic steatosis and fibrosis simultaneously in adult obese patients.

Abstract #1975

Intragastric balloon for managing weight loss in non-alcoholic steatohepatitis (NASH) patient—systematic review

Hanifa, Rachmadianti Sukma, Khairunissa, Seruni Tyas, Nuromah, Siti, [4]Afiff, Raysha, Sulaiman, Andri Sanityoso

Hepatobiliary Division, Internal Medicine Department, Faculty of Medicine, Universitas Indonesia, Indonesia.

Introduction: NASH is one of the health problems that continue to rise in obese patients. There is no definitive treatment for NASH other than weight loss and exercise. Bariatric surgery has shown its capability to improve weight loss, but not all NASH patients are suitable for that. Thus, intragastric balloon can be an alternative option.
Objectives: This study aimed to evaluate the role of intragastric balloon in managing weight loss for NASH patient
Methods: An electronical literature search was conducted through Pubmed and Cochrane. Study inclusion criteria were the following: $\geq$ 1 NASH patient having BMI $\geq$ 27 kg/m^2 and undergoing IGB placement. The primary outcome for this study was weight loss, while the ad ditional outcome was the histological improvement after 6 months of IGB placement.
Result: 1 case report and 1 RCT study were identified. Weight loss as much as 39.2% (181 pounds to 110 pounds) was found after 6 months of IGB treatment. Furthermore, it was also found that IGB significantly induced BMI loss from 30.3 $\pm$ 5.7 kg/m^2 to 28.7 $\pm$ 8.1 kg/m^2 ($P < 0.05$) after 6 months of placement. When it compared to the control group, the median of BMI loss among patients receiving IGB for 6 months are higher (1.52 vs 0.8; $P < 0.01$ respectively). However, the mean of ALT and AST levels in the end of the treatment were not significantly improved both in control and IGB groups.
Conclusion: Intragastric balloon can be a potential alternative treatment for managing weight loss for NASH patient with obesity

Abstract #1997

Essential phospholipids in the treatment of non-alcoholic fatty liver disease associated with type 2 diabetes or obesity: a systematic review and network meta-analysis.

Dajani AI[1] and Popovic Branko[2]

[1]ADSC, Sharjah, United Arab Emirates, [2]Sanofi-Aventis Deutschland GmbH, CHC Global Medical Affairs, Industriepark Höchst, 65926 Frankfurt am Main, Germany.

Introduction: Non-alcoholic fatty liver disease (NAFLD) has a global prevalence of 25.24%. This prevalence is markedly higher in individuals with type 2 diabetes mellitus (T2DM), obesity, or hyperlipidemia. Even though there are currently few pharmacological interventions, essential phospholipids (EPLs) have been used for the treatment of liver diseases, including NAFLD.

Objectives: To systematically review the evidence on the efficacy of EPLs in the treatment of NAFLD in patients with obesity or T2DM, and to conduct meta-analyses on the efficacy of EPLs.
Methods: Search strategy: A systematic search for clinical trials in which patients with NAFLD and T2DM or obesity received treatment with EPLs (alone or in combination with antidiabetic therapy) was performed.
Endpoints: Levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol, triglycerides, disease response (based on ultrasonography) and disease severity.

Statistical methods: Direct-, indirect- and cohort-meta-analysis were performed.
Results: EPLs were associated with a significant reduction in ALT in all three analyses, a significant reduction of AST in the cohort analysis, a significant reduction in triglycerides level in the direct and indirect meta-analyses, a significant reduction of cholesterol in the direct meta-analysis and improved disease response as measured by ultrasonography improvement of liver steatosis in the direct meta-analysis and cohort analysis.
Conclusion: The current analyses provide evidence for a benefit of EPLs in NAFLD patients with T2DM and obesity. Therefore, EPLs warrant further investigation in large-scale studies with a long duration of follow-up.

Abstract #1998

Heme oxygenase-1 alleviated non-alcoholic fatty liver disease via suppressing ros—dependent endoplasmic reticulum stress

Li Dongdong[1,2], Zhao Dandan[1,2], Dong Shiming[1,2], Du Jinghua[1,2], Du Huijuan[1,2], Yuan Xiwei[1,2,] Zaid[1,2], Nan Yuemin[1,2]

[1]Department of Traditional and Western Medical Hepatology, Third Hospital of Hebei Medical University, 050051 Shijiazhuang, China, [2]Director of Hebei Provincial Key Laboratory of liver fibrosis in chronic liver diseases

Background/Aims: As non-alcoholic fatty liver disease (NAFLD) develop, endoplasmic reticulum (ER) stress plays a crucial role in hepatic modulation of imbalanced oxidative stress, apoptosis. Our previous study found that heme oxygenase-1 (HO-1) could anti-oxidative and ameliorate hepatic apoptosis and inflammation in NAFLD. This study aimed to clarify the mechanism of HO-1 in regulation of ER stress through NAFLD animal and cell models.
Methods: To induce NAFLD models, the male wild-type (WT) C57BL/6 J mice at 8 weeks were fed with methionine and choline deficient diet (MCD) for 4 weeks or high fat-high carbohydrate-high cholesterol diet (HFD) for 16 weeks (6–7 mice per group). HO-1 chemical inducer (hemin) or HO-1 chemical inhibitor zinc protoporphyrin IX (ZnPP-IX) was administered to mice fed with MCD, respectively. Liver biopsies, Oil Red O and blood biochemistry were applied to evaluate hepatic steatosis. Furthermore, pex-DNA-HO-1 plasmid and HO-1 sh-RNA were transfected to human LO-2 hepatocytes. The changes of endoplasmic ultrastructural and structure were assessed by TEM and confocal microscopy. Hepatic HO-1, ER stress marker and related apoptosis factors were detected via qRT-PCR and Western blotting, IHC. Meanwhile, hepatic reactive oxygen species (ROS) and LO-2 cells apoptosis were measured by flow cytometry.
Results: We found that hepatic HO-1 and ROS contents were dramatically increased in fatty liver tissues inducing by MCD or HFD (Fig. 1 M). Similarly, ER stress markers including phosphor-inositol-requiring enzyme-1 (p-IRE1), protein kinase R-like ER kinase (PERK), activating transcription factor 6 (ATF6), glucose-regulated protein 78 (GRP78) (Fig 2C and D), and apoptotic factors such as CCAAT/enhancer—binding protein homologous protein (CHOP), cysteinyl aspartate specific proteinase 12 (caspase12) were significantly increased, meanwhile, B-cell lymphoma 2 (BCL2) was remarkably decreased (Fig 3B). On the contrary, ER stress markers and related apoptotic proteins, the hepatic steatosis and necrosis were significantly ameliorated by hemin administration on MCD diet-fed mice. Under TEM, swelled and broken rough endoplasmic reticulum were presented in fatty liver tissues (Fig 2A). Overexpression of HO-1 in LO-2 cells could downgrade of ROS contents, the expression of ERS markers (GRP78, p-IRE1, PERK, ATF6) and apoptotic genes (CHOP, Caspase12). However, these showed opposite results in sh-HO-1 LO-2 cells. Confocal microscope analysis also revealed that the integrity of endoplasmic reticulum was much deteriorated in sh-HO-1 LO-2 cells compared to the control (Fig 3A, C, D).
Conclusions: HO-1, which suppress hepatocyte excessive ER stress, is a protective regulatory factor in the progression of nutritional steatohepatitis. It is certified that HO-1 might be a potential serum biomarker for the selective, diagnosis and personalized therapy of nutritional steatohepatitis.

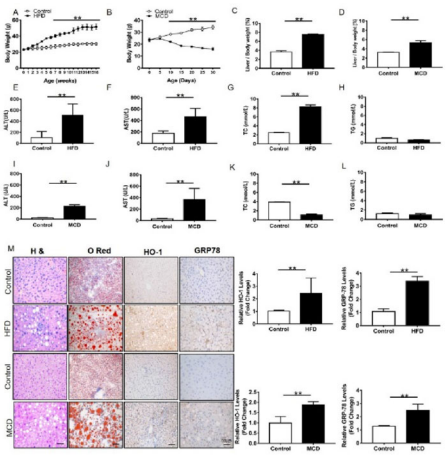


Fig. 1 Feeding HFD or MCD induced HO-1 and ER Stress in mice

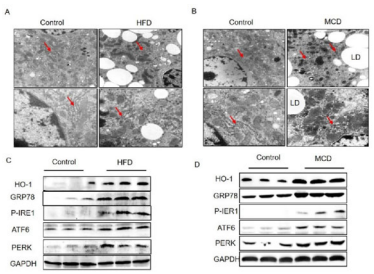


Fig.2 Feeding HFD or MCD induced HO-1 and ER Stress in nutritional steatohepatitis in mice

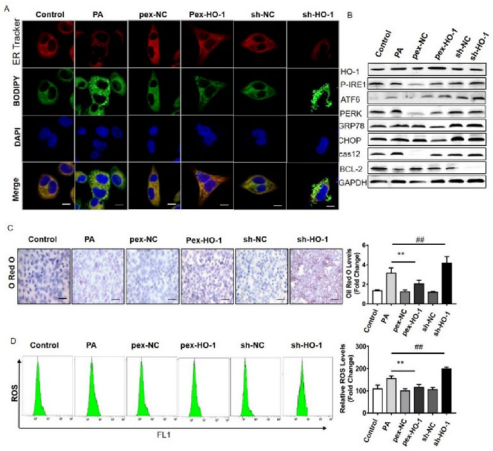


Fig.3 HO-1 attenuate ER stress via alleviating ROS in hepatocytes

Abstract #2005

The clinical value of BTG model in the progression of non-alcoholic fatty liver disease

Yiqi Wang, Xiwei Yuan, Dongdong Li, Yuhui Tang, Ningning Xue, Yuemin Nan

Department of Traditional and Western Medical Hepatology, Third Hospital of Hebei Medical University, Director of Hebei Provincial Key Laboratory of liver fibrosis in chronic liver diseases, Shijiazhuang 050051, China

Objective: To investigate the clinical value of Body mass index, Triglycerides and Golgi glycoprotein 73 (BTG) model in the diagnosis of the progression of nonalcoholic fatty liver disease (NAFLD).
Methods: A total of 335 patients who selected from the Physical examination center and the Department of Traditional and Western Medical Hepatology of Third Hospital of Hebei Medical University from June 2017 to December 2017. A combination of ultrasound and liver elastography were used to screen NAFLD patients, and the healthy population of 117 cases was included as the control group (HC). The peripheral blood cell counts and liver biochemical tests of the included subjects were collected simultaneously, and blood samples were collected. Plasma GP73 level was detected by ELISA, and TG GLU series was detected by Olympus AU2700 automatic biochemical analysis. Synchronization into the object of study of general information collection peripheral blood cell count and liver biochemical tests were performed. SPSS 21.0 statistical software was used for statistical analysis, the binary Logistic regression model was used to calculate the diagnostic model of non-alcoholic fatty liver disease, and the significant indicators of NAFLD were selected by step by step regression method, and the prediction probability was calculated according to the formula($0 < P<1$):$P = 1/1 + e^{-(a+b1x1+b2x2+b3x3+\ldots+bnxn)}$ (a stands for a constant, b stands for the non-normalized coefficient, and stands for the predictive index). The receiver operating characteristic curve (ROC) was used to evaluate the diagnostic efficacy of BTG model for nonalcoholic fatty liver disease (NAFLD).
Results: A total of 335 patients with NAFLD were included, including 191 males and 144 females. The healthy control group included 117 cases, including 37 males and 80 females. The observation group was divided into non-metabolic syndrome (N-MetS) group (185 cases) and metabolic syndrome (MetS) group (150 cases) according to the clinical characteristics and liver biochemical results. Body mass index (BMI), serum triglyceride (TG), and plasma golgi glycoprotein 73 (GP73) increased successively with the onset of NAFLD, and the non-metabolic syndrome group of the healthy control group increased successively with the metabolic syndrome group, with statistical differences among the groups ($P < 0.05$). The ROC curve of NAFLD diagnosis model established on the basis of these three factors showed that the area under the curve (AUC) was 0.971, and the sensitivity and specificity were up to 88.7% and 94.0%, respectively.
Conclusion: BTG model can effectively evaluate the risk of NAFLD and is expected to be a new diagnostic model for NAFLD.

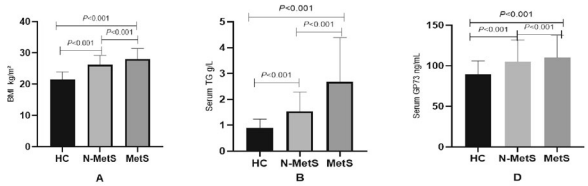


Figure 1: The levels of BMI、TG、GP73 in different patient populations.

Table 1 : Evaluation of the diagnostic value of the new model in patients with NAFLD

Variable	Nagelkerke R^2	Cut-off value	AUC	Se，%	Sp，%	*P*	OR 95% CI	
							Lower	Upper
RM	0.799	0.747	0.974	0.901	0.940	0.000	0.962	0.986
GRM/BTG model	0.790	0.744	0.971	0.887	0.940	0.000	0.958	0.985
TGRM[ab]	0.686	0.770	0.944	0.860	0.889	0.000	0.921	0.966

Abstract #2068

Correlation between liver stiffness measurement and FIB-4 or APRI for the assessment of liver fibrosis in Prof. R.D. Kandou Hospital patients with nonalcoholic fatty liver disease

Irawaty A[1], Waleleng B J[2], Tendean N[2], Gosal F[2], Rotty L[2], Winarta J[2], Waleleng A[2]

[1]Department of Internal Medicine, Faculty of Medicine Sam Ratulangi University, Manado, Indonesia, [2]Division of Gastroentero-Hepatology, Department of Internal Medicine, Faculty of Medicine Sam Ratulangi University/Prof. Dr. R.D.Kandou Hospital, Manado, Indonesia

Introduction: Nonalcoholic fatty liver disease (NAFLD) is being increasingly recognized as a cause of chronic liver disease. Noninvasive assessment of liver fibrosis is of great value for therapeutic decision making in patients with NAFLD.
Objective: To assess liver stiffness measurement (LSM) using transient elastography (FibroScan, Echosens, Paris) and to correlate the results to Fibrosis-4 (FIB-4) and AST platelet ratio Index (APRI) scores.
Method: A cross-sectional study was conducted on NAFLD patients who underwent FibroScan examination between October 2018 and October 2019. Demographic data was collected, including sex, age, serum alanine aminotransferase level, serum aspartate aminotransferase level and platelet counts. Fibrosis stages were defined according to LSM categories for NAFLD in kiloPascal (kPa).
Results: A total of 79 cases were retrieved during the study period; 43 (54.4%) of them were men. Patients' mean age was 49.2 ± 12.6 years. The mean liver stiffness score was 9.1 ± 7.9 kPa. There was a significant positive correlation with Spearman test, between Fibroscan results and APRI scores ($p < 0.005$) and FIB-4 ($p < 0.005$)
Conclusion: FIB-4 and APRI score can predict liver stiffness in fibrosis liver of NAFLD.

Abstract #2086

Impact of low-carbohydrate diet compared to low-fat diet on hepatic fat content in patients with non-alcoholic fatty liver disease

Irsan Hasan[1], Primasari Deaningtyas[1]

Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Lifestyle modification, including diet, is the cornerstone of non-alcoholic fatty liver disease (NAFLD) management. Low-carbohydrate diet (LCD) and low-fat diet (LFD) are both associated with weight loss which have a favorable effect on reducing hepatic fat content (HFC)
Objectives: This study compares hepatic fat content in NAFLD patients receiving LCD compared to LFD.
Methods: Online search of PubMed, EBSCO, and Scopus databases led to two articles (one meta-analysis and one randomized controlled trials). The selection of articles is based on inclusion and exclusion criteria. Inclusion criteria were articles published within the last 5 years, written in English, and involving adult human subjects. Animal and pediatric studies, review articles, and case reports were excluded. HFC was measured with magnetic resonance imaging or computed tomography.
Results: Gepner et al reported that LCD significantly decrease HFC after 18 months compared to LFD ($4.2 \pm 7.1\%$ vs $3.8 \pm 6.7\%$, $p = 0.036$). Decrease of HFC after 6 months was not significant between the two diets ($7.3 \pm 9.2\%$ vs $5.8 \pm 7.2\%$, $p = 0.079$). Ahn et al reviewed 11 clinical studies in their meta-analysis. 6 studies evaluating HFC showed no significant difference in HFC between the two diets (mean difference 1.39 [-0.25, 3.02], $p = 0.10$, $I^2 = 91\%$. Weight loss and decrease of HFC were observed in both diets.
Conclusion: Evidence to recommend LCD over LFD in patients with NAFLD is still lacking. Both diets can be recommended for NAFLD patients as both are associated with a decrease in HFC and weight loss. Additional investigations should be conducted.

Abstract #2089

Prevalence and risk factors of non-alcoholic fatty liver disease among adults in an urban Indonesian population

Irsan Hasan[1], Monica Raharjo[1], Gita Aprilicia[1], Andri Sanityoso Sulaiman[1], Cosmas Rinaldi A Lesmana[1], Juferdy Kurniawan[1], Chyntia Olivia Maurine Jasirwan[1], Kemal Fariz Kalista[1], Saut Horas Hatoguan Nababan[1], Rino Alvani Gani[1]

Hepatobiliary Division, Department of Internal Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: The prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing in Asia due to urbanization which sets the stage for sedentary lifestyle and overnutrition. Few studies have documented the prevalence of NALFD in Indonesia.
Objectives: The aim of this study is to estimate the prevalence and risk factors of NAFLD in an urban Indonesian population.
Methods: A cross-sectional study was conducted in a single medical check-up center located in Jakarta, an urban area of Indonesia, between January to December 2018. Demographic data were collected followed by laboratory testing and abdominal ultrasound. Multivariate logistic regression analysis was performed to identify risk factors of NAFLD.
Results: 1300 adults, aged 21–62 years old (median 35 years) and predominantly male (83.4%), were included in this study. NAFLD was diagnosed by abdominal ultrasound in 52.5% of study participants. Age, body mass index, waist circumference, transaminases, fasting blood glucose, total cholesterol, triglyceride, and uric acid were significantly higher in adults with NAFLD compared to without NAFLD. Multivariate analysis showed that diabetes, hypertriglyceridemia, hyperuricemia, obesity, and central obesity were significantly associated with NAFLD ($p = 0.000$). Adults with diabetes, hypertriglyceridemia, hyperuricemia, obesity, and central obesity are at risk for developing NAFLD with odds ratio of 4.57 (95% CI 2.234–9.352), 2.484 (95% CI 1.880–3.283), 2.032 (95% CI 1.562–2.643), 3.401 (95% CI 2.394–4.833), and 1.932 (95% CI 1.398–2.670) respectively.
Conclusion: Around half of the adult population in Jakarta is affected by NAFLD. Individuals with diabetes, hypertriglyceridemia, hyperuricemia, obesity, and central obesity are at greater risk for developing NAFLD.

Abstract #2095

Association between hyperuricemia and non-alcoholic fatty liver disease among adults in an urban Indonesian population

Monica Raharjo[1], Mutiara Lirendra[1], Irsan Hasan[1]

Hepatobiliary Division, Department of Internal Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Serum uric acid (SUA) is a metabolic parameter considered to play a role in non-alcoholic fatty liver disease (NAFLD). Hyperuricemia was reported to be associated with higher prevalence of NAFLD and was found to be an independent risk factor of significant fibrosis in NAFLD. Few studies have documented the association of hyperuricemia and NAFLD in Indonesia.
Objectives: This study aims to study the association of hyperuricemia and NAFLD in an urban Indonesian population.
Methods: A cross-sectional study was conducted in a single medical check-up center in Jakarta between January to December 2018. Subjects with heavy alcohol consumption were excluded. Demographic data were collected followed by laboratory testing and abdominal ultrasound. Hyperuricemia was defined as SUA > 6.8 mg/dl. Bivariate analysis was performed in all subjects. Multivariate analysis was performed in subjects with hyperuricemia.
Results: 1300 adults, aged 21–62 years old and predominantly male (83.4%), participated in this study. 565 subjects (43.5%) had hyperuricemia. NAFLD was diagnosed by abdominal ultrasound in 359 subjects (63.5%) with hyperuricemia. NAFLD subjects with hyperuricemia had significantly older age along with higher BMI, waist circumference, transaminases, fasting blood glucose, and triglyceride. Bivariate analysis of all subjects showed that hyperuricemia was significantly associated with NAFLD (odds ratio [OR] 3.22 95% CI 2.56–4.05, $p = 0.000$). Multivariate analysis showed that hypertriglyceridemia and obesity were associated with NAFLD in subjects with hyperuricemia (OR 1.87 95% CI 1.28–2.75, $p = 0.001$ and 5.15 95% CI 2.82–9.38, $p = 0.000$ respectively).
Conclusion: Hyperuricemia is associated with NAFLD in an urban Indonesian adult population.

Abstract #2110

Correlation between an elevated serum uric acid and non-alcoholic fatty liver disease: a meta-analysis

Effendi, GB[1], Simanihuruk, V[1], Pramesthi, DE[1], Widodo B[2]

[1]Faculty of Medicine, Universitas Airlangga, Surabaya-Indonesia, [2]Gastroenterology and Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya-Indonesia

Introduction: Non-alcoholic fatty liver disease (NAFLD) is the most common hepatic disease in the world. Globally, the prevalence of NAFLD increase from 15% in 2005 to 25% in 2010. The incidence of NAFLD is commonly associated with metabolic syndrome which often has an elevated serum uric acid. However, the correlation between hyperuricemia and NAFLD is still controversial. Thus, a meta-analysis was carried out to evaluate the correlation between those two.
Objective: To evaluate the correlation between hyperuricemia and the incidence of NAFLD.
Method: A meta-analysis was conducted using RevMan 5.3 software to identify studies regarding correlation between hyperuricemia and NAFLD by a search on PubMed, EMBASE, and Cochrane Library, analyzing the odd ratios (OR) with 95% confidence intervals (95% CIs) using a random-effects model.
Result: Twenty-two studies involving 296.814 subjects were included. Our pooled analysis showed that subjects with hyperuricemia had an increased risk of NAFLD compared those without hyperuricemia (OR = 1.88; 95% CI 1.74–2.04, $p < 0.00001$). Subgroup analyses were done based on study design and gender. Increased risk of NAFLD was significantly associated with hyperuricemia in both men (OR = 1.61; 95% CI 1.44–1.80, $p < 0.00001$) and women (OR = 2.16; 95% CI 1.93–2.42, $p < 0.00001$).
Conclusion: Hyperuricemia is associated with an increased risk of NAFLD.

Abstract #2115

SGLT-2 Inhibitor for improving hepatic fibrosis and steatosis in patients with non-alcoholic fatty liver disease and type 2 diabetes mellitus: a systematic review

Michael Dwinata[1], David Dwi Putera[2], Irsan Hasan[3], Monica Raharjo[3]

[1]Department of Internal Medicine, Depati Hamzah General Hospital, Pangkalpinang, Indonesia, [2]Faculty of Medicine, Public Health and Nursing, Gadjah Mada University, Yogyakarta, Indonesia, [3]Hepatobiliary Division, Department of Internal Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia.

Introduction: Until present, there is no approved pharmacotherapy for patients with Non-Alcoholic Fatty Liver Disease (NAFLD). Recent animal studies showed sodium-glucose co-transporter-2 inhibitors (SGLT2i) can delay the progress of NAFLD.
Objectives: To evaluate the efficacy of SGLT2i to improve hepatic fibrosis and steatosis in NAFLD patients with type 2 diabetes mellitus (T2DM)
Methods: We searched studies in journal databases (CENTRAL, MEDLINE, and EMBASE) from November 2019 to January 2020. We included trials involving patients with NAFLD and T2DM aged $\geq$ 18 years old comparing efficacy of SGLT2i and other antidiabetic drugs in improving fibrosis and steatosis; irrespective of publication status, year of publication, and language.
Results: Five RCTs were included. One study reported significant improvements in controlled attenuation parameter 314.6 $\pm$ 61.0 dB/m to 290.3 $\pm$ 72.7 dB/m ($p = 0.04$) in SGLT2i group compared to control ($p = 0.04$), measured by transient elastography. In patients with significant fibrosis, dapagliflozin treatment significantly decreased liver stiffness measurement from 14.7 $\pm$ 5.7 kPa at baseline to 11.0 $\pm$ 7.3 kPa after 24 weeks ($p = 0.02$). One study reported a significant decrease in liver fat content 16.2%-11.3% ($p < 0.001$) in SGLT2i group compared to control ($p < 0.001$). Three studies reported change in liver-to-spleen ratio in SGLT2i group compared to control 0.96 (0.86–1.07) to 1.07 (0.98–1.14), $p < 0.01$; 0.80 $\pm$ 0.24 to 1.00 $\pm$ 0.18, $p < 0.001$; and 0.91 (0.64–1.04) to 1.03 (0.80–1.20), $p < 0.001$ respectively). All studies reported significant decrease in alanine aminotransferase with SGLT2i.
Conclusion: SGLT2i significantly improves alanine aminotransferase in NAFLD patients with T2DM. Further studies are needed to confirm the impact of SGLT2i to hepatic fibrosis and steatosis.

Abstract #2176

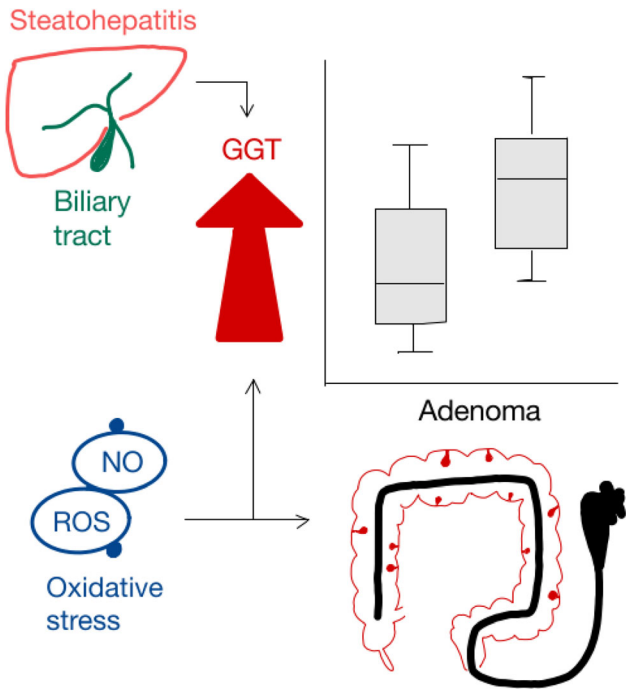
Relationship between serum gamma-glutamyl transferase level and colorectal adenoma

Tzu-Chan Hong, M.D. [1], Hung-Chih Yang, M.D., Ph.D.[1,2], Chi-Ling Chen, Ph.D.[2], Jia-Horng Kao, M.D., Ph.D.[1,2], Chun-Jen Liu, M.D., Ph.D[1,2], Ming-Jen Chen, M.D., M.S.[3], Horng-Yuan Wang, M.D., Ph.D.[3], Yang-Che Kuo, M.D., Ph.D.[3,4], Lo-Yip Yu, M.D., Ph.D.[3,4], Kuang-Chun Hu, M.D., Ph.D.[3,4],

[1]Department of Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei 10051, Taiwan, [2]Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei 10048, Taiwan, [3]Division of Gastroenterology, Department of Internal Medicine, MacKay Memorial Hospital, Taipei 10449, Taiwan, [4]Health Evaluation Center, MacKay Memorial Hospital, Taipei 10449, Taiwan

Introduction: Cost-effective serology tests may increase the predictive accuracy of colonoscopy for colorectal cancer screening. Reportedly, gamma-glutamyl transferase (GGT) is associated with oxidative stress and carcinogenesis and has been found to be elevated in the serum of cancer patients and colorectal adenoma tissue.
Objectives: We aimed to investigate the association between serum GGT levels and colorectal adenoma.
Methods: This single-center, health examination-based cohort enrolled 4669 subjects from 2006 to 2015. Baseline characteristics, laboratory data, bidirectional gastrointestinal endoscopy, and transabdominal ultrasonography were used to evaluate the severity of fatty liver.
Results: We found an elevated median GGT level in subjects with tubular adenoma compared with those without (23 IU/L and 20 IU/L, $p < 0.001$). A GGT cutoff of $\geq$ 20 IU/L reached a maximal Youden index in receiver operating curve (ROC) analyses. Subsequent regression analyses showed an odds ratio of 1.46 (95% CI 1.17–1.82, $p < 0.001$) for age, body mass index, diabetes diagnosis, total cholesterol, triglycerides, low-density lipoprotein cholesterol, and positive Helicobacter pylori urease test, all being associated with an increased incidence of colon adenoma. Subgroup analysis showed that the odds ratio (OR 1.27, 95% CI 1.15–1.68, $p < 0.001$) is only significant and highest in patients with a negative or mild fatty liver and an ALT level of $\leq$ 40 IU/L.

Conclusion: The results suggested a positive correlation of GGT with colon adenoma incidence and a predictive value with a cutoff point of > 20 IU/L, which is within the normal range. The effect may be most prominent for those without steatohepatitis.



Abstract #2219

Association between non-alcoholic fatty liver disease and diabetic retinopathy in diabetic patients: a systematic review and meta-analyses of cross-sectional studies

Fanny Budiman[1], Ignatius Ivan[1], Rivaldi Ruby[1]

[1]School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia

Introduction: The link between Non-Alcoholic Fatty Liver Disease (NAFLD) and diabetic retinopathy in diabetes mellitus (DM) patients still possessed variable results. Our aim is to elucidate the association between NAFLD and diabetic retinopathy in patients having DM.
Methods: This systematic review was based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We searched Pubmed, EBSCOhost, and ProQuest for articles published in English from 2000 to 2020. Titles and abstracts extracted were reviewed for relevance. Quality of study was evaluated using Newcastle-Ottawa Scale (NOS) determining quality of selection, comparability and outcome.
Results: Search strategy identified 60 studies. Six relevant full-text articles met our inclusion criteria with adequate reporting qualities and NOS scale of 8–9. Our meta analysis using fixed-effect failed to show significant association between NAFLD and diabetic retinopathy (OR, 1.16; 95% CI 0.94–1.43; p = 0.16, I^2 = 77%; p = 0.0002). Meanwhile, random-effect also showed an insignificant association (OR, 1.23; 95% CI 0.77–1.98; p = 0.39, I^2 = 77%; p = 0.0002). Results showed a high statistical heterogeneity and imbalance weight between study. Thus, results from random-effect may be more appropriate.
Conclusion: Our findings showed an insignificant association between NAFLD and diabetic retinopathy in patients having DM. Due to limited studies available and high heterogeneity, current evidence still lacking and thus further studies with larger sample size need to be conducted.

Abstract #2220

Association between non-alcoholic fatty liver disease and diabetic nephropathy in diabetic patients: a systematic review and meta-analyses of cross-sectional studies

Fanny Budiman[1], Ignatius Ivan[1], Rivaldi Ruby[1]

[1]School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia

Introduction: The link between Non-Alcoholic Fatty Liver Disease (NAFLD) and diabetic nephropathy in diabetes mellitus (DM) patients is still uncertain. Our aim is to elucidate the association between NAFLD and diabetic nephropathy in patients having DM.
Methods: This systematic review was based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We searched Pubmed, EBSCOhost, and ProQuest for articles published in English from 2000 to 2020. Titles and abstracts extracted were reviewed for relevance. Quality of study was evaluated using Newcastle-Ottawa Scale (NOS) determining quality of selection, comparability and outcome.
Results : Search strategy identified 76 studies. Four relevant full-text articles met our inclusion criteria with adequate reporting qualities and NOS scale of 8–9. Our meta-analysis using fixed-effect failed to show significant association between NAFLD and diabetic nephropathy (OR, 1.00; 95% CI 0.95–1.05; p = 0.93, I^2 = 75%; p = 0.007). Meanwhile, random-effect also showed an insignificant association (OR, 0.86; 95% CI 0.54–1.36; p = 0.51, I^2 = 75%; p = 0.007). Results showed a high statistical heterogeneity and imbalance weight between study. Thus, results from random-effect may be more appropriate.
Conclusion: Our findings showed an insignificant association between NAFLD and diabetic nephropathy in patients having DM. Due to limited studies available and high heterogeneity, current evidence still lacking and thus further studies with larger sample size need to be conducted.

Drug Induced Liver Injury

Oral Presentations

Abstract #741

Prognostic factors to predict abnormal liver function with severe cutaneous adverse reactions: a retrospective analysis from a medical center

Bo-Huan Chen, MD[1], Ching-Chung, MD[3], Pin-Cheng Chen, MD[1], Chien-Hao Huang, MD, Ph.D. [1,2], Sen-Yung Hiseh, MD, Ph.D. [1,2], Wen-Hung Chung, MD, Ph.D.[4]

[1]Division of Hepatology, Department of Gastroenterology and Hepatology, Chang-Gung Memorial Hospital, Linkou Medical Center, Taiwan, [2]Chang-Gung University, College of Medicine, Taiwan, [3]Department of Internal Medicine, Chang-Gung Memorial Hospital, Linkou Medical Center, Taiwan, [4]Department of Dermatology, Chang-Gung Memorial Hospital, Linkou Medical Center, Taiwan

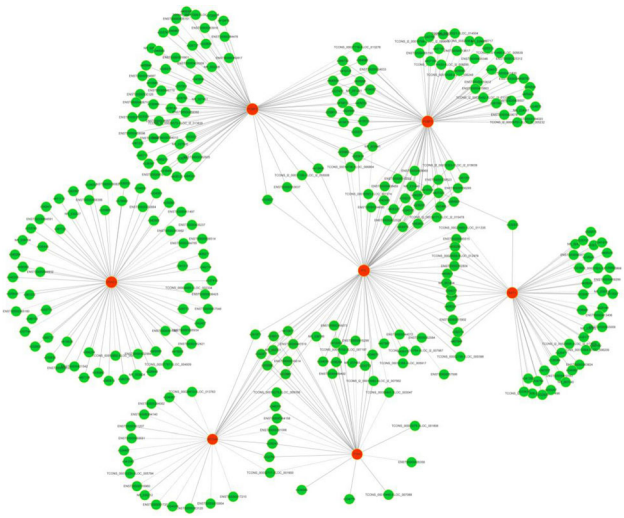
Background: Drug induced liver injury (DILI) is important that is responsible for the most frequency cause of acute liver failure (ALF). Unfortunately, the diagnosis of drug-induced is particularly challenging. However, the most organ involved by adverse drug reaction is not liver but skin and mucous membranes. During the past decade, major advance has been made in the accurate diagnosis of severe cutaneous adverse reactions (SCARs) to drug. In addition, there's a group of SCARS patient with abnormal liver function. Since they might belong to one kind of DILI, we try to investigate the risk factor and prognostic factor for these patients
Methods: This is a retrospective cohort study between Oct 1999 and Jan 2018, a total of 1093 patients diagnosed with SCARs at the Linkou Chang Gung Memorial Hospital were enrolled. Patients were divided into two groups: one is the abnormal group (defined as the values of alanine amoinotransferase (ALT) > 2X upper limits of normal range (ULNs), and another is the normal ALT group. (the values of ALT within normal range). Clinical features and pathologic information were also collected to analyze prognostic factors. Specific clinical parameters were used to predict abnormal liver function by univariable and multivariable logistic regression analysis.
Results: A total 254 patients in abnormal ALT group and 590 patients in normal ALT group entered the final analysis (249 patients had excluded due to data). Median ALT was 262 in abnormal ALT group and 28 in normal ALT group. Patients in abnormal cohort significantly differed from comparison group in median age (57 vs. 64, p = 0.006), drug exposure days (17 days vs. 6 days, P = 0.035). Creatine > 1.2 mg/dL (21% vs. 13%, P < 0.001). Eosinophil > 10% (24.7% vs. 14.4%, P < 0.001). Some implicated agents were significantly different between two group including antibiotic (50.2% vs. 57.1%, p = 0.013), NSAID (18.4% vs. 15.3%, p = 0.017) but not other such as proton pump inhibitor: 8.2%% vs. 7.1%, p = 0.571, anti-tuberculosis agent: 7.8% vs. 10.2%, P = 0.076, and Chinese herbs: 15.7% vs. 16.7%, p = 0.981. In univariable analysis, significant predicter to abnormal liver function were age < 60 years (p = 0.003), drug exposure days more than 10 days (p < 0.001), Creatine greater than 1.2 mg/dL (p = 0.002), Eosinophil > 10% (p < 0.001). Antibiotic agent (p = 0.003), NSAID agent (p = 0.001). In multivariate analysis using binary logistic regression model, significant factors predicting abnormal liver function are drug exposure days (95% CI 2.26–11.38, p < 0.001) and eosinophil > 10% (95% CI 10.45–24.6, p < 0.001)
Conclusion: In this retrospective study, we reported abnormal liver function of 23.2% among patients with severe cutaneous adverse reactions. Significant prognostic factors to predicting were drug exposure days and eosinophil > 10%.

Abstract #1496

Ferroptosis-related regulatory protein NCOA4 and its lncRNA-mRNA co-expression network in patients with anti-tuberculosis drug-induced liver injury

Jun Chen

Background: The pathogenesis of anti-TB related DILI is not very clear. In this study, we aimed to investigate important signaling pathways and construct profile of lncRNA-mRNA co-expression network to further understand the pathogenesis.
Method: Totally 16 patients with anti-TB related DILI and 16 patients without DILI (as control) were enrolled in this study. Total serum RNA was collected, Affymetrix Human Transcriptome Array and the Metascape platform was applied to analysis of differentially expressed mRNAs, and gene interaction matrix was constructed based on Pearson correlation coefficient. Total RNA was extracted from serum, and the selected important genes were verified by RT–PCR.
Results: Contrast to control group, there were 568 deferentially expressed coding genes. KEGG enrichment on significantly different mRNAs highlighted the ferroptosis involving in anti-TB DILI that presenting as one of the top 20 signaling pathways, which referred to FTH1 (Log FC = 2.05), FTL (Log FC = 2.94), NCOA4 (Log FC = 1.65), PCBP1 (LogFC = 2.5), PCBP2 (Log FC = 2.32) and SAT1 (Log FC = 1.97). Co-expression analysis of mRNAs and ncRNAs showed that NCOA4, which was closely related to FTH1 (correlation P = 0.97) probably involved in the process of anti-TB DILI. In addition, the network suggested that FTH1P3 (Log FC = 1.27) contemporary connecting to FTH1, FTL and NCOA4 (p = 0.97, 0.97 and 0.96, respectively) (Figure 1). Furthermore, RT-PCR results confirmed both expression of NCOA4 and FTH1P3 were significantly higher in patients with DILI than no DILI patients (p < 0.05).
Conclusion: NCOA4 acting as a selective cargo receptor for autophagic turnover of ferritin (ferritinophagy) and FTH1P3, have a co-expression relationship with NCOA4 may play an important role in anti-TB DILI, worthy to be further studied.



Abstract #2103

Hepatoprotective effect of *Tylophora villosa Blume* leaves extract on aspartate aminotransferase and alanine aminotransferase blood concentrations of sprague-dawley rat models induced by rifampicin and isoniazid

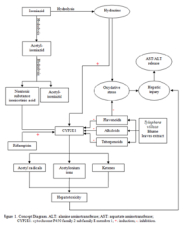
Khazmi, Sara Yulus[1], Ruyani, Aceng[2], Putri, Sylvia Rianissa[3]

[1]Undergraduate Program in Medicine, Faculty of Medicine and Health Sciences, University of Bengkulu, Bengkulu, Indonesia, [2]Department of Biology, Faculty of Teacher Training and Education, University of Bengkulu, Bengkulu, Indonesia, [3]Department of Biochemistry and Molecular Biology, Faculty of Medicine and Health Sciences, University of Bengkulu, Bengkulu, Indonesia.

Introduction: The use of isoniazid may cause hepatotoxicity effects due to Cytochrome P450 Family 2 Subfamily E Member 1 (CYP2E1) oxidative reactions. Meanwhile, rifampicin can increase the production of isoniazid toxic metabolites which can cause liver cell damage. Secondary metabolites of *Tylophora villosa* Blume leaves extract, such as flavonoids, alkaloids, and triterpenoids can inhibit CYP2E1 activity and may provide hepatoprotective effect.
Objectives: This research was conducted to study the effects of *Tylophora villosa* Blume leaves extract on serum aspartate

aminotransferase (AST) and alanine aminotransferase (ALT) concentrations of rats exposed to rifampicin and isoniazid.
Methods: This study was a post test only control group experimental study, involving 25 Sprague-Dawley rats that were divided into 5 groups. Two groups were receiving different extract dosages (0.077 and 0.154 mg/g body weight). Following 21 days of treatment, blood were collected to measure AST and ALT concentrations. Data were analyzed using one way ANOVA followed by Tukey HSD test.
Results: Statistically, there were significant differences in AST and ALT concentrations between group with $p < 0.001$ for both markers. Post hoc test showed that concentrations of AST in 2 groups receiving leaves extracts are comparable to healthy rats group. Moreover, AST concentrations in 0.154 mg/g body weight group were significantly different from control group. The same group also showed similar pattern in ALT concentrations.
Conclusion: The administration of *Tylophora villosa* Blume leaves extract with dosage of 0.154 mg/g body weight alleviated AST and ALT levels comparable to healthy rats group.

Patient	A	B	C
Age	51	44	52
Gender	Female	Female	Male



Poster Presentations

Abstract #236

Use of steroids in drug induced liver injury: a case series from Singapore

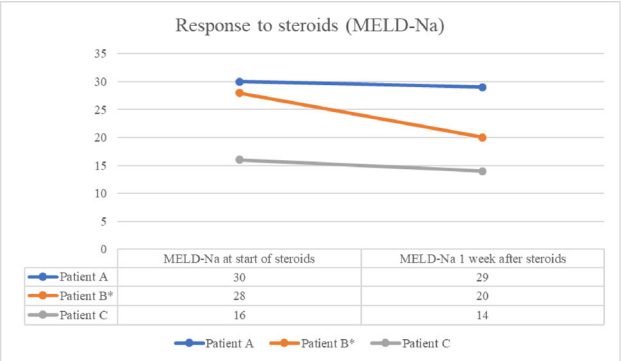
Tan Bernice[1], Lee YM[1]

[1]Division of Gastroenterology and Hepatology, National University Hospital, Singapore

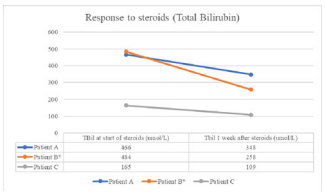
Introduction: Drug-induced liver injury (DILI) is a leading cause of liver failure worldwide. However, there is still no fixed consensus on management apart from holding off the inciting drug. The hepatologist often has to decide on the utility of anecdotal treatment such as steroid therapy. Current data does not support the use of steroids in DILI.
Objectives: This case series aims to review existing literature on current management strategies and ascertain the indications for steroid use in DILI.
Methods: This is a retrospective review of electronic case records of three cases of DILI from a tertiary liver transplant centre in Singapore (2019).
Results: Mean MELD-Na at presentation was 26.3. All three patients received oral prednisolone. Patient A had the highest peak MELD-Na of 33. Histology showed submassive hepatic necrosis and interface hepatitis, and she underwent plasma exchange before her eventual demise. Patient B had positive autoimmune serologies, extensive hepatic necrosis and interface hepatitis, and underwent plasma exchange before eventually undergoing liver transplant. Patient B was managed as DILI-induced autoimmune hepatitis (AIH) and hence, will remain on long-term steroids. Patient C had lobular necroinflammation and mild-moderate periportal inflammation; he has since fully recovered and stopped steroids with no adverse events.
Conclusion: The use of steroids in DILI may be considered in cases with autoimmune features, or when histology shows interface and lobular hepatitis. However, the risks may outweigh potential benefits in patients with severe liver injury, i.e. MELD-Na > 30. Large-scale prospective studies are needed before formal recommendations can be made.

Inciting drug	TCM (mixture)	Herbal slimming tea (Garcinia Cambogia)	Male performance supplements (Horny Goat Weed Extract)
Total bilirubin at presentation (umol/L)	549	419	299
ALT at presentation (U/L)	493	1038	1969
MELD-Na at presentation	33	28	18
Peak MELD-Na	33	29	24
Serology **- Anti-nuclear Ab** **- Immunoglobulin G** **- Anti smooth muscle Ab**	 Negative 11.98 Not done	 **Positive** **25.5** **33**	 Negative 10 13
Liver histology	Submassive hepatic necrosis; Interface hepatitis with lymphoplasmacytic predominance; Cholestasis	Extensive multilobular necrosis and collapse; Lymphoplasmacytic infiltrate; Tortuous interlobular bile ducts	Marked cholestatic lobular necroinflammation with perivenular confluent necrosis; Mild to moderate periportal inflammation (only few plasma cells)
Use of plasma exchange	Yes	Yes	No
Use of steroids	Yes	Yes	Yes
Outcome	Demised	Liver transplant	Recovered

Patient B: MELD-Na was calculated 5 days post-steroids as patient underwent liver transplant that day.



Graph2: Response to steroids (MELD-Na). For



Graph 3: Response to steroids (Bilirubin). For Patient B: Bilirubin value was taken at 5 days post-steroids as patient underwent liver transplant that day.

Abstract #460

Anti-nuclear antibody, CD8/CD4 ratio and the granulomatous change could be biomarkers for liver damage induced by anti-PD-1 orPD-L1 treatment

Yasuteru Kondo[1,2], Ryo Fukuda[1,2], Junichi Akahira[3], Mareyuki Endoh[3], Yukihiro Toi[4], Shunichi Sugawara[4], Yasuhito Tanaka[5]

[1]Department of Hepatology, Sendai Kousei Hospital, Sendai city, Miyagi, Japan, [2]Treatment Center for Liver Cancer, Sendai Kousei Hospital, Sendai city, Miyagi, Japan, [3]Department of Pathology, Sendai Kousei Hospital, Sendai city, Miyagi, Japan, [4]Department of Pulmonary Medicine, Sendai Kousei Hospital, Sendai city, Miyagi, Japan, [5]Virology & Liver unit, Nagoya City University Graduate School of Medical Sciences, Nagoya City, Japan.

Introduction: The Department of Respiratory Medicine in our institute has reported various kinds of immune-related adverse events (irAEs) in advanced non-small cell lung cancers patients treated with anti-PD-1 (JAMA oncology 2018). However, the detailed characteristics of liver damage induce by treatment with anti-PD-1 and PD-L1 have not been clear yet.
Objectives: The aim of this study is to identify useful biomarkers and the histological characteristics of liver inflammation induced by anti-PD-1 and anti-PD-L1.
Methods: Permission for the study was obtained from the ethics committee at our institute. The medical record analysis retrospectively evaluated 182 advanced non-small cell lung cancer patients who received nivolumab, pembrolizumab or atezolizumab monotherapy at our institute in Japan between January 2016 and April 2018. Immune staining with CD3, CD4, CD8, CD20 and CD138 antibodies was carried out.
Results: The frequency of ANA positive patients among nivolumab treated patients with liver damage was significantly higher than in those without liver damage (53.8% vs 23.9%, $p = 0.003$). Moreover, the ratio of CD4/CD8 in the inflamed liver induced by iCI was significantly lower than that in the inflamed liver induced by typical AIH and DILI. Granulomatous change, especially large granulomatous change with necrosis was significantly increased in patients with ICIs patients compared with DILI and AIH patients ($p < 0.05$).
Conclusion: ANA could be a useful biomarker to identify patients at high risk for liver damage induced by nivolumab. Moreover, the dominance of CD8 positive T cells and granulomatous change in the inflamed liver might be important characteristics of liver damaged by iCIs.

Abstract #1092

Incidence of drug induced liver injury due to category one anti-tuberculosis drug and the relationship of drug induced liver injury with the decline in the activity of glutathione S-transferase

Samuel M Lukas[1], Djumhana Ali[2], Bestari Begawan[2], Abdurachman A Siti[2]

[1]GastroenteroHepatology Division, Internal Medicine, Maranatha Christian University/Immanuel Hospital, [2]GastroenteroHepatology Division, Internal Medicine, Padjadjaran University/Hasan Sadikin General Hospital

Introduction: One of the side effects of anti-TB drugs is drug-induced liver injury (DILI). There is an increased risk of hepatotoxicity associated with decreased activity of Glutathione-S-transferase (GST) enzyme and glutathione levels in serum.
Objective: This purpose of this study is to determine the decrease in the activity of serum Glutathione-S-transferase in patients who experience DILI due to the use of anti-TB drugs, the incidence of DILI, and when does the incidence occur.
Methods: This is a prospective cohort study with research subjects comprising of new TB patients who will receive anti-TB drugs in Inpatient and Outpatient Installation of Department/SMF of Internal Medicine RSUP Dr. Hasan Sadikin and RS Immanuel, Bandung. The study was conducted from October 2013 to July 2014.
Results: There were 197 research subjects comprising of a larger male to female proportion and the median age was 36 (15–91) years. The most prevalent nutritional status, either by measuring the BMI or albumin level, is the normoweight proportion. A total of 20 research subjects experienced DILI (10.15%). The activity of GST enzyme in this group changed significantly between before and after the administration of anti-TB drugs ($p = 0.01$). A total of 14 people (70%) experienced drug induced liver injury at week 2, 3 people (15%) at week4, 1people (5%) at week 6, and 2 people (10%) at week 8. The result of survival analysis shows that the average estimate of the incidence of DILI is at week 3.1 with a 95% confidence level between 2.2 to 4.
Conclusion: This research shows that there is a significant decrease in the GST enzyme activity between before and after the use of anti-tuberculosis drugs in the group of research subjects that experienced DILI. The incidence of DILI is 10.15% with the highest incidence found on the 2nd week after the use of anti-tuberculosis drugs.
Keywords: anti-tuberculosis drugs, drug-induced liver injury, Glutathione-S transferase

Abstract #1196

Complementary and alternative medicine use in adults with liver disease: A single center experience from south India

Kumar P, Rao P N, Rani U, Vennela, Rao S

[1]Department of hepatology, Asian Institute of gastroenterology hospitals, Hyderabad, India, [2]Department of pharmacy practice, Bhaskar pharmacy college, Hyderabad, India.

Introduction: Use of complementary and alternative medicine (CAM) is not well characterized among Indian patients with liver diseases. We did a hospital-based patient interview survey about usage of CAM.
Methods: We interviewed adult patients attending OPD with a CAM questionnaire. It contained 50 questions about the patient demography, etiology, and severity of the liver disease, CAM-related questions like source, type, administration, and effect on disease status.
Results: Of the 300 adults with liver disease, 46% (n = 140) reported using of CAM during an interview after the onset of illness. The most common etiology was chronic hepatitis B in 39% followed by alcohol-related liver disease in 27%, chronic hepatitis C in 13%, fatty liver in 11% and Unconjugated hyperbilirubinemia in 11%. The most common modality was Homeopathy (37%) followed by herbal medicine (30%), Ayurveda (28.5%) and naturopathy in 4%. The physical characteristics include tablet (43%), Liquid (25%), Herbal (18%), and powder in 13.5% of patients. The vehicle for consumption was water in 58.5%, Milk in 8% and without a vehicle in 38.5% of patients. 37.1% of patients took CAM in fasting, 29% without fasting, and 35% took before and after fasting. Complete symptomatic improvement reported in 15%, partial recovery in 14%, no recovery in 50% and worsening of symptoms reported in 21%.
Conclusions: CAM use, particularly Homeopathy, Herbal medicine, and Ayurveda, is prevalent among Indian adults with liver disease. Many patients do not disclose their use to health care providers, despite some using potentially hepatotoxic substances.

Abstract #1252

Hepatoprotective activity of pineapple (*Ananas comosus*) juice on paracetamol-induced rats

Eva Pravitasari Nefertiti[1,2], Troef Soemarno[1,2], Iswan A Nusi[2], Poernomo Boedi Setiawan[2], Herry Purbayu[2], Titong Sugihartono[2], Ummi Maimunah[2], Ulfa Kholili[2], Budi Widodo[2], Husin Thamrin[2], Amie Vidyani[2], IGM Sanies Ermawan[3]

[1]Faculty of Medicine, Hang Tuah University, Surabaya, East Java, Indonesia. [2]Division of Gastroentero-Hepatology, Department on Internal Medicine, Faculty of Medicine, Airlangga University, Soetomo Hospital, Surabaya, East Java, Indonesia.[3]Mataram Hospital, Mataram, West Nusa Tenggara, Indonesia

Introduction: Pineapple fruit (*Ananas comosus*) were collected from West Nusa Tenggara, Indonesia, can inhibit the activity of cytochrome 2E1 (CYP2EI). Paracetamol is a nonsteroidal antiinflammatory drug (NSAID) used largely for a acute treatment of pain and it undergoes hydrolysis in the liver via an enzymatic reaction with CYP2EI, resulting in the formation of hepatotoxic compounds.
Objectives: Extracts of ethanol and water from pineapple fruit can decrease damage of liver cells in rats. The aim of this study was to evaluate the hepatoprotective activity of pineapple juice in Paracetamol-induced rats.
Methods: Rats were divided into four groups. The normal group (Group 1) was treated with water. The negative group (Group 2) was induced with Paracetamol, the postive group (Group 3) wastreated with silymarin and the test group (Group 4) was treated with pineapple juice. The treatment for all groups were administered orally for 8 weeks. Levels of hepatocyte damage were determinated using morphologi histopathology method. Data were analyzed using the one-way analysis of variance test with a 95% confidence inter4val.
Results: Based on the data analysis, pineapple juice exhibited hepatoprotective activity, as it decreased the hepatocyte damage levels.
Conclusions: Pineapple juice, protective the rats hepatocytes by inhibiting the hepatocytes damaged

Abstract #1334

The prevalence of oxaliplatin induced portal hypertension in colorectal cancer patients who were treated with oxaliplatin based therapy

Katsumi Terashita

Background: Oxaliplatin is one of the key chemotherapeutic drugs for patients with colorectal cancer. During oxaliplatin-based chemotherapy, portal hypertension as adverse events of oxaliplatin, is sometimes observed. However, it has been not clarified well how Oxaliplatin affect portal hypertension and the risk factors regarding incidence of portal hypertension in patients with colon cancer who are treated with oxaliplatin-based chemotherapy. In this retrospective single center study, we aimed to evaluate the effect of oxaliplatin-based chemotherapy on portal hypertension.
Methods: In this study, we screened the patients who had colorectal cancer and been conducted radical surgery between 2008 April and 2018 March in JCHO Hokushin hospital. Patients were included if they had adjuvant chemotherapy for 6 months after surgery. Included patients were divided in two groups according to chemotherapy regimen; Oxaliplatin included regimen (XELOX and FOLFOX) or non-Oxaliplatin included regimen (S-1 and Capecitabin) and were evaluated the occurrence of portal hypertension and the risk.
Results: Overall, a total of 50 patients who met the inclusion criteria were include in this study. Of 50 patients, 33 patients are males and 17 patients were females. The Oxaliplatin group are 36 patients, and Non-Oxaliplatin are 14 patients. In Oxaliplatin-base therapy group alone, PLT count significantly decreased after treatment, and APRI and fib-4 index significantly increased after treatment. Additionally, in Oxaliplatin-base therapy group alone, development of esophagus varix (n = 4) and its rupture (n = 1).
Conclusions: Oxaliplatin-based chemotherapy cause portal hypertension

Abstract #1372

Unusual case of acute liver dysfunction associated with drug-induced rhabdomyolysis and acute kidney injury: a case report

Fatwiadi Apulita Ginting Munte[1], Deka Larasati[2], Eny Ambarwati[3], Ruswhandi[4]

[1]Department of Cardiology and Vascular Medicine, National Cardiovascular Center Harapan Kita, Jakarta, Indonesia, [2]Division of Gastroenterology and Hepatobiliary Disease, Internal Medicine Department, Gatot Soebroto Central Army Hospital, Jakarta, Indonesia, [3]Division of Nephrology and Hypertension, Internal Medicine Department, Gatot Soebroto Central Army Hospital, Jakarta, Indonesia, [4]Division of Gastroenterology and Hepatobiliary Disease, Head of Internal Medicine Department, Gatot Soebroto Central Army Hospital, Jakarta, Indonesia

Introduction: Rhabdomyolysis is an uncommon clinical condition caused by injury to skeletal muscle and involves the release of potentially toxic intracellular contents into the circulation. The presence of liver damage in patients with rhabdomyolysis has not been well recognized.
Objective: To present a case report.
Methods: A 31-year-old man admitted with right upper abdominal pain, generalized jaundice and nausea since 4 days ago. He also complained general weakness with a paralysis episode at home, muscle ache and dark-colored urine. He had medical history of heart failure due to valvular heart disease since 6 months ago and took bisoprolol, furosemide, spironolactone, digoxin, clopidogrel, acetylsalicylic acid and alprazolam as medication. He denied any rigorous exercise, fever or exposure to extreme heat. At admission, his vital sign was unremarkable. His physical examination showed generalized jaundice, distended abdomen and shifting dullness. There was tenderness in right upper and epigastric region of abdomen. Other clinical findings included jugular vein distention, systolic murmur, and mild leg edema. Laboratory test revealed AST 11160U/L, ALT 4270U/L, total bilirubin 7.99 mg/dL, direct bilirubin 4.04 mg/dL, BUN 107 mg/dl, creatinine 4.5 mg/dL, INR 1.82, CPK 566U/L with normal troponin I. There was no sign of myocardial infarct or ischemia on ECG. Abdominal ultrasound scan showed ascites with hepatic congestion and dilated hepatic vein. During hospitalization, his kidney function was deteriorating with an anuric period, so we decided to hemodialyse the patient. We found that AST, ALT and bilirubin concentrations decreased in concert with BUN, creatinine and CPK concentrations normalization.
Results: When interpreting liver function tests in rhabdomyolysis, we needs to consider that AST is also released from damaged muscle, whereas elevation of ALT to the degree seen in this case is rarely occurred in rhabdomyolysis. In this patient, liver function normalized with hemodialysis and after all possible culprit medicine had been stopped. This, as well as classical clinical triad and the absence of other identifiable causes of liver dysfunction, gave us further confidence in the diagnosis.
Conclusion: Acute reversible liver dysfunction could be rare manifestation of rhabdomyolysis.

Abstract #1681

Unusual case of severe herbs-induced systemic manifestations

Sargsyants Narina

Elit-Med Medical Center, Yerevan, Armenia

Introduction: The last few decades have seen a rise in the use of herbal supplements, natural products, and traditional medicines. These herbal medicines are associated with complications such as liver damage with a high incidence of mortalities and morbidities.
Case report: Patient 52 years old, female, with diabetes mellitus, obesity, NAFLD, psoriasis. Liver enzymes in normal range, Fibromax result in December 2016-F0/A0/S3/N2/H0. From April 2017 complains on diarrhea, abdominal cramps, nausea. Patient exclude any drugs administration, besides antidiabetic and antihypertensive. Primary diagnosis: acute enteric infection?Pancreatitis? Abdomen US-mild thickness of distal ileum. During following month worsening of complains (painful numerous aphtha's in oral cavity and perianal region, profuse diarrhea, abdominal pains, weight loss) and laboratory parameters (ALT 100U/l, AST 82U/l, GGT 180U/l, FERR 288.85, Fibrinogen 612 mg/dL, CPR 10.9 mg/dL, RBC 3.13, Hb 103 g/L, ESR 86 mm/h) aggravate Cronh's disease. Evaluations continuing: Clostridium Difficile toxin A + B, Helminth ova and larvae/Protozoa cysts and oocysts, Giardia a/g in faeces negative; Fecal Calprotectin 2000 μg/g and Lactoferrin positive. In May 2017 performed capsule endoscopy (total transit 8 h 29 m): erosive antral gastritis, duodenitis, terminal ileitis, total colitis. Short-term corticosteroids improve condition. After 3 months, all symptoms repeated with Fecal Calprotectin 529 μg/g and patient finally noticed unknown composition Chinese herbs intake for psoriasis treatment, which was withdrawn with subsequent short-term improvement in physical and laboratorial parameters without relapse.
Conclusion: Herbs self-administration can leads to severe multiorgan systemic manifestations with persistent diarrhea, abdominal pain, aphtous stomatitis and perianal erosions, hepatitis, weight loss.

Abstract #1731

A case report with toxic hepatitis due to Didrogosterone

Elif Yorulmaz[1], Mehmet Emin Gundogdu[2], Zehra Sucuoglu[2], Emre Yuce[2], Emircan Erecan[2]

Bağcılar Education and Research Hospital, Department of Gastroenterology, Istanbul, Turkey. Bagcılar Education and Research Hospital, Department of Internal Diseases, Istanbul, Turkey

Introduction: Didrogesterone is a progesterone-derived drug used in some gynecological diseases and rarely causes cholestasis table. In this paper, a case having mixed type of cholestasis due to didrogesterone use is submitted.
Case descriptions: 32-year-old female patient admitted to the hospital due to fatigue, dizziness, and jaundice complaints for 1 week. A week ago, didrogesterone tablet treatment was started due to menstrual irregularity. In her physical examination, sclera and skin were icteric. In the laboratory examination; Hb: 9.7 mg/dl, WBC: 13000 mm^3, PLT: 123000 mm^3, ALT: 614 U/L, AST: 1029 U/L, GGT: 64 U/L, ALP: 100 U/L, Total bilirubin: 16.6 mg/dl, Direct bilirubin: 14.5 mg/dl, INR: 2.0, AFP: 420 ng/ml were found. Viral hepatitis and autoimmune markers were negative detected. Seruloplasmin, 24-hr urinary copper, and Alpha-1 antitrypsin level were normal. Transabdominal ultrasonography was assessed as normal. In abdominal MRI, increase in the wall thickness of the gall bladder and free fluid between the perihepatic, perisplenic, and bowel loops were observed. Since the biochemical tests did not regress during the follow-ups, 1 mg/kg/day prednisolone treatment was started. In the control on the third month after the treatment, the values were detected as AST: 27 U/L, ALT: 28 U/L, GGT: 52 U/L, ALP: 51 U/L, T.Bil: 1.2 mg/dl, D.Bil: 1.0 mg/dl, INR: 1.2, AFP: 3.4 ng/ml. Imaging methods were evaluated as normal at the control and prednisolone treatment was reduced and discontinued.
Discussion: Drug-induced liver toxicity is a clinical picture that can last from weeks to months. As in the case presented in this paper, prednisolone treatment can be used in drug-induced jaundice prolonged due to the progesterone-derived drugs.

Abstract #1973

Evaluation of MELD score in acute liver failure patients with drug-induced injury

Hong Zhao, Qi Wang, Ting Zhang, Yan Bin Wang, Jie Yan, Ying Fan, Jingjing Wang, Cheng Cheng, Rui Ding, Ying Cao, Wen Xie

Background: We aimed to evaluate the value of MELD (model for end-stage liver disease) score in acute liver failure patients with DILI.
Methods: A single-center, retrospective, cross-sectional study was conducted. We collected data from 970 patients with DILI hospitalized at Beijing Ditan Hospital from January 1, 2012 to December 31, 2014, includes laboratory data at initial and during disease progression.
Results: 124 of 970 cases of drug-induced liver injury progressed to acute or subacute liver failure, with a rate of 12.78%. Multivariate logistic regression analysis showed that high levels of TBIL, high levels of INR, and low levels of ALB were independent risk factors for the development of liver failure. MELD score was used to assess the risk of liver failure. It was calculated using the DILI recognition, highest level of bilirubin, and highest level of INR, respectively. The MELD score calculated at highest level of bilirubin had the highest predictive value for liver failure, with sensitivity: 64.4%, specificity: 91.8%, area under the curve: 0.846, 95% CI (0.784, 0.908).
Conclusions: The MELD score has a high assessment value for drug-induced liver failure. MELD score calculated at the highest bilirubin was the most sensitive and specific to predict liver failure.

Complications of Liver Cirrhosis

Oral Presentations

Abstract #40

Disparities in cirrhosis complications and mortality in migrant communities in australia: competing risk analysis

Belaynew W Taye[1,2], Paul J Clark[1,3,4], Gunter Hartel[2], Elizabeth E Powell [4], Katharine Irvine[1], Patricia C. Valery [1,2]

[1]University of Queensland, Brisbane, QLD, Australia, [2]QIMR Berghofer Medical Research Institute, Herston, QLD, Australia, [3]Department of Gastroenterology and Hepatology, Mater Hospitals, Brisbane, QLD, Australia, [4]Department of Gastroenterology and Hepatology, Princess Alexandra Hospital, Brisbane, QLD, Australia

Background & Aims: Chronic liver disease disproportionately affects migrant communities in Australia. In this cohort study, we examined the etiology, complications, and mortality from cirrhosis

and non-cirrhosis causes in migrants from Africa, Middle East or Asia regions and compared with other Australians.
Methods: Hospital data on cirrhosis admissions for 11,377 patients from 2008 to 2017 in Queensland were obtained. Cumulative incidence function curves were used present the probability of death due to cirrhosis and non-cirrhosis causes. We used the Fine-Gray competing-risk regression to identify predictors for cirrhosis and non-cirrhosis deaths.
Results: At ten years, the cumulative incidence of cirrhosis-related (39.2% vs 50.0%, $p < 0.001$) and non-cirrhosis-related (24.8% vs 32.7%, $p < 0.0001$) deaths was significantly different between migrants and Australian-born patients. Independent predictors of cirrhosis-related deaths were country of origin (SHR = 1.39, 95% CI 1.19–1.63), alcohol use (SHR = 1.54, 95% CI 1.43–1.66), ascites (SHR = 1.62, 95% CI 1.49–1.75), acute peritonitis (SHR = 1.31, 95% CI 1.09–1.58), hepatic encephalopathy (SHR = 1.30, 95% CI 1.10–1.54), hepatorenal syndrome (SHR = 2.74, 95% CI 2.26–3.32) and gastrointestinal bleeding (SHR = 1.10, 95% CI 1.02–1.19). Predictors of non-cirrhosis-related deaths were country of birth, insurance status, congestive heart failure, renal disease, cancers, and Charlson Comorbidity Index.
Conclusions: Better survival in migrants may reflect differing etiology of liver disease and other differing rates of socio-economic characteristics, and lower rates of comorbidities, higher rates of complications, and concurrent drug and alcohol use.

Abstract #454

Effect of simplifying protein counting tool and educational intervention on the nutritional status of patient with cirrhosis: a randomized clinical trial

Sankhaanurak A, Thongsawat S, Leerapun A

Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Introduction: Protein-calorie malnutrition (PCM) is common problem in cirrhotic patients, and is associated with an increased morbidity and mortality. Diet plays a key role as a nutritional therapy in chronic liver disease. However, most of cirrhotic patients are not received the adequate nutrition counseling from their physicians and very few patients have access to a registered dietician.
Methods: An open, randomized clinical trial was conducted at GI clinic from November 2018 to November 2019. After a short period of nutrition counseling, participants were randomly assigned to the intervention group who received simplified protein counting tool and the control group. The outcomes were nutritional status: serum albumin, transferrin, CTP score, MELD score, Patient-Generated Subjective Global Assessment score (PG-SGA) and protein counting skill at 3 and 6 months.
Results: A total of 53 patients, 15 (53.6%) of intervention group and 13 (52%) of control group had albumin improvement at 3 months. Protein counting skill archived in 13 (46.4%) in the intervention group compared with 9 (36.0%) in the control group ($P = 0.578$). Among 22 patients (41.5%) who complete protein counting record were statistically significant improvement of albumin ($P < 0.001$), CTP score ($P < 0.001$), MELD score ($P = 0.047$), and PG-SGA ($P = 0.005$) at 3 months. More than 60% of patients in both groups had significant albumin improvement at 6 months compare to baseline.
Conclusion: Simplifying protein counting tool can improve protein counting skill. Nutrition advice may encourage the cirrhotic patient to have adequate protein intake to maintain the good nutritional status.

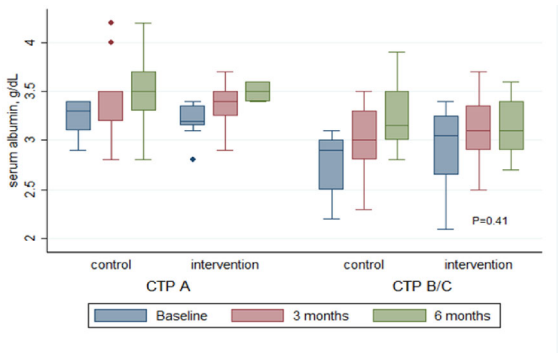


Figure 1. Box plot of serum albumin level by CTP score in control and intervention group.

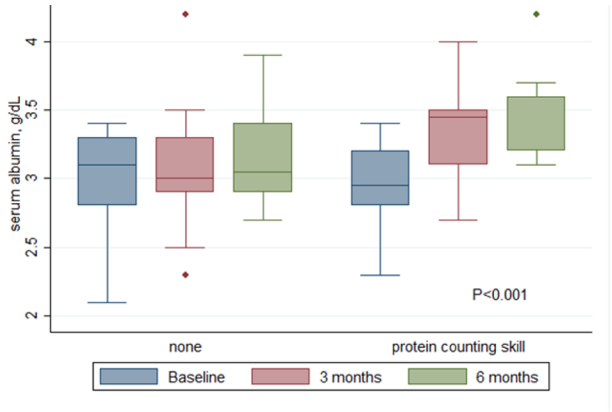


Figure 2. Effect of protein counting skill on serum albumin level.

Abstract #492

Antifibrotic Chinese patent medicine reduce the risk of death in decompensated cirrhosis patients with hepatorenal syndrome

Bingbing Zhu [1,2], Xianbo Wang[1]

[1]Center for Combined TCM and Western Medicine,Beijing Ditan Hospital Affiliated to Capital Medical University, Beijing 100015, China, [2]Department of Gastroenterology, Third Affiliated Hospital of Beijing University of Chinese Medicine, Beijing 100029, China.

Introduction: Antifibrotic Chinese patent medicines have been used for several decades to treat liver cirrhosis, and many studies have found them works well. But there are few studies about these medicines' affection on hepatorenal syndrome (HRS) patients.
Objective: In this study, we are intended to investigate the effect of anti-fibrotic Chinese medicine on the prognosis of decompensated cirrhosis complicated with HRS patients.
Methods: We collected 190 inpatients retrospectively from Beijing Ditan Hospital from August 2008 to August 2016. We classified these patients into treatment group (72, defined as $\geq$ 90 cumulative defined daily doses [cDDD]) and control group (118, defined as $<$ 90 cDDD), the follow-time was 2 years.
Results: There are statistically significant differences in baselines between the two groups, then we used Propensity Score Matching (PSM) method to match the two groups in 1:1 ratio, 65 cases were fuzzily matched, and the median survival time of control group and treatment group were 687 days and 315 days ($p = 0.024$), while the risk of death in the control group was significantly higher than that in

treatment group (76.9% vs. 41.5%, $p < 0.001$). Mortality rates in treatment group with different Child-Turcotte-Pugh (CTP) grades were reduced (CTP-B 75.0% vs. 41.38%, p = 0.0249, CTP-C 93.9% vs. 36.4%, $p < 0.001$)), so did them in patients with different etiology (CHB: 32.3% vs 73.3%, $p < 0.001$, ALD: 33.3% vs. 81.2%, p = 0.0119).

Conclusion: Antifibrotic Chinese patent medicines can reduce the mortality of decompensated cirrhosis patients with HRS and prolong their survival time.

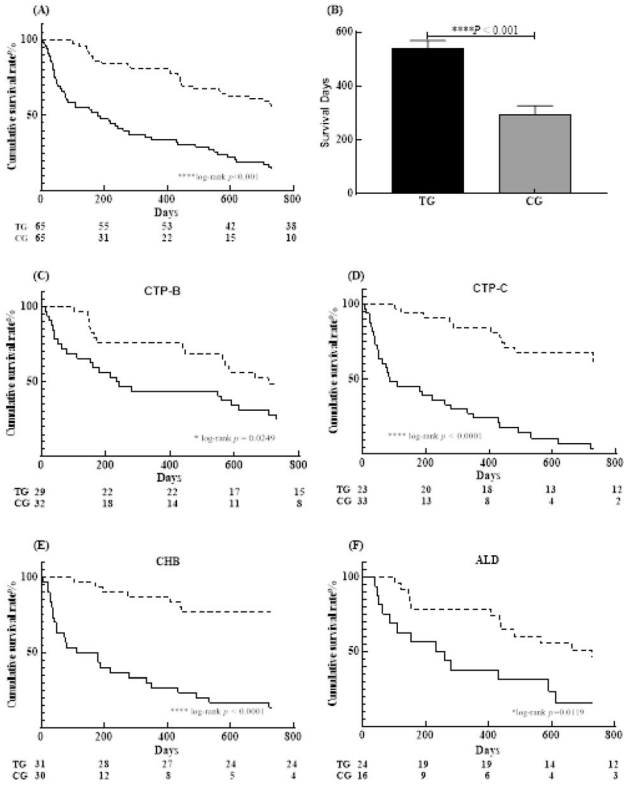


Figure 1 Legend:TG - - - - CG ——
(A) Cumulative survival plot for patients in control group(CG) and treatment group(TG).
(B) Survival days in control group(CG) and treatment group(TG).
(C) (D) Cumulative survival plot for patients with different Child-Turcotte-Pugh grades--CTP-B and CTP-C.
(E) (F) Cumulative survival plot for patients with different etiology--CHB and ALD.
* statistically significant differences between the two groups.

Abstract #586

Clinical profile, etiology, outcome and predictors of outcome in upper gastrointestinal bleed patients presenting to emergency in A Tertiary Care Centre in India

Sachan Anurag[1], Dhibar Deba prasad[2], Bhalla Ashish[3], Sharma Navneet[4], Taneja Sunil[5], Sharma Vishal[6]

[1]Junior Resident, Department of Internal Medicine, PGIMER, Chandigarh, India, [2]Assistant Professor, Department of Internal Medicine, PGIMER, Chandigarh, India, [3]Professor, Department of Internal Medicine, PGIMER, Chandigarh, India, [4]Professor, Department of Internal Medicine, PGIMER, Chandigarh, India, [5]Assistant Professor, Department of Hepatology, PGIMER, Chandigarh, India, [6]Assistant Professor, Department of Gastroenterology, PGIMER, Chandigarh, India

Introduction: Upper Gastrointestinal (UGI) Bleed is a common presentation in any medical emergency and peptic ulcer bleed has been shown to be the major etiology in western literature. Many scores are available for predicting need of intervention and outcome.

Objective: To determine the etiology; outcome in terms of re-bleed, mortality, need for blood transfusion, need for surgery and need for mechanical ventilation; and predictors of these outcome measures.

Methods: A prospective observational study was conducted in a tertiary care institute in India; enrolling 268 UGI bleed subjects. Complete clinical data was recorded and they were followed for 60 days. Glasgow Blatchford score (GBS), Pre-Endoscopy Rockall score (PRS), Complete Rockall score (CRS), AIMS65 and Modified Early Warning Score (MEWS) were calculated for each patient. Area under curve -receiver operating characteristic (AUC-ROC) was calculated for each score and compared.

Results: Out of 268 subjects, UGI endoscopy could be done in 236 patients out of which 150 (63.55%) patients had gastro-esophageal varices. Only 249 patients could be followed upto 60 days. Re-bleed occurred in 15.26%, total mortality was 28.51% with in-hospital mortality as much as 11.24%, blood component transfusion was required in 126 (47%) patients; mechanical ventilation was required in 9.3% of patients and requirement of surgery in only 2 patients. GBS best predicted the need for transfusion (AUC-ROC = 0.678) and in hospital mortality (AUC-ROC = 0.626) whereas AIMS65 was best in predicting re-bleed and overall mortality.

Conclusions: Most common etiology in UGI bleed patients is variceal. AIMS65 is a simple score with a cutoff as 2 is a good predictor of re-bleed, mortality and need for intervention.

Abstract #589

Early use of oral PEG3350 plus lactulose vs. lactulose alone enables early and sustained recovery of overt hepatic encephalopathy in patients with acute on chronic liver failure: an open label randomized controlled trial

Syed Ahmed[1], Madhumita Premkumar[2], Radhakrishna Dhiman[2]; Saurabh Mishra[2]; Rohit Mehtani[2]; Ajay Duseja[2]

[1]Department of Internal Medicine, Post Graduate Institute of Medical Education and Research, Chandigarh, India, [2]Department of Hepatology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Objective: Polyethylene glycol electrolyte solution (PEG-3350) can ensure rapid catharsis of gut which may resolve hepatic encephalopathy (HE) more effectively than lactulose. We compared PEG plus lactulose versus lactulose alone in patients with Acute-on-chronic Liver Failure (ACLF) admitted to hospital with HE$\geq$2 for efficacy and outcome.

Methods: This open label randomized controlled trial enrolled 60 patients with ACLF with HE grades $\geq$2. Participants were randomised to receive PEG (2 litre dose;12 h apart) followed by lactulose (30mlq8h) or standard of care lactulose (30mlq8h) alone. Primary end point was improved HE grade at 24hrs, 48hrs and 1 week determined using HE scoring algorithm (HESA) score and mortality benefit. Secondary outcomes included time to HE resolution and ammonia reduction.

Results: Of 60 patients, 29 patients were randomised to PEG + Lactulose (Arm 1)and 31 patients to Lactulose alone (Arm 20. Seventeen (58.6%) in Arm 1 improved HESA score by 1 point at 24hrs vs. 10 (32.2%) in Arm 2; $P = 0.04$. Time to HE resolution in Arm 1 was 5.76 3.39) days compared to 8.28 (3.73) days in arm 2 ($P = 0.023$). (Figure 1) On univariate analysis, MELD > 26 ($P = 0.000$), AARC score > 10 ($P = 0.001$) ammonia > 148 μmol/L (p = 0.007) predicted 28-daymortality but only AARC score predicted outcome on multivariate analysis. Ammonia level did not

correlate with HE grades at any time point. Adverse events included excessive diarrhoea in Arm 1 needing dose reduction, but no dyselectrolytemia/fluid overload or pain was noted in either arm.
Conclusions: Although PEG resulted in early and sustained, HE resolution, there was no mortality benefit at 28 or 90 days.

Table 1. Results of interventions on the outcome on hepatic encephalopathy in either arms

Variables	All Patients n=60	Arm 1 (Lactulose +PEG) n=29	Arm 2 (SMT) n=31	Significant difference
Baseline HESA score 3 2	 23 37	 09 (31.0%) 20 (68.9%)	 14 (45.16%) 17 (54.84%)	 *P=0.298*
One or more improvement in HESA score at 24 hours, n	27	18 (62.1%)	10 (32.2%)	***P = 0.021****
24-hour HESA score, Mean ± SD	1.91 ± 0.72	1.69 ± 0.71	2.12 ± 0.67	***P = 0.014****
48-hour HESA score, Mean ± SD	1.42 ± 0.75	1.11 ± 0.64	1.70 ± 0.74	***P = 0.001****
24-hour HESA score change, Mean ± SD	0.46 ± 0.29	0.62 ± 0.49	0.47 ± 0.32	***P = 0.037****
48-hour HESA score change, Mean ± SD	0.92 ± 0.62	1.14 ± 0.53	0.73 ± 0.63	***P = 0.012****
Resolution of HE at 48 hours, n	7 (11.6%)	4 (13.78%)	3 (9.68%)	*P=0.702*
Resolution of HE at 1 week, n	23 (42.5%)	17 (65.38%)	6 (21.43%)	***P = 0.002****
Duration for resolution of HE, (days) Mean ± SD	7.07 ± 3.76	5.76 ± 3.39	8.28±3.73	***P = 0.023****

Abstract #869

Fibrosis index predicts subsequent esophageal variceal bleeding in patients with compensated cirrhosis and initial small varices without beta-blocker or band ligation prophylaxis

Sheng-Fu Wang[1], Chien-Hao Huang[1,2,3,4], Yu-tung Huang[4], Yu-Ling Chen[4], Pin-Cheng Chen[1], Bo-Huan Chen[1], Wen-Juei Jeng, MD[1,2], Yi-Chung Hsieh[1,2], Wei Teng[1,2], Yi-Cheng Chen[1,2], Wei-Ting Chen[1,2], Yu-Pin Ho[1,2], Chun-Yen Lin[1,2], I-Shyan Sheen[1,2]

[1]Division of Hepatology, Department of Gastroenterology and Hepatology, Chang-Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan, [2]School of Medicine, College of Medicine, Chang-Gung University, Taoyuan, Taiwan, [3]Graduate Institute of Clinical Medical Sciences, College of Medicine, Chang-Gung University, Taoyuan, Taiwan, [4]Center for Big Data Analytics and Statistics

Aim: To predict subsequent esophageal variceal (EV) bleeding within 1 year and 2 years in compensated liver cirrhotic patients with initial small esophageal varices without beta-blocker prophylasix by non-invasive of markers.
Method: The data source was obtained from the Chang-Gung Research Database (CGRD) after IRB approval. Non-invasive parameters including CTP score, MELD score, MELD-Na score, PALBI score, gamma-glutamyl transpeptidase-to-platelet ratio (GPR), gamma-glutamyl transpeptidase-to-albumin ratio (GAR), AST/ALT, AST to platelet ratio index (APRI), platelet count to spleen diameter (PC/SD), spleen diameter, portal vein size, fibrosis-4-index (FIB-4), fibrosis index (FI), King's Score, Lok score, Lok index, and Forn's index were measured to predict esophageal bleeding within 1 year and 2 years.
Result: The study included 6803 cirrhotic patients with small EV, no red-color sign, who had not used non-selective beta-blocker until event of EV bleeding. 539 patients (7.92%) and 710 patients (10.44%) had esophageal variceal bleeding within in 1 year and 2 years, respectively. By multivariate analysis, the FI and GPR significant predicted EV bleeding within 1 year. In addition, the FI, GPR and age significantly predicted EV bleeding within 2 years. Among them, fibrosis index possessed the best AUROC of 0.630 and 0.623 respectively.
Conclusion: Fibrosis index appears to be an acceptable non-invasive predictor of subsequent EV bleeding in compensated cirrhotic patients with initial small EV without beta-blocker prophylasix, and hence could be served as an initial screening tool for these cirrhotic subgroup patients.

Abstract #926

Assessment of small fiber neuropathy in HCV-related cirrhosis with or without diabetes mellitus: a pilot study in Egyptian patients

El-Sayed Tharwa[1], Mohamed Abdel-Samiee[1], Anwar Mohamed[1], Mohsen Salama[1], Mohamed I. Youssef[2], Mohammed Saied Bakeer[2], Doaa Elwazzan[3], Hosam Aldeen Salah Shabana[2], Mahmoud Abdelrashed Allam[2], Sherief M. Alshazly[4], Elsayed Fathi Ali Hamed[4], Hany Abdelbary Abdelaziz Elbasyouni[5], A. S. Seif[6], Ayman Ahmed Sakr[7], Marwa F. Youssef[8], Sally Waheed Elkhadry[8], Mohammad AbdelElhameed Ahmed Alwaseef[9] and Helmy Elshazly[1].

[1]Department of Hepatology and Gastroenterology, National Liver Institute, Menoufia University, Menoufia, Egypt, [2]Department of Internal Medicine, Al-Azhar University, Cairo, Egypt, [3]Department of Tropical Medicine, Faculty of Medicine, Alexandria University, Alexandria, Egypt, [4]Department of Neurology, Al-Azhar University, Cairo, Egypt, [5]Department of Internal Medicine, Faculty of Medicine, Menoufia University, Menoufia, Egypt, [6]Tropical Medicine Hepatology and Gastroenterology Department, Shebin Elkom Teaching Hospital, Menoufia, Egypt, [7]Department of Tropical Medicine, Faculty of Medicine, Menoufia University, Menoufia, Egypt [8]Epidemiology and Preventive Medicine Department, National Liver Institute, Menoufia University, Menoufia, Egypt, [9]Clinical Pathology department, Al-Azhar University, Cairo, Egypt

Introduction: Hepatitis C Virus (HCV) infection can affect the neurological system and neuropathy is one of these manifestations. HCV infection is associated with diabetes mellitus (DM) type II and diabetic patients are at higher risk of acquiring HCV infection. Sweat function has been proposed to assess early autonomic neuropathy.
Objectives: This study aimed to evaluate small fiber neuropathy in asymptomatic HCV-related cirrhotic patients with or without diabetes mellitus through sweat function assessment.
Methods: Three groups were involved: 47 healthy controls, 48 HCV-related cirrhotic patients without DM (Group 1) and 49 HCV-related cirrhotic patients with DM type II (Group 2). All participants were subjected to liver panel tests, renal function tests, cell blood counts, HbA1c, abdominal ultrasound. Sweat function was assessed in all patients and controls by measuring hand and feet Electrochemical Skin Conductance (ESC, μS) using Sudoscan.
Results: Peripheral neuropathy was detected in none of the controls, 39% of Group 1 patients and in 62% of Group 2 patients ($p < 0.0001$). The mean feet ESC (FESC) was 88.3 ± 6.8 μS in controls, 67.2 ± 19.2 μS in Group 1 and 57.9 ± 19.4 μS in Group 2 ($p < 0.0001$). A significant correlation was observed between FESC and bilirubin, albumin, creatinine, international normalized ratio, transaminases and splenic size.
Conclusion: The integration of circulating mi-RNA panel achieved to diagnose NAFLD cases and to discriminate between SS and NASH. Large scale study is still needed to verify the other miRNAs profile and their role in NAFLD pathogenesis and targeting therapy.

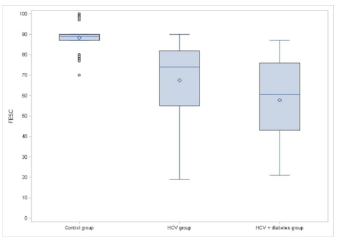


Figure 1: Box-plots of feet ESC (FESC) in controls, patients with HCV-related cirrhosis and patients with HCV-related cirrhosis as well as DM. FESC is decreased in HCV-related cirrhosis as compared to controls, and more profoundly decreased in patients with DM in addition.

	Control group (N=47)	Group 1 (N=48)	Group 2 (N=49)	P-value
Age	55.14 ± 10	57.86 ±7.59	57.94 ±8.85	0.653
Female	20 (42.6%)	20 (41.7%)	23 (46.9%)	0.8545
Ascites	0(0)	28(58.3%)	33(67.35%)	<0.0001
ALT	4.8 ± 0.5	2.9 ± 0.4	2.9 ± 0.5	<0.0001
AST	20.6 ± 6.1	59.1 ± 22.3	66.1 ± 63.1	<0.0001
Bilirubin	21.9 ± 6.4	79.3 ± 33.2	92.3 ± 76.2	<0.0001
BMI	0.9 ± 0.1	2.2 ± 1.7	3.7 ± 4.3	<0.0001
Systolic BP	26.5 ± 3.5	28.0 ± 5.5	29.4 ± 6.9	0.1554
Diastolic BP	117.9 ± 4.1	119.3 ± 18.0	113.1 ± 15.5	0.1645
HbA1c	76.9 ± 4.6	74.0 ± 8.7	72.6 ± 7.6	0.0087
Hb	4.6 ± 0.4	4.6 ± 0.4	8.6 ± 1.1	<0.0001
INR	12.0 ± 1.2	10.6 ± 1.3	10.2 ± 1.4	<0.0001
Platelets	1.0 ± 0.2	1.8 ± 0.5	1.8 ± 0.5	<0.0001
PV Diameter	245553 ± 53721	114581 ± 121E3	99245 ± 50989	<0.0001
Spleen Size	8.8 ± 1.5	16.5 ± 1.8	15.6 ± 2.1	<0.0001
Splenic vein	9.2 ± 1.3	17.8 ± 2.1	17.5 ± 2.7	<0.0001
	9.4 ± 1.3	14.0 ± 1.2	13.7 ± 1.7	<0.0001

Abstract #975

Five year experience with 2-octyl cyanoacrylate injection in gastric varices in cardinal Santos Medical Center

Chua PB, Adraneda C, Agas F Jr, Co JL, Dee G, Miranda R, Sy P, Yu Kim Teng K, Lapus I Jr

Section of Gastroenterology, Cardinal Santos Medical Center, Philippines

Significance: Gastric variceal hemorrhage (GVH) is linked with significant morbidity and mortality, limited endoscopic therapeutic options and lack of consensus regarding optimal management. Cyanoacrylate injection have been shown to be effective and safe in European countries. As an alternative to N-butyl-2-cyanoacrylate, 2-octyl-cyanocrylate (2-OCA) has been used. The aim of this study was to evaluate the efficacy and safety of 2-OCA in patients with gastric varices.
Methodology: A single center retrospective analysis was performed among patients who underwent 2-OCA injection for gastric variceal obturation (GVO) over a 5-year period (May 2014–April 2019). Rates of hemostasis, predictors of bleeding or rebleeding and cyanoacrylate-injection related adverse events were assessed.
Result: A total of 19 patients all with cirrhosis underwent a total of 28 cyanoacrylate injection during the study period. Mean age was 60 and 57% were males. The median Child Pugh classification was 8B, and MELD sodium score was 12. Mean volume injected was 1.3 cc and median number of varices injected per session was 2. Gastric varices were categorized as GOV-1 (42.11%), GOV-2 (26.31%) and isolated gastric varices type 1 (31.48%) per Sarin classification. A successful GVO, which was defined as sustained hemostasis within 1 month after injection, was achieved in all 19 (patients. Immediate hemostasis was achieved in three (15%) active bleeders; while eight (42%) each were done for primary and secondary prophylaxis. There were no reported in-hospital re-bleeding and associated glue related adverse events.
Conclusion: Endoscopic injection with 2-OCA was effective, safe and cheaper in achieving hemostasis and as primary and secondary prophylaxis.

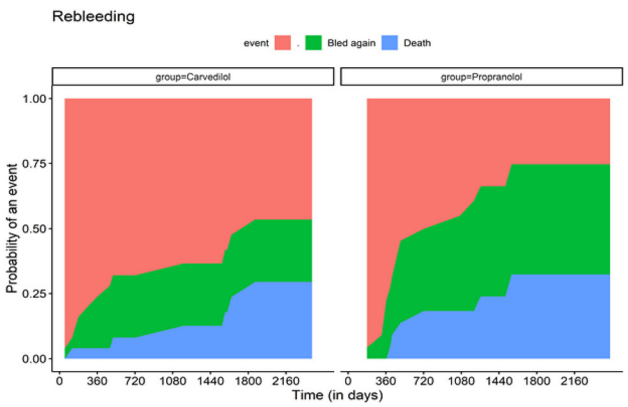
Abstract #1008

Long term outcomes with carvedilol versus propanolol in patients with index variceal bleed: 6-year follow-up of a randomised controlled trial

Mohta S[1], Agarwal S[1], Sharma S[1], Gunjan D[1], Gupta V[1], Kaushal K[1], Rawat R[1], Shalimar[1], Poudel S[1], Anand A[1], Gopi S[1], Saraya A[1]

[1]Department of Gastroenterology and Human Nutrition, All India Institute of Medical Sciences, New Delhi, India 110029

Aims and Background: There is limited information on comparison of clinical outcomes with carvedilol for secondary prophylaxis following acute variceal bleed (AVB) when compared to propranolol. We report long-term clinical and safety outcomes of a randomised controlled trial comparing carvedilol with propranolol with respect to reduction in hepatic venous pressure gradient (HVPG) in patients post AVB.
Methods: Patients randomized to receive either carvedilol or propranolol following AVB were followed up for rebleed events, survival, additional decompensation events and safety outcomes. Rebleed and other decompensations were compared using competing risks analysis, taking death as competing event, and survival was compared using Kaplan-Meier analysis. Univariate and multivariable adjusted predictors of rebleed and survival were identified.
Results: 48 patients (25 taking carvedilol; 23 propranolol) were followed-up for 6 years from randomization. Comparable 1-year and 3-year rates of rebleed (16.0% and 24.0% for carvedilol versus 8.9% and 36.7% for propranolol; p = 0.457) and survival (94.7% and 89.0% for carvedilol versus 100.0% and 79.8% for propranolol; p = 0.76) were obtained. New/ worsening ascites was more common in those receiving propranolol (69.5% vs 40%; p = 0.04). Multivariate analysis identified MELD (model for end-stage liver disease) as predictor of rebleed [subdistributional hazards ratio (HR): 1.166 (1.014–1.341); p = 0.031]. MELD more than 12 [HR: 2.4 (1.04–5.4); p = 0.04] and ascites at baseline [HR: 2.7 (1.01–7.4); p = 0.049] predicted mortality, HVPG response being non-significant. Drug-related adverse-events were similar in both groups.
Conclusion: Long-term clinical, survival and safety outcomes in carvedilol are similar to those of propranolol with limited value of HVPG response.



Abstract #1076

Cost analysis of hospitalized liver cirrhosis patients in tertiary referral hospital

Kemal F. Kalista, Saut H. H. Nababan, Chyntia O. M. Jasirwan, Juferdy Kurniawan, C. Rinaldi A. Lesmana, Andri S. Sulaiman, Irsan Hasan, Rino A. Gani

Divison of Hepatobiliary, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo General Hospital

Background: Liver cirrhosis is the end stage of every causes of chronic liver disease. Liver cirrhosis can cause several complication. Patient with liver cirrhosis tend to hospitalized many times due to the complications and cause high economic burden.
Aim: To perform cost analysis of hospital admission of patients with liver cirrhosis for 1 year period.
Method: This is a restropective study. Demographic, clinical and medical cost data were collected from liver cirrhosis patients who hospitalized in 2017 at Cipto Mangunkusumo Hospital, Indonesia.
Result: There were 93 patients hospitalized in 2017. Majority of the patients was male (69.9%), mean age was 53.8 + 12.6 yo. The number of hospitalization was 223 hospitalization/year with average hospital admission 2 times/year and average length of stay 16 days. Most common reason of hospital admission in CP-A patients was ligation procedure, CP-B patients was variceal bleeding and ligation procedure, CP-C patients was infection. Mean medical cost for 1 year period was 32.3 million IDR (2294 USD) and mean medical cost every admission was 15.2 million IDR (1085 USD). CP-A patients had highest number of average length of stay (19 days) and highest total medical cost in 1 year period (44.4 million IDR; 3154 USD). Meanwhile CP-C patients had highest medical cost per admission (17.3 million IDR; 1231 USD).
Conclusion: Liver cirrhosis patients requires high medical cost due to hospital admission. It is associated with recurrent hospitalizations and longer length of stay. Variceal related complications was the most common reason to hospitalization

Abstract #1170

Effect of propofol sedation during upper gastrointestinal endoscopy in cirrhotics and utility of psycometric tests, inhibitory control test and critical flicker frequency in assesment of recovery from sedation

Amit Agrawal, Kabir, Chandra Shekhar, Anil Bharani

Division of Gastroenterology, Department of Medicine, MGM Medical College, Indore

Introduction: Minimal hepatic encephalopathy (MHE) impairs health–related quality of life and predicts overt hepatic encephalopathy (HE) in cirrhotic patients. Cirrhotics are at increased risk of development of complications related to sedation.
Aim: To study effect of propofol sedation during upper gastrointestinal (UGI) endoscopy in cirrhotics and utility of psycometric tests, inhibitory control test (ICT) and critical flicker frequency (CFF) in assesment of recovery from sedation.
Methods: 204 cirrhotic patients were taken to assess the effect of propofol sedation during UGI endoscopy. Out of 100 cirrhotic patients 49% (49 patients) were diagnosed as MHE on the basis of psychometric tests.. All patients underwent CFF test, ICT and combination of psychometry (NCT A, B); digit symbol test (DST), line tracing test (LTT) and serial dotting test (SDT) at baseline CFF and ICT done at 30 min and repeated every 30 mins for 2 h. Psychometry repeated at 2 h.
Results: 125/204 cirrhotics (61%) had MHE before the endoscopy. In propofol group there was no significant deterioration in psychometry. Significant deterioration from baseline was seen in CFF at 30 min (38.8 ± 2.3 Hz, $p = 0.001$) and 1 hr (39.2 ± 2.4 Hz, $p = 0.001$) but no difference thereafter. Cirrhotics with MHE had significantly higher lures (22 ± 7.8 vs 11 ± 5.6) and lower target response compared with Controls.
Conclusions: Propofol sedation for UGI endoscopy is safe and associated with improved recovery in cirrhotics. CFF is less time consuming, easy to perform, more sensitive and more specific than ICT to diagnose MHE

Abstract #1180

Validation of AKI-CLIF-SOFA: a novel prognostic score for cirrhotic patients with acute kidney injury

Sriram PB, A R Venketeshwaran,

Institute of Medical Gastroenterology, Madras Medical, College, Chennai, India

Introduction: AKI is a strong predictor for mortality in patients with critically ill cirrhosis. There is a need to develop a new score for critically ill cirrhotic patients with AKI in order to improve the predicting accuracy of the CLIF-SOFA score for hospital mortality.
Objectives: The aim of this study were to validate a specific prognostic score for critically ill cirrhotic patients with AKI, the acute kidney injury—Chronic Liver Failure—Sequential Organ Failure-Assessment score (AKI-CLIF-SOFA) score. In the current AKI-CLIF-SOFA score, parameters consist of 24 h creatinine, bilirubin, age, lactate and vasopressin used (0 or 1 for each variable, range 0–5 points)
Materials and methods: A total of 200 cirrhotic patients with AKI admitted to intensive care unit were included and constructed a new scoring system, the AKI-CLIF-SOFA, which can be used to prognostically assess mortality in these patient population. Parameters included in this model were analysed by cox regression. The area under the receiver operating characteristic curve (auROC) of AKI-CLIF-SOFA scoring system was 0.78 in 30 days, 0.78 in 90 days, 0.76 in 270 days and 0.74 in 365 days. Additionally, this study demonstrated that the new model had more discriminatory power than chronic liver failure-sequential organ failure assessment score (CLIF-SOFA), SOFA, model for end stage liver disease (MELD), kidney disease improving global outcomes (KDIGO) and simplified acute physiology score II (SAPS II) (auROC: 0.74, 0.68, 0.66, 0.64, 0.65 and 0.66 respectively, all $P < 0.05$) for the prediction of the 365-days mortality. we used an optimal cutoff point of 2 for the 365-days mortality with reported sensitivity and the specificity of 63.1% and 83.32% respectively.
Conclusion: Therefore, AKI-CLIF-SOFA demonstrated a valuable discriminative ability compared with KDIGO, CLIF-SOFA, MELD, SAPS II and SOFA in critically ill cirrhotic patients with AKI.

Abstract #1223

Role of terlipressin on kidney function in cirrhotic patients with acute gastrointestinal bleeding

Le Thi Thu Hien[1], Dong Duc Hoang[1], Le Quoc Tuan[2], Nguyen Quang Duat[3], Nguyen Khac Hung Manh[1]

[1]Thai Nguyen University of Medicine and Pharmacy, [2]Thanh Ba Hospital, [3]103 Military Hospital

Introduction: Acute gastrointestinal bleeding (AGB) reduces effective blood volume, thereby developing acute kidney injury in cirrhotic patients. Terlipressin is recommended for the management of esophageal variceal bleeding and hepatorenal syndrome.
Objectives: To determine the role of Terlipressin on kidney function in cirrhotic patients with AGB.
Methods: Study group included 69 cirrhotic patients with AGB from May 2018 to April 2019. These patients received Terlipressin more than 3 days and the control group included cirrhotic patients with AGB had no Terlipressin. Renal dysfunction was defined as serum creatinine > 133 μmol/l at admission and/or any time poin during hospitalization in this study.
Results: The in-hospital mortality was not significantly different between patients treated with or without Terlipressin. Renal dysfunction was significantly associated with higher in-hospital mortality in cirrhotic patients with AGB in overall. Terlipressin significantly decreased the in-hospital mortality in patients with kidney funtion damage (9% vs. 29.5%, $p < 0.01$). The in-hospital mortality was significantly different between patients treated with or without Terlipressin. The rate of decrease in serum creatinine was not significantly different between patients treated with or without Terlipressin.
Conclusions: Renal dysfunction increased the in-hospital mortality of cirrhotic patients with AGB. Terlipressin might improve the survival of cirrhotic patients with AGB and renal dysfunction.

Abstract #1283

A study of thyroid and parathyroid dysfunction in patients with decompensated HCV-related liver cirrhosis

Hassan El-Shennawy[1], El-Sayed Tharwa[1], Mohamed Abdel-Samiee[1]*, Shimaa Abdelsattar[2] and Sayed Abu-Hatab[3]

[1]Hepatology and Gastroenterology Department, National Liver Institute, Menoufia University, Shebin Elkom, Menoufia, Egypt, [2]Clinical Biochemistry Department, National Liver Institute, Menoufia University, Shebin Elkom, Menoufia, Egypt, [3]General Physician, Ministry of Health, Damanhor, Behaira, Egypt

Introduction: The liver has an important role in thyroid hormones (THs) metabolism, as it is the most important organ in the peripheral conversion of tetraiodothyronine (T4) to triiodothyronine (T3) by type 1 deiodinase. T4 and T3 regulate the basal metabolic rate (BMR) of all cells, including hepatocytes, and thereby modulate hepatic function. Parathyroid hormone (PTH) has a half life time of less than 5 minutes and its clearance from the circulation is undertaken by the kidney and liver.
Objectives: We investigated the status of thyroid and parathyroid hormones and calcium homeostasis in patients with advanced liver cirrhosis.
Methods: This study included (50) patients who had been randomly recruited from either the outpatient clinics or the inpatient unit of clinical Hepatology and Gastroenterology department, National Liver Institute hospital, Menoufia University as well as (50) healthy subjects with matched age and sex had been enrolled in this study as a control group. Full history and clinical examination, abdominal ultrasonography were done. Liver function tests, viral markers, AFP, hormonal analysis, electrolytes were measured.
Results: There was a significant positive correlation in both studied groups as regards free T3, free T4, TSH and parathyroid hormonal levels. A significant correlation was found between the studied variables FT3 and FT4 with Parathormone and TSH. Also, there was a significant correlation between FT4 with serum calcium, ionized calcium and serum phosphorus. A significant correlation also found as regard between FT3&TSH with TgAb, TPOAb and MELD score. The studied variables FreeT3, FreeT4, TSH, Total Calcium, Phosphorus, Ionized Calcium and Vitamin D level had a positive significant correlation as regard both MELD score and TPO Ab.
Conclusion: Derangement in thyroid profile is common in patients with cirrhosis of liver. Low free T3 and T4 levels are associated with more severe liver injury in patients with cirrhosis of liver. Chronic liver disease in advanced stages is complicated by bone disease, the clinical relevance of vitamin D &PTH disturbances in hepatic osteodystrophy.

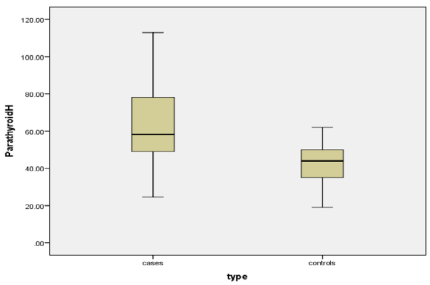


Figure 1: Scatter plot of parathyroid hormone level in the studied groups

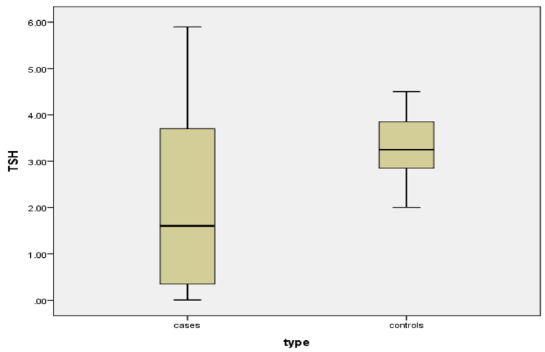


Figure 2: Scatter plot of TSH level in the studied groups.

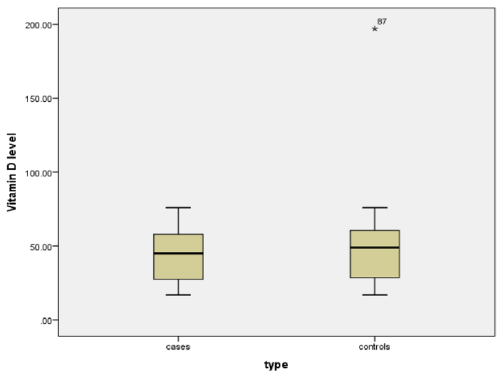


Figure 3: Scatter plot of vitamin D level in the studied groups.

Abstract #1360

Quantitative collagen pattern has independent prognostic value in predicting short-term survival in cirrhosis patients with acute decompensation

Wang, Yan[1,2]; Bihari, Chhagan[3]; Rastogi, Archana[3]; Shasthry, Saggere M.[4]; Zhou, Jie[5], Jiang, Ze-Sheng[6]; Hou, Jin-Lin[1]; Sarin, Shiv K.[4]

[1]Guangdong Provincial Research Center for Liver Fibrosis, Department of Infectious Diseases and Hepatology Unit, Nanfang Hospital, Southern Medical University, Guangzhou, China, [2]Biomedical Research Center, Southern Medical University, Guangzhou, China, [3]Department of Pathology, Institute of Liver and Biliary Sciences, New Delhi, India, [4]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India, [5]Department of Medical Imaging Systems, GE Healthcare, China, [6]Department of Hepatobiliary Surgery, Zhujiang Hospital, Southern Medical University, Guangzhou, China

Introduction: Histologic fibrosis in patients with acute decompensation of cirrhosis (ADC) has not been intensively evaluated.
Objectives: We quantified histologic fibrosis in a large cohort with ADC and identified correlations with short-term survival.
Methods: To describe fibrosis patterns fully in cirrhosis with diverse etiologies, we established a dual-photon microscopy-based computerized image analysis tool. It measures the quantitative collagen pattern (QCP), comprising both collagen spatial network and collagen geometry within septal, sinusoidal, and nodular regions. Associations with clinicopathologic parameters and prognostication of 90d-survival were evaluated in patients who underwent liver biopsy on admission to Institute of Liver and Biliary Sciences with ADC from 2012 to 2014.
Results: In a total of 413 subjects, including a 227-patient subset with data on 90d-survival, 4121 image tiles were used to determine QCP. QCP varied greatly with etiology but correlated with Laennec stages and model for end-stage liver disease (MELD) scores. QCP predicted 90d-mortality better than did MELD or Child-Turcotte-Pugh scores, hepatic venous pressure gradient (HVPG), Laennec stages, and collagen proportionate area (AUROC 0.81 versus 0.66–0.63, $p < 0.001$ for all). QCP discriminated probability of survival more efficiently than did MELD or Child-Turcotte-Pugh scores, HVPG, and Laennec stages. On multivariable Cox analysis, QCP was the most important predictor of 90d-survival (adjusted hazard ratio 6.26; $p < 0.0001$). Collagen spatial network had overall higher predictive relevance than did collagen geometry.
Conclusion: Quantifying fibrosis pattern is feasible for intensively assessing liver-biopsy findings in ADC. It reflects disease severity and provides high accuracy in short-term prognostication, independent of other clinical predictors.

Abstract #1485

Association of thromboelastrography with severity of liver cirrhosis and portal venous system thrombosis

Yanglan He[1,2], Xiaozhong Guo[1], Xiangbo Xu[1], Shixue Xu[1], Walter Ageno[3], Xingshun Qi[1*]

[1]Department of Gastroenterology, General Hospital of Northern Theater Command (formerly General Hospital of Shenyang Military Area), Shenyang, China, [2]Postgraduate College, China Medical University, Shenyang, China, [3]Dipartimento di Medicina e Chirurgia Università degli Studi dell'Insubria-Varese, Via Guicciardini 9, 21100 Varese-Italy

Background and Aims: Liver cirrhosis has a complicated hemostasis profile, which may be associated with thrombotic complications. Thromboelastography (TEG) is a global hemostasis test recommended by the current practice guideline. This cross-sectional study aimed to evaluate the association of TEG profile with severity of liver cirrhosis and presence of portal venous system thrombosis (PVST).
Methods: Among the 109 eligible patients, TEG and conventional coagulation tests (CCTs) were compared between 31 non-cirrhotic patients and 78 cirrhotic patients. Comparisons were further performed in cirrhosis with and without acute decompensated events, Child–Pugh class A and B/C cirrhosis, and cirrhosis with and without PVST. The correlation between TEG and CCTs in cirrhosis was also assessed.
Results: Both CCTs and TEG profile showed a relative hypocoagulation in cirrhosis as compared to non-cirrhosis with or without gastrointestinal bleeding. However, the median values of most TEG parameters in cirrhosis were within the reference range (reactive time: 6.25 [reference range 5–10]; coagulation time: 2.80 [reference range 1–3]; angle: 65.90 [reference range 53–72]). Reactive time was significantly shorter in cirrhosis with decompensated events (7.20 versus 5.90, $P = 0.012$) and Child–Pugh class B/C (6.80 versus 5.80, $P = 0.028$). Most of TEG parameters were not significantly different between cirrhosis with and without PVST. Coagulation time ($P < 0.001$), angle ($P < 0.001$), and maximum amplitude ($P < 0.001$), but not reactive time ($P = 0.780$), significantly correlated with platelet count.
Conclusion: TEG profile suggested a relative hypercoagulation indicated by a shorter reactive time in more advanced liver cirrhosis. Additionally, hypercoagulation might not be associated with presence of PVST in liver cirrhosis.

Abstract #1493

Transjugular intrahepatic portosystemic shunt using 8-mm versus 10-mm covered stents for patients with cirrhosis: a meta-analysis

Wang Xiaoze, Wang Haoran, Luo XuefengYang Jinlin, Yang Li

Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, Chengdu, China.

Introduction: The portosystemic pressure gradient (PPG) reduction during transjugular intrahepatic portosystemic shunt (TIPS) primarily depends on the stent diameter.
Objectives: We performed a systemic review and meta-analysis to compare the clinical outcomes of 8-mm versus 10-mm covered stents for TIPS.
Methods: Databases including PubMed, Embase, Web of Science, Scopus and Cochrane library were searched. Mortality, recurrence of complications of portal hypertension, hepatic encephalopathy, and decline of PPG were the major endpoints.
Results: A total of 5 studies with 489 patients were eligible. Meta-analyses showed that TIPS using 8-mm and 10-mm covered stents had no significant difference in aspects of mortality (RR = 0.91, 95% CI 0.59–1.40, $P = 0.66$) and decline of PPG (MD = -1.30, 95% CI -2.94 to 0.34, $P = 0.15$). Additionally, 8-mm group might have a higher risk of recurrence of portal hypertensive complications (RR = 1.87, 95% CI 1.17–2.97, $P = 0.008$) and a lower risk of post-TIPS hepatic encephalopathy (RR = 0.64, 95% CI 0.47–0.88, $P = 0.005$). However, in subgroup analyses, there was no significant differences between two groups on recurrence of complications in Asian population (RR = 1.35, 95% CI 0.57–3.22, $P = 0.49$) and on hepatic encephalopathy in Western population (RR = 0.69, 95% CI 0.34–1.41, $P = 0.31$).

Conclusion: Overall survival remains similar in both groups. TIPS using 8-mm covered stents are sufficient to decompress portal hypertension with a lower risk of hepatic encephalopathy in an Asian population. Nevertheless, as for the Western population, 10-mm TIPS may be more suitable.

Abstract #1540

Comparative study of granulocyte colony stimulating factor versus combination of granulocyte colony stimulating factor and darbopoietin in decompensated liver cirrhosis in terms of one-year survival

Sudhamshu K. C., Dipendra Khadka, Niyanta Karki, Dilip Sharma, Sandip Khadka

Introduction: Various studies have proved that the colony stimulating factor (G-CSF) and darbopoietin (DPO) lead to enhance hepatic regeneration and improved survival in patients with advanced liver disease.
Objective: We aimed to see the clinical response of G-CSF in combination with DPO in decompensated chronic liver disease patients in terms of complications, disease progression and survival in patients who were unable to afford liver transplantation.
Methodology: Consecutive patients of decompensated liver cirrhosis meeting inclusion and exclusion criteria from June 2016 to September 2017 were enrolled. Patients were randomized into GDP group receiving G-CSF and DPO both, GCSF group receiving G-CSF and SMT group receiving standard medical therapy. Patients were followed up for 1 year.
Results: 150 patients were enrolled, 60 excluded and remaining 90 were divided into three groups. Ascites was major decompensating event (40%) followed by acute variceal bleeding and hepatic encephalopathy. New onset complications were more in SMT group. Improvement in CTP score and decrease in MELD score was observed in both GCSF and GDP group as compared to SMT. Need of large volume paracentesis was required more in SMT group. There were of 50 deaths during study. Overall survival was highest in GDP group (66.7%) followed by GCSF group (50%) and least in SMT group (16.7%) which was statistically significant (P = < 0.001). Both G-CSF and DPO were well tolerated.
Conclusion: Our study concluded that G-CSF and DPO therapy improved liver disease severity score, decreased new onset complications and increased overall survival in decompensated liver cirrhosis.

Abstract #1594

Long-term effect of growth hormone therapy in decompensated cirrhosis

Kumari Sunita[1], De Arka[1], Singh Akash[1], Kalra Naveen[2], and Singh Virendra[1]

[1]Department of Hepatology, [2]Radiodiagnosis and Imaging, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Background and Aim: Malnutrition is common in decompensated cirrhosis (DC) and is associated with a poor prognosis. It is commonly associated with protein catabolism which is accompanied by severe growth hormone (GH) resistance leading to overall effective deficiency of GH. The supplementation of GH may revert this process. The effect of long-term GH therapy on the malnutrition and nitrogen metabolism in these patients is not known. Therefore, we plan to study the safety and efficacy of GH therapy and its effect on malnutrition and nitrogen metabolism in patients with DC.
Methods: 34 patients with DC were openly randomized to either standard medical therapy (SMT) plus GH (started at a dose of 1 IU/day subcutaneously and increased to 2 IU/day by titrating the dose according to IGF-1 levels) (GH Group; n = 17) or SMT alone (Control Group; n = 17) and followed-up monthly for 12 months. We studied clinical scores (CTP and MELD), malnutrition parameters [body mass index (BMI), mid-arm muscle circumference (MAMC), hand grip strength (HGS) and skeletal muscle index (SMI)] and nitrogen balance at baseline and then 3 monthly till 12 months.
Results: The baseline characteristics were comparable between two groups. There was significant improvement in malnutrition parameters [BMI (22.92 ± 3.03 vs 25.71 ± 3.20, p = .016), MAMC (22.6 ± 2.5 vs 27.5 ± 8.1 cm, p = 0.02), HGS (21.10 ± 5.77 vs 27.5 ± 6.4 kg, p = 0.006)and SMI (56.6 ± 8.4 vs 60.6 ± 9.5 cm^2/m^2, p = 0.005)] and CTP score (7.7 ± 2.2 vs 6.2 ± 1.4, p = 0.024) and a trend of improvement in nitrogen balance (3.0 ± 6.4 vs 8.43. ± 6.16 g/day, p = 0.09) in GH group at 12 months. There was no significant improvement in clinical scores, malnutrition parameters and nitrogen balance in control group. There were no adverse events related to long-term use of growth hormone in these patients.
Conclusions: GH therapy is safe and effective in patients with DC and long-term use improves CTP, malnutrition and nitrogen balance. However, a larger study is required to validate our findings.

Abstract #1665

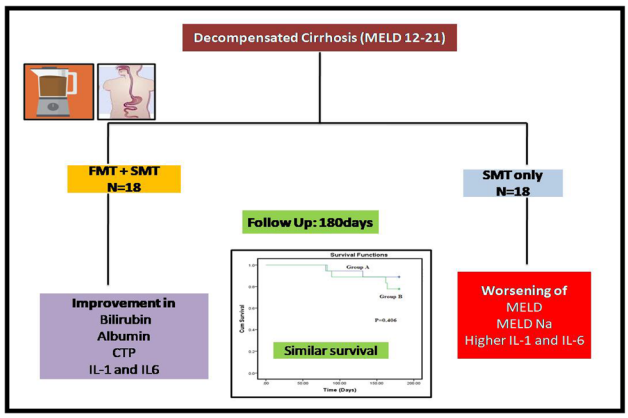
Role of fecal microbiota transplantation in decompensated cirrhosis: an initial experience of clinical endpoints

Dhiman K Radha,[1] Roy Akash,[1] Premkumar Madhumita,[1] Duseja K Ajay,[1] Taneja Sunil,[1] Verma Nipun,[1] De Arka[1]

[1]Department of Hepatology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

Introduction: Gut dysbiosis (GD) worsens with transition from compensated to decompensated cirrhosis (DC) and accelerates complications.
Objectives: To assess the impact of FMT on liver disease severity, prognostic scores, inflammatory markers [(Interleukin -1 (IL-1) and 6 (IL-6)] and 180-day mortality in patients with DC.
Methods: Consecutive patients with advanced but stable DC (MELD12-21) were assigned to receive FMT (30 g freshly prepared stool from selected family member through nasojejunal tube) plus standard medical therapy (FMT group) or SMT alone (SMT group). Outcomes were assessed at day 7, 28 and 90 and 180.
Results: Eighteen patients each with similar baseline characteristics (88.8% males; mean age, 46.12 ± 6.23 vs 47.0 ± 4.54; mean CTP, 9.5 ± 0.71 vs 9.6 ± 0.80; mean MELD, 16.1 ± 1.71 vs 1.62 ± 1.81) were allocated to FMT or SMT alone. Haemoglobin (p = 0.05), serum bilirubin (p = -.001) and serum albumin (p = 0.001) showed improving trends till day 180 in FMT group. CTP scores improved in FMT group (P = 0.01) whereas MELD (P = 0.03) and MELD Na (P = 0.04) worsened in SMT group. Ammonia reduction was similar at day 7 and day 28 (P = 0.21; P = 0.17). IL-1 (P = 0.01) and IL 6 (P = 0.005) levels reduced significantly in FMT group at day 28. 180 day survival were similar (HR, 2.02; 95% CI 0.37–11.05; P = 0.41). Although, transient gastrointestinal side-effects were common (56.2%), no SAE (serious adverse events) were noted.

Conclusion: In a stable but advanced population of DC, FMT improves prognostic scores and leads to a reduction in pro-inflammatory cytokines, but does not improve 180 day survival.



Abstract #1678

Prognosis of secondary IgA nephropathy in liver cirrhosis

Divyaveer S[1], Kumar P[2], Dasgupta S[3], Das Bhattacharya T[3], Bagur V[3], Banerjee A[3], Raychaudhury A[3], Pandey R[3]

[1]Department of Nephrology, Post Graduate Institute of Medical Education and Research, Chandigarh, India, [2]Department of gastroenterology, Institute of Gastrosciences, Apollo Gleaneagles Hospital, Kolkata, India, [3]Department of Nephrology, Institute of Post Graduate Medical Education and Research, Kolkata, India.

Introduction: Prognosis of secondary IgA Nephropathy with cirrhosis on conservative management in relation to (Mesangisal Mesangial cellularity, Endocapillary proliferation, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, Crescents) MEST-C classification is not well known.
Objectives: Change in estimated glomerular filtration rate (eGFR) by Modified Diet in Renal Disease (MDRD) 6 formula and proteinuria (PU) in secondary IgAN in relation to the MEST C.
Methods: All patients with biopsy proven IgAN with MEST C classification and liver cirrhosis were included. All recieved conservative management with Renin angiotensin blockers. Outcomes: eGFR and proteinuria at 6 months in relation to each of M, E, S, T, C component of IgAN classification.
Results: Of 62 IgAN patients, 8 had cirrhosis. All were Child Pugh class A. MEST-C was: M0E1S0T0C0, M1E1S1T1C0, M0E0S1T2C0, M1E0S0T0C0, M0E0S0T0C0, M1E1S0T1C0, M0E0S1T1C0 and M0E0S0T1C0. Baseline: mean eGFR : 54.33 ± 14.3 and median eGFR : 60.4; IQR 44.62 to 68.56 ml/min/m2. Baseline mean Proteinuria was 1.4 and median was 1.2 with IQR 0.77 to 2.4gm/day. eGFR mean and median at 6 months was 50.54 ± 12.33 and median eGFR was 52.34 (IQR 37.54 to 54.46) ml/min/m2; p = 0.03. At 6 months the proteinuria was mean 1.4 gm/day, median 1.3gm/day IQR (1.0 to 2.97 gm/day); p = 0.24. Those with E1 had higher decline in eGFR. Proteinuria did not differ in those with E0 and E1.
Conclusion: In patients with cirrhosis and secondary IgAN there is no significant change in proteinuria but there is significant decline in eGFR at 6 months. E1 is associated with worse decline in eGFR.

Abstract #1700

Risk of spontaneous bacterial peritonitis with use of proton pump inhibitors among patients with liver cirrhosis—a systemic review and meta-analysis

Sy, Marianne Linley[1]; Janairo, Jose Isagani [2]; Mariano, Patricia[3]; Cervantes, Juliet[1]; and Cua, Ian Homer[1]

[1]Institute of Digestive and Liver Diseases, St. Luke's Medical Center—Global City, Philippines, [2]Biology Department, De La Salle University, Philippines. [3]Department of Medicine, St. Luke's Medical Center-Quezon City, Philippines.

Introduction: Spontaneous bacterial peritonitis (SBP) is a frequent complication seen among cirrhotic patients resulting to increased morbidity and mortality. The use of proton pump inhibitors (PPIs) has been associated with higher incidence of SBP. Previous studies were inconclusive. Newer studies were done to re-evaluate the causality of PPI use and development of SBP.
Objective: We aim to re-assess the association between PPI use and SBP incidence with larger and better quality data.
Methods: Database of Medline, Cochrane, and Google scholar were used to search for relevant articles. Two reviewers independently assessed the quality of each included study. Disagreements were resolved by the third author.
Results: A total of twenty-two studies: eight case–control, thirteen cohort, and one randomized controlled trial, involving 10,828 patients were analyzed. The overall results showed a statistically significant association between SBP and PPI use (pooled odds ratio (OR): 2.03, 95% CI of 1.67 to 2.45). On sugbgroup analysis involving cohort and randomized controlled trial, association was weaker (OR: 1.88 with 95% CI of 1.51 to 2.34 $p < 0.00001$) while the case control studies, showed pooled OR of 2.64 with 95% CI of 1.91 to 3.64. The pooled OR for high quality studies is 1.93 with 95% CI of 1.57 to 2.38, $p < 0.00001$).
Conclusion: The present meta-analysis showed that there is a weak association, although statistically significant, between SBP and PPI use. Thus, this updated meta-analysis suggests judicious use of PPI among cirrhotic patients with ascites.

Abstract #1706

Serial saliva proteomic analyses can predict the outcome of plasma exchange in severe alcoholic hepatitis patients

Jaswinder Singh Maras[1], Gaurav Yadav[1], Adil Bhat[1], Arun Thakur[1], Meenu Bajpai[3], Vinod Arora[2], Rakhi Maiwal[2], V Rajan[2], Shiv Kumar Sarin[1,2]

[1]Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi-110070, [2]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi-110070, [3]Department of transfusion medicine, Institute of Liver and Biliary Sciences, New Delhi-110070

Background and Aims: Severe alcoholic hepatitis (SAH) has high mortality with limited medical treatment options such as corticosteroids or Therapeutic Plasma Exchange (TPE). However, response to patients undergoing TPE procedures is variable and decision for further TPE remains empirical. We explored the utility of baseline saliva proteomics in identifying patients who are unlikely to survive or require additional TPE.
Methods: Saliva cotton swab from SAH patient (n = 20) undergoing TPE was collected at baseline ie (Before TPE) and 24 h after TPE (Post-TPE). Proteins were isolated form the saliva swab and were

subjected to reduction, alkylation and trypsin digestion followed by label free quantification using nano liquid chromatography coupled to high-resolution mass spectrometry. Most significant determinants (proteins) in nonsurvivors were correlated with severity and subjected to evaluation of their diagnostic accuracy.
Results: A total of 2000 proteins were identified in the saliva samples and were linked to B-lymphoblast, tongue, bone marrow, bronchial epithelial cells and CD34 + cells (human gene atlas). Baseline saliva of SAH patients showed 248 upregulated proteins which were linked to IL-17 signaling, detoxification of ROS, MAPK6/MAPK4 signaling whereas 432 downregulated proteins were linked to platelet activation and glycolysis ($FC > \pm 1.5$; $p < 0.05$). As compared to baseline SAH, post-TPE SAH patients who survived, showed 125 differently expressed proteins, of which 110 were upregulated and linked to platelet degranulation, and gluconeogenesis while 15 proteins were downregulated linked to NOD1/2 signaling and ketone metabolism ($FC > \pm 1.5$; $p < 0.05$). SAH patients who died post-TPE, showed 258 differently expressed proteins of which 241 were upregulated; linked to cytokine signaling; mTOR signaling and MAP2K/MAPK activation and 17 were downregulated linked to regulation of energy metabolism as compared to baseline SAH. In comparision to survivors, the nonsurvivors documented significant increase in pathways linked to Rap1 signaling, MAPK signaling and chemokine signaling ($p < 0.05$). Inflammatory pathway linked proteins; High mobility group box 1 protein (HMGB1) and Heat Shock 60 kDa Protein 1 (HSPD1) significantly correlated with the severity ($r > 0.3$; $p < 0.05$) and documented highest diagnostic efficiency for predicting non-survival ($AUC > 0.85$; $p < 0.05$) in SAH patients. **Conclusions:** Post-TPE measurement of alarmins; High mobility group box 1 protein (HMGB1) and Heat Shock 60 kDa Protein 1 (HSPD1) in saliva could predict the outcome in SAH patients. Study of saliva proteins could serve as a simple way for serial assessment of SAH patients undergoing TPE.

Abstract #1818

Quality of life, psychosocial burden and mental health disorders in primary caregivers of patients with cirrhosis

Hareendran Atul[1], Devadas Krishnadas[2]

[1]Department Of Medical Gastroenterology, Government Medical College Trivandrum, [2]Professor and Head of Department Of Medical Gastroenterology, Government Medical College Trivandrum

Introduction and Objectives: Caregivers are needed for cirrhotic patients as it is a chronic illness with progressive decline in cognition and self-care. Very less is studied about the psychosocial problems of caregivers. We intend to study their quality of life (QOL), caregiver burden and prevalence of mental health disorders in them.
Methods: Cross sectional study in south India. Primary caregivers of cirrhotic patients, defined as person who takes responsibility of providing care to patient, were included. Short form 36 health survey (SF-36) to assess QOL, Zarit Burdern Index12 (ZBI) for caregiver burden (CB). Patient Health Questionnaire (PHQ) identified depression and Generalized Anxiety Disorder (GAD -7) questionnaires, anxiety.
Results: Of 132 caregivers, mean age was 41.2 ± 10.3yrs with female preponderance. Mean age of patients 51 ± 9yrs with male preponderance. Mean MELD 21.4 ± 7 and majority were CHILD C. Comparing SF36 score of caregivers to normal population showed lower level of QOL for caregivers. Mean ZBI score was 14 ± 5.8, 64% had CB. Mean GADscore was 8.1 ± 5.1, 54 (41%) had anxiety. Mean PHQscore was 7.8 ± 5.2, 45 (34%) had depression.
Multiple logistic regression

Alcoholic cirrhosis (ODDS-22), Hepatic encephalopathy (ODDS-29) & recidivism (ODDS-10) predicted CB. Treatment costs (ODDS—1.15), alcoholic cirrhosis (ODDS—29), Hepatic encephalopathy (ODDS—15) caregiver duration (ODDS—0.25) correlated with the anxiety. Treatment costs (ODDS—1.05), caregiver age (ODDS—0.87), spouse as caregiver (ODDS—10.9) and post-secondary education (ODDS—0.79) were predictors of caregiver depression.
Conclusions: Caregivers of cirrhotic patients have high prevalence of CB with a lower QOL and high incidence of anxiety and depression, compared to general population. Alcoholism in patients precipitates while higher education helps cope up with mental disorders.

Abstract #1849

No Difference in efficacy among terlipressin combined with somatostatin, somatostatin or terlipressin treatments in cirrhotic patients with esophagogastric variceal bleeding

Li Xiaolu, Ding Huiguo, Zeng Ajuan, Lv Xinyue, Gao Zhuqing, Li Lei

Department of Gastroenterology and Hepatology, Beijing You'an Hospital affiliated with Capital Medical University, Beijing, China.

Introduction: Terlipressin and somatostatin are commonly used in the treatment of esophagogastric variceal bleeding (EVB). However, it is unclear whether the efficacy of terlipressin combined with somatostatin is better than somatostatin or terlipressin alone.
Objective: To observe whether terlipressin combined with somatostatin is superior to somatostatin or terlipressin in the treatment of EVB.
Methods: 73 patients were included in this retrospective study. Under acid-suppressing treatment, 43 patients treated with somatostatin and 8 patients treated with terlipressin served as the control group; and 22 patients treated with terlipressin combined with somatostatin served as the observation group. The 24-h hemostatic success rate, hemostatic time, early rebleeding rate, delayed rebleeding rate, improvement rate of acute kidney injury (AKI) and half-year cumulative survival rate were compared among the three groups.
Results: Treatment success was achieved within 24 h in 54.5%, 41.9% and 37.5% of the observation group and the control group, respectively ($P = 0.618$), the hemostatic time was 1.00 (1.00 ~ 3.00) d, 2.00 (1.00 ~ 3.00) d, 2.00 (1.00 ~ 3.00) d ($P = 0.513$), with similar rates of early rebleeding (25%, 27.5% and 16.7%; $P = 1.000$), delayed rebleeding (16.7%, 27.3% and 40%; $P = 0.466$) and half-year cumulative survival ($P = 0.436$). There was no AKI in terlipressin group, and the improvement rates of AKI in combined group and somatostatin group were 100% and 50% respectively ($P = 0.429$), the difference was not statistically significant.
Conclusion: There was no difference in efficacy among terlipressin combined with somatostatin, somatostatin or terlipressin treatments in EVB. Compared with somatostatin, the improvement rate of AKI in the combination treatment group has an upward trend.

Abstract #1867

Serum Cystatin C as a predictor of 90-day mortality in patients admitted with complications of cirrhosis

Anuchit Suksamai[1], Amnart Chaiprasert[2], Sakkarin Chirapongsathorn[1]

[1]Division of Gastroenterology, Department of Medicine, Phramongkutklao Hospital and College of Medicine, [2]Division of Nephrology, Department of Medicine, Phramongkutklao Hospital and College of Medicine.

Background and aims: Model for end-stage liver disease (MELD) score has been shown to be the best predictor of mortality in cirrhotic patients. Cystatin C is not affected by muscle mass like serum creatinine therefore, cystatin C may be a good predictor of mortality in cirrhotic patients. We evaluated to compare predictive performance of serum cystatin C level and MELD score and develop a new model to predict 90-day mortality in patients admitted with complications of cirrhosis.
Methods: A prospective cohort study was performed during December 2018 to December 2019. All patients had laboratory values measured within 48 h of admission. Cox regression analysis and a c-statistic measured by AUROC curve were used to predict 90-day mortality.
Results: A cohort of 223 cirrhotic patients was admitted during study period. Sixty-two patients were eligible for analysis. Twenty-seventh of these patients died within 90 days of follow up, comprised of 45 males (72%). The median of MELD score was 20.5 (15, 24). Serum cystatin C level of > 1.44 mg/L has the highest 90-day mortality prediction with the sensitivity, specificity and diagnostic accuracy of 66.7%, 68.4% and 67.6%, respectively. Cystatin C and MELD score were predictive of 90-day mortality: Cystatin C HR = 1.98 (95% CI 1.92–3.29, p = 0.008); MELD score HR = 1.08 (95% CI 0.99–1.17, p = 0.058). C-statistic of cystatin C and MELD score to predict 90-day mortality were 0.63 and 0.58, respectively. Adding cystatin C to the MELD score improved the predictive of 90-day mortality.
Conclusion: Serum cystatin C is as good as MELD score and the new MELD-cystatin C model is superior to the MELD score in predicting mortality in cirrhotic patients admitted with complications.

Abstract #1959

The Periscreen strip show a good value in diagnosing spontaneous bacterial peritonitis in patients with acute-on-chronic liver failure

Chen Li, Hai-bin Su, Jin-hua Hu

Liver Failure Treatment and Research Center, The Fifth Medical Center of Chinese PLA General Hospital, Beijing 100039, P. R. China

Introduction: Application of leukocyte esterase reagent strips may help diagnose spontaneous bacterial peritonitis (SBP), but application evidence on acute-on-chronic liver failure (ACLF) are still unclear.
Objectives: This study aimed to assess the performance of the periscreen strip for the rapid diagnosis of SBP in patients with ACLF.
Methods: The strip was used to test 261 ascites samples from 252 inpatients with ACLF between October 2014 and June 2019. The color of the reagent strip was divided into four colorimetric graduations ("negative", "trace", "small" and "large") and the detection time was 3 minutes. The polymorphonuclear leukocyte of ascites (PMN) $> 250/mm^3$ was used as the gold standard for the diagnosis of SBP.
Results: Ninety-two (35.2%) ascites samples were SBP. The colorimetric graduations of the strip was positively correlated with the PMN of ascites (r = 0.867, $P < 0.001$), but was not correlated with the grade of total bilirubin (r = -0.100, $P = 0.106$). When using the "trace" threshold as the detection of SBP, for all patients sensitivity was 100.0% and specificity was 91.1%, for non-LF patients sensitivity was 100.0% and specificity was 95.0%, for LF patients sensitivity was 100.0% and specificity was 90.6%. Multivariate logistic regression showed that the PMN of ascites (OR = 1.029) and the WBC of ascites (OR = 1.007) were independent predictors of false positive.
Conclusion: Jaundice did not affect the detection of the periscreen strip, and it showed a good application value in the rapid diagnosis of SBP in ACLF patients.

Abstract #1968

Nutritional status, dietary intake and misconceptions of diet in patients with cirrhosis

Grover I[1], Singh N[2], Gunjan D[3], Sati H C [4], Saraya A[5]

[1]Senior Research Fellow, Department of Gastroenterologyand Human Nutrition Unit, All India Institute of Medical Sciences, New Delhi, India, [2]Dietician, Department of Gastroenterologyand Human Nutrition Unit, All India Institute of Medical Sciences, New Delhi, India, [3]Assistant Professor, Department of Gastroenterology and Human Nutrition Unit, All India Institute of Medical Sciences, New Delhi, India, [4]Statistical Assistant, Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India, [5]Professor& Head, Department of Gastroenterology and Human Nutrition Unit, All India Institute of Medical Sciences, New Delhi, India

Introduction: Malnutrition and poor nutritional status negatively affects disease prognosis and survival in the patients with cirrhosis. Unnecessary dietary restrictions can also lead to insufficiencies and malnutrition
Objective: To see association between nutritional status and dietary intake (also dietary restrictions) in cirrhotics.
Methods: Subjective global assessment (SGA) modified for liver disease was used to assess nutritional status. Three days 24 h dietary recall was used to calculate the nutrient intake. Questions related to dietary restrictions were enquired. Disease severity was assessed by Child-Turcotte-Pugh score (CTP) and categorized into compensated (CTP A) and decompensated cirrhosis (CTP B and C).
Results: Patients with cirrhosis (n = 342, age 43.79 $\pm$ 11.95 yrs, 272 male, compensated: 204) were enrolled. SGA grades revealed that 9.06%, 49.71% and 41.23% patients were well nourished, moderately malnourished and severely malnourished, respectively. Corrected BMI was lower in severely malnourished (20.57 $\pm$ 5.22 Kg/m^2) as compared to well nourished (22.86 $\pm$ 3.79) patients (p = 0.02) Energy intake reduced as the nutritional status worsened ($p < 0.0001$). Intake of all three macronutrients was lower in severely malnourished as compared to well nourished patients ($p < 0.0001$).) Diet intake based on dietary restrictions: salt restriction (prescribed) vs spices and oil (self imposed) along with salt, was similar in both groups.
Conclusion: Worsening of SGA was associated with decrease in dietary intake and low BMI. In spite of unpalatable food, nutrient intake of the patients with self imposed restrictions was found to be similar as patients with prescribed salt restriction. During nutritional counselling self imposed restrictions should be discouraged.

Abstract #2020

Urine liver-type fatty-acid binding protein (L-FABP); a novel biomarker for predicting mortality in hospitalized cirrhotic patients

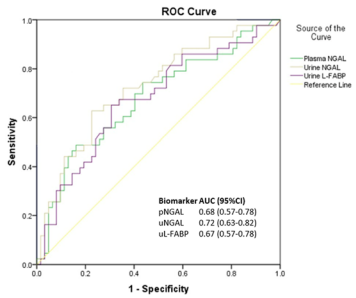
Salisa Wejnaruemarn, MD.[1], Chonlada Phathong, B.Sc.[2], Nattachai Srisawat, MD.[3], Sombat Treeprasertsuk, MD., Ph.D.[2,4]

[1]Department of Medicine, Faculty of Medicine, Chulalongkorn University, and Thai Red Cross, Bangkok, Thailand, [2]Department of Medicine, Division of Gastroenterology, Faculty of Medicine,

Chulalongkorn University, and Thai Red Cross, Bangkok, Thailand, [3]Department of Medicine, Division of Nephrology Critical Care Medicine, Faculty of Medicine, Chulalongkorn University, and Thai Red Cross, Bangkok, Thailand, [4]Liver Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Introduction: Acute kidney injury (AKI) causes high mortality in cirrhotic patients. Urine Liver-type Fatty-Acid Binding Protein (uL-FABP) and urine Neutrophil Gelatinase-Associated Lipocalin (uNGAL) increased in kidney injury, and related to AKI progression.
Objectives: We aim to identify role of novel biomarkers for prediction of AKI and 28-day mortality.
Methods: We prospectively enrolled hospitalized cirrhotic patients at tertiary care university hospital during June 2018 and November 2019. Novel biomarkers were collected within 48 h of admission. Cut-off value of novel biomarkers for AKI diagnosis derived from ROC curve. Logistic regression analysis was used to identify independent factors for AKI and 28-day mortality.
Results: We enrolled 109 patients, 45 of them (41.3%) had AKI. Median uL-FABP, uNGAL, and plasma NGAL (pNGAL) in AKI group were higher than non-AKI group; 8.05 vs. 2.82 ng/mL ($p = 0.002$), 40.45 vs. 10.1 ng/mL ($p < 0.001$), and 195.7 vs 81.4 ng/mL ($p = 0.001$). AUC-ROC curve of novel biomarkers for diagnosing of AKI was shown in figure 1. Mortality in AKI group was higher than those without (42.2% vs. 12.5%, $p < 0.001$). UL-FABP, uNGAL, and pNGAL in deceased patients were higher than survivors; 14 vs. 2.72 ng/mL ($p < 0.001$), 104.7 vs. 10.3 ng/mL ($p < 0.001$), and 209.3 vs. 91.3 ng/mL ($p = 0.005$). Using multivariate analysis, predictors for 28-day mortality were uL-FABP with cut-off of 4.68 ng/mL (OR 3.94, $p = 0.021$), malignancy (OR 4.21, $p = 0.013$) and AKI (OR 4.60, $p = 0.006$).
Conclusion: UL-FABP, uNGAL, and pNGAL were significantly higher in cirrhotic patients with AKI. The presence of AKI, malignancy and uL-FABP were predictors for 28-day mortality in hospitalized cirrhotic patients.

Figure 1. AUC-ROC curve indicating performance of each biomarker in discriminating patients with cirrhosis who developed AKI and no AKI



Abstract #2047

Gastrointestinal bleeding is complication of acute-on-chronic liver failure

Do Seon Song[2], Jin Mo Yang[2], Hee Yeon Kim[2], Chang Wook Kim[2], Sung Won Lee[2], Eileen L. Yoon[1], Han Ah Lee[3], Young Kul Jung[3], Hyung Joon Yim[3], Jeong-Ju Yoo[4], Soung Won Jeong[4], Sang Gyune Kim[4], Jae Young Jang[4], Seong Hee Kang[5], Moon Young Kim[5], Jung Gil Park[6], Won Kim[7], Baek Gyu Jun[8], Ki Tae Suk[9], Dong Joon Kim[9], on behalf of Korean Acute-on-Chronic Liver Failure (KACLiF) Study Group

[1] Department of Internal Medicine, The Catholic University of Korea, Seoul, Republic of Korea, [2]Department of Internal Medicine, Inje University, Seoul, Republic of Korea, [3] Department of Internal medicine, Korea University, Seoul, Republic of Korea, [4] Department of Internal Medicine, Soonchunhyang University, Seoul, Republic of Korea, [5] Department of Internal Medicine, Wonju College of Medicine, Yonsei University, Wonju, Republic of Korea, [6] Department of Internal Medicine, Yeungnam University College of Medicine, Daegu, Republic of Korea, [7] Department of Internal Medicine, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, Republic of Korea, [8] Department of Internal Medicine, University of Ulsan College of Medicine, Gangneung, Republic of Korea, [9]Department of Internal Medicine, Hallym University College of Medicine, Chuncheon, Republic of Korea

Background: Two acute-on-chronic liver failure (ACLF) definitions, proposed by Asian Pacific Association for the Study of the Liver ACLF research Consortium (AARC) and European Association for the Study of Liver-Chronic Liver Failure (EASL-CLIF) consortium are most commonly used. However, two definitions had different criteria in terms of predisposing factor, especially gastrointestinal bleeding (GIB). This study is to investigate whether GIB acts as predisposing factor of ACLF.
Method: Total 1490 chronic liver disease patients (1762 events) who admitted with acute deterioration were enrolled. The association between GIB and ACLF were analyzed by logistic regression analysis.
Results: GIB was present in 664 events at the time of admission, and new GIB developed during hospitalization in 32 patients without GIB at the time of admission. In the patients without ACLF at the time of admission, there was no significant association between GIB and new ACLF development ($P = 0.251$ for AARC and $P = 1.000$ for EASL-CLIF ACLF). However, in the patients without GIB at the time of admission, AARC ACLF and EASL-CLIF ACLF showed significant association with new GIB development (Odds ratio (OR) 4.606, $P < 0.001$ for AARC ACLF and OR 2.789, $P = 0.005$ for EASL-CLIF ACLF). Both ACLF definitions were independent factors for new GIB during hospitalization after adjusting by C-reactive protein, hyponatremia, and presence of ascites which were significant factors by univariate analysis.
Conclusion: GIB is likely the complication of ACLF rather than predisposing factor of ACLF. Therefore, caution is required for the GIB in patients with ACLF.

Abstract #2096

Glomerular filtration rate in liver cirrhosis

Niza Amalya,*Rini Rachmawarni Bachtiar, Fardah Akil, Muhammad Luthfi Parewangi, Nu'man AS Daud, Susanto H Kusuma, Amelia Rifai

Centre of Gastroenterology-Hepatology HAM Akil/DR. Wahidin Sudirohusodo General Hospital. Division of Gastroenterology-Hepatology, *Department of Internal Medicine, University of Hasanuddin, Makassar-Indonesia

Introduction: The accurate assessment of glomerular filtration rate (GFR) in patients with liver disease especially in liver cirrhosis (LC) is a crucial aspect of their clinical care and outcomes. It determines when renal dysfunction is recognized, potentially lessening side effects of inappropriate drug dosing, while also facilitating early therapeutic interventions and decisions about liver transplantation.
Objectives: To identify and evaluate the correlations of GFR with clinical data of LC patients.
Methods: This retrospective study using 199 LC patients between year 2017–2018. Demographic, laboratory, and radiology data were collected and calculate estimated glomerular filtration rate (eGFR) by chronic kidney disease epidemiology collaboration (CKD-EPI)

formula divided into two groups eGFR: ≥60 ml and < 60 ml/min/1.73m2. Statistic analysis using Chi-square, Fisher-exact, Spearmen coefficient-correlation and ROC methods.

Results: We found 179 (89.9%) without organic renal disease and 111 patients were included in this study. Majority patients were male 84 (75.7%) and age > 40 y.o in 100 (90.0%). Etiology of LC: viral/non-viral 100 (90%)/11 (10%) with ascites gr2-3 78 (70.2%), Child-Turcotte-Pugh A-B 71 (63.9%). Median of laboratory data: albumin 2.8 g/dl, billirubin 2.15 mg/dl, INR 1.29. Based on eGFR: ≥60 ml 83 (74.8%) and < 60 ml 28 (25.2%) patients with median 89.9 ml/min/1.73m2; eGFR < 60 ml was significantly correlated with bilirubin > 3 mg/dl (p = 0.017), viral etiology (p = 0.018) and ascites gr2-3 (p = 0.000). Logistic regression analysis revealed that ascites gr 2-3 and viral etiology at diagnosis correlated with eGFR < 60 ml (OR.16.941;95% CI 2.193–130.848; p = 0.000 and OR.4.255;95% CI 1.186–15.266; p = 0.018) with 75.5% of accuracy.

Conclusion: Our study suggests that viral etiology/bilirubin/ascites gr 2-3 correlate with decrease of eGFR and viral etiology/ascites gr 2-3 are independent risk factors of renal dysfunction in LC.

Abstract #2137

Ascites or encephalopathy in acute-on-chronic liver failure—which is more ominous?

Anand V. Kulkarni[1], Padaki Nagaraja Rao[1], Bindu Reddy[1], Ashok K. Choudhury[2], Shiv K. Sarin[2], and AARC collaborators.

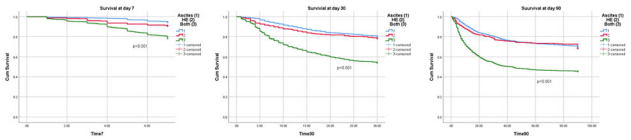
[1]Department of Hepatology, Asian Institute of Gastroenterology, Hyderabad, India, [2]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Development of ascites or encephalopathy is an ominous sign in a cirrhotic patient. Acute-on-chronic liver failure (ACLF) is a syndrome of acute portal hypertension, and both ascites and encephalopathy are part of the definition of APASL ACLF. We evaluated the impact of the development of ascites and hepatic encephalopathy (HE) at baseline on the outcome of ACLF patients.

Methods: Prospective data from the multi-national APASL-ACLF Research Consortium (AARC) was analyzed using SPSS 25.

Results: Of the 3343 patients {Males-84.5%; alcohol-49.8%} with completed outcomes 1770 presented with ascites (Gr. A), 393 with HE only (Gr. B), and 1180 with both ascites and HE (Gr.C). HVPG data was available in 481 patients. Baseline HVPG was similar in all the three groups (Gr. A-18.46 ± 5.7, Gr. B-17.71 ± 4.59, Gr.C-17.53 ± 4.74; p = 0.29). Baseline ammonia was higher in Gr. B and C than A (Gr. A-82.89 ± 50.18, Gr. B-152.21 ± 90.5, Gr.C-165.32 ± 99.86; p < 0.001). Baseline severity scores were higher in Gr. B and C than Gr. A {AARC-Gr. A-9.3 ± 1.86, Gr. B-10.46 ± 2.09, Gr. C-10.95 ± 1.96; p < 0.001; CLIF SOFA-Gr. A-12.87 ± 4.76, Gr. B-14.56 ± 4.8, Gr. C-14.48 ± 4.01; p < 0.001}. Day 7, 30, and 90 mortality in the whole cohort was 11.5%, 29%, and 38.4%, respectively. Day 7, 30 and day 90 mortality was similar in Gr. A and B (Day 7-Gr. A-5.4% Gr. B-9.2%; Day 30-Gr. A-19.4% Gr. B-21.6%; day 90-Gr. A-29.3%, Gr. B-31.1%). However, patients who presented with ascites and encephalopathy had higher mortality (Gr. C-day 7–21.4%; day 30–45.8%; 90–54.4%) than Gr. A and Gr. B (Figure).

Conclusions: ACLF patients presenting with ascites or encephalopathy have similar outcomes, while those who present with both ascites and HE have higher mortality. Thus, upholding the definition of ACLF.



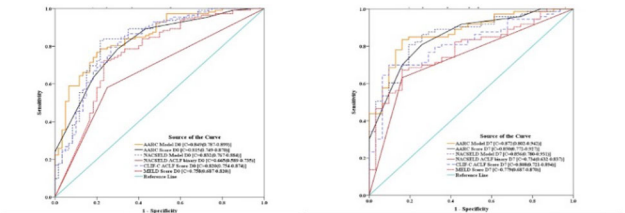
Abstract #2139

Comparative accuracy of prognostic models for short-term mortality among acute-on-chronic-liver-failure (ACLF) patients: an analysis beyond receiver operator curve (ROC)-CAPSACLF study

Verma Nipun[1], Dhiman Radha Krishan[1], Duseja Ajay[1], Choudhury Ashok[2], Sharma ManojKumar[2], Maiwall Rakhi[2], Eapen CE[3], Devarbhavi Harshad[4], Mahtab MamunAl[5], Rahman Salimur[5], Shukla Akash[6], Hamid Saeed Sadiq[7], Jafri Wasim[7], Butt Amna Shubhan[7], Ning Quin[8], Chen Tao[8], Tan Soek Siam[9], Lesmana LaurentiusA.[10], Lesmana Cosmas Rinaldi[10], Sahu Manoj K[11], Hu Jinhua[12], Lee Guan Huei[13], Sood Ajit[14], Midha Vandana[14], Goyal Omesh[14], Ghazinian Hasmik[15], Kim Dong Joon[16], Treeprasertsuk Sombat[17], Mohan Prasad VG[18], Dokmeci A Kadir[19], Sollano Jose D[20], Shah Samir[21], Payawal Diana Alcantara[22], Rao PN[23], Kulkarni Anand[23], Lau George K[24], Yuen Man Fung[25], Duan Zhongping[26], Yu Chen[26], Yokosuka Osamu[27], Abbas Zaigham[2], Karim Fazal[29], Chowdhury Debashish[30], Prasad Ananta Shrestha[31], Sarin Shiv Kumar[2], APASL ACLF Working Party

[1]Department of Hepatology, PGIMER, Chandigarh, India, [2]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India, [3]Department of Hepatology, CMC, Vellore, India, [4]Department of Hepatology, St John Medical College, Bangalore, India, [5]Department of Hepatology, Bangabandhu Sheikh Mujib Medical university, Dhaka, Bangladesh, [6]Department of Hepatology, STNMC Medical College, Mumbai, India, [7]Department of Medicine, Aga Khan University Hospital, Karachi, Pakistan, [8]Department of Medicine, Tongji Hospital, Tongji Medical College, China, [9]Department of Medicine, Hospital Selayang, Bata Caves, Selangor, Malaysia, [10]Department of Medicine, Medistra Hospital, Jakarta, Indonesia, [11]Department of Hepatology, IMS &SUM hospital, Bhuvaneswar, Odisa, India, [12]Department of Medicine, 302 Millitary Hospital Beijing, China, [13]Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, [14]Department of Gastroenterology, DMC, Ludhiana, India, [15]Department of Hepatology, Nork Clinical Hospital of Infectious Disease, Armenia, [16]Deparment of Internal Medicine, Hallym University College of Medicine, Seoul, Korea, [17]Department of Medicine, Chulalongkorn University, Bangkok, Thailand, [18]Department of Gastroenterology, VGM Hospital, Coimbatore, India, [19]Department of Medicine, Ankara University School of Medicine, Turkey, [20]Department of Medicine, University of Santo Tomas, Manila, Philippines, [21]Global Hospitals, Mumbai, India, [22]Department of Medicine, Cardinal Santos Medical Center, Metro Manila, Philippines, [23]Asian Institute of Gastroenterology, Hyderabad, [24]Department of Medicine, Humanity and Health Medical Group, Hong Kong, [25]Department of Medicine, Queen Mary Hospital Hong Kong, China, [26]Translational Hepatology Institute Capital Medical University, Beijing You'an Hospital, China, [27]Chiba University Japan, [28]Department of Medicine, Ziauddin University Hospital, Karachi, Pakistan, [29]CMOSH Medical College, Agrabad, Chittagong, Bangladesh, [30]Sir Salimullah Medical College, Mitford Hospital, Dhaka, Bangladesh, [31]Department of Hepatology, Foundation Nepal Sitapaila Height, Kathmandu, Nepal

Introduction: Accurate prediction of mortality is important to prognosticate and stratify management in acute-on-chronic-liver-failure (ACLF) patients.
Objective: To evaluate the accuracy of prognostic models for 30-day mortality among ACLF patients.
Methods: Data from APASL-ACLF Research Consortium (AARC) was analyzed from April-2009 till December-2019. ACLF was graded utilizing AARC-criteria. AARC-model, AARC-score, CLIF-C ACLF-score, NACSELD ACLF-model, NACSELD ACLF-binary, CLIF-C OF, SOFA, APACHE-II, MELD, and CTP-scores were evaluated in both static and dynamic modes. Model performance was evaluated using C-statistics, Akaike and Bayesian information criteria (AIC and BIC), Nagelkerke-R^2, correct-predictability (%) and odds-ratios.
Results: Thirty-day survival of cohort (n = 2864) was 64.9% and was lowest for baseline grade-III (31%) than grade-II (69%) and grade-I (87%) ACLF; $P < 0.001$. Patients satisfying CANONIC or NACSELD definition had a poor 30-day survival as compared with others (38.2% and 24.8% vs. 75.4% and 47.6%; $P < 0.001$ for both). Individual-performance characteristics of most day7-models were better than day0-models (Table1). On comparison (Figure1), day7 AARC-model [C = 0.872 (0.802–0.942)], AARC-score [C = 0.850 (0.772–0.972)], NACSELD-model [C = 0.856 (0.780–0.931)] and CLIF-C ACLF-score [C = 0.808 (0.721–0.894)] had the best discrimination for 30-day mortality (P = NS). Overall-prediction of 30-day-outcome was best for day7 AARC-Model (84.0%). Day7 NACSELD ACLF-binary had minimum AIC/BIC (12/17), highest odds-ratio [8.859 (3.043–25.791)] and correct-prediction of mortality (100%). Day7 AARC-model had the best C-statistic [C = 0.847 (0.797–0.888)] for APASL with CANONIC ACLF.
Conclusions: ACLF is often a progressive disease and dynamic models, assessed up to day7 reliably predict 30-day mortality. Day7 AARC-model is best at classifying risk (discrimination) of 30-day mortality and correctly predicting overall-outcome (calibration) among ACLF patients. ACLF patients satisfying NACSELD-definition at day7 has highest odds of 30-day mortality.



Day 0 Models

Parameters	C-statistics	AIC	BIC	Nagelkerke R^2	% Overall prediction correct	% Prediction correct for mortality	% Prediction correct for survival	Odds Ratio Mortality (95%CI)
AARC Model	0.847 (0.797–0.895)	143	151	0.458	84.0	90.3	63.3	-
AARC Score	0.833 (0.749–0.876)	33	29	0.373	78.0	89.3	37.0	1.516 (1.536–2.363)
NACSELD Model	0.822 (0.751–0.884)	164	170	0.421	80.0	89.9	62.0	-
NACSELD ACLF-binary*	0.695 (0.559–0.730)	15	20	0.133	65.1	100.0	0.0	4.149 (2.075–8.859)
CLIF-C ACLF Score	0.831 (0.724–0.914)	168	174	0.306	77.3	87.5	58.3	1.183 (1.120–1.249)
MELD Score*	0.697 (0.592–0.820)	175	115	0.276	73.8	85.9	55.6	1.186 (1.136–1.239)

Day 7 Models

Parameters	C-statistics	AIC	BIC	Nagelkerke R^2	% Overall prediction correct	% Prediction correct for mortality	% Prediction correct for survival	Odds Ratio Mortality (95%CI)
AARC Model	0.872 (0.802–0.942)	82	100	0.609	84.0	89.0	71.0	-
AARC Score	0.850 (0.772–0.927)	62	31	0.438	81.0	92.0	34.0	2.111 (1.220–2.862)
NACSELD Model	0.856 (0.780–0.931)	102	120	0.442	80.8	87.7	64.2	-
NACSELD ACLF-binary*	0.734 (0.632–0.837)	13	17	0.255	70.2	100.0	0.0	8.859 (3.043–25.791)
CLIF-C ACLF Score	0.808 (0.721–0.894)	128	132	0.334	74.0	86.3	43.1	1.162 (1.087–1.242)
MELD Score*	0.779 (0.687–0.870)	109	114	0.271	71.2	86.3	35.8	1.171 (1.094–1.254)

Poster presentations

Abstract #63

Autologus haemopoitic stem cell transplantation in decompensated cirrhotics via portal venous route—initial experience from Bangladesh

Mahtab Mamun[1], Rahim Abdur[2], Noor-E-Alam Sheikh[1], Alam Ashraful[3], Khondokar Faiz[4], Moben Lutful[5]

[1]Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, [2]Department of Hepatology, Abdul Malek Ukil Medical College, Noakhali, [3]Department of Hepatology, Shaheed Tajuddin Ahmod Medical College, Gazipur, [4]Department of Hepatology, Shaheed Suhrawardy Medical College, Dhaka, [5]Department of Medicine, Kurmitola General Hospital, Dhaka

Introduction: Decompensated cirrhosis of liver is associated with decreased functional hepatocytes. Liver transplantation is only curative option, but unavailable in Bangladesh. Autologous haemopoitic stem cells administered to liver may help hepatocyte mobilization and reversal of decompensation. **Objectives:** To assess safety and efficacy of autologous haemopoitic stem cell transplantation in decompensated cirrhosis.
Methods: 33 decompensated cirrhotics were included after ethical approval of BSMMU. All received G-CSF injection (60 IU) s/c daily for 3–4 days with standard medical therapy. CD34-positive cells were isolated from peripheral blood using cell sorter (Fresenius Kabi, Germany) and transfused via trans-hepatic route into portal vein. Patients were followed up initially for 90 days.
Results: Of the 33, 23 were males and 10 females. Age was 50.6 years. 22 had hepatitis B, 4 NASH, 2 hepatitis C and 5 cryptogenic cirrhosis. Mean serum bilirubin improved from 4.09 mg/dl at baseline to 1.87 mg/dl and 1.64 mg/dl at 30 and 90 days. Mean serum albumin rose from 3.08 gm/L to 3.4 gm/L at 90 days. Mean prothombin time improved from 17.57 sec to 16.65 sec and 15.55 sec at 30 and 90 days. While moderate to marked ascites was present in 9 patients at baseline, 4 and 1 patient had similar ascites at 30 and 90 days respectively. 1/33 patient died within 90 days of follow up due to hepatic encephalopathy. No rise in AFP and no hepatic SOL was detected in ultrasonography.
Conclusion: Autologus haemopoitic stem cell transplantation appears, safe and moderately beneficial in decompensated cirrhosis.

Abstract #88

Efficacy of spironolactone and furosemide combination in comparison to spironolactone alone as treatment of ascites in liver cirrhosis patient: an evidence based case report

Bany Faris Amin[1], Hasan Maulahela[2]

[1]Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia, [2]Department of Internal Medicine, Gastroenterohepatology Division, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia

Introduction: Ascites is one of the main complications of cirrhosis which is associated with increased mortality. Diuretics are the main management of ascites in patients with cirrhosis. Spironolactone and furosemide are diuretics that are often used as an initial therapy.
Objective: This evidence-based case report aims to determine whether the combination of spironolactone and furosemide compared with spironolactone as initial therapy has better efficacy.
Method: Literature search uses databases such as Pubmed, Ebscohost, Scopus, and Cochrane with keywords "Ascites", "cirrhosis", "Spironolactone", "Furosemide", and "Efficacy". Result is then sorted using inclusion criteria, exclusion criteria, and removing duplicates
Result: Two relevant studies were obtained. Research by Santos et al. found that weight loss, time of response, ascites response rate and incidence of adverse events amongs the group were not significant ($P > 0.05$), the need for dose reduction was higher in the combination group (68% vs 34%) ($P = 0.002$). Research by Fogel et al. found that weight loss, loss of ascites, loss of edema, need for increased dosage, and the need to reduce dosage is not significant ($p > 0.05$). the onset of diuresis was faster in the combination group (9 ± 1 vs 13 ± 1) ($p < 0.05$)
Conclusion: The selection of spironolactone can be given as initial therapy and then raised based on the response to ascites. Giving

combination therapy as a patient's initial therapy can be done to accelerate the onset of diuresis in hospitalized patients who can be periodically monitored.

Abstract #93

The effect of long-term human albumin administration on the mortality of adult patients with decompensated liver cirrhosis: a meta-analysis and systematic review

Ramon Larrazabal Jr

Introduction: Liver cirrhosis is currently the 11th most common cause of death globally. The common hallmark in its pathophysiology is circulatory dysfunction. Targeting circulatory dysfunction appears to be a promising therapeutic approach to decrease the development of complications; and therefore, mortality. Human Albumin have been shown to be useful in improving circulatory function in patients with advanced cirrhosis.
Objectives: This study aims to determine the effect of long-term human albumin administration on the mortality rate of adult patients with decompensated liver cirrhosis.
Methods: Meta-Analysis and Systematic Review
Results: Results showed that there is a 27% decrease in mortality [RR = 0.73 (0.51 to 1.04, 95% CI, Z = 1.73, p 0.08)] after long term human albumin administration with standard medical therapy as compared to those who received standard medical therapy alone. A subgroup analysis excluding the heterogenous study of Sola et al. showed that there was a 32% decrease in mortality [RR = 0.68 (0.47 to 0.99, 95% CI, Z = 1.99, p = 0.05)] in patients given long term human albumin. There was also a 62% decrease in cirrhosis-related complications [RR = 0.38 (0.26 to 0.54, 95% CI, Z = 5.39, $p < 0.00001$)] in the treatment group.
Conclusion: Long term human albumin administration might have a beneficial effect in reducing mortality and the incidence of cirrhosis-related complications among adult patients with decompensated liver cirrhosis. However, larger, multi-centered, and double-blinded randomized controlled trials with longer follow-up periods are needed to generate more robust data.

Abstract #112

Prevalence and outcomes of acute kidney injury in patients with acute on chronic liver failure: a single centre experience

Khatua Chitta Ranjan,[1] Sahu Saroj Kanta,[1] Singh Shivaram Prasad[1]

[1]Srirama Chandra Bhanja Medical College, Cuttack, Odisha, India

Introduction: Acute on chronic liver failure (ACLF) is a life-threatening condition in patients of chronic liver disease (CLD) and acute kidney injury (AKI) further decreases the survival of patients.
Objectives: There are scant data regarding the impact of AKI on survival in ACLF in this region of Asia. Hence we performed a prospective study to evaluate the spectrum of ACLF and the impact of AKI in outcomes of these patients
Methods: This study was conducted in consecutive ACLF patients (defined as per APASL consensus criteria), hospitalised in SCB Medical College, India between October 2016 and December 2018. AKI was defined and classified as per AKIN criteria. Demographic, clinical, and laboratory parameters were recorded, and outcomes were compared during hospitalisation and also at 28 days and 90 days.
Results: 154 (26.7%) out of 576 CLD patients had ACLF, of which 71.4% had AKI. 39% had stage 1, 17.5% had stage 2, and 14.9% had stage 3 AKI. Mortality during hospitalisation increased with higher grades of AKI ($p < 0.001$). Furthermore, they had decreased survival both at 28 days ($p < 0.001$) and 90 days ($p < 0.001$). ACLF patients with AKI had significantly higher serum creatinine, serum urea, total bilirubin, INR and higher MELD UNOS, MELD Na + , CTP score, and increased duration of hospitalisation ($p < 0.001$).
Conclusion: In our institution, about one fourth of CLD patients had ACLF and over two thirds of them had AKI during hospitalisation. AKI patients had prolonged hospitalisation, and decreased survival during hospitalisation, and also at 28 days and 90 days.

Abstract # 152

Association of portal venous system thrombosis with endoscopic variceal treatment: an observational study with a systemic review and meta-analysis

Xingshun Qi

Background: The association of endoscopic variceal treatment (EVT) with the development of portal venous system thrombosis (PVST) in liver cirrhosis remains uncertain.
Methods: In an observational study, cirrhotic patients were screened. PVST was confirmed by contrast-enhanced computer tomography (CT) or magnetic resonance imaging (MRI). History of previous EVT before CT or MRI scans was reviewed. In a systematic review, all relevant studies regarding the association of EVT with PVST were searched. Meta-analyses were performed by random-effect model. Risk ratios (RRs) with 95% confidence intervals (CIs) were calculated.
Results: In the observational study, patients who underwent EVT had a significantly higher incidence of PVST than those who did not undergo EVT (37.3% versus 22.6%, P = 0.003). According to the site of PVST, patients who underwent EVT had significantly higher incidence of thrombosis within main portal vein, superior mesenteric vein, and splenic vein. According to the degree of PVST, patients who underwent EVT had a significantly higher incidence of partial occlusion. The incidence of PVST remained higher in patients who underwent endoscopic variceal ligation (EVL) combined with endoscopic cyanoacrylate glue injection (ECGI) (55.3% versus 22.6%, $P < 0.001$) and those who underwent EVT for controlling bleeding (40.0% versus 22.6%, P = 0.001). In the meta-analysis of 13 studies, the pooled incidence of PVST after EVT was 10.4%, and EVT significantly increased the risk of PVST (RR: 2.25; 95% CI, 1.15–4.41; P = 0.02).
Conclusions: EVT may increase the risk of PVST in liver cirrhosis, especially in those who underwent EVL combined with ECGI and who underwent EVT for controlling bleeding.

Abstract #153

Correlation of serum cardiac markers with acute decompensated events in liver cirrhosis

Miaomiao Li [1,2*], Zeqi Guo [1*], Jie Liu [3*], Xiangbo Xu [1,3*], Jingqiao Zhang [1,3], Ruirui Feng [1], Xinmiao Zhou [1], Cen Hong [1], Hemant Goyal [4], Xingshun Qi[1]

[1] Liver Cirrhosis Group, Department of Gastroenterology, General Hospital of Northern Theater Command (formerly General Hospital of Shenyang Military Area), Shenyang, China, [2] Department of Clinical Laboratory, The First Hospital of Lanzhou University,

Lanzhou, Gansu 730000, P. R. China, [3]Department of Pharmaceutical Sciences, Shenyang Pharmaceutical University, 103 Wenhua Road, Shenyang, Liaoning, 110016, China, [4]Department of Internal Medicine, The Wright Center for Graduate Medical Education, 111 North Washington Avenue, Scranton, PA, 18503, USA.

Background and aim: Liver cirrhosis is often accompanied by insidious cardiac dysfunction. A retrospective cross-sectional study aimed to explore the correlation between serum cardiac markers and decompensated events in liver cirrhosis.
Methods: Cirrhotic patients who were consecutively admitted to our department between January 2016 and March 2019 were screened. Serum cardiac biomarkers, including N-Terminal pro-B-Type natriuretic peptide (NT-pro BNP), Troponin T-hypersensitivity (TnT-HSST), creatine kinase (CK), creatine kinase MB (CK-MB), and lactate dehydrogenase (LDH) were tested. Acute decompensated events at admission, including ascites, acute gastrointestinal hemorrhage, and acute-on-chronic liver failure (ACLF), were recorded.
Results: NT-pro BNP level was significantly higher in cirrhotic patients with acute decompensated events than those without decompensated events. NT-pro BNP level significantly correlated with ascites, acute gastrointestinal hemorrhage and ACLF. TnT-HSST level was significantly higher in cirrhotic patients with ascites and acute gastrointestinal hemorrhage than those without decompensated events. TnT-HSST level significantly correlated with acute gastrointestinal hemorrhage, but not ascites or ACLF. LDH level was significantly higher in cirrhotic patients with ascites and ACLF than cirrhotic patients without decompensated events. LDH level significantly correlated with ascites and ACLF, but not acute gastrointestinal hemorrhage. CK and CK-MB levels were not significantly different between cirrhotic patients with and without decompensated events.
Conclusion: Elevated NT-pro BNP level is more closely related to the development of acute decompensated events in liver cirrhosis. NT-pro BNP may be a sensitive marker to predict early cardiac dysfunction caused by advanced cirrhosis.

Abstract # 154

No benefit of hemostatic drugs on acute upper gastrointestinal bleeding in cirrhosis

Yang An[1,2#], Zhaohui Bai[1,2#], Xiangbo Xu[1,2#], Xiaozhong Guo[1#], Fernando Gomes Romeiro[3], Cyriac Abby Philips[4], Yingying Li[5], Yanyan Wu[1,6], Xingshun Qi[1*]

[1] Department of Gastroenterology, General Hospital of Northern Theater Command (formerly General Hospital of Shenyang Military Area), Shenyang, 110840, P. R. China, [2] Postgraduate College, Shenyang Pharmaceutical University, Shenyang 110016, P. R. China, [3]Department of Internal Medicine, Botucatu Medical School, UNESP-Univ Estadual Paulista. Av. Prof. Mário Rubens Guimarães Montenegro, s/n Distrito de Rubião Jr. Botucatu, Brazil, [4] The Liver Unit and Monarch Liver Lab, Cochin Gastroenterology Group, Ernakulam Medical Center, Kochi 682028, Kerala, India, [5] Department of Gastroenterology, The First People's Hospital of Huainan, Huainan 232007, P. R. China, [6] Postgraduate College, Jinzhou Medical University, Jinzhou 121001, P. R. China.

Background and Aims: Acute upper gastrointestinal bleeding (AUGIB) is a life-threatening condition. Hemostatic drugs are often prescribed to control AUGIB in clinical practice, but have not been recommended by guidelines. The aim of this study was to investigate the therapeutic effect of hemostatic drugs on AUGIB in cirrhosis.
Methods: All cirrhotic patients with AUGIB were retrospectively included. Patients were divided into hemostatic drugs and no hemostatic drug groups. A 1:1 propensity score matching (PSM) analysis was performed by adjusting age, gender, Child–Pugh score, MELD score, hematemesis, red blood cell transfusion, vasoactive drugs, antibiotics, proton pump inhibitors, and endoscopic variceal therapy. Primary outcomes included 5-day rebleeding and in-hospital mortality.
Results: Overall, 982 patients were included. In overall analyses, hemostatic drugs group had a significantly higher 5-day rebleeding rate (18.10% versus 5.40%, P = 0.001); in-hospital mortality was not significantly different (7.10% versus 4.50%, P = 0.293). In PSM analyses, 170 patients were included. Hemostatic drugs group still had a significantly higher 5-day rebleeding rate (17.60% versus 5.90%, P = 0.017); in-hospital mortality remained not significantly different (4.7% versus 4.7%, P = 1.000). Statistical results remained in PSM analyses according to the different hemostatic drugs.
Conclusions: Use of hemostatic drugs did not improve the in-hospital outcomes of cirrhosis with AUGIB.

Abstract #186

Fungal Urinary Tract Infection Among Chronic Liver Disease Patients With Hepatic Encephalopathy And Its Treatment Outcomes

Dr. Hamid Ali, Dr. Lubna kamani

Introduction: -Candiduria is a common nosocomial infection afflicting the urinary tract. Candida urinary tract infections are an increasingly prevalent nosocomial problem with uncertain significance. CLD patients are known to have various functional immune abnormalities, ignoring a possible Candida infection in such patients can have fatal consequences.
Objective: To determine the frequency of fungal urinary tract infection among chronic liver disease patients with hepatic encephalopathy and its treatment outcomes, at a tertiary care hospital, Karacchi
Subject & methods: All patients who fulfilled the inclusion criteria in the Department of Gastroenterology, Liaquat National Hospital, Karachi were included. After taking informed written consent clinical examination and lab investigations were done to determine the outcome i-e fungal urinary tract infection and its different species. After diagnosis patients were treated with fluconazole and treatment outcomes in term of discharge or death was observed.
Results: A total of 236 CLD patients presenting with fever or porto systemic encephalopathy were selected to conduct this study with mean age of 51.27 + 5.56 years, 165 patients (70%) were females. 200 patients (85%) had child class C. 141 patients (60%) had fungal UTI of which non-albicans Candida spp. emerged as the predominant pathogen and was responsible for 30% (70 patients) of nosocomial fungal UTI. Candida Albicans accounted for 13% (30 patients) of the cases. After treatment with fluconazole 98/141 patients (69.5%) were improved and discharged.
Conclusion: Nosocomial Candida UTIs in CLD patients is common as these patients are immunocompromised & there is cumulative pressure of contributing factors such as urinary instrumentation and prolonged use of broad-spectrum antibiotics. Non-albicans Candida were found to outnumber. Treatment with fluconazole results in better outcome.

Abstract #201

Cytoglobin-expressing cells in the splenic cords contribute to splenic fibrosis in cirrhotic patients

Yuji Iimuro[1,3], Toshihiro Okada[1], Norifumi Kawada[2], Etsuro Hatano[1], Jiro Fujimoto[1]

[1]Department of Surgery, Hyogo College of Medicine, [2]Department of Hepatology, Graduate School of Medicine, Osaka City University, and [3]Department of Surgery, Yamanashi Central Hospital

Background and Aim: Spleen stiffness measured by ultrasound increases in patients with portal hypertension (PH), while the underlying mechanism is obscure. We previously reported that splenic fibrosis progresses along with advancement in PH. In the present study, we investigated characteristics of cells which play significant roles in splenic fibrosis.
Methods: Histological examination and Western Blot analysis were performed using splenic tissues from patients with PH, in comparison with those from non-PH patients.
Results: Diffuse fibrosis was detected in the splenic cords in the red pulp of PH patients, and the degree of the fibrosis well correlated with severity in thrombocytopenia ($p = 0.011$) and splenomegaly ($p < 0.001$). Cytoglobin (Cygb)-expressing cells, which have been reported in rat spleen to be reticular cells, a kind of pericytes, were also detected in the human splenic cords (IHC and Western Blot), and its shape dramatically changed in patients with PH, elongating their cytoplasm to surround the splenic sinus. These transformed fibroblast-like cells expressed significant amount of a-smooth muscle actin, implying these cells were the origin of fibrous tissues observed in the cords. Expressions of nicotinamide adenine dinucleotide phosphate oxidases (NOX) 2, nitrotyrosine, and transforming growth factor-b were markedly upregulated in the red pulp of PH patients. The expression of NOX2 was localized to mononuclear cells/macrophages in the cords, suggesting oxidative stress produced by these cells play significant roles in the fibrogenic process.
Conclusion: Splenic fibrosis progresses along with advancement of portal hypertension. Cygb-expressing cells in the splenic cord possibly participate in this process through mechanisms including oxidative stress.

Abstract #215

Performance of AST to platelet ratio index (APRI) in predicting variceal bleeding among patients with upper gastrointestinal bleeding

Nattida Sribuathong, MD. And Chalermrat Bunchorntavakul, MD.

Division of Gastroenterology, Rajavithi Hospital, Bangkok, Thailand

Introduction: Various non-invasive liver fibrosis tests, including APRI, have been studied aiming to predict liver fibrosis and the presence of esophageal varices in patients with cirrhosis. However, the use of APRI to predict variceal bleeding (VB) in the setting of upper gastrointestinal (UGIB) remains unexplored.
Objective: This study aimed to evaluate the diagnostic accuracy of APRI in predicting VB as cause of bleeding in patients presenting with UGIB.
Methods: Consecutive patients presented with UGIB who underwent esophagogastroduodenoscopy EGD, between June 2018 and August 2019 at Rajavithi Hospital, Bangkok, were prospectively enrolled. Baseline clinical characteristics, basic laboratory variables, including APRI, and treatment outcome were evaluated.
Results: A total of 215 patients with UGIB were included; 75% were men, mean age was 56.4 years, mean Glasgow-Blatchford Score was 9.8, and 39.5% were VB. Mortality rates were 5.4% in non-VB group and 8.2% in VB group ($p = 0.408$). AUCs of APRI in predicting VB in all UGIB patients and in patients without known cirrhosis ($n = 132$) were 0.857 and 0.895, respectively. At the cut-off of 0.5, APRI showed sensitivity of 90.6% and 86.7%, and specificity of 75.4 and 81.2% in all UGIB patients and in patients without known cirrhosis, respectively.
Conclusions: APRI score has good performance in predicting VB in patients presenting with UGIB regardless of known cirrhosis status. It can be useful in clinical practice for prompt administration of vasoactive agents and urgent EGD.

Abstract #330

Changes in liver biopsy indications over 18 years and its safety

Young Chang[1*], Jun Il Kim[2*], Bora Lee[3], Sang Gyune Kim[2], Min Jung Jung[4], Young Seok Kim[2], Soung Won Jeong[1], Jae Young Jang[1], Jeong-Ju Yoo[2*]

[1]Department of Internal Medicine, SoonChunHyang University School of Medicine, Seoul, Korea, [2]Department of Internal Medicine, SoonChunHyang University School of Medicine, Bucheon, Korea, [3]Department of Biostatistics, Graduate School of Chung-Ang University, Seoul, Republic of Korea, [4]Department of Pathology Soonchunhyang University College of Medicine, Bucheon, South Korea,

Background: Liver biopsy (LB) remains the gold standard for evaluation of liver disease. However, many noninvasive tests have been developed and utilized in clinical practice as alternatives to LB during the past two decades. The aim of this study is to evaluate the clinical use and safety of LB in the era of noninvasive assessment of liver fibrosis.
Methods: This retrospective study included 1944 consecutive cases of LB performed between 2001 and 2018 in a tertiary hospital. All the LBs were conducted under ultrasonography guidance with 18-gauge cutting needles.
Results: LB was performed on average approximately 108 times per year during the study period. Chronic hepatitis B (25.3%) and suspected malignancy (20.5%) were the two most common indications for LB. The use of LB for nonalcoholic fatty liver disease increased from 8.1% to 17.2% in the recent 5 years compared with the last 10 years, and viral hepatitis decreased from 40.3% to 18.9%. The discordance rate between the suspected diagnosis and the final diagnosis was 2.6% (51 cases). The overall rate of major AE was 0.05% (1 case), and involved delayed bleeding at the biopsy site. Liver cirrhosis was observed in 563 cases (28.9%), and presence of cirrhosis did not affect the frequency of complications ($P = 0.289$).
Conclusion: LB is widely used in clinical practice as an irreplaceable diagnostic tool even in the era of noninvasiveness. Ultrasound-guided LB can be performed safely in patients with liver cirrhosis.

Abstract #357

The value of serum pro-calcitonin in diagnosis of spontaneous bacterial peritonitis (SBP) and predicting response to treatment

Allam Mahmoud, Elbasuony Reham, Salman Tary

Hepatology & Gastroenterology department, National Liver Institute, Menoufiya University

Background: spontaneous bacterial peritonitis (SBP) is a fatal complication of liver cirrhosis. Early diagnosis and appropriate management is crucial as regard patients' survival.
Method: Forty eight patients with ascites and suspicion of peritoneal fluid infection were enrolled. Diagnosis of SBP was confirmed by ascitic fluid analysis in 24 patients. Serum Procalcitonin was measured at time of admission for all enrolled patients and after 5 days of antibiotic treatment for those with SBP.
Results: At a cut-off of value of 0.55 ng/mL, procalcitonin had the best sensitivity (100%), specificity (83.3%) and (99.9%) accuracy in predicting SBP diagnosis. After 5 days of antibiotic treatment, thirteen patients (54.2%) responded to treatment. Procalcitonin had a (100%) sensitivity, (87.5%) specificity and (100%) accuracy at a cut-off value of 0.45 ng/mL in predicting response to antibiotic treatment.
Conclusion: procalcitonin may be a valuable non-invasive marker for diagnosis and guiding antibiotic therapy for patients with SBP.

Abstract #365

Quick sequential organ failure assessment in acute-on-chronic liver failure patients

Do Seon Song[1], Hee Yeon Kim[1], Young Joo Jin[2], Dong Hyun Sinn[3], Eileen L. Yoon[4], Chang Wook Kim[2], Young Kul Jung[5], Ki Tae Suk[6], Sang Soo Lee[7], Hyun Chin Cho[7], Chang Hyeong Lee[8], Hwi Young Kim[9], Tae Hun Kim[9], Baek Gyu Jun[10], Hyung Joon Yim[5], Sung Eun Kim [11], Sung Won Lee[1], Jung Hyun Kwon[1], Seong Hee Kang[12], Soon Koo Baik[12], Byung Seok Lee[13], Jae Young Jang[14], Jeong Ill Suh[15], Hyoung Su Kim[16], Seong Woo Nam[17], Hyeok Choon Kwon[17], Young Seok Kim[18], Sang Gyune Kim[18], Hee Bok Chae[19], Jin Mo Yang[2], Joo Hyun Sohn[20], Jung Gil Park[21], Heon Ju Lee[21,] Yoon Jun Kim[22], In Hee Kim[23], Ju Yeon Cho[24], Man Woo Kim[24], Sang young Han[25], Won Kim[26], Dong Joon Kim[6], on behalf of the Korean Acute-on-Chronic Liver Failure (KACLiF) Study Group

[1]Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea, [2]Department of Internal Medicine, Inha University Hospital, Inha University School of Medicine, Incheon, Republic of Korea, [3] Department of Internal Medicine, Samsung Medical Center, Seoul, Republic of Korea, [4]Department of Internal Medicine, Inje University Sanggye Paik Hospital, Seoul, Republic of Korea.[5] Department of Internal Medicine, Korea University Ansan Hospital, Ansan, Republic of Korea, [6] Department of Internal Medicine, Hallym University College of Medicine, Chuncheon, Republic of Korea, [7]Department of Internal Medicine, Gyeongsang National University Hospital, Jinju, Republic of Korea, [8]Department of Internal Medicine, Catholic University of Daegu School of Medicine, Daegu, Republic of Korea, [9]Department of Internal Medicine, Ewha Womans University School of Medicine, Seoul, Republic of Korea, [10]Department of Internal Medicine, Gangneung Asan Hospital, Gangneung, Republic of Korea, [11] Department of Internal Medicine, Hallym University Sacred Heart Hospital, Anyang, Republic of Korea, [12] Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea, [13] Department of Internal Medicine, Chungnam National University, School of Medicine, Daejeon, Republic of Korea, [14] Department of Internal Medicine, Soonchunhyang University College of Medicine, Seoul, Republic of Korea, [15] Department of Internal Medicine, Dongguk University Gyeongju Hospital, Gyeongju, Republic of Korea, [16] Department of Internal Medicine, Hallym University Kangdong Sacred Heart Hospital, Seoul, Republic of Korea, [17]Department of Internal medicine, National Medical Center, Seoul, Republic of Korea, [18]Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, Bucheon, Republic of Korea, [19]Department of Internal medicine, College of Medicine and Medical Research Institute, Chungbuk National University, Cheongju, Republic of Korea, [20]Department of Internal Medicine, Hanyang University Guri Hospital, Guri, Republic of Korea, [21]Department of Internal Medicine, Yeungnam University College of Medicine, Daegu, Republic of Korea, [22]Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea, [23]Department of Internal Medicine, Chonbuk National University Medical School and Hospital, Jeonju, South Korea, [24]Department of Internal Medicine, School of Medicine, Chosun University, Gwangju, South Korea, [25]Department of Internal Medicine, Dong-A University Hospital, Busan, [26]Department of Internal Medicine, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, Republic of Korea.

Background: Quick Sequential Organ Failure Assessment (qSOFA) have been suggested to screen for sepsis. In this study, we aimed to evaluate the ability of qSOFA in patients with acute-on-chronic liver failure (ACLF).
Methods: We prospectively collected data of 1199 chronic liver disease patients who admitted due to acute deterioration. ACLF was defined according to Asian Pacific Association for the Study of the Liver ACLF Research Consortium (AARC) and European Association for the Study of the Liver Chronic Liver Failure Consortium (EASL-CLIF) definitions.
Results: The qSOFA was ≥ 2 was independent prognostic factor for 90-day mortality ($P = 0.02$), but not 28-day mortality (P = 0.117) by Cox proportional hazard model. The area under receiver operating characteristics (AUROC) values of qSOFA for 28-day and 90-day mortality were 0.758 and 0.666 in patients with bacterial infection and 0.562 and 0.539 in patients without bacterial infection. The AUROC for 28-day and 90-day mortality were 0.542 and 0.515 in patients with AARC-ACLF, and 0.659 and 0.553 in patients with EASL-CLIF ACLF. By Kaplan-Meier analysis, patients with qSOFA ≥ 2 showed significantly lower 28-day survival rate than those with qSOFA < 2 in total patients regardless of bacterial infection ($P < 0.001$), and in patients with EASL-CLIF ACLF ($P = 0.001$). However, there were no significant differences in 28-day survival rate in patients with AARC-ACLF ($P = 0.077$) and in 90-day survival rate in both ACLF groups ($P = 0.464$ and $P = 0.171$).
Conclusion: qSOFA was useful tool to assess the short-term mortality in patients with bacterial infection. qSOFA was more accurate in patients with EASL-CLIF ACLF than patients with AARC-ACLF for predicting 28-day mortality mortality.

Abstract #397

Efficacy and tolerance of maximally tolerable dose of propranolol in the prevention of esophageal variceal rebleeding

Lee Changhyeong, MD., Kim Byungseok, MD., Song Jungeun, MD.

Gastroenterology and hepatology department, Daegu Catholic University Hospital, Daegu, South Korea

Introduction: The aim of this study was to assess the tolerance of maximal dose (MTD) and rebleeding rates of propranolol in liver cirrhosis patients for the prevention of EV rebleeding. **Objectives and Methods:** A total of 122 patients, who were treated with endoscopic band ligation for acute EV bleeding were enrolled. The definition of MTD is the maximal dose of propranolol that is being administered when the patient's pulse rate at rest is reduced to 75% of baseline or to 55 beats per minute. Low dose (LD) means a dose of

propranolol with 40 mg/day or less. End of follow-up was the time of the recurrence of EV rebleeding after at least 1 month after propranolol therapy or end of study.
Results: Sixty-eight patients were included in MTD group, and 54 patients were included LD group. The mean dose of propranolol of MTD group and LD group were 154.71 ± 68.82 mg/day and 38.15 ± 5.85 mg/day, and the mean duration of treatment was 45.5 ± 24.3 months and 57.5 ± 37.3 months. Rebleeding occurred 23 (33.8%) in MTD group and 29 (53.7%) in LD group, respectively (P = 0.027). There was no statistically significant difference in drug withdrawal rates between the two groups (P = 0.143). In MTD group, 18 patients experienced dose reduction compared to 2 patients in LD group. But, 12 patients maintained high dose of propranolol (≥ 80 mg/day) after dose reduction. The most common cause of dose reduction was bradycardia (30%) and other reasons were dizziness (25%) and hypotension (15%).
Conclusion: MTD is well tolerable and significant effect in reduction of EV rebleeding.

Abstract #458

Effects of exercise on frailty in patients with hepatocellular carcinoma

Takumi Kawaguchi[1], Shunji Koya[2], Keisuke Hirota[2], Jin Tsuchihashi[3], Noboru Koga[4], Hayato Narao[5], Manabu Tomita[6], Dan Nakano[1], Ryuki Hashida[2,7], Hiroo Matsuse[2,7], Taku Sanada[8], Kazuo Notsumata[8], Takuji Torimura[1]

[1]Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine, Kurume, Japan [2]Division of Rehabilitation, Kurume University Hospital, Kurume, Japan [3]Division of Rehabilitation, Fukui-ken Saiseikai Hospital, Fukui, Japan [4]Department of Rehabilitation, Chikugo City Hospital, Chikugo, Japan [5]Department of Rehabilitation, Yame General Hospital, Yame, Japan [6]Department of Rehabilitation, Saga Central Hospital, Saga, Japan [7]Department of Orthopedics, Kurume University School of Medicine, Kurume, Japan [8]Department of General Internal Medicine, Fukui-ken Saiseikai Hospital, Fukui, Japan

Introduction: Frailty is a geriatric syndrome of physiological decline including physical inactivity. Frailty is recently reported as a prognostic factor for patients with hepatocellular carcinoma (HCC).
Objectives: We aimed to investigate effects of exercise on frailty in patients with HCC.
Methods: This is a multi-center prospective observational study. We enrolled 94 patients with HCC (median age 77 years, female/male 36/58). Patients were classified into the Exercise group (n = 46) or Non-exercise group (n = 48) according to the intention of patients. In the Exercise group, patients performed exercise (2.5–4 metabolic equivalents/20 min/day) during the hospitalization. Frailty was assessed by Liver Frailty Index (LFI). Factors for an improvement of LFI during the hospitalization were examined by multivariate analysis and decision-tree analysis.
Results: There is no significant difference in age, sex, ALBI grade at the baseline between the two groups. BMI and the prevalence of sarcopenia in the Exercise group were significantly lower than those in the Non-exercise group. LFI was significantly improved in the Exercise group (P = 0.0191), but not in Non-exercise group. In multivariate analysis, male was identified as independent factor for the improvement of LFI (HR 2.80, 95% CI 1.067–7.3512, P = 0.0365). In decision-tree analysis, the improvement of LFI was seen in 70% of patients with male and exercise. While, the improvement was seen in 42.9% of patients with male and no exercise.
Conclusion: We demonstrated that exercise improved frailty in patients with HCC. However, the improvement was only remarkable in male, suggesting that exercise program according sex is required for improvement of frailty.

Abstract #477

The association between character of portal blood flow and post TIPS incidence of hepatic encephalopathy

Helmy El-Shazly[1], Mohamed Abdel-Samiee[1]*, El-Sayed Tharwa[1], Hassan Zaghla[1], Shrief Abass[1], Mohamed El-Warraky[2] and El-Sayed Ibrahim[1].

[1]Hepatology and Gastroenterology Department, National Liver Institute, Menoufia University, Shebin Elkom, Menoufia, Egypt, [2]Radiology Department, National Liver Institute, Menoufia University, Shebin Elkom, Menoufia, Egypt

Introduction: Hepatic encephalopathy (HE) is one of the serious complications observed post TIPS operations in patients with different complications of portal hypertension as refractory ascites, refractory hydrothorax, bleeding varices, and hepatorenal syndrome.
Objectives: Here in, we aimed to clarify predisposing factors for post-TIPS incidence of HE according to Pre-TIPS hemodynamics.
Methods: Fifty patients were enrolled in this study with different complications of portal hypertension most of them Child A and B, patients were evaluated by Ultrasound Doppler for the flow inside the portal vein and clinically recorded into two groups: group 1; 31 patients with hepatopetal flow, group 2; 19 patients with hepatofugal flow then TIPS was performed and patients were reassessed 1 month later to detect HE.
Results: Multiple variables as age, gender, weight, etiology of liver disease, indication for TIPS had no significant differences. The incidence of HE post-TIPS was observed more at group 1 more than group 2. (P = 0.12)
Conclusion: Post-TIPS incidence of HE was interestingly related to Pre-TIPS flow in the portal vein (hepatopetal group more than hepatofugal group). Patients with hepatofugal flow in the portal vein are perfect candidate for TIPS than patients with hepatopetal flow in the portal vein. Patient with previous history of HE are contraindicated for TIPS except as a bridge for Liver transplantation.

Table 1. Clinical characteristics of the studied groups before TIPS

	Hepatofugal group (no=19)		Hepatopetal group (no=31)		X^2 test	P value
	No	%	No	%		
Gender						
Male	9	47.4 52.6	11	35.5	0.69	0.41
Female	10		20	64.5		(>0.05)
Ascites						
Negative	1	5.3	1	3.2		
Mild	1	5.3	3	9.7	0.43	0.94
Moderate	4	21.1	6	19.4		(>0.05)
Severe	13	68.4	21	67.7		
History of Paracentesis						
Negative	1	5.3	4	12.9	0.83	0.64
Positive	18	94.7	27	87.1		(>0.05)
HE before TIPS						
Negative	19	100	29	93.5	1.96	0.52
Positive	0	0	2	6.5		(>0.05)
Child score						
A	2	10.5	2	6.5		0.48
B	17	89.5	27	87.1	1.48	(>0.05)
C	0	0	2	6.5		

Table 2. Comparison of the studied variables in relation to post TIPS incidence of Hepatic encephalopathy.

Variables	Post TIPS hepatic encephalopathy		P
	Negative	Positive	
Age in years (Mean±SD)	44.67±7.38	47.36±6.36	0.372 (>0.05)
MAP (Mean±SD)	79.10±7.96	80.18±5.96	0.663 (>0.05)
MELD Score	11.72±2.98	14.73±7.16	0.304 (>0.05)
HARI (Mean±SD)	0.58±0.10	0.61±0.05	0.459 (>0.05)
IVC pressure mmHg (Mean±SD)	5.18±0.89	5.37±0.84	0.403 (>0.05)
PVP mmHg (MeanSD)	33.90±11.10	34.45±5.66	0.934 (>0.05)

Table 3. Comparison between the studied groups regarding liver functions before TIPS:

	Hepatofugal group (no=19)	Hepatopetal group (no=31)	Mann Whitney test	P Value
	Mean±SD	Mean±SD		
ALT (IU/L)	57.2±51.7	40.5±35.1	1.22	0.22(>0.05)
AST (IU/L)	57.6±50.3	52.5±37.3	0.62	0.54(>0.05)
ALP (IU/L)	136.U66.4	129.7±40.9	0.09	0.93(>0.05)
Albumin(g/dL)	2.5±0.56	2.8±1.03	1.33	0.18(>0.05)
T. Biliiuhin (mg/dL)	1.5±0.58	1.6±0.53	0.62	0.54(>0.05)
D. Bilirubin (mg/dL)	0.95±0.77	0.98±1.03	0.22	0.83(>0.05)
INR	1.46±0.22	1.45±0.23	0.23#	0.82(>0.05)
Na^+	132.1±3.1	130.2±4.2	1.79#	0.08(>0.05)
K^+	3.8±0.47	3.7±0.57	0.31#	0.76(>0.05)

Table 4. Comparison between the studied groups regarding post HE.

		Hepatofugal group (no=19)		Hepatopetal group (no=30)		Fisher Exact test	P value
		No	%	No	%		
Post HE	Negative	17	89.5	22	71.0	2.55	0.12
	Positive	2	10.5	9	29.0		

Abstract #526

Evaluating outpatient elective paracentesis

Emilia Prakoso

Background: An elective large volume paracentesis (LVP) programme started in this tertiary hospital in July 2015.
Aim: To evaluate the utilisation of elective LVP in an outpatient setting and adherence of management to current guidelines.
Method: Retrospective analysis of cohort undergoing LVP from July 2015–June 2018. Clinical, laboratory and patient characteristics were collected using the electronic medical record.
Results: 66 patients (47 male, 19 female) underwent LVP. Mean age was 65.3 years (range 27–84 years). The most common aetiologies of liver disease were viral hepatitis (n = 23, 34.8%), non-alcoholic steatohepatitis (n = 21, 31.8%), alcohol-related liver disease (n = 16, 24.2%), and other (n = 3, 4.5%). 219 LVP procedures were performed. Mean volume (recorded in 90 LVP, 41%) was 6.4 L. Albumin infusion (recorded in 81 LVP, 37%) was adequate for 68 patients (84.0%). Albumin infusion was inadequate in 8 LVP (9.9%) with $\geq$ 5L fluid drained and 5 LVP (6.2%) with $\leq$ 5L fluid drained, although by a small albumin deficit (mean 7.8 g albumin per LVP). Ascitic fluid analyses were performed in 182 (83.1%) encounters. There were 10 cases of SBP (5.5%). 19 patients were on antibiotics for secondary SBP prophylaxis. 6 patients were not on antibiotics despite an indication for secondary prophylaxis.
Conclusion: Rates of SBP for an outpatient LVP setting (5.5%) is high compared with reported rates of 1.5–3.5%. Adherence to guidelines for utilisation of secondary SBP prophylaxis was suboptimal and may be clinically relevant.

Abstract #533

Relationship between hepatic venous pressure gradient with PH Risk Score, APRI Index and Fib-4 Score in patients with liver parenchymal diseases

Ellik Zeynep[1], Asiller Özgün Ömer[1], Özercan Mübin[1], Kartal Çalışkan Aysun[1], Örmeci Necati[1]

[1]Ankara University Faculty of Medicine, Department of Gastroenterology, Ankara/Turkey

Introduction: Portal hypertension is very important antitea for liver parenchymal disease.
Object: In order to evaluate the diagnostic accuracy of Apri index, Fib-4, Portal Hypertension (PH) risk score (PH risk score = -5.953 + 0.188 x LS +1.583 x sex (1: male; 0: female) + 26.705 x spleen diameter/platelet count ratio) for clinical significant portal hypertension in patients with compensated liver parenchymal disease.
Material: Twenty seven patients with compensated liver cirrhosis due to 6 hepatitis B, 2 hepatitis C virus infection, 8 non-alcoholic steatohepatitis, 6 autoimmune hepatitis, 5 cryptogenic cirrhosis, 1 portal vein thrombosis and 1 primary sclerosing cholangitis were approved for the study. All patients were measured for Hepatic Venosus Pressure Gradient (HVPG) by using right jugular vein. All patients underwent fibroscan and upper abdominal ultrasonographic examination to detect liver stiffness and spleen size.
Results: Fourteen patients were female; 13 patients were male. HVPG of 18 patients were higher than 5 mm Hg. FHVP, WHVP and HVPG were 12.78±5.33 (24–5), 22.93±8.23 (37–9), and 10.15±6.75 (27–2), respectively. PH risk score was 37.23±24.11 (84.25–4.27), Fib-4 was 3.94±2.24 (9.38–1.25), APRI was 0.81±0.44 (1.59–0.19). Area under the curve for PH risk score was 0.74 (p = .043, 95% CI 0.54–0.94), Fib-4 was 0.73 (p = .056, 95% CI 0.53–0.93), APRI was 0.63 (p = 0.28, 95% CI 0.40–0.85). Three patients had pain on the puncture side after the examination.
Conclusion: The measurement of HVPG is the gold standard examination to notice clinically significant portal hypertension and the risk of variceal bleeding. However, LS, PH risk score, APRI index and Fib 4 index were also useful in order to predict the patients with high risk for variceal bleeding.

Abstract #547

Determinants of rebleeding and mortality in acute variceal haemorrhage

Tin Tin Hlaing (Bi-Zhen Kao), Hwai-Jeng Lin, Ming-Yao Chen, Chia-Shin Wu, Sheng-Tsai Lin, Yu-Xin Lai, Ming-Zhe Tay, Chung-Ying Lee

Division of Gastroenterology and Hepatology, Department of Internal Medicine, Shuang Ho Hospital, New Taipei, Taiwan

Introduction: Acute variceal hemorrhage (AVH) is the most serious encountered complication of liver cirrhosis and carries high mortality rate.
Objectives: To determine patients' characters, and identify parameters associated with rebleeding and mortality after AVH.
Method: Retrospective analysis on cirrhotic patients admitted with AVH to Taipei Medical University-Shuang Ho hospital between 2012 and 2018.
Result: Among 263 patients, sources of bleeding were oesophageal varices (90.5%) and gastric varices (9.5%). The aetiologies of cirrhosis were alcohol 46.8% and viral hepatitis 47.9%. Patient

characteristics were male 73.4%, mean age 57.9 years: thrombocytopenia 67.7%: present of ascites 53.2%: mean MELD score 17.5: mean Child–Pugh (CP) score 8.2: CP class A 25.9%, CP class B 46.0%, CP class C 28.1%, active bleeding at inclusion 44.8%: taking non-selective beta-blocker (NSBB) 17.1%, bacterial infection 24.3%, presence of ascites 53.2%, encephalopathy 28.1%, hepatocellular carcinoma (HCC) 28.1% and portal vein thrombosis (PVT) 6.4%. Recurrent variceal bleeding rates were 3.0% at day-5, 7.2% at week-6 and 20.7% at year-1. The parameters associated with recurrent bleeding at week-6 were active bleeding (odds ratio (OR) 12.8), CP-class C (OR 4.4), MELD score > 20 (OR 2.8), ascites (OR 6.1), and HCC (OR 3.1). CP score > 7, MELD score > 20, active bleeding, ascites and PVT predicted rebleeding at year-1 (OR 3.9; OR 2.1; OR 5.1; OR 2.8 and OR 6.5, respectively). The mortality rates were 3.8%, 14.1% and 26.7% at day-5, week-6 and year-1 respectively: CP class A (0%, 2.9% and 7.8%), CP class B (3.3%, 7.4% and 22.9%), and CP class C (8.1%, 35.1% and 49.2%). The parameters associated with 6-weeks mortality were old age > 60 years (OR 2.3), CP score > 7 (OR 7.3), MELD score > 16 (OR 2.6), creatinine > 1.3 mg/dL (OR 3.7), albumin < 2.8 mg/dL (OR 2.1), bilirubin > 3 mg/dL (OR 5.2), ascites (OR 6.9), encephalopathy (OR 2.8), bacterial infection (OR 7.4), HCC (OR 4.1), and NSBB use (OR 0.5). The parameters associated with 1-year mortality were old age (OR 2.6), CP score > 7 (OR 5.5), MELD score > 20 (OR 2.3), ascites (OR 4.1), HCC (OR 6.5), PVT (OR 3.1) and NSBB use (OR 0.3).

Conclusion: In this study, variceal rebleeding and mortality rate of cirrhotic patients were substantially high in liver decompensation and presence of HCC or PVT. Use of NSSB could reduce mortality but not rebleeding rate.

Abstract #638

Non-invasive prediction of esophageal varices by splenic elasticity and platelet count (P-SEP criteria) in elderly patients with liver cirrhosis

Yasunori Yamamoto,[1] Masashi Hirooka,[1] Takaaki Tanaka,[1] Yohei Koizumi,[1] Yoshio Tokumoto,[1] Eiji Takeshita,[1] Yoshiou Ikeda,[1] Masanori Abe,[1] Bunzo Matsuura,[1] and Yoichi Hiasa[1]

Department of Gastroenterology and Metabology, Ehime University Graduate School of Medicine, Ehime, Japan

Introduction: We reported that SEP score (Splenic elasticity X 1.63–2.88) measured by real-time tissue elastography showed a good correlation to hepatic venous pressure gradient. We aim to identify that P-SEP criteria (platelet count > 150,000 /μl and SEP score < 6) be useful to rule out high-risk varices and be possible to avoid a unnecessary EGDs in elderly patients with liver cirrhosis

Methods: A total of 63 patients over 70 years old with liver cirrhosis of different aetiology, were analysed. Varices needing treatment (VNT) was defined as any varices with a red colour sign, and a grade F2 esophageal and gastric varices.

we examined the association between P-SEP criteria and the complication of any varices and VNT.

Results: The median age of patients was 74 (70–90) years. The gender ratio was 38:25. The cause was NASH 19, HCV 18, PBC 9, Alcohol 6, HBV 4, AIH 2, unknown 5 cases. Child–Pugh classification A/B/C were 42/19/2. Esophageal and gastric varices were found in 27.0% of all cases and VNT in 9.5%. 39.6% of patients were within P-SEP criteria, and both Esophageal and gastric varices and VNT complication rates were 0%. Patients with P-SEP criteria were significantly less to have a complication with any varices and VNT ($P < 0.0001$, $P = 0.012$).

Conclusion: P-SEP criteria were useful for the extraction of patients without VNT. P-SEP criteria may be able to avoid about 40% of endoscopic screening In elderly cirrhosis patients.

Abstract #711

Changing trends in etiology and severity of cirrhotic patients in South Korea: a multicenter retrospective study from 2008 to 2017

Kim, Jeong Han[1], Yoon, Jae Hyun[2], Jun Chung Hwan[2], Yoon, Eileen L.[3], Kim, Byung Seok[4], Suk, Ki Tae[5], Kim, Moon Young[6]; Korean Epidemiology of Liver Cirrhosis (KELC) Study Group.

[1]Department of Internal Medicine, Konkuk University School of Medicine, Seoul, Korea, [2]Department of Internal Medicine, Chonnam National University Hospital, Gwangju, Korea, [3]Department of Internal Medicine, Inje University Sanggye Paik Hospital, Seoul, Korea, [4]Department of Internal Medicine, Daegu Catholic University School of Medicine, Daegu, Korea, [5]Department of Internal Medicine, Hallym University College of Medicine, Chunchueon, Korea, [6]Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea

Introduction: Chronic hepatitis B has occupied the largest portion for liver cirrhosis in South Korea but clinical implications have been changing since introduction of antiviral agents for hepatitis B. On the other hands, alcoholic cirrhosis is still not well controlled and has shown increasing trends.

Objectives: We aimed to investigate the change in etiology and clinical severity of cirrhotic patients in Korea.

Methods: Ten years (2008–2017) of 16,328 visit records from 9282 cirrhotic patients in six tertiary hospitals in Korea were retrospectively reviewed.

Results: Most common etiologies were hepatitis B and alcohol (38.6% and 39.7% in 2008, and 37.2% and 36.6% in 2017, respectively). Child–Pugh score and prevalence of decompensation showed decreasing trends (6.52 to 6.21 and 45.2% to 35.5% from 2008 to 2017, respectively). Admission rate and overall mortality decreased from 50.5% to 33.9% and 8.8% to 5.2% as well. Among complications, variceal bleeding incidence reduced most significantly from 12.3% to 6.8%. Although alcoholic liver cirrhosis group had poorer liver function than HBV group (Child–Pugh score 7.15 vs. 5.79), both two groups showed trends of liver function improvement. There was no decrement of hepatocellular carcinoma occurrence (9.8% to 9.9%) but it was more prevalent in HBV group than alcohol group (11.3% vs. 6.2%) during 10 year period.

Conclusions: Overall clinical status showed improving trends irrespective of cirrhosis etiology. Despite no change in proportions of alcohol and HBV in cirrhosis, alcohol group showed dismal liver functions and higher rates of decompensation than HBV group.

Abstract #715

Urinary neutrophil gelatinase-associated lipocalin, kidney injury molecule-1 and cystatin C are not useful markers of moderate kidney function impairment in patients with liver cirrhosis

Szymanek-Pasternak Anna

Background: Kidney function impairment worsens prognosis in patients with liver cirrhosis therefore early diagnosis of chronic kidney disease is improtant but challenging for clinicians.

The aim of the study was to establish possible usefulness of urinary neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1) and cystatin C (CysC) as early markers of moderate impairment of kidney function in patients with liver cirrhosis.
Materials and methods: Urine samples from 95 consecutive patients with liver cirrhosis of different etiologies were collected within 24 h after admission to the 1st Department of Infectious Diseases Regional Specialistic Hospital, Wroclaw, Poland. Urinary concentrations of NGAL, KIM-1, CysC and proteinuria were mesured. eGFR according to Modification of Diet in Renal Disease equation was calculated and Child-Turcotte-Pugh score (CTP) was performed.
ANOVA and t-Student tests were used. P value 0.05 was considered statistically significant.
Results: There were 57 patients with A score according to CTP, 32 patients—B, 6 patients—C. Mean eGFR did not differ significantly between CTP A, B and C groups (95.3 ml/min/1.73 m^2, 87.4 ml/min/1.73 m^2 and 88.2 ml/min/1.73 m^2, respectively). Mean NGAL, KIM-1 and CysC concentrations between the group with higher eGFR ($\geq$ 60 ml/min/1.73 m^2, N = 85) and lower eGFR ($<$ 60 ml/min/1.73 m^2, N = 10) did not differ significantly (NGAL: 32.66 pg/mL vs 38.57 pg/mL, KIM-1: 1.66 ng/mL vs 2.52 ng/mL, CysC: 24.11 ng/mL vs 37.86 ng/mL, respectively).
Conclusions: Urinary NGAL, KIM-1 and CysC probably will not play a role as early markers of moderate impairment of renal function in patients with liver cirrhosis.

Abstract #729

Relation of ascitic fluid cholesterol level with serum ascites albumin gradient in cirrhotic and non-cirrhotic ascites

Hossain R M M[1], Azam M G[1], Bhuiyan T M [1], Datta I K [1], Mamoon A A[1], Mustafa M A S[1] and Rahman M A[1]

[1]Department of Gastrointestinal, Hepatobiliary and Pancreatic Disorders (GHPD), BIRDEM General Hospital, Dhaka, Bangladesh.

Background: The most common cause of ascites is cirrhosis with portal hypertension (C-PHT) and high serum ascites albumin gradient (SAAG) is highly suggestive of portal hypertension. Common causes of low-SAAG ascites include tubercular peritonitis (TB-per), peritoneal metastasis (P-met), pancreatitis, hypothyroidism, etc. The differentiation between malignancy-related ascites (MRA) and non-malignant ascites in low-SAAG settings is challenging. Some studies found high level of ascitic fluid cholesterol (AFC) in MRA.
Objectives: This study was planned to evaluate any relation of AFC level with SAAG and MRA.
Methodology: This was a cross-sectional study. A total of 41 patients with ascites were included. This study was carried out at the Gastroenterology Department of BIRDEM General Hospital, Dhaka, Bangladesh.
Results: Among 41 patients with ascites, 13 were cirrhosis with HCC (C-HCC), 10 were C-PHT, 12 were P-met and 6 were TB-per. SAAG was low in P-met (7.76 $\pm$ 2.48) and T-per (6.40 $\pm$ 1.08) but high in C-HCC (18.92 $\pm$ 6.94) and C-PHT (16.4 $\pm$ 2.96). AFC levels were higher in low-SAAG ascites (values of 91.67 $\pm$ 38.17 mg/dL for P-met and 116.00 $\pm$ 13.14 mg/dL for TB-per) than in high-SAAG ascites (values of 34.31 $\pm$ 29.21 mg/dL for C-HCC and 21.50 $\pm$ 9.19 mg/dL for C-PHT), where p-value was less than 0.001. Among low SAAG ascites settings, AFC of P-met was not significantly different from that of TB-per (p-0.154). Using a cut-off limit of 61.0 mg/dL, AFC had sensitivity and specificity for low-SAAG of 92.3% and 85.0% respectively. So, AFC is a sensitive marker to differentiate cirrhotic from non-cirrhotic ascites.
Conclusion: This study showed that AFC is a reflection of SAAG.

Abstract #744

Correlation of different grades of esophageal varices with non -invasive liver fibrosis markers in liver cirrhosis patients

Haryono, Muhammad Begawan Bestari, Dolvy Girawan, Nenny Agustanti, Yudi Wahyudi, Siti Aminah Abdurachman

Division of Gastroenterology Hepatology, Department of Internal Medicine, Faculty of Medicine Universitas Padjadjaran-Hasan Sadikin Hospital, Bandung, Indonesia

Background: Esophageal variceal bleeding is a potentially fatal consequence of portal hypertension in cirrhotic patients. The risk of hemorrhage has been related to the size and appearance of the varices, as well as the degree of hepatic dysfunction. There is a particular need for non -invasive predictors for esophageal varices. The aim of the present study is to evaluate correlation of different grades of esophageal varices and Child Pugh (CP) class, APRI, FIB-4, ALBI and Lock Score as 5 non -invasive parameter in liver cirrhosis patients.
Method: This is a cross-sectional study of patients at the Hasan Sadikin hospital Bandung between October 2018 to October 2019 with the diagnosis of cirrhosis based on clinical, biochemical examination and ultrasound. Meanwhile esophageal varices were examined using esophagogastroduodenoscopy. CP, APRI, FIB-4, ALBI and Lock Score were analyzed for all patients.
Results: We gathered 120 patients with mean age 50 $\pm$ 12 years with Child–Pugh B (53.3%), Child Pugh C (25%), Child–Pugh A (21.7%) The cause of liver cirrhosis were Hepatitis B 32 (26.7%), Hepatitis C 18 (20%) and others 70 (58.3%). Esophageal varices grades were F3 (65%), F2 (27.5%), F1 (7.5%). The result showed the higher grade of esophageal varices was found in the more advanced classification of Child–Pugh (p value $<$ 0.05). However, for the other methods of assessment there were no statistically significant correlation to the grade esophageal varices.
Conclusion: Child–Pugh classification is significantly associated with esophageal varices and remains as a good non-invasive predictor of esophageal varices in Cirrhosis patients

Abstract #772

Chronic liver disease profile in elderly population in a big community based university hospital

Huang Yuan[1], Sun Chunyan[1], Wei Lai[1], Dong Jiahong*[2]

[1]Division of Hepatology, Beijing Tsinghua Changgung Hospital, Tsinghua University, Beijing 102218, China, [2]Hepatopancreatobiliary Surgery, Medical Center, Beijing Tsinghua Changgung Hospital, Tsinghua University, Beijing 102218, China

Introduction: The increasing aging population is a worldwide issue, and societies are facing various problems including long-term care for elderly populations with chronic liver disease (CLD).
Objectives: This study aims to provide a detailed community-level description of the CLD profile in elderly population.
Methods: We consecutively assembled a retrospective cohort of elderly patients with CLD at Beijing Tsinghua Changgung Hospital from 1/11/2015 to 1/10/2019.
Results: Out of total 2269 patients with CLD at our hospital, 625 (59.0% male) were elderly patients. The first three etiologies were chronic hepatitis B (CHB) (n = 401, 64.2%), nonalcoholic fatty liver disease (NAFLD) (n = 179, 28.6%) and chronic hepatitis C (CHC)

(n = 58, 9.3%). The top two was similar to the non-elderly patients (n = 1134, 69.0%; n = 670, 40.8%), but the third etiology of the latter group was drug-induced liver injury (DILI) (n = 75, 4.6%). There were 152 (24.3%) elderly patients with decompensated cirrhosis. The top two symptoms of decompensated cirrhosis in the elderly were ascites (65.8%) and gastrointestinal bleeding (25.7%). So were those in non-elderly patients (n = 117, 60.6%; n = 55, 28.5%). CHB was the most important etiology of decompensated cirrhosis both in the elderly (40.1%) and the non-elderly patients (57.5%). However, there was 30.9% elderly patients with unknown etiology for decompensated cirrhosis.

Conclusion: The elderly populations with CLD Increase social burden. CHB is the first etiology for both CLD and decompensated cirrhosis in the elderly.

Abstract #805

Screening varices in the era of anti-HBV treatment: baveno VI (platelets + LSM) or platelets alone?

Bingqiong Wang[1], Jialing Zhou[1], Xiaoning Wu[1], Yameng Sun[1], Shanshan Wu[1], Yiwen Shi[1], Shuyan Chen[1], Jinwen Huang[2], Xiaojuan Ou[1], Jidong Jia[1], Hong You[1]*

[1]Liver Research Center, Beijing Key Laboratory of Translational Medicine in Liver Cirrhosis, National Clinical Research Center for Digestive Disease, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [2]Beijing Chao-Yang Hospital, Capital Medical University, Beijing, China.

Introduction & Objectives: Non-invasive assessment criteria used to rule out varices needing treatment (VNT) in HBV related compensated cirrhotic patients underwent anti-viral therapy remains unclear.
Methods: HBV related compensated cirrhotic patients underwent endoscopy screening during anti-viral therapy from two multi-center studies were enrolled and divided as training and validation cohort. VNT was defined as medium-large varices or small with red signs. Univariable and multivariable logistic analysis was used to determine parameters associated with VNT.
Results: In the training cohort (N = 234, 21.8% with VNT), a median anti-viral therapy duration was 4 years. Platelets and total bilirubin (OR [95% CI] = 0.97 [0.96–0.98] and 1.02 [1.01–1.05], both $P < 0.05$) were identified as the most significantly different variables in patients with VNT and without VNT after uni-and multi-variable analysis, whereas liver stiffness was not selected (OR [95% CI] = 1.03 [1.00–1.07], $P > 0.05$). The diagnostic value of single platelets vs. platelets plus total bilirubin were similar (AUROC [95% CI] = 0.831 [0.771–0.891] vs. 0.840 [95% CI] = 0.780–0.899, $P = 0.43$ by DeLong test). The cut off value of platelets was recommended as 115 $x10^9$/L, which could spare 110 (47.0%) patients with unnecessary endoscopies, with a risk of missing VNT of 4.5% (5/110). In validation cohort (N = 246, 12.6% with VNT), the proportion of safely spared endoscopy identified by new single cut-off value of PLT (115) was superior than Baveno VI criteria (57.0% vs. 35.0%) with acceptable risk of missing VNT (2.5% vs. 0.0%).
Conclusion: Platelets higher than 115 $x10^9$/L could safely spare more endoscopies without increasing the risk of VNT missed in post-treatment HBV related compensated cirrhotic patients.

Table 1. Validation of single platelets to predict the presence of VNT compared with Baveno VI.

	Training set		Validation set	
	PLT 115 in our study	Baveno VI criteria	PLT 115 in our study	Baveno VI criteria
Saving EGDS, n (%)	110 (47.0)	67 (28.6)	162 (57.0)	100 (35.0)
VNT missed, n (%)	5 (4.5)	2 (3.0)	4 (2.5)	0 (0.0)
SEN (%)	90.2	96.1	91.1	100.0
SPE (%)	57.4	35.5	65.8	40.0
PPV (%)	37.1	29.3	33.3	18.9
NPV (%)	95.5	97.0	97.5	100.0

Abstract #806

Clinical characteristics in cirrhotic patients with non-forward flow of superior mesenteric vein

Soichiro Kiyono,[1] Miyuki Sensui,[1] Hitoshi Maruyama,[1] Takayuki Kondo,[1] Kazufumi Kobayashi,[1] Susumu Maruta,[1] Kengo Kanayama,[1] Hiroaki Kanzaki,[1] Masato Nakamura,[1] Naoya Kanogawa,[1] Tomoko Saito,[1] Sadahisa Ogasawara,[1] Eiichiro Suzuki,[1] Yoshihiko Ooka,[1] Shingo Nakamoto,[1] Akinobu Tawada,[1] Tetsuhiro Chiba,[1] Jun Kato,[1] Naoya Kato[1]

Department of Gastroenterology, Chiba University School of Medicine, Chiba, Japan

Introduction: Non-forward or reversed flow is exclusively found in the portal vein system. We have reported that non-forward or hepatofugal flow of splenic vein was associated with gastric varices bleeding. However, the influence of non-forward flow of superior mesenteric vein (NFSMV) has not been determined yet. Thus, we retrospectively examined the clinical characteristics of NFSMV in patients with chronic liver disease.
Methods: From March 2012 to June 2018, 380 patients with chronic liver disease had Doppler ultrasound examination for hemodynamics in portal vein system. Flow direction was judged using reference of color Doppler findings. The cases of bidirectional blood flow were also included to NFSMV cases.
Results: Among the candidate patients, 96 cases were included, including 18 cases of NFSMV and 78 cases of non-forward flow of splenic vein. NFSMV was detected at the main level of SMV in 13 cases, of which 8 were continuous reversed flow and 5 were bidirectional. Occlusion of portal vein system was found, in 7 cases due to thrombus and in 4 cases due to tumor invasion. Of the 17 cases with NFSMV and liver cirrhosis, 1 case was Child–Pugh classification A, 9 cases for B, and 7 for C. Hepatic encephalopathy was observed in 8 cases, of which 3 cases had difficulty in treating. Moderate ascites was observed in 4 cases.
Conclusion: Patients with reversed, non-forward flow of superior mesenteric vein were accompanied by severe decompensated liver symptoms. Deep attention in the treatment of chronic liver disease is required.

Abstract #832

Efficacy and safety of lusutrombopag prior to endoscopic treatment in patients with esophageal varices and thrombocytopenia

Kentaro Ito, Akira Uchiyama, Eisuke Nakadera, Hiroo Fukada, Kyoko Fukuhara, Kazuyoshi Kon, Shunhei Yamashina, Kenichi Ikejima

Department of Gastroenterology, Juntendo University School of Medicine, Tokyo, Japan

Introductions: Thrombocytopenia is a frequent finding in chronic liver disease (CLD). The pathophysiology of thrombocytopenia in liver disease has long been associated with the hypersplenism and portal hypertension. It frequently increases the risk of hemorrhage with invasive procedures. Lusutrombopag is a small molecule thrombopoietin receptor agonist designed to temporarily increase the platelet count in patients with CLD for whom elective invasive procedures are planned. Here, we show the efficacy and safety of lusutrombopag prior to EVL (Endoscopic variceal ligation) for high-risk varices.
Methods: Eight patients with high-risk varices who had a platelet count < 50000/mL prior to received lusutrombopag (3 mg/day) orally for t days between 2016 and 2018. The following were compared: the effect of lusutrombopag to increase the platelet count, the rate of avoiding platelet transfusion and any complications associated with endoscopic treatment.
Results: The mean age of patients (5 men and 3 women) was 59.5 ± 10.6 years. Four patients had alcoholic liver, one had non-alcoholic steatohepatitis, one patient was autoimmune hepatitis, one patient is primary biliary cholangitis and one is Budd-Chiari syndrome. The mean Child–Pugh score was 6.25 ± 1.19. Platelet counts significantly increased compared with baseline (44000 ± 8180 /μL vs83600 ± 35400μL)($p < 0.05$). None of the patients required platelet transfusion. None of the patients developed clinical symptoms such as portal vein thrombosis, bleeding, or any other serious adverse events prior to EVL.
Conclusions: Lusutrombopag is an effective and safe drug for thrombocytopenia and can reduce the frequency of platelet transfusions prior to EVL.

Abstract #860

The effects of L-carnitine on reducing hospital admissions in patients with hepatic encephalopathy

Joji Tani[1], Asahiro Morishita[1], Teppei Sakamoto[1], Kei Takuma[1], Mai Nakahara[1], Koji Fujita[1], Kyoko Oura[1], Tomoko Tadokoro[1], Shima Mimura[1], Takako Nomura[1], Hirohito Yoneyama[1], Hideki Kobara[1], Takashi Himoto[2], Tsutomu Masaki[1]

[1]Department of Gastroenterology and Neurology, Kagawa University, Faculty of Medicine, Kagawa, 761-0793, Japan [2]Department of Medical Technology, Kagawa Prefectural University of Health Sciences, Kagawa, 761-0123, Japan

Aim: The aim of this study was to determine whether oral L-carnitine administration reduces the serum ammonia concentration and number of hospital admissions for hepatic encephalopathy (HE) in patients with advanced cirrhosis.
Methods: Of 68 patients with HE treated with oral L-carnitine supplementation from April 2013 to March 2016, we enrolled 19 patients who had received full standard treatment. We analyzed serum ammonia concentration, number of hospital admissions, and prognosis to determine how effective L-carnitine was in achieving mid- to long-term suppression of recurrent HE.
Results: Median serum ammonia concentrations at the start, 1 week, 12 weeks, 24 weeks, and 48 weeks were 159 μg/dL, 79 μg/dL, 75 μg/dL, and 82 μg/dL, respectively. Serum ammonia concentrations 12 week, 24 weeks, and 48 weeks after L-carnitine administration were significantly lower than those at the start ($P < 0.0001$, respectively). During the 3 years prior to oral L-carnitine administration, the enrolled patients were hospitalized a total of 29 times for HE. However, during the 3 years following oral L-carnitine administration, they were admitted a total of six times for HE ($P < 0.001$). Median survival time was 40.9 months. Child–Pugh scores before and after oral L-carnitine administration differed significantly, whereas liver reserve function, nutritional status, and muscle index did not change significantly.
Conclusions: Oral L-carnitine administration is effective and free of adverse effects in patients with hyperammonemia and reduces the number of hospital admissions for HE.

Abstract #865

Relationship between hepatic venous pressure gradient with PH risk score, APRI index and Fib-4 score in patients with liver parenchymal diseases

Ellik Zeynep[1], Asiller Özgün Ömer[1], Özercan Mübin[1], Kartal Çalışkan Aysun[1], Örmeci Necati[1]

[1]Ankara University Faculty of Medicine, Department of Gastroenterology, ANKARA/TURKEY

Introduction: Portal hypertension is very important antitea for liver parenchymal disease.
Object: In order to evaluate the diagnostic accuracy of Apri index, Fib-4, Portal Hypertension (PH) risk score (PH risk score = -5.953 + 0.188 x LS +1.583 x sex (1: male; 0: female) + 26.705 x spleen diameter/platelet count ratio) for clinical significant portal hypertension in patients with compensated liver parenchymal disease.
Material: Twenty seven patients with compensated liver cirrhosis due to 6 hepatitis B, 2 hepatitis C virus infection, 8 non-alcoholic steatohepatitis, 6 autoimmune hepatitis, 5 cryptogenic cirrhosis, 1 portal vein thrombosis and 1 primary sclerosing cholangitis were approved for the study. All patients were measured for Hepatic Venosus Pressure Gradient (HVPG) by using right jugular vein. All patients underwent fibroscan and upper abdominal ultrasonographic examination to detect liver stiffness and spleen size.
Results: Fourteen patients were female; 13 patients were male. HVPG of 18 patients were higher than 5 mm Hg. FHVP, WHVP and HVPG were 12.78±5.33 (24–5), 22.93±8.23 (37–9), and 10.15±6.75 (27–2), respectively. PH risk score was 37.23±24.11 (84.25–4.27), Fib-4 was 3.94±2.24 (9.38–1.25), APRI was 0.81±0.44 (1.59–0.19). Area under the curve for PH risk score was 0.74 ($p = .043$, 95% CI 0.54–0.94), Fib-4 was 0.73 ($p = .056$, 95% CI 0.53–0.93), APRI was 0.63 ($p = 0.28$, 95% CI 0.40–0.85). Three patients had pain on the puncture side after the examination.
Conclusion: The measurement of HVPG is the gold standard examination to notice clinically significant portal hypertension and the risk of variceal bleeding. However, LS, PH risk score, APRI index and Fib 4 index were also useful in order to predict the patients with high risk for variceal bleeding.

Abstract #872

Co-relation of ascitic fluid (AF) appearance, symptoms and severity of cirrhosis in predicting spontaneous bacterial peritonitis (SBP) in patients of chronic liver disease

Kandpal Ajay, Revathy MS, Sumathi B, Chitra, Manimaran, Sathya

Department of Medical Gastroenterology, Govt Stanley Medical College, Chennai, India

Background: SBP is major cause of mortality in cirrhotics. Timely initiation of antibiotics reduces burden of disease. Ascitic fluid (AF) cell count is definitive to diagnose SBP. Timely availability of cell

count is crucial especially in peripheral setting. Limited labs at periphery compels to look at other options. Here patient's symptoms, severity of disease and appearance of AF comes handy.
Objectives: To identify Co-relation of AF appearance, symptoms & severity of cirrhosis in predicting SBP in patients of chronic liver disease which in turn provides evidence to justify empirical use of antibiotics in these high risk patients before availibility of AF analysis reports.
Materials and Methods: 75 chronic liver disease patients with acites enrolled between Nov 2018 and June 2019. Baseline characteristics noted. AF sampling done. Combination of AF appearance, symptoms, Child and MELDS scores, were used to predict SBP which was later matched with AF cell count
Result: 37 patients had SBP. Chi square test was used. 92% patients with SBP had pain abdomen ($P < 0.0001$). Apperance of AF was opaque for 38% patients with SBP ($P < 0.0001$). MELD scores of patients with SBP was 19.5676 ± 4.4630 and without SBP was 14.3214 ± 3.6823. ($P < 0.0001$). 76% patients having SBP had child grade C. No association with fever.
Conclusion: A chronic liver disease patient with ascites presenting with pain abdomen, opaque ascitic fluid with advanced cirrhosis can be started on broad spectrum empirical antibiotics without waiting for AF analysis reports. Fever has low predictive value for SBP in cirrhotics.

Abstract #890

Clinical profile of patients with gastric variceal hemorrhage and outcome after cyanoacrylate (histoacryl) injection: a single center experience

Kerwin Ang

Background: Gastric variceal bleeding is a complication of liver cirrhosis that causes significant morbidity and mortality. The substantial variability in its prevalence is related to the difference in patient characteristics. With the advancement of endoscopic techniques, cyanoacrylate injection has become the most accepted intervention. In the present study we tried to identify the clinical profile of patients with gastric variceal bleeding. We also determined the outcomes of cyanoacrylate injection in relation to primary hemostasis and rebleeding.
Methods: This is a descriptive cross sectional study of 108 adult patients who were diagnosed with bleeding gastric varices from April 2007 to April 2018 at Metropolitan Medical Hospital. Medical records of the enrolled patients were reviewed.
Results: Patients had a mean age of 63 ± 5.9 years with a male to female ratio of 3:2. Melena was the most common presentation in 64 patients (59%). The main etiology was hepatitis B related cirrhosis in 31 patients (29%), followed by alcohol induced liver cirrhosis in 26 patients (24%). Sarin classification of GOV 1 were seen in 43 patients (40%) and IGV 1 in 33 patients (30%), and GOV 2 in 32 patients (30%). 78 patients were treated with cyanoacrylate injection wherein primary hemostasis were achieved in all patients. The incidence of rebleeding occurred in 9 (12%) patients.
Conclusion: Bleeding gastric varices were mainly seen among males in the 6^{th} decade. The most common presentation was melena. GOV 1 was the most frequent Sarin classification. Hepatitis B related cirrhosis was the main etiology followed by alcoholic liver cirrhosis. Cyanoacylate injection is an effective modality in achieving primary hemostasis however there still remains a significant risk of rebleeding.

Abstract #894

Prevelance of fragmented QRS in patients with cryptogenic cirrhosis and relationship between the presence of fragmented QRS and systolic dysfunction and diastolic dysfunction

Mehmet Demir

Background/Aim: Cirrhotic cardiomyopathy is associated with increased morbidity and mortality particular in advenced cirrhosis. Cardiac hypertrophy, patchy fibrosis and subendothelial edema may play a role in cirrhotic cardiomyopathy of patogenic mechanism. Latterly, fragmented QRS complex (fQRS) in ECG is associated with myocardial fibrosis. The aim of this study was to determine the relationship between the presence of fQRS and diastolic and systolic dysfunction in patients with cryptogenic cirrhosis.
Methods: The study included patients with cryptogenic cirrhosis admitted to Mustafa Kemal University department of gastroenterology between January 2014 and January 2019. Patients with organic valvular heart disease, bun-dle branch block, TIPS and hepatoma were excluded. fQRS pattern was described as presence of RSR' manifested as existence of additional R wave and notching in either R or S waves in ECG recordings. Conventional echocardiography and tissue Doppler echocardiography were performed in all patients
Results: The prevalence of fQRS was 22% (21/96) in patients with cryptogenic cirrhosis. Patients with cryptogenic cirrhosis with fQRS were of a higher age ($p = 0.03$), higher Child-Turcot-Pugh score ($p = 0.01$) and higer MELD score ($p = 0.009$) in comparison to the without fQRS. The patients with fQRS had worse diastolic and systolic functions in comparison to the patients without fQRS (DT, 185 ± 53 vs. 229 ± 12 ms, $p < 0.01$; IVRT, 76 ± 18 vs. 97 ± 42 ms, $p < 0.01$; Em, 8.5 ± 4.7 vs. 10.9 ± 3.7 cm/s, $p < 0.01$; E/Em ratio, 10 ± 7 vs. 8 ± 6, $p < 0.05$).
Conclusions: This study showed that the relationship between the presence of fQRS and diastolic and systolic dysfunction in patients with cryptogenic cirrhosis.. These data suggest that fQRS may represent a novel noninvasive marker for cardiac involvement cryptogenic cirrhosis and further studies will be needed to confirm these findings.

Abstract #924

Spontaneous bacterial peritonitis in patients with chronic liver disease

Nikhil Gupta

Objective: To determine the prevalence of SBP in patients with chronic liver disease as well as to identify any difference in biochemical parameters of the ascitic fluid in patients with and without SBP.
Methods: 120 patients with cirrhosis of liver and ascites between the age ranging from 9 to 80 years were included in the study.. The diagnosis of cirrhosis was made from history, clinical examination and the ultrasonographic findings. These patients were subjected to ascitic fluid paracentesis and were divided into SBP and non-SBP groups on the basis of ascitic fluid culture and routine examination. The SBP group was further divided into culture positive SBP, culture negative neutrocytic ascites (CNNA) and monomicrobial nonneutrocytic bactcrascites (MNB) on the basis of culture reports and absolute polymorphonuclear leukocyte count/ml of ascitic fluid.
Results: The study included total 120 cases (89 males and 31 females) having
cirrhosis of liver and ascites. On the basis of routine examination and culture of ascitic fluid from these cases, 31 (26%) were diagnosed to

have SBP. Seventeen (14.16%) and 1 (.83%) case respectively were diagnosed as having CCNA and MNB respectively. E. coli was the most frequent cultured organism. It was isolated in 12 (85%) cases with SBP. One case (7%) of Klebsiella species and one case (7%) of Staphylococcus aureus was also reported

Conclusion: This study reaffirms that SBP is a common and potentially fatal complication in cirrhotic patients with ascites. E. coli is the most frequent offending organism m this condition.

Abstract #943

Dyspepsia in cirrhotic hepatitis C patients

Talal Khurshid, Muhammad Umar, Mashhood Ali

Background: To determine the frequency of patients with dyspepsia, its patterns of presentation and causes along with their associations with gender and age, amongst HCV cirrhotic patients presenting to a tertiary care health facility of Rawalpindi.

Methods: In this cross sectional study 207 HCV cirrhotic patients, above 25 years of age irrespective of gender, were included. Patients receiving prolonged treatment of acid suppression prior to hospitalization were excluded. After taking history and performing thorough physical examination, routine laboratory investigations, abdominal ultrasonography and endoscopies were performed to determine the cause of dyspepsia.

Results: Amongst 207 HCV cirrhotic patients 146 (70.5%) were presented with dyspepsia. Pain in epigastrium 92 (63.0%), heart burn 81 (55.5%) and water brash 65 (44.5%) were most common patterns of presentation of dyspepsia in HCV cirrhotic patients. Portal hypertensive gastropathy 77 (52.7%) came out as leading etiology of dyspepsia, followed by gastritis 9 (6.2%), ulcer 6 (4.1%) and cholelithiasis 4 (2.7%). Amongst those diagnosed with Dyspepsia, 25 (17.1%) patients were found to have functional dyspepsia i.e. no organic cause was found.

Conclusion: Dyspepsia is very frequent phenomenon in HCV cirrhotic patients with most common patterns of presentation as pain in epigastrium and heart burn. The leading cause of dyspepsia was portal hypertensive gastropathy.

Abstract #985

No association between ischemic stroke and portal vein thrombosis in liver cirrhosis

Kexin Zheng [1,2], Xiaozhong Guo [1], Fangfang Yi [1,3], Le Wang [1,3], Andrea Mancuso [4], Xingshun Qi [1]

[1] Liver Cirrhosis Study Group, Department of Gastroenterology, General Hospital of Northern Theater Command (formerly General Hospital of Shenyang Military Area), Shenyang, Liaoning Province, China, [2] Postgraduate College, Jinzhou Medical University, Jinzhou, Liaoning Province, China, [3] Postgraduate College, Dalian Medical University, Dalian, Liaoning Province, China, [4] Medicina Interna 1, Azienda di Rilievo Nazionale ad Alta Specializzazione Civico-Di Cristina-Benfratelli, Piazzale Leotta 4, 90100, Palermo, Italy.

Background and aims: There seems to be a higher risk of ischemic stroke and portal vein thrombosis in liver cirrhosis. Both of them may be associated with hypercoagulability. We aim to explore the association between ischemic stroke and portal vein thrombosis in liver cirrhosis.

Patients and methods: We selected patients from our prospectively established database of liver cirrhosis from December 2014 to July 2019. The difference between patients with and without stroke was compared. A 1:1 propensity score matching (PSM) analysis was performed to adjust the effect of age, sex, Child–Pugh score, and MELD score on our statistical results.

Results: There were 349 cirrhotic patients in the cross-sectional study. The prevalence of stroke, ischemic stroke, hemorrhagic stroke, and portal vein thrombosis were 8.88% (31/349), 8.31% (29/349), 1.15% (4/349), and 28.65% (100/349) in liver cirrhosis, respectively. Patients with ischemic stroke were significantly older, and had significantly higher proportions of alcohol abuse, smoking, and arterial hypertension and levels of white blood cell and low density lipoprotein. However, statistical analyses with and without PSM did not find any significant association between ischemic stroke and portal vein thrombosis in patients with liver cirrhosis.

Conclusion: Ischemic stroke might not be associated with portal vein thrombosis in liver cirrhosis.

Abstract #999

Risk factors for esophageal collateral veins in cirrhosis with and without previous endoscopic esophageal variceal therapy

Qianqian Li[1,2], Xiaozhong Guo[1], Xiangbo Xu[1,3], Saurabh Chawla[4], Hongyu Li[1], Xingshun Qi[1*]

[1]Department of Gastroenterology, General Hospital of Northern Theater Command, Shenyang, 110840, P. R. China, [2]Postgraduate College, Dalian Medical University, Dalian 116044, P. R. China, [3]Postgraduate College, Shenyang Pharmaceutical University, Shenyang, 110840, P. R. China, [4]Department of Medicine, Division of Digestive Diseases, Emory University School of Medicine, Atlanta, USA.

Introduction and Objectives: Presence of portosystemic collateral vessels is a sign of portal hypertension in liver cirrhosis. Esophageal collateral veins (ECVs) are one major type of portosystemic collateral vessels, which increase the recurrence of esophageal varices and bleeding after variceal eradication. However, the risk factors for ECVs were still unclear.

Materials and Methods: We retrospectively screened cirrhotic patients who had contrast-enhanced computed tomography (CT) images and upper gastrointestinal endoscopic reports at our hospital. ECVs were evaluated on CT scans. Univariate and multivariate logistic regression analyses were performed to explore the independent risk factors for ECVs. Odds ratios (ORs) were calculated. Subgroup analyses were performed in patients with and without previous endoscopic variceal therapy which included *endoscopic variceal ligation (EVL) and endoscopic injection sclerotherapy (EIS).*

Results: Overall, 243 patients were included, in whom the prevalence of ECVs was 53.9%. The significant independent risk factors for ECVs were hepatitis C virus infection (OR = 0.250, p = 0.026), previous *EVL* (OR = 1.929, p = 0.044), platelet (PLT) (OR = 0.993, p = 0.008), and esophageal varices needing treatment (EVNTs) (OR = 2.422, p = 0.006). The prevalence of ECVs was 60.8% (73/120) in patients undergoing EVL, 50% (10/20) in those undergoing EIS, and 47.5% (48/101) in those without previous endoscopic variceal therapy. The significant independent risk factors for ECVs were PLT (OR = 0.991, p = 0.029) and EVNTs (OR = 3.912, p = 0.004) in subgroup analyses of patients with and without previous endoscopic variceal therapy, respectively.

Conclusions: Presence of ECVs should be closely associated with the severity of portal hypertension in liver cirrhosis. Risk of ECVs might be increased by previous EVL.

Abstract #1003

Role of terlipressin in cirrhotic patients with ascites and without hepatorenal syndrome: a systematic review of current evidence

Zhaohui Bai[1,2], Yang An[1,2#], Xiaozhong Guo[1#], Rolf Teschke[3], Nahum Méndez-Sánchez[4], Hongyu Li[1*], Xingshun Qi[1*]

[1]Department of Gastroenterology, General Hospital of Northern Theater Command, Shenyang, 110840, P. R. China, [2]Postgraduate College, Shenyang Pharmaceutical University, Shenyang 110840, P. R. China. Department of Internal Medicine II, Division of Gastroenterology and Hepatology, Klinikum Hanau, D-63450, Hanau, Germany, [4] Liver Research Unit, Medica Sur Clinic and Foundation and Faculty of Medicine, National Autonomous University of Mexico, Mexico.

Ascites, a common complication in cirrhosis, is prone to the development of acute kidney injury or hepatorenal syndrome and can be complicated by circulatory dysfunction after paracentesis. Terlipressin has not been considered as the mainstay treatment option for ascites in cirrhosis yet. The present work aimed to systematically review the current evidence regarding use of terlipressin in cirrhosis with ascites without hepatorenal syndrome. PubMed, EMBASE, and Cochrane Library databases were searched for relevant studies. Twelve studies were eligible. Among the 3 studies (1 randomized controlled trial and 2 single-arm studies without controls) involving 32 patients who received terlipressin for non-refractory ascites, terlipressin improved hemodynamics by decreasing heart rate and cardiac output and increasing mean arterial pressure and systemic vascular resistance. Among the 5 studies (1 randomized controlled trial, 2 single-arm studies without controls, and 2 comparative studies with controls) involving 67 patients who received terlipressin for refractory ascites, terlipressin improved renal function by increasing glomerular filtration rate, renal blood flow, urinary sodium, and urine output and decreasing serum creatinine. Among the 4 studies (4 randomized controlled trials) involving 71 patients who received terlipressin for preventing from paracentesis-induced circulatory dysfunction, terlipressin prevented from paracentesis-induced circulatory dysfunction by increasing mean arterial pressure and systemic vascular resistance and decreasing plasma renin. Terlipressin may improve hemodynamics, severity of ascites, and renal function and prevent from paracentesis-induced circulatory dysfunction in cirrhosis with ascites without hepatorenal syndrome. However, no study has evaluated the effect of terlipressin for prevention of acute kidney injury.

Abstract #1027

Prevalence and outcomes of spontaneous bacterial peritonitis in patients with cirrhosis: a single centre experience

Singh Shivaram Prasad,[1] Khatua Chitta Ranjan,[1] Sahu Saroj Kanta,[1] Meher Dinesh,[1] Nath Gautam,[1] Khandelwal Resu[1]

[1]Srirama Chandra Bhanja Medical College, Cuttack, Odisha, India

Introduction: Spontaneous bacterial peritonitis (SBP) is a common and life-threatening condition in patients with cirrhosis, and it occurs as the result of intestinal bacterial overgrowth and translocation to mesenteric lymph nodes.
Objectives: The prevalence of SBP and its outcome are poorly understood from this resource constrained region of Asia. So we performed a prospective study to evaluate the spectrum of SBP and their outcome in hospitalized patients.
Methods: This study was conducted in consecutive cirrhosis patients with ascites hospitalised in SCB Medical College, India between October 2016 and December 2018. Demographic, clinical, laboratory and microbiological parameters were recorded and survival was compared between patients with and without SBP during hospitalisation and also at 28 days and 90 days.
Results: 330 (50.3%) out of 656 patients had infection, of which 17.3% (n = 57) had SBP. Culture positivity was seen in 10.5% (n = 6) of SBP patients and E. coli was the commonest isolated organism. Cirrhotics with SBP had increased prevalence of ACLF as per EASL-CLIF criteria (82.2% vs 37.6%; $p < 0.001$). Furthermore, they had increased duration of hospitalisation ($p = 0.007$), increased hospital death (28.1% vs 10.7%; $p < 0.001$), decreased survival both at 28 days (61.4% vs 76%; $p = 0.016$) and 90 days (31.6% vs 58.8%; $p < 0.001$).
Conclusion: In our institution, more than half of decompensated cirrhotics had associated infection at the time of hospitalisation and one sixth of them had spontaneous bacterial peritonitis. Patients with SBP had increased proportion of ACLF, longer hospital stay, increased in hospital mortality and decreased survival both at 28 days and 90 days.

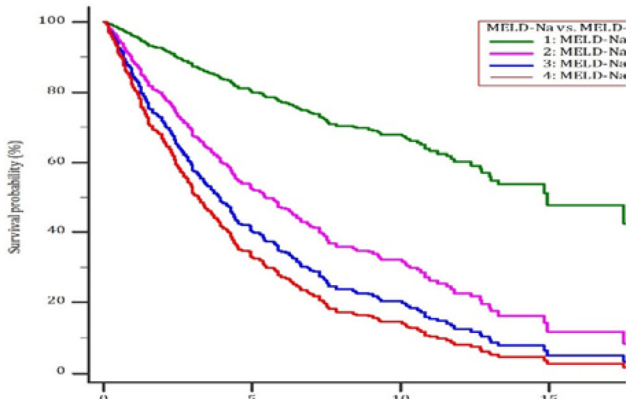
Abstract #1074

Addition of AST to the MELD–Na score is more likely to predict long-term prognosis comparing to MELD-Na

Prof. Ulus Salih Akarca1, Dr. Huseyin Semiz2, Dr. Ilker Turan[1], Dr. Zeki Karasu[1], Prof. Fulya Gunsar[1], Prof. Galip Ersoz[1], Dr. Nilay Danis[1] and Prof. Omer Ozutemiz[1]

[1]Ege University, Medical Faculty, Department of Gastroenterology, [2]Ege University, Medical Faculty, Department of Internal Medicine

Background: Although MELD–Na has been accepted as a good parameter to select the patients for liver transplantation, its value to predict long-term prognosis is not clear.
Aim: To investigate the prognostic value of the implementation of AST on MELD–Na.
Methods: Patients with decompensated cirrhosis who had been followed from 1995 to 2018 were retrospectively analyzed. 428 patients included into the study. Serum creatinine > 0.99 mg/dl, Na ≤ 134 mEq/dl, AST > 42 U/l, and presence of hepatic encephalopathy were found to be related to survival. As creatinine and Na already exist in MELD-Na, and hepatic encephalopathy is a subjective criterion to some extent, AST > 42 has been implemented on MELD–Na. The new formula (MELD–Na–AST) is calculated as follows: (If AST $>$ 42 U/l, then MELD–Na + EXP (10/MELD–Na), otherwise MELD–Na x 0.7).
Results: The mean follow–up for the study population was 5.4 ± 4.2 years, and the mean age was 63 ± 11. On ROC curve analysis, the MELD–Na–AST score had better prognostic accuracy in predicting survival for 1-year, 5-year, and entire follow-up compared to the MELD–Na score. The AUCs of MELD–Na and MELD–Na–AST were 0.811 and 0.843 for entire follow–up ($p = 0.0026$), 0.718 and 0.748 for 5-year ($p = 0.0087$), 0.648 and 0.704 for 1-year ($p = 0.0027$), respectively. In order to validate the MELD–Na–AST, half of the study population was selected randomly for three times and underwent the same statistics. MELD–Na–AST was always found to be superior to MELD–Na in every tests.
Conclusion: MELD–Na–AST is superior to predict the 1-year and long-term survival of the patients with decompensated cirrhosis comparing to MELD–Na.



Abstract #1124

Effect of vitamin D treatment in patients with decompensated cirrhosis of liver-report from a Tertiary Centre, Bangladesh

Mohd Harun or Rashid

Aim: To assess the vitamin D (VD) deficiency and prognosis of treatment of VD on mortality in decompensated cirrhosis.
Methods: A total of 71 VD deficient patients (< 20 ng/mL) randomly enrolled in two groups: Treatment group (n = 36) and control group (n = 35). Treatment group received cholecalciferol 50000 IU weekly for 7 weeks as loading dose and 2000 IU/d oral as maintenance dose with 1000 mg oral calcium suppliment. The VD level, clinical parameters and survival of both the groups compared for 6-months.
Results: The mean (SD) age of the patients in the treatment group (M:F: 30:06) and control group (M:F: 28:07) were 34.5 (± 10.5) years and 39.58 (± 9.58) years, respectively. Baseline mean (CI) VD (ng/mL) in control group and treatment group 9.15 (8.35–9.94) and 9.65 (8.63–10.7), respectively. Mean (CI) serum VD level (ng/mL) at 6-month in control group and treatment group 9.05 (6.85–11.15) and 30 (22–34), respectively. Over the period of time the VD, calcium and phosphorus level improved in treatment group compared to control group. There was non-significant trend seen in greater survival (70% *vs* 65%; $P > 0.05$) and longer survival (158 d *vs* 144 d; $P > 0.05$) in treatment group compared to control group. VD level had no significant association with mortality ($P > 0.05$).
Conclusion: VD deficiency is very common in patients of decompensated cirrhosis of Liver. Treatment of VD may improve survival in patients with decompensated cirrhosis of liver.

Abstract #1135

Non-invasive parameters and plasma Mac-2 binding protein glycosylation isomer level as predictors of high-risk esophageal varices in cirrhosis

Saut Horas H Nababan, Monica Raharjo, Kemal F Kalista, Chyntia OM Jasirwan, Juferdy Kurniawan, C. Rinaldi Lesmana, Andri Sanityoso Sulaiman, Irsan Hasan, Rino A Gani.

Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Background: Cirrhotic patients with variceal bleeding have higher mortality. Therefore, screening esophagogastroduodenoscopy (EGD) is recommended but is expensive and invasive. Previous studies showed that Mac-2 binding protein glycosylation isomer (M2BPGi) is a reliable biomarker for liver fibrosis, but its role for predicting high-risk esophageal varices (HREV) in liver cirrhosis is not widely studied.
Objectives: The purpose of this study was to determine whether plasma measurement of M2BPGi level, in addition to other non-invasive parameters, can help predict HREV in cirrhosis patients.
Methods: A total of 93 patients with cirrhosis, referred to our tertiary centre from May 2018 to November 2019 for screening endoscopy, underwent a clinical examination, abdominal ultrasonography (USG), liver stiffness measurement (LSM), and laboratory tests including plasma M2BPGi levels.
Results: Based on endoscopy results, HREV were present in 31 patients (33.3%). On univariate analysis, variables associated with HREV were Child–Pugh score, platelet counts, bipolar spleen diameter, portal vein diameter, LSM and plasma M2BPGI levels. The multivariate analysis showed that higher bipolar spleen diameter (p = 0.011) and higher plasma M2BPGi levels (p = 0.009) were independent predictors of HREV. Plasma M2BPGi level ≥ 5 COI (cutoff index) had 77.4% diagnostic accuracy for predicting HREV with sensitivity 83.9% and specificity 71.0%.
Conclusion: Plasma M2BPGi levels may predict HREV in liver cirrhotic patients. The screening value of plasma M2BPGi for HREV should be evaluated by further studies.

Abstract #1159

Glycated albumin to glycated hemoglobin ratio as a predictor of esophageal varices bleeding risk

Abd ElAtti E,[1] Elshayeb E,[1] Badr M,[1] Montaser B,[2] Hewezy M[1]

[1]Internal Medicine Department, Faculty of Medicine-Menoufia University, Egypt, [2]Clinical pathology Department, Faculty of Medicine-Menoufia University, Egypt.

Introduction: Bleeding from ruptured esophageal varices (EV) is the most severe complications of patients with liver cirrhosis. Upper endoscopy is the golden standard for diagnosis of esophageal varices. Noninvasive diagnosis of esophageal varices in cirrhotic patients is beneficial because it help us to select the patients likely to have esophageal varices to do endoscopy for them.
Objectives: To evaluate glycated albumin to glycated hemoglobin ratio (GA/HbA1c ratio) as a predictor of presence of esophageal varices and bleeding risk in patients with liver cirrhosis.
Patients and methods: The study included 100 patients with chronic hepatitis C-related cirrhosis from Menoufia University Hospitals (Egypt). The patients divided into 3 groups: group 1 (40 cirrhotic patients with esophageal varices and history of bleeding), group 2 (40 cirrhotic patients with esophageal varices without history of bleeding) and group 3 (20 cirrhotic patients without esophageal varices). They underwent physical examination and laboratory investigations (CBC, liver profile {ALT, AST, serum albumin, bilirubin, PT %} urea, creatinine, AFP, FBG). Abdominal ultrasound and upper endoscopy were done for all patients. Glycated hemoglobin (HbA1c) and glycated albumin (GA) were measured. GA/HbA1c ratio was calculated for all patients.
Results: GA and GA/HBA1c ratio was significantly higher in group 1 (GA 23.2 ± 2.4) (GA/HBA1c 5.1 ± 0.3) than group 2 (GA 16.1 ± 1.4) (GA/HBA1c 3.8 ± 0.3) and group 3 (GA 11.7 ± 1.5) (GA/HBA1c 2.8 ± 0.3) (p = 0.001) and they were significantly higher in group 2 than group 3 (p = 0.001). HBA1c was significantly higher in group 1 (4.60± 0.42) than in group 2 (4.24 ± 0.15) and group 3 (4.14 ± 0.11) (p = 0.001) but there was no significant difference between group 2 and group 3 (p = 0.21). Binary logistic regression analysis for independent predictors of presence of

esophageal varices are GA, portal vein diameter and GA/HbA1c ratio ($P < 0.05$). Linear regression analyses for independent predictors of variceal bleeding are platelet count, grades of esophageal varices, risk signs and GA/HbA1c ratio.
Conclusion: GA/HbA1c ratio is a non-invasive parameter for prediction of presence of varices in HCV-positive cirrhotic patients. GA/HbA1c ratio may help in discrimination of low risk from high-risk varices and can predict the risk of bleeding. It can be provide a method for selecting patients for endoscopic surveillance.

Abstract #1175

Serum ascites cholestrol gradient in benign (cirrhotic) versus malignant ascites

Arun P[1], A R Venkateswaran[2]

[1]Senior Resident, Institute Of Medical Gastroenterology, Madras Medical College, Chennai, India, [2]Director, Institute Of Medical Gastroenterology, Madras Medical College, Chennai, India

Introduction: Ascites is a very common clinical problem. However, the ability to distinguish malignant from non-malignant and tubercular causes of ascites using various biochemical techniques would obviate the need of many expensive and time-consuming diagnostic studies on patients presenting with ascites of unknown etiology.
Aims: Therefore, this study was planned to evaluate usefulness of ascitic fuid albumin, protein, and SAAG and ascitic fluid cholesterol level in diagnosis of malignant, non-malignant and tubercular ascites.
Materials and methods: We conducted a prospective observational study in Department of medical gastroenterology, Madras Medical College from time period of January 2018 to December 2018. All cases of ascites of unknown etiology were evaluated and were grouped into malignant and benign ones. Patient having peritonitis were excluded from the study. In this groups, serum albumin, ascitic fluid albumin, cholesterol, serum ascitic fluid cholesterol gradient (SACG) were done. The data was processed in MS Excel and analysis was carried out using SPSS Ver. 23.
Results: Out of 80 patients, 30 were malignant (37.5%) and 50 were benign (62.5%). Cirrhosis was the most common cause of benign ascites and carcinoma stomach was the most common cause of malignant ascites. Ascitic fluid cholesterol above the level of 100 mg/dl has a specificity of 100% in detecting malignant ascites. Serum cholesterol ascitic fluid gradient of 100.2 ± 25.2 occurred in cirrhotic ascites, 49 ± 22 occurred in malignant ascites. Mean value of ascetic fluid cholesterol in cirrhosis was 27 mg/dl.
Conclusion: SAAG, SACG, ascitic fluid cholesterol having high specificity, can be used for differentiating between non-malignant and malignant ascites. It can also be used to differentiate cirrhotic ascites from malignant ascites

Abstract #1176

Faecal calprotectin as a screening test for hepatic encephalopathy in cirrhotic patients

Arun P[1], A R Venkateswaran[2]

[1]Senior Resident, Institute Of Medical Gastroenterology, Madras Medical College, Chennai, India, [2]Director, Institute Of Medical Gastroenterology, Madras Medical College, Chennai, India

Introduction: Calprotectin is a calcium zinc binding protein mainly found in neutrophils. It serves as a marker for intestinal inflammation. Bacterial translocation from the gut causing intestinal inflammation is one of the key pathogenic mechanisms of hepatic encephalopathy.
Aim: To assess the correlation between values of fecal calprotectin and degree of liver cirrhosis and minimal hepatic encephalopathy.
Methods: We included 100 patients with liver cirrhosis and 40 healthy patients as controls. Patients having other causes of abnormal calprotectin values (gastrointestinal bleeding or inflammatory bowel disease) were excluded from the study. The degree of hepatic insufficiency was assessed using the Child–Pugh classification and Model of End Stage Liver Disease (MELD), and extent of hepatic encephalopathy by Modified West-Haven criteria.
Results: Mean value of fecal calprotectin in cirrhotic patients was 169.1 ± 128.0 μg/g, and 25.0 ± 16.0 μg/g in the control group, respectively. We have confirmed statsically significantly higher values of fecal calprotectin in patients with cirrhosis ($p < 0.001$). There were not much significant differences in values of fecal calprotectin between the patients having different stages of liver cirrhosis using the Child–Pugh classification and MELD score ($p > 0.05$). We have observed statistically significant difference by comparing fecal calprotectin with West-Haven criteria of hepatic encephalopathy ($p < 0.001$).
Conclusion: We have found out significantly higher values of fecal calprotectin in cirrhotic patients, especially in hepatic encephalopathy according to West-Haven criteria.

Abstract #1238

Correlation between severity of cirrhosis based on child turcotte pugh score and lipid profile

Permadi GA[1], Nusi IA[2], Purbayu H[2], Sugihartono T[2], Kholili U[2], Soelistijo SA[3], Setiawan PB[2]

[1]Department of Internal Medicine, Faculty of Medicine, Airlangga University-Dr. Soetomo General Hospital, Surabaya, Indonesia, [2]Gastroenterohepatology Division, Department of Internal medicine, Faculty of Medicine, Airlangga University-Dr. Soetomo General Hospital, Surabaya, Indonesia, [3]Endocrinology Metabolic and Diabetes Division, Department of Internal medicine, Faculty of Medicine, Airlangga University-Dr. Soetomo General Hospital, Surabaya, Indonesia

Introduction: Lipoproteins such as LDL and HDL are also associated to cardiovascular disease as one of the causes of death in patients with liver cirrhosis. Hepatocyte's function will decrease in cirrhosis especially in lipoprotein synthesis. Therefore lipid profile evaluation in liver cirrhosis is very important, and the correlation between the severity of liver cirrhosis with serum lipid profile levels needs to be further investigated
Objective: To analyze the correlation between liver cirrhosis severity with lipid profile levels.
Methods: An observational analytic study crosses sectional, involving 35 subjects of liver cirrhosis. The severity of cirrhosis is measured by the Child-Turcotte Pugh score (CTP). Lipid profile measurements using Cbas C311-C501 with homogeneous enzymatic colorimetric methods. Data analysis using SPSS 23.0, output p value and the correlation coefficient (r) to determine the correlation.
Results: The study subjects dominated by men (74.3%). The mean age was 51.54 years. The mean LDL, HDL, and total cholesterol level was 69.31 mg/dL, 32.74 mg/dL, 113.71 mg/dL, respectively. Triglycerides had a median 69 mg/dL with the lowest value 30 mg/dL and the highest 171 mg/dL. The median of Child-Turcotte Pugh scores was 8 with the lowest score 5 and the highest 13. Obtained a significant, strong negative correlation for LDL levels (r-0.696; p 0.000), HDL (r-0.777; p0.000), Total Cholesterol (r-0.777; p0.000),

while Triglyceride levels was significantly weak negative (r -0.381; p 0.024).
Conclusion: Cirrhosis's severity has been shown to be strongly related to LDL, HDL, and Total Cholesterol levels. Triglyceride level has not been proven to be strongly related.

Abstract #1239

Association between plasma fibrinogen level and severity of decompensated liver cirrhosis measured with model for end stage liver disease (MELD) and Child–Turcotte–Pugh (CTP) score

Marfu'ah NO[1], Maimunah U[2], Jannah L[1], Ayudi C[1], Vidyani A[2], Thamrin H[2], Miftahussurur M[2], Sedana MP[3], Setiawan PB[2]

[1]Resident of Internal Medicine Department, Universitas Airlangga, Surabaya Indonesia, [2]Division of Gastroenterology and Hepatology, Internal Medicine Department, Universitas Airlangga, Dr. Soetomo General Hospital, Surabaya Indonesia, [3]Division of Hematology-Oncology, Internal Medicine Department, Universitas Airlangga, Dr. Soetomo General Hospital, Surabaya Indonesia

Introduction: Decompensated liver cirrhosis (LC) is associated with high mortality due to portal hypertension and coagulation impairment. One of that being impaired is fibrinogen. LC severity can be assessed with scoring system, such as Child Turcotte Pugh (CTP) and Model for End Stage Liver Disease (MELD) score. The relationship between fibrinogen and LC severity is still controversial.
Objectives: To determine the correlation between plasma fibrinogen level and decompensated LC severity measured with MELD or CTP score.
Methods: This was a cross sectional study involved patients with decompensated LC who visited Soetomo General Hospital from January 2018 until January 2019. Correlation between plasma fibrinogen level and MELD and CTP score was assessed using Spearman correlation test.
Results: There were 30 subjects, 63.3% male and 36.7% female, age average was 51.86 ± 8.79 years old. The mean of fibrinogen level was 173.02 ± 11.97 mg/dL. The mean fibrinogen level in MELD score < 10; 10–19; > 20 were 217.82 ± 44.56; 147.14 ± 55.15; 164.50 ± 100.18 mg/dL, respectively. The mean fibrinogen level in Child A; Child B; Child C were 198.95 ± 50.95; 158.69 ± 67.47; 155.40 ± 88.06 mg/dL, respectively. There was a significant negative correlation between fibrinogen level and MELD (r = -0.391; P = 0.033), but not significant with CTP score (r = -0.272; P = 0.146).
Conclusion: Patients with decompensated LC have reduced serum fibrinogen levels as result of decreased fibrinogen synthesis, dysfibrinogenemia, increased fibrinolysis, and consumptive coagulopathy.

Abstract #1254

Encephal App (Stroop test) for screening covert encephalopathy patients in our tertiary care centre

G N Gireesh, K Premkumar, A R Venketeshwaran, K Muthukumar, R Murali, A Chezhian

Institute of Medical Gastroenterology, Madras Medical College, Chennai

Background and Aim: Covert hepatic encephalopathy (CHE) is difficult to screen because of a large number of patients. We aimed Stroop Test as a screening method for CHE.
Methods:All patients attending medical gastroenterology department in our hospital with decompensated chronic liver disease was screened using phone based Encephal app. The time required to do the test number with subtask on (naming the color of signs) and off (naming the color of the word in discordant coloring) were recorded.
Results: 130 patients were included; 58 (44.61%) patients were diagnosed with CHE by psychometric hepatic enchephalopathy score. The cutoff of > 98 s for off time and > 213.43 s for on time + off time was taken & had the maximum area under the curve values (0.78) in all patients. The cutoff of 213.43 s had the highest sensitivity (0.88) but the specificity was low (0.59). Age and alcoholic hepatitis (odds ratio = 1.03 and 2.18, both with $P < 0.05$) had a positive correlation with the risk of developing CHE. Compared with PHES, EncephalApp was 32% time saving. It proved superior to PHES in terms of accessibility, acceptability and convenience to use (all $P < 0.05$).
Conclusions: The EncephalApp Stroop Test is an efficient screening tool to diagnose CHE in cirrhotic patients. Further studies are needed with larger sample size to increase its validity

Abstract #1284

Correlation between albumin serum and severity of decompensated liver cirrhosis measured with model for end stage liver disease (MELD)

Cahyani C[1], Nusi IA[2], Kholili U[2], Widodo B,[2] Thamrin H[2], Vidyani A[2], Jannah L[1], Setiawan PB[2]

[1]Resident of Internal Medicine Department, Universitas Airlangga, Surabaya Indonesia, [2]Division of Gastroenterology and Hepatology, Internal Medicine Department, Universitas Airlangga, Dr. Soetomo General Hospital, Surabaya Indonesia.

Introduction: Model for End-Stage Liver Disease (MELD) is a scoring system used to estimate the severity of chronic liver disease. Score is based on objective variables and predicts survival among different populations of patients. However, in the past, the first model like Child–Pugh score signified the importance of serum Albumin, a protein producing in liver. It is, thus, expected that the serum Albumin has correlation with MELD score.
Objectives: To determine the correlation between albumin serum and decompensated liver cirrhosis severity measured with MELD score in the Gastroenterohepatology Outpatient Installation at Dr. RSUD Soetomo Surabaya.
Methods: This was a cross sectional study involved patients with decompensated liver cirrhosis who visited Soetomo General Hospital from January 2018 until January 2019. Data analysis and correlation between albumin serum and MELD score was assessed using SPSS 25.0 with Spearman test, output p value and correlation coefficient (r) to find out the correlation.
Results: There were 31 subjects, 61.3% male and 38.7% female, age average was 52.23 ± 8.80 years old. The mean of albumin serum was 3.09 ± 0.65 mg/dL. Mean MELD score was 12.61 ± 0.958 with minimum score was 7 and maximum score was 31. There was a statistically significant correlation between albumin serum level and MELD score (r = -0.536; p = 0.002).
Conclusion: Patients with lower serum albumin level are presenting higher MELD score. Thus it's necessary to modify the MELD score by including serum albumin to assess the severity of liver cirrhosis.

Abstract #1286

Correlation between mid-upper arm circumference and body mass index in liver cirrhosis

Kurniawan Andree[1], Lugito Nata Pratama Hardjo[1], Prasetya Ignatius Bima[1], Raffaello Wilson Matthew[2], Halim Devina Adella[2], Renaldi Renaldi[2]

[1]Internal medicine, Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia, [2]Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia

Introduction: Malnutrition is highly prevalent in patients with liver cirrhosis especially in advances stage and underwent liver transplantation. Mid upper arm circumference (MUAC) is recognized recently as an effective means of screening for poor nutritional status in adults. Body mass index (BMI) is widely used as an anthropometric indicator for nutritional status, but BMI has several limitations in patients with edema and ascites which were found in liver cirrhosis. There was still limited data about the correlation between MUAC and BMI especially in liver cirrhosis patients.
Objectives: To know the correlation between MUAC and BMI in liver cirrhosis patients
Methods: This cross-sectional study was done in one of private hospital in Tangerang, Banten, Indonesia. Liver cirrhosis patients diagnosed by abdominal ultrasound were included. Nutritional assessment was performed by BMI and MUAC. The correlation between BMI and MUAC were evaluated using Pearson or Spearmen correlation test based on normality distribution data.
Results: A total of 27 subjects were recruited from November to December 2019. Twenty-four (88.8%) were male. The median of age was 52 (25–87) years old. More than 50% subjects were grouped into Child T. Pugh C. The median of MUAC was 26 (20–33) cm. The median of BMI was 23 (17–39) kg/m^2. The correlation between BMI and MUAC was r 0.189 (p 0.484).
Conclusion : The mid-upper arm circumference did not correlate with body mass index in liver cirrhosis. MUAC might be used for nutritional parameter especially in advance liver cirrhosis.

Abstract #1305

Prevalence and prognostic significance of pre-sarcopenia and sarcopenia in cirrhosis

Anand Abhinav[1], Agarwal Samagra[1], Mohta Srikant[1], Gunjan Deepak[1], Kaushal Kanav[1], Poudel Shekhar[1], Sharma Sanchit[1], Gopi Srikant[1], KS Madhusudhan[2], Mahajan Sandeep[3], Singh Namrata[1] and Saraya Anoop[1]

[1]Department of Gastroenterology and Human Nutrition, All India Institute of Medical Sciences, New Delhi, India 110029, [2]Department of Radiology, All India Institute of Medical Sciences, New Delhi, India 110029, [3]Department of Nephrology, All India Institute of Medical Sciences, New Delhi, India 110029

Introduction: Consensus on the definition of pre-sarcopenia and sarcopenia in patients with cirrhosis is lacking.
Objectives: Determining skeletal muscle index (SMI) based cut-offs for sarcopenia and pre-sarcopenia and assessing its impact on mortality.
Methods: A healthy cohort (HC) comprising of kidney donors and a diseased cohort (DC) of patients with cirrhosis were chosen. Computed tomography (CT) images at third lumbar vertebra were analyzed to calculate SMI. Mean-2 (standard deviation) value of SMI from the HC was defined as the cut-off for sarcopenia. SMI value as a predictor for mortality in the DC was obtained by a receiver operating curve and used to define pre-sarcopenia.
Results: The CT images of 180 patients (144 males and 36 females, age 42.9 ± 9.9 years) with cirrhosis and 180 age and sex-matched controls were evaluated. The cut-offs for pre-sarcopenia and sarcopenia were 41.5 cm^2/m^2 and 37.3 cm^2/m^2 respectively for males, and 34.3 cm^2/m^2 and 26.7 cm^2/m^2 respectively for females. The prevalence of sarcopenia and pre-sarcopenia was 18.3% and 19.4% respectively. The mortality in the non-sarcopenic, pre-sarcopenic and sarcopenic group was 6.2%, 17.1% and 30.3% ($p < 0.001$). On multivariate analysis, sarcopenia (hazard ratio (HR) 3.1, $p = 0.029$), model for end stage liver disease (MELD) score more than 20 (HR 3.8, $p = 0.03$) and ascites (HR 4.9, $p = 0.005$) were independent predictors of mortality. Pre-sarcopenia showed an insignificant but positive trend for predicting mortality (HR 2.7, $p = 0.072$).
Conclusion: No sarcopenia, pre-sarcopenia and sarcopenia represent a continuum of worsening muscle mass. Identification of pre-sarcopenic patients provides a therapeutic window to prevent the development of sarcopenia and reduce mortality.

Abstract #1307

Correlation between hand grip strength and health-related quality of life in liver cirrhosis

[1]Raffaello Wilson Matthew, [2]Kurniawan Andree, [2]Prasetya Ignatius Bima, [1]Josephine Andrea Pasha, [1]Sanjaya Gisela Meydilin, [1]Vanessa Maria Gabrielle [1]Suciningtias Marlyn

[1]Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia

Introduction: Liver Cirrhosis (LC) may affect patient's quality of life causing higher economic burden and adverse clinical outcome. Sarcopenia is associated with unfavourable H-QOL in LC. Muscle function is one of the components of sarcopenia and easily measured by hand grip strength (HGS). However, there has been limited data on association between H-QOL and HGS in LC.
Objective: The aim of this study is to see the correlation between hand grip strength and H-QOL in LC.
Methods: A cross-sectional study with 27 patients diagnosed with LC by ultrasonography in our general hospital was conducted. H-QOL is measured using Short Form 36 (SF-36) questionnaire and HGS is measured using Southampton protocol with JAMAR handgrip. Pearson or Spearman correlation test will be used according to data distribution.
Results: Twenty seven patients with LC were included. Twenty-two (81%) patients were male with mean age 52±14.35 years. The average of HGS was 20.7±11.68. Fifteen male (68%) patients and 4 (80%) female patients were low HGS according to Indonesian's cut off. The correlation between HGS and H-QOL were the physical functioning ($r = 0.260$ $p = 0.191$), role physical ($r = 0.099$ $p = 0.622$), bodily pain ($r = -0.196$ $p = 0.327$), general health ($r = 0.042$ $p = 0.834$), vitality ($r = 0.162$ $p = 0.420$), social functioning ($r = 0.016$ $p = 0.939$), role emotional ($r = 0.130$ $p = 0.519$), and mental health ($r = 0.161$ $p = 0.421$), respectively.
Conclusions: Hand grip strength did not correlate with H-QOL in most domain in LC. Further study with bigger sample size is needed.

Abstract #1309

Correlation between skeletal muscle mass index and health-related quality of life in liver cirrhosis

Saroso Olivia J. D. A.,[1] Kurniawan Andree,[2] Prasetya Ignatius B,[2] [1]Law Natasha K.,[1] Heriyanto Rivaldo S.,[1] Sanjaya Gisela M.,[1] Angel Patricia[1]

[1]Faculty of Medicine, Universitas Pelita Harapan, [2]Department of Internal Medicine, Faculty of Medicine, Universitas Pelita Harapan

Introduction: Liver cirrhosis is the end-point of many liver diseases which leads to advanced hepatic fibrosis. Liver cirrhosis has been associated with worse health-related quality of life (HRQOL). Sarcopenia or loss of skeletal muscle loss is one of many complications of liver cirrhosis that has been associated with increased mortality, risk of development of other complications, worse post-liver transplant outcomes and decreased quality of life.
Objective: The aim of this study is to know the correlation between muscle mass and health-related quality of life in liver cirrhosis.
Methods: This cross-sectional study collected 18 liver cirrhotic patients who are diagnosed with ultrasonography. Muscle mass was measured using body impedance analysis (BIA) and then adjusted by height to get skeletal muscle mass index (SMI). HRQOL was measured using Short Form 36 (SF-36) questionnaire. Correlation statistical analysis will be done using Pearson or Spearman according to data distribution normality test.
Results: Eighteen patients with liver cirrhosis were included in this study. Sixteen (89%) patients were male with mean age 52.72±15.76 years. Mean score of SMI is 7.41±1.65 kg/m^2. Correlation between SMI and 8 domains of SF-36 were r = 0.137 p = 0.589 (physical functioning), r = 0.298 p = 0.230 (role-physical), r = -0.155 p = 0.539 (bodily pain), r = 0.495 p = 0.037 (general health), r = 0.432 p = 0.073 (vitality), r = -0.158 p = 0.532 (social functioning), r = -0.067 p = 0.791 (role-emotional), r = 0.468 p = 0.050 (mental health), respectively.
Conclusions: SMI is correlated with HRQOL domains in mental health and general health. SMI might also correlate with vitality, but bigger sample size is needed.

Abstract #1310

Correlation between sleep disturbance and quality of life in liver cirrhosis

[1]Sanjaya Gisela Meydilin, [2]Kurniawan Andree, [2]Prasetya Ignatius Bima, [1]Saroso Olivia Jeany Darmawan Adji, [1]Law Natasha Karlina, [1]Hamdoyo Audrey

[1]Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia

Introduction: Cirrhosis have been predicted to be the 12th leading cause of death in 2020. Sleep disturbances is associated with a decrease in quality of life. The underlying pathophysiological mechanism for sleep disturbances are correlated with disturbed metabolism of melatonin and glucose. Study shows that sleep disturbance as an independent predictor of lower quality of life for patients with liver cirrhosis, but there is limited data in Indonesian population.
Objective: The aim of this study is to evaluate the association between sleep disturbance and quality of life in liver cirrhosis.
Method: We performed a cross-sectional study. Nineteen patients with liver cirrhosis were recruited voluntarily from the hospital. Participants completed the Pittsburgh Sleep Quality Index (PSQI) questionnaires and Short Form 36 (SF-36) questionnaires for evaluation of sleep quality and quality of life respectively. Pearson or Spearman correlation test will be used according to data distribution normality test.
Results: Nineteen patients were evaluated with average age 52±13 years. The average of PSQI score was 9.02±3.79. The correlation between PSQI and SF-36 in several domains were the physical functioning (r = −0.262 p = 0.278), role physical (r = − 0.094 p = 0.701), energy (r = − 0.13 p = 0.957), bodily pain (r = -0.200 p = 0.412), general health (r = -0.097 p = 0.691), vitality (r = 0.041 p = 0.868), social functioning (r = 0.539 p = 0.017), role emotional (r = − 0.123 p = 0.617), mental health (r = 0.231 p = 0.342) respectively.
Conclusion: Sleep disturbance related to a lower SF-36 in social functioning domain but not with the others. Further study with bigger sample is needed to confirm this result.

Abstract #1312

Correlation between physical activity and hand grip strength in liver cirrhosis

Heriyanto Rivaldo S., [2] Kurniawan Andree, [2]Prasetya Ignatius Bima, [1]Law Natasha K., [1]Saroso Olivia Jeanny Darmawan Adji, [1]Renaldi renaldi, [1]Rachmaputri Salma S.

[1]Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia

Introduction: Physical inactivity along with sarcopenia are highly prevalent, independent predictors of morbidity and mortality in patients with cirrhosis. Many patients with liver cirrhosis perceive lower physical functioning and more fatigue than non-cirrhotic individuals which leads to physical inactivity. Loss of muscle strength is one aspect of sarcopenia that can be measured using hand grip strength (HGS) test. However, there has been scarcity of data in regard to correlation of physical activity and HGS.
Objective: The objective of this study is to see the correlation between hand grip strength and physical activity in liver cirrhosis.
Methods: Cross sectional study was conducted. A total of 14 subjects liver cirrhosis diagnosed by abdominal ultrasound were gathered from our general hospital. Structured interview using International Physical Activity Questionnaire (IPAQ) was conducted to assess patients physical activity. The HGS were measured using utilizing standardized JAMAR handgrip procedures. Pearson or Spearman correlation test will be used according to data distribution.
Results: Fourteen patients were included in this study. Ten (71%) patients were male and 4 (29%) patients were female. The average age was 48 ± 14.33 years. The mean of METS/IPAQ was 2142.64± 3022.6. The average of HGS was 23.5 ± 13.01 kg. The correlation between IPAQ and HGS in liver cirrhosis was (r = 0.1 p = 0.962).
Conclusions: Physical activity did not correlate with hand grip strength in most domain in liver cirrhosis. Further study with bigger sample is needed to confirm this result.

Abstract #1316

Correlation between mid-upper arm circumference and hand grip strength in patients with liver cirrhosis

Josephine Andrea Pasha[1], Kurniawan Andree[2], Prasetya Ignatius Bima[2], Heriyanto Rivaldo Steven[1], Raffaello Wilson Matthew[1], Hamdoyo Audrey[1]

[1]Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia

Introduction: Malnutrition is common in patients with liver cirrhosis (LC) and is associated with the severity and survival of the patients. Mid-upper arm circumference (MUAC) and handgrip strength (HGS) are great indicators for malnutrition and easy to perform even on the most debilitated individuals. Both anthropometric measurements can be taken for evaluation but there has been limited data on the association between the two in LC patients.
Objectives: The aim of this study is to see the correlation between mid-upper arm circumference and handgrip strength in patients with LC.
Methods: A total of 16 hospitalized and non-hospitalized LC diagnosed patients by ultrasonography in a general hospital in Indonesia participated in this cross-sectional study. MUAC was measured using a measuring tape on the midpoint of the upper arm according to the standard protocol. HGS was measured using a JAMAR handgrip dynamometer with Southampton protocols. Spearman or Pearson correlation test will be used to evaluate the correlation between MUAC and HGS according to data distribution normality test.
Results: A total of 16 LC patients participated in this study. Fifteen (93.75%) patients were male with the average age of 51.38 ± 11.34. The median of MUAC was 25.5 (20–31) cm and the mean of HGS was 21.44 ± 10.28 kg. Twelve patients had low HGS according to HGS cut-off in Indonesia (30 kg in male and 19 kg in female). The correlation between MUAC and HGS was (r = 0.495, p = 0.051).
Conclusion: MUAC might have correlation with HGS, but bigger sample size is needed to confirm this result.

Abstract #1320

Diagnostic performance of splenic shear wave elastography for predicting esophageal varices in patients with compensated liver cirrhosis

Ishwar Amalazari, Venkatesawaran, Premkumar

Institute of medical gastroenterology, MMC

Objectives: The purpose of this study was to investigate the diagnostic performance of splenic shear wave elastography (SWE) for predicting the presence of esophageal varices and high-risk esophageal varices in patients with compensated cirrhosis and to compare it with other nonspecific predictors and according to the presence of splenomegaly
Methods: Clinical data from 103 patients with compensated cirrhosis who underwent sonography, SWE of spleen, and endoscopy were collected consecutively. splenic stiffness was measured by SWE. Comparisons of the accuracy of prediction between groups were made by areas under the receiver operating characteristic curves (AUROCs), and regression analyses were performed for the multiple variables related to the presence of esophageal varices and high-risk varices.
Results: The optimal cutoff values for predicting the presence of esophageal varices and high-risk varices were 40.9 and 56.1 kPa, respectively. The AUROC of spleen stiffness for prediction of esophageal varices was significantly higher than the AUROCs of platelet count, spleen diameter, and platelet count/spleen diameter ratio ($P = .025$; $P = .001$; $P = .027$). For predicting esophageal varices in patients without splenomegaly, the AUROC of spleen stiffness was higher than that of the platelet count/spleen diameter ratio. In multivariate logistic regression analysis, spleen stiffness and the platelet count/spleen diameter ratio were independent predictors of esophageal varices ($P < .001$; $P = .038$). For the presence of high-risk varices, only liver stiffness was a statistically significant independent predictor ($P = .012$).
Conclusions: In patients with compensated cirrhosis, spleen stiffness measured by SWE is a new effective noninvasive diagnostic tool for predicting the presence of esophageal varices. It is more accurate than the platelet count/spleen diameter ratio, especially in patients without splenomegaly. In addition, the SWE value was the only effective independent factor for predicting high-risk esophageal varices.

Abstract #1321

Liver and spleen stiffness measurements for assessment of portal hypertension severity in patients with Budd Chiari syndrome

Ishwar Amalazari, Venkatesawaran, Premkumar

Institute of medical gastroenterology, MMC

Background: Budd-Chiari Syndrome (BCS) is a rare vascular disease of the liver caused by the obstruction of the hepatic venous outflow located from the small hepatic venules up to the entrance of the inferior vena cava (IVC) into the right atrium. Current prognostic indexes are suboptimal for an individual prognostic assessment and subsequent management of patients with BCS. Liver (LSM) and spleen (SSM) stiffness measurements are widely validated prognostic tools in hepatology, but the evidence in patients with BCS is limited. This paper describes LSM and SSM in patients with BCS and their correlation with clinical, biochemical, and ultrasound findings from the same patients.
Methods: We investigated a case series of 20 patients with BCS diagnosis and available LSM and SSM evaluated by transient elastography (TE). Biochemical, imaging, and endoscopic findings nearest to the TE evaluation were recorded. Clinical outcomes and BCS evolution were described for each patient. When available, repeated TE assessments were also recorded.
Results: Patients with acute nonfulminant manifestation of BCS presented near-the-upper-limit values (75 kPa) of LSM and SSM, which often persist until the placement of a transjugular intrahepatic portosystemic shunt (TIPS). On the other hand, TE values were markedly lower in patients with compensated BCS. In some patients with repeated TE measurement years after TIPS placement, LSM had decreased to values of < 10 kPa years. SSM changes in these patients were, however, less evident.
Conclusions: Extremely elevated values of LSM and SSM are suggestive of BCS. The evaluation of both LSM and SSM by TE could help clinicians in the initial evaluation, risk stratification, and therapy response monitoring of patients with BCS.

Abstract #1329

Correlation between physical activity and muscle mass in liver cirrhosis patients

Hamdoyo Audrey[1], Kurniawan Andree[2], Prasetya Ignatius Bima[2], Fahman Julang[1], Angel Patricia[1], Suciningtias Marlyn[1], Rachmaputri Salma Shafira[1]

[1]Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia

Introduction: Loss of muscle mass is the most common and clinically significant complication of liver cirrhosis. It is often associated with increased morbidity and mortality. One of the other conditions accompanying liver cirrhosis is decreased physical activity. There is a paucity of data regarding the correlation between physical activity and muscle mass.
Objective: The aim of this study is to see the correlation between physical activities and muscle mass in liver cirrhosis patients.
Methods: A cross-sectional study was conducted on 13 liver cirrhosis patients diagnosed by ultrasonography from a general hospital in Indonesia. Participants completed the International Physical Activity Questionnaire (IPAQ). Bio-electrical Impedance Analysis (BIA) was performed and skeletal muscle mass index (SMI) was used to determine the muscle mass of participants. Spearman or Pearson correlation test will be used to evaluate the correlation between physical activity and muscle mass in liver cirrhosis patients according to the data distribution.
Results: Thirteen liver cirrhosis patients were involved in this study. Eleven (84.62%) were male with a mean age of 48.385±13.482 years. The mean of IPAQ/METS was 2163.923±3144.996 while the mean of muscle mass was 7.435±1.859. The correlation between physical activity and muscle mass in liver cirrhosis patients was (r = -0.453, p = 0.120).
Conclusions: Physical activities inversely correlate to the muscle mass in liver cirrhosis patients. Further studies with a bigger sample size may be needed to confirm this result.

Abstract #1332

Inflammation associated with leaky gut syndrome causes poor response and relapse of water retention in decompensated liver cirrhosis patients treated by Vasopressin V2-recepor antagonist

Masato Nakai, Takashi Kitagataya, Ren Yamada, Taku Shigesawa, Kazuharu Suzuki, Akihisa Nakamura, Machiko Umemura, Takuya Sho, Goki Suda, Kenichi Morikawa, Koji Ogawa, Naoya Sakamoto

Gastroenterology and Hepatology, Hokkaido University Hospital, Sapporo, Japan

Introduction: Tolvaptan (TVP), vasopressin V2 receptor antagonist is available for Water retention (WR) due to decompensated liver cirrhosis (LC) in Japan, and several predictors for the response to TVP have been reported. But the criteria of relapsewas not defined in Asia and the predictive factors for relapse is unclear.
Objective: To analysis the predictors for TVP response and relapse of WR in decompensated LC patients.
Method: Ninety five LC patients were treated with TVP. Short term response was judged by the decrease in body weight ($\geq$ 1.5 kg) within 7 days. The relapse of WR was judged due to EASL criteria in practice guidelines (J Hepatol. 2018). Blood biochemical tests including serum soluble CD14 (sCD14), a marker of leaky gut syndrome, and urinary tests were performed before start of TVP. Predictive factors for the short-term response and the relapse of WR were analyzed statistically.
Results: The response rate to TVP was 55.8% and 42 patients was non-responders (*NR* group). The relapse could be judged in 41 patients, and the rate was 34.1% (14 patients:*Rep* group). 27 patients were long-term responders without relapse(*LR* group). CRP$\leqq$0.9 mg/dl and urinary Na/K ratio$\geqq$2.5 were significant predictors of short-term response. Higher CRP was also one of the predictors of relapse. By using CRP, the stratification of these groups (*NR, Rep, LR*) was possible (p = 0.01). sCD14 was positively correlated with CRP and also useful for the stratification of three groups (p = 0.03)
Conclusion: Inflammation associated with leaky gut syndrome might be a predictive factor for not only poor response but also relapse of WR after TVP treatment.

Abstract #1361

Correlation between minimal hepatic encephalopathy and sleep quality in liver cirrhosis

Renaldi Renaldi[1], Kurniawan Andree[2], Prasetya Ignatius Bima[2], Josephine Andrea Pasha[1], Raffaello Wilson Matthew[1], Vanessa Maria Gabrielle[1], Suciningtias Marlyn[1]

[1]Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia, [2]Internal Medicine, Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia

Introduction: Minimal Hepatic encephalopathy (MHE) is the beginning of a potentially reversible, metabolically caused disturbance of the central nervous system function that occurs in patients with acute or chronic liver disease. Sleep disturbances and excessive daytime sleepiness have been reported in patients with liver cirrhosis. A study showed the prevalence of sleep disturbances in patients with liver cirrhosis ranging from 48% to 81%. The pathophysiology of how MHE can cause sleep disturbances is still not fully understood. Moreover, research about this problem is still lacking.
Objective: The aim of this study is to find the correlation between minimal hepatic encephalopathy and sleep quality in liver cirrhosis.
Methods: This cross-sectional study was done with a total of 16 patients. MHE is measured using Number Connection Test (NCT) questionnaire during the interview and sleep disturbance is measured using Pittsburgh Sleep Quality Index (PSQI) questionnaire. Pearson or Spearman correlation test will be used according to data distribution normally test.
Results: A total of 16 patients were included with the average age of 58 ±4.76 years. Thirteen (81%) patients were male and 3 (19%) patients were female. The mean of NCT was 126.12 ± 62.8 and PSQI score was 9 ± 4.01. The correlation between NCT and PSQI in liver cirrhosis was (r = 0.260 p = 0.331).
Conclusions: Minimal hepatic encephalopathy did not correlate with sleep quality in liver cirrhosis. Further study with a bigger sample size and another measurement of MHE are needed to confirm this result.

Abstract #1363

Correlation between hand grip strength and minimal hepatic encephalopathy in liver cirrhosis patients

[1]Natasha Karlina Law, [2]Andree Kurniawan, [2]Ignatius Bima Prasetya, [1]Rivaldo Steven Heriyanto, [1]Gisela Meydilin Sanjaya, [1]Patricia Angel, [1]Johanna Valentina

[1]Faculty of Medicine, Universitas Pelita Harapan, [2]Department of Internal Medicine, Faculty of Medicine, Universitas Pelita Harapan

Introduction: Minimal hepatic encephalopathy (MHE) is considered as the mildest type of hepatic encephalopathy (HE), which are frequently encountered in patients with liver cirrhosis (LC) and may affect patients quality of life. Detection of MHE determines the patients' psychometric performance, attention, working memory, psychomotor speed, and visuospatial ability, likewise to neurology measurements. In general, patients with cirrhosis can appear with muscular depletion due to a deficiency in the synthesis of muscular proteins. Handgrip strength (HGS) test often evaluated amongst liver dysfunction patients. However, There has been no further evidence related to MHE.
Objectives: This study aimed to investigate the correlation between MHE and HGS.
Method: This cross-sectional study was conducted with a total of 22 LC patients. Handgrip is measured with JAMAR handgrip using southampton method. Early signs of MHE is evaluated using Number Connection Test (NCT). According to the data distribution normality test, Spearman's correlation test was used to measure between HGS and MHE.
Results: A total of 22 samples involved in the study. Eighteen (81.8%) male patients and 4 (18.2%) female patients. The average age was 52.45 ± 15.25 years. The mean of the NCT and HGS was 118.95 ± 56.75 and 23.14 ± 9.83 respectively, where the correlation of these two variables were (r = -0.11, p = 0.62).
Conclusion: There is no significant correlation between the HGS and MHE. Further studies with a larger sample size is needed.

Abstract #1381

Correlation between muscle mass and minimal hepatic encephalopathy in liver cirrhosis

[1]Angel Patricia, [2]Kurniawan Andree, [2]Prasetya Ignatius Bima, [1]Fahman Julang, [1]Hamdoyo Audrey, [1]Vanessa Maria Gabrielle, [1]Valentina Johanna

[1]Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia

Introduction: Sarcopenia refers to the loss of muscle mass and function, affecting nearly 10% of the world's population. It has shown to be an increasingly common condition in cirrhosis patients, along with hepatic encephalopathy. Evidence regarding the relation between the two is thought to be due to metabolic errors that occur due to declining muscle mass. Reduced muscle mass is thought to impair ammonia clearance, leading to accumulation and further impairment along with the liver's reduced function. Increased concentrations of ammonia then impairs muscle synthesis, resulting in a vicious cycle, contributing towards a worse prognosis in cirrhosis patients.
Objectives: The aim of this study is to evaluate the correlation between muscle mass and minimal hepatic encephalopathy in liver cirrhosis.
Methods: Admitted patients who were diagnosed with liver cirrhosis by abdominal ultrasound were evaluated in this cross-sectional study. Muscle mass was evaluated using bio-impedance analysis method and adjusted by height. Minimal hepatic encephalopathy was evaluated using the numbers connection test. The correlation between them was evaluated using either Spearman or Pearson correlation test based on data distribution normality.
Results: 19 subjects were evaluated. The mean muscle mass was 7.57 ± 1.75 kg/m2, while the mean results for the number connection test was 119 ± 66.5 seconds. The correlation is r = 0.274 and p = 0.256.
Conclusion: The correlation between muscle function and minimal hepatic encephalopathy was shown to be insignificant. Muscle mass does not correlate with minimal hepatic encephalopathy. Further study with bigger sample size is needed to confirm this result.

Abstract #1384

The impact of sarcopenia in liver cirrhosis on mortality and rehospitalization after one month being admitted: a preliminary study

Kurniawan Andree[1], Prasetya Ignatius Bima[1], Lugito Nata Pratama Hardjo[1], Raffaello Wilson Matthew[2], Halim Devina Adella[2], Jodhinata Claudia[2], Renaldi Renaldi[2], Saroso Olivia Adji[2]

[1]Internal Medicine, Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia, [2]Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia

Introduction: Sarcopenia is decreased of muscle mass and or muscle strength and physical performances. We evaluated the impact of sarcopenia to liver cirrhosis patients on mortality and rehospitalization in 1 month after been admitted. There is still limited data about the impact of it especially in Indonesian patients.
Objectives: To evaluate the impact of sarcopenia in liver cirrhosis on mortality and re-hospitalization after 1 month being admitted.
Methods: This cohort study included liver cirrhosis diagnosed by abdominal ultrasound who admitted in our hospital. They were evaluated if they had decreased muscle mass (evaluated by Bioelectrical Impedance analysis) and or muscle strength (evaluated by hand grip strength using Southampton protocol). The Indonesian cut-off of low muscle mass and strength are less than 5.52 kg/m2 in female and 7.71 kg/m2 in male and 19 kg in female and 30 kg in male. The outcome is mortality and re-hospitalization after 1 month being admitted.
Results: A total of 27 subjects were collected. Twenty-four (88.8%) were male. The median of age was 52 (25–87) year old. More than 50% subjects were grouped into Child T. Pugh C. One patient had HCC. Fifteen (55%) subjects had low muscle mass and twenty (74%) subjects had low muscle strength. They were followed up around average 2.8 months. One subject found died and two subjects were re-hospitalized. All three subjects were male and had sarcopenia
Conclusion: One (6.67%) subject with sarcopenia died in 1 month follow up. Two (10%) subjects with sarcopenia have been re-hospitalization in 1 month.

Abstract #1386

Serum ferritin—an independent prognostic marker in predicting early mortality in advanced liver disease

Shujaath Asif

Introduction: Various prognostic models were devised to predict the future events in patients with advanced liver disease. MELD-Na is usually preferred for organ allocation whereas CTP score is preferred in daily practice. The efficacy of serum ferritin in predicting future events is uncertain.
Aim of The Study: To study whether serum ferritin can independently predict the 30 day mortality in patients with advanced liver disease.
Materials and Methods: This study was a prospective analytical evaluation, conducted at tertiary referral center, AIG Hospitals,

Hyderabad, from Sep 2018 to Nov 2019. Total of 75 Adult patients in age group 12 years and above with chronic liver disease were enrolled with all relevant data and investigations including *serum ferritin levels.* Patients enrolled were followed up and Mortality was assessed at 30th day. Patients were also classified into 3 groups based on serum Ferritin values. GROUP A-SERUM FERRITIN < 200 ng/ml. GROUP B-SERUM FERRITIN 200 TO 400 ng/ml. GROUP C-SERUM FERRITIN > 400 ng/ml. Serum ferritin was analysed as trichotomous variable. Majority of the patients had serum ferritin value above 400 ng/ml. 29 patients out of 36 patients in this group had early mortality. Serum ferritin was assessed as a categorical variable using Pearson's Chi-square test. It was found to be highly significant *P* Value < 0.001.

Conclusion: Though CTP score, MELD and serum ferritin were found to be useful in predicting outcome, but serum ferritin was superior. Addition of serum ferritin to MELD was found to increase the accuracy which was significant. Serum ferritin as an independent prognostic appears to be convincing but large prospective studies should be carried out before being recommended.

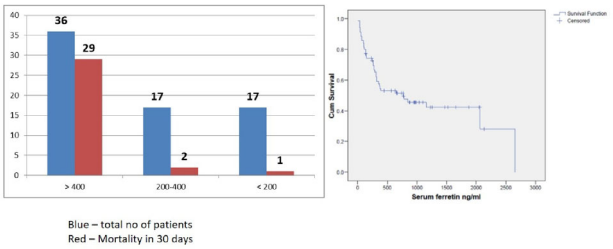


Figure 1. 30 day outcome and Kaplan-Meyer survival curves.

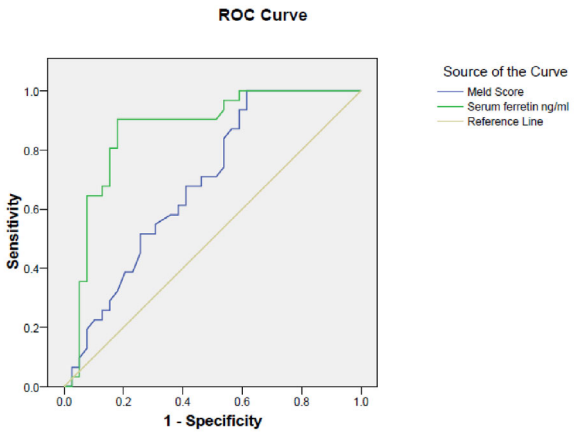


Figure 2. ROC Curve Analysis For Serum Ferritin + Meld-Na

Abstract #1406

Demographic makeup of a diverse patient population with a diagnosis of cirrhosis in a single Urban Centre, in Toronto, Ontario, Canada

Jammu A[1], Dallali H[2], Lee J[3], Mahmood M K[4], Kausar S[5], Magnes M[6], Elkhashab M[7]

Research, Toronto Liver Centre, Toronto, Canada

Background: Understanding the demographic composition of patient populations is of great interest in today's medical landscape where there is a growing appreciation for the impact of patient history on medical diagnosis/prognosis.

Objective: A descriptive study of a diverse population of cirrhotic patients in a single urban centre (Toronto Liver Centre) in Toronto, Ontario, Canada may provide insight into the context in which a cirrhosis diagnosis was made.

Methods: Retrospective review of 5748 charts to identify cases of cirrhosis diagnosis (n = 470). Patient age, sex, comorbid conditions and cancer history was examined to generate a demographic summary.

Results: Of 5748 charts, 470 had a positive history of cirrhosis. Ethnicity spans five continents: Asia (34.6%), Commonwealth of Independent States (4.7%), Eastern Europe (3.1%), Latin America & Caribbean (3.1%), Near East (5.8%), Northern Africa (23.6%), North America (1.6%), Sub-Saharan Africa (8.4%) and Western Europe (15.2%). 65% were male and 35% were female. In terms of age distribution: < 30:0.2%, 31–40:1.3%, 41–50:6.8%, 51–60:21.9%, 61–70:27.9%, 71–80:18.5%, 81–90:18.7%, > 90:4.7%. Major comorbid conditions: obesity (25.7%), dyslipidemia (27.4%), hypertension (43%), diabetes (35.1%), GERD (14.0%), depression (10.9%), CAD (9.1%), colonic polyps (6.8%), sleep apnea (1.9%). Of the patients, chronic HCV (42.3%), chronic HBV (17.4%), alcoholic liver disease (18.1%), NAFLD (3.6%), NASH (9.8%), autoimmune hepatitis (3.6%). Of this cohort, hepatomegaly (22.6%), splenomegaly (33.6%), focal liver lesion (16.6%), alpha-1-antitrypsin deficiency (21.3%), sarcoidosis (21.3%), hepatic encephalitis (10.2%), esophageal varices (42.3%), gastric varices (13.8%), ascites (33.8%), portal hypertension (48.3%). Major cancer history includes liver cancer (13%), breast cancer (1.7%), colon cancer (0.9%), non-Hodgkin's lymphoma (0.9%).

Conclusion: Majority of patients were above 50 (91.7%) and male (65.0%). The diverse patient population had numerous comorbid burdens including hypertension (43%), diabetes (35.1%), dyslipidemia (27.4%) and obesity (25.7%). Most commonly observed cancer diagnoses include liver and breast cancer. 4.7% had liver transplant.

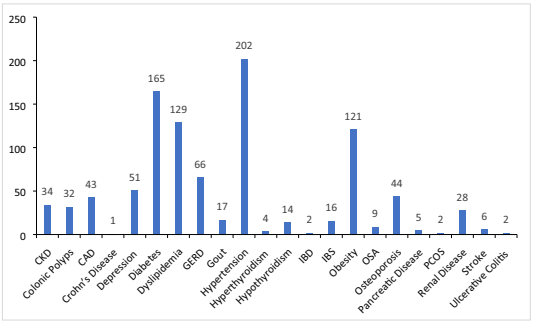


Figure 1: Comorbid condition history of patients with a cirrhosis diagnosis at a single urban centre in Toronto, Ontario, Canada (n=470).

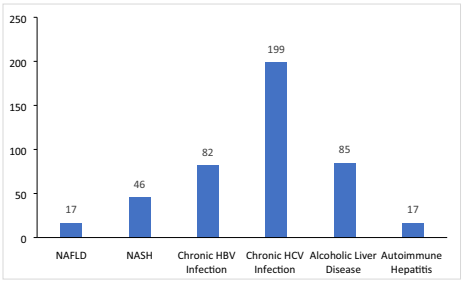


Figure 2: Liver condition history of patients with a cirrhosis diagnosis at a single urban centre in Toronto, Ontario, Canada (=470).

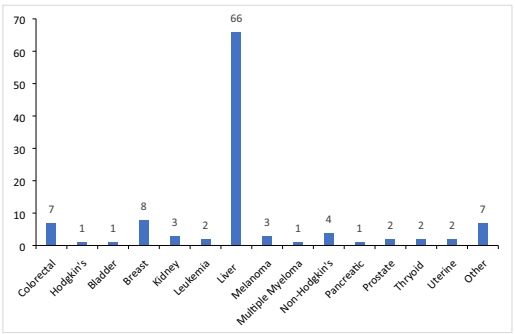


Figure 3: Prevalence of hepatic and extra-hepatic malignancies among patient with a liver cirrhosis diagnosis (n=470).

Abstract #1426

Surgical management in patient with non-cirrhotic portal hypertension

Tri Asih Imroati[1], Aditya SF[2], Budi W[3], Titong S[3], Ulfa K[3], Poernomo BS[3], Iswan AN[4]

[1]Resident of Gastroentero-Hepatology Division, Internal Medicine Departement, Faculty of Medicine, Airlangga University, Dr. Soetomo-Teaching Hospital, Surabaya, Indonesia, [2]Resident of Internal Medicine Departement, Faculty of Medicine, Airlangga University, Dr. Soetomo-Teaching Hospital, Surabaya, Indonesia, [3]Teaching staff of Gastroentero-Hepatology Division, Internal Medicine Departement, Faculty of Medicine, Airlangga University, Dr. Soetomo-Teaching Hospital, Surabaya, Indonesia, [4]Head of Gastroentero-Hepatology Division, Internal Medicine Departement, Faculty of Medicine, Airlangga University, Dr. Soetomo-Teaching Hospital, Surabaya, Indonesia

Introduction: Noncirrhotic portal hypertension (NCPH) causes can be classified as prehepatic, hepatic, and posthepatic. Several studies from 1980 to 1990 found that there were 23% cases of portal hypertension in India, 3–5% in Western countries, and 14–27% of cases were NCPH. The management of NCPH includes preventing and treating hemorrhagic varices as well as managing portal hypertension, stopping related drugs, and treating the following medical conditions. Primary and secondary prevention of varicose bleeding can use non-selective beta blockers, varicose ligation or sclerotherapy. If varicose hemorrhage recurs and fails with pharmacotherapy or endoscopic therapy, surgery can be done by creating portoportal or portosystemic shunt.
Case: A 23-year-old man with recurring blood vomiting since the last 6 months, as much as 500 ml each time vomiting, initially occurs every 2 weeks and then more often. Fibroelastography showed 4.3 kPa (F0). Endoscopy found gr II-III esophageal varices. Abdominal CT-scan showed portal hypertension. The patient was diagnosed as NCPH and received propranolol 20 mg TID in the last 5 months. Because hematemesis still occurs, edoscopic varicheal ligation was performed, but could not overcome the problem, and pancytopenia was getting worse. Due to the treatments failure, the patient underwent modified Sugiura operation.
Discussion/conclusion: Surgery on NCPH can be performed on patients with portal hypertension complications who fail medical and endoscopic treatments, to decrease portal pressure and thus prevent and treat portal hypertension complications.

Abstract #1432

Hand grip strength as a prognostic tool in liver cirrhosis

Suciningtias Marlyn[1], Kurniawan Andree[2], Prasetya Ignatius Bima[2], Saroso Olivia Jeany Darmawan Adji[1], Fahman Julang[1], Renaldi Renaldi[1], Rachmaputri Salma Shafira[1]

Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia, [2] Internal Medicine, Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia

Introduction: Liver Cirrhosis (LC) has a variety of complications including ascites, varices, hepatic encephalopathy, infection, malnutrition, and sarcopenia. Sarcopenia is a condition that's characterized by loss of skeletal muscle mass and strength that's usually present in liver cirrhosis with malnutrition. Sarcopenia in liver cirrhotic is associated with worse outcomes. Comparison of muscle strength between hospitalized and non-hospitalized patients could be a prognostic tool in LC.
Objectives: The aim of this study is to compare handgrip strength (HGS) between hospitalized and non-hospitalized LC patients.
Methods: A cross-sectional study was conducted at our general hospital has reported a total of 27 hospitalized and non-hospitalized patients diagnosed with LC using ultrasonography. HGS is measured using JAMAR hand dynamometer following the Southampton protocol.
Results: There were 27 patients in total. Ten patients were non-hospitalized and 17 patients were hospitalized. The mean age was 52±14.35 years. The mean HGS for outpatient is 19.30 ± 11.96 kg and for inpatient is 21.53 ± 11.80 kg (p = 0.641).
Conclusion: The difference in mean HGS between hospitalized and non-hospitalized LC patients is not significant. Further studies with a bigger sample size were needed to confirm these results.

Abstract #1462

Treating Budd Chiari syndrome: an opportunity to reset

Vishwanathan D[1], Ingle MA[1], Pandey V[1], Khairnar HB[1], Chauhan SG[1], Walke SS[1], Jadhav RP[1], Chaudhari VS[1], Shukla AP[2]

[1]Department of Gastroenterology, Lokmanya Tilak Municipal Medical college and general Hospital, Sion, Mumbai, India, [2]Department of Gastroenetrolog, Seth GSMC and King Edward Memorial Hospital, Parel, Mumbai

Introduction and Objectives: With improved survival in patients with Budd Chiari Syndrome (BCS), the outcomes should now be focusing on the quality of life (QOL). There is paucity of data on QOL in patients with BCS. We did this study to determine the QOL after treatment in these patients and identify the predictors.

Methods: Forty-three patients [23 (53.5%) women, 32.3 + 10.8 years], with BCS who had received therapy [anticoagulation only (7%), radiological interventions (93%)] at least 2 months prior to enrolment were administered the Chronic Liver disease Questionnaire (CLDQ) validated in Hindi, with 29 items divided into sub-groups: abdominal symptoms (AS), fatigue (F), systemic symptoms (SS), activity (A), emotional functioning (EF), worry (WO). Response to treatment was defined as absence of ascites and encephalopathy, normal AST/ALT, bilirubin < 1.5 mg/dL, and no portal hypertension related bleed after starting therapy.
Results: The median duration after therapy was 7.3[2–93] months. 83.72% patients had a response to therapy. Overall CLDQ score was 6.26 + 0.99 out of maximum of 7. The domain scores were as follows: AS:6.3{SD:{1.090}, F:6.08{SD:1.122}, SS:6.33{SD:0.982}, A:6.29{SD:1.1.87}, EF:6.17{SD:1.076}, WO:6.31{1.148}. Response to therapy was the most important predictor of overall CLDQ score [6.4726 (SD:0.7568923) in responders Vs 5.1412 (SD:1.367) in non-responders (P = 0.01)]. Other factors associated with low CLDQ score were presence of gastrointestinal bleed, hepatic encephalopathy and co-morbidities before therapy. The overall CLDQ score was not affected by the disease severity scores, age, vein involved, the category of administered treatment, thrombophilic disorder or the requirement of re-intervention.
Conclusion: Patients with BCS who respond to treatment have excellent overall CLDQ scores irrespective of baseline severity scores.

Abstract #1474

Diastolic dysfunction manifests early in patients with liver cirrhosis: a malaysian tertiary centre experience

Zulkifli, Khairil Khuzaini[1,2], Abdul Aziz, Khairul Azlan[1,3], Wan Isa, Wan Yus Haniff [1,4], Wong, Mung Seong [1,4], Lee, Yeong Yeh[1,4], Mustaffa, Nazri[1,4]

[1]Medical Department, Hospital Universiti Sains Malaysia, Kota Bharu, Malaysia. [2]Gastroenterology Unit, Universiti Teknologi Mara, Sungai Buloh, Malaysia. [3]Medical Department, Hospital Teluk Intan, Teluk Intan, Malaysia. [4]School of Medical Sciences, Universiti Sains Malaysia, Kota Bharu, Malaysia

Introduction: Diastolic dysfunction, a recognized characteristic of cirrhotic cardiomyopathy, is associated with poor prognosis in patients with liver cirrhosis. Despite this, current guidelines only recommend echocardiography in those with more severe disease.
Objectives: To explore the proportion of patients with diastolic dysfunction in different stages of liver cirrhosis, and to identify its associated factors at Hospital Universiti Sains Malaysia (HUSM).
Methods: A cross-sectional, prospective study was performed at HUSM Gastroenterology Clinic from 1 September 2018 until 30 November 2018. Adult patients with liver cirrhosis but without known cardiac disease or hepatocellular carcinoma were included. Demographic data, severity of liver disease, medication history and relevant laboratory investigations were recorded. Echocardiography was then done by trained personnel.
Results: Thirty-three subjects were recruited. Median age was 60 years, 17 (51.5%) were female. Diastolic dysfunction was detected in 78.8% (n = 26, CI 0.64–0.94) of subjects. This included all patients with hypertension (n = 13, 39.4%) and 65% (n = 13) of non-hypertensives. No association noted between diastolic dysfunction and severity of liver cirrhosis by both Child–Pugh (CP) score (p = 0.607) and Model for End-Stage Liver Disease (MELD) score (p = 0.607). Diastolic dysfunction was notably high in least-severe patients with CP score A (82.4%, n = 14) and MELD score < 10 (82.4%, n = 14). Using multiple logistic regression analysis, serum sodium and age were identified as independent risk factors.
Conclusion: Diastolic dysfunction was very common among liver cirrhosis patients. Although limited by small sample size, we showed that diastolic dysfunction already manifested overwhelmingly during early stages of liver cirrhosis.

Abstract #1475

Efficacy and safety of esophageal band ligation in acute esophageal variceal bleeding: mono-center Experience in Calmette Hospital, Cambodia

KY Vutha[1,2], CHEA Khang[2,3]

[1]University of Health and Sciences, Cambodia, [2]Liver and GI unit at Calmettre Hospital, Phnom Penh, Cambodia, [3]Ekip liver and GI specialist clinic, Phnom Penh, Cambodia.

Introduction: Endoscopic band ligation (EBL) is the most effective treatment for acute esophageal variceal bleeding (EVB). However, there is no data demonstrating the efficacy of this procedure in patients whose prothrombin time (PT) < 50% and/or platelet (Plt) < 50.000.
Objectives: The aim of this study was to evaluate the efficacy and safety of EBL in the management of cirrhotic patient with EVB.
Methods: It was a retrospective mono-center study of 141 cirrhotic patients with acute EVB between 2012 to 2013, who underwent EBL procedure. We analyzed the characteristic epidemiological, the rebleeding and mortality rate by comparing the group 1 (PT > 50% and Plt > 50.000) to the group 2 (PT < 50% and/or Plt < 50.000).
Results: The mean age was 55 years. Male was predominant. Group 1 (83 cases) versus group 2 (58 cases). There were 13% of overall rebleeding rate and 3% of the mortality rate. The rebleeding rate in group 2 was no significant different in group 1 (16% vs 11% for overall rebleeding and 9% vs 5% for overt rebleeding with a p = 0.450 and p = 0.208 respectively). However, there was a significant difference in mortality rate between the two groups (7% vs 0%, p = 0.015).
Conclusion: This study reported the low risk of overall rebleeding rate and mortality rate, which was comparable to other studies confirming the efficacy and safety of this procedure therapeutic. The coagulopathy in cirrhotic might not the risk factor for rebleeding, but it does affect the mortality rate.

Abstract #1477

Per-rectal portal scintigraphy and hepatic venous pressure gradient for the assessment of portal hypertension in patients with chronic liver disease

Kohei Kotani[1], Sawako Uchida-Kobayashi[1], Akira Yamamoto[2], Naoshi Odagiri[1], Kanako Yoshida[1], Hiroyuki Motoyama[1], Etsushi Kawamura[1], Atsushi Hagihara[1], Hideki Fujii[1], Masaru Enomoto[1], Ken Kageyama[2], Atsushi Jogo[2], Shigeaki Higashiyama[3], Joji Kawabe[3], Akihiro Tamori[1], Norifumi Kawada[1]

Department of Hepatology, [2]Diagnostic and Interventional Radiology and [3]Nuclear Medicine, Osaka City University Graduate School of Medicine, Osaka, Japan

Introduction: Per-rectal portal scintigraphy (PRPS) can estimate portal hemodynamics noninvasively. However, there are few reports examined the association between PRPS and hepatic venous pressure

gradient (HVPG) measurement which is a gold standard for the diagnosis of portal hypertension.
Objectives: To investigate the association between HVPG and PRPS in patients with chronic liver disease, including cirrhosis.
Methods: We included 21 patients with chronic liver disease who underwent HVPG measurement and PRPS between October 2018 and March 2019. For PRPS, 370 MBq of Tc-99 m-pertechnetate was administered into the upper rectum, and time-activity curves for the liver and heart were obtained. The transit times from injection of the radiotracer to its inflow into the liver (TTL) and heart (TTH) were set and the time difference between TTL and TTH (TDLH) was calculated, while the shunt index (SI) was measured. We examined the relationship between those quantitative values of PRPS, HVPG, and presence of esophageal varices (EV).
Results: Eighteen patients (86%) had cirrhosis, 12 patients (57%) had EV, and the median HVPG was 13 mmHg. HVPG ($p = 0.028$), TTL ($p = 0.018$), TDLH ($p = 0.003$), and SI ($p = 0.033$) were higher in patients with EV. The area under the curve for presence of EV was 0.88 for TDLH and 0.80 for HVPG. TDLH was significantly correlated with the risk of EV rupture ($p = 0.004$).
Conclusion: Patients with chronic liver disease are recommended to undergo upper gastrointestinal endoscopy when the TDLH is high.

Abstract #1478

Prognostic performance of CTP, MELD and MELD variants in predicting 3 month, 6 month and 12 month mortality in a cohort of decompensated liver disease DCLD

David Mathew Thomas

Aims and objectives: Decompensated Liver disease carries a high mortality and is important to prognosticate to channel high risk patients for Liver transplantation. MELD and CTP were widely tested in terms of mortality prediction in various studies. Studies comparing MELD, CTP and MELD variants are few. This study aims to compare the prognostic performance of MELD, CTP and MELD variants in predicting 3, 6- and 12-month mortality in a cohort of decompensated cirrhotics.
Materials and Methods: Retrospective study. 321 patients taken. MELD, MELD-Na, MESO, I-MELD, UKELED and CTP were calculated on the date of admission from the medical records and patient/patient relatives were telephonically contacted regarding mortality status at 3, 6 and 12 months. Data was assessed and scores compared using AUROC therby obtaining cutoffs.
Results: CTP had maximum AUROC in predicting 3 month mortality (0.767, cut off > 11, sensitivity 71%, specificity 73.8%) followed by MELD-Na (0.735, cut off > 25 sensitivity 65%, specificity 72%). CTP had maximum AUROC in predicting 6 month mortality (0.761, cut off > 11 sensitivity 58%, specificity 80.5%) followed by I-MELD (0.746, cut off > 3.2 sensitivity 72%, specificity 73.6%). I-MELD had maximum AUROC in predicting 12 month mortality (0.749, cut off > 0.6 sensitivity 74.6%, specificity 73%) followed by CTP (0.745, cut off > 10 sensitivity 70%, specificity of 67%)
Conclusion: CTP is superior to MELD and comparable to MELD variants in predicting 3- and 6-month mortality. I-MELD is the best prognostic model in predicting 12-month mortality.

Abstract #1479

Simple predictor variables to differentiate bland versus malignant PVT in cirrhotics

David Mathew Thomas

Background And Aims: Differentiation of bland versus tumoral PVT is important because management and prognosis varies for both. This study was done to analyze the profile of PVT in cirrhotics and hence derive predictive variables for differentiating the two types.
Methods: Cross-sectional study, All patients with cirrhosis with PVT were includedStatistical analysis for significant variables were done using t test and Chi-Square test.
Results: 104 patients with PVT (31 bland and 73 tumoral). HBV was the most common cause of both tumoral (56%) and bland (32.3%) PVT. 45% bland and 46% of tumoral PVT in Child A cirrhosis patients were due to HBV. Among the variables analyzed Age, Bilirubin, INR, Eosinophil count, Portal vein diameter and AFP were statistically significant between bland and malignant thrombus. Portal Vein diameter of > 14 mm had AUROC of 0.887 in predicting nature of thrombus. AFP level of > 15 had AUROC of 0.962 in predicting nature of thrombus. Eosinophil count of < 155 had AUROC of 0.732 in predicting the nature of thrombus.
Conclusions: Eosinophil count < 155, AFP > 15 and PV diameter > 14 were able to predict the nature of thrombosis with AUROC of 0.73, 0.887 and 0.96 respectively. Simple scores can avoid contrast imaging which could worsen RFTs in cirrhotics. Further studies are required so as to find out the utility of eosinophil count, AFP and PV diameter in characterization of the nature of PVT.

Abstract #1484

Demographic and clinical profile of non-variceal upper gi bleeding in liver cirrhosis patients in Makassar-Indonesia

Andi Arny Megawaty*, Rini Rahmawarni Bachtiar, Fardah Akil, Andi Muhammad Lutfi Parewangi, Nu'man AS Daud, Susanto H Kusuma, Amelia Rifai

Centre of Gastroenterology-Hepatology HAM Akil/DR. Wahidin Sudirohusodo General Hospital. Division of Gastroenterology-Hepatology, *Department of Internal Medicine, University of Hasanuddin, Makassar-Indonesia

Introduction: Gastrointestinal bleeding is one of liver cirrhosis (LC) complication which is due to variceal and non variceal bleeding. Clinical and endoscopic features of cirrhotic patients with nonvariceal upper gastrointestinal bleeding (NVUGIB) have been rarely reported.
Objectives: To describe demographic and clinical profile of NVUGIB in liver cirrhosis patients.
Methods: This retrospective study using endoscopy data from 857 liver cirrhosis patients between year 2014–2018. Clinical features and endoscopic findings data were collected to analyse.
Results: From 272 (31.7%) NVUGIB, 197 patients were included in this study. Male 143 (72.6%) and female 54 (27.4%), age > 45 y.o in 133 (67.5%) with mean age 52 ± 12 y.o. Ethnic majority are buginese 103 (52.3%), makassarese 71 (24.8%), torajanese 23 (11.7%) and works as a farmers 60 (30.4%). Common etiology was HBV 89 (45.2%), NAFLD 61 (30%), HCV 30 (15.2%) with CTP class A/B/C 94 (47.7%)/92 (46.7%)/11 (5.6%). Endoscopy indication and findings were as follows: dyspepsia 101 (51.3%), melena 62 (31.5%), hematemesis 34 (17.3%); and erosive mucosa 116 (58.9%), gastric ulcer 63 (32%), duodenal ulcer 31 (15.8%), portal hypertensive gastropathy 32 (16.3%). Risk factors founding were *Helicobacter pylori* 54 (27.4%), alcohol 35 (17.8%), OAINS 63 (32%), herbal 33

(16.8%); gastric and duodenal ulcer associated with *H. pylori* infection (p = 0.002).
Conclusion: Prevalance of NVUGIB in this study are 31.7%. Dyspepsia was the common symptoms with sources included erosive disease stomach and duodenum, peptic ulcer, and portal hypertensive gastropathy. Screening of *H. pylori* in peptic ulcer liver cirrhosis is recommended.

Abstract #1530

Correlation of Child–Pugh Score and esophageal varices severity in patients with liver cirrhosis

Pratiwi, Irma Chandra[1]; Supriono[2]; Pratomo, Bogi[2]; Mustika, Syifa[2]

[1]Resident of Internal Medicine, Faculty of Medicine, Universitas Brawijaya, Saiful Anwar Malang General Hospital. [2]Supervisor, Consultant in Gastroenterohepatology Division, Department of Internal Medicine, Faculty of Medicine, Universitas Brawijaya Malang, Saiful Anwar Malang General Hospital

Introduction: Bleeding esophageal varices are a major complication of portal hypertension in liver cirrhosis. Not all hospitals in Indonesia have endoscopy. Child–Pugh score can be used to evaluate the prognosis of liver cirrhosis. Clinically, it used to assess liver dysfunction.
Objectives: To correlate Child–Pugh score and severity of esophageal varices in liver cirrhosis patient.
Methods: This cross sectional retrospective study from January 2016 to August 2019. Classification of esophageal varices using Paquet's classification. Liver cirrhosis was diagnosed from history taking and abdominal ultrasonography.
Results: A total 92 liver cirrhotic patients. Among them, 5.4% without esophageal varices, 8.7% had grade I varices, 38% had grade II varices, 45.7% had grade III varices and 2.2% had grade IV varices Child–Pugh score and severity of esophageal varices have significant correlation (r = 0.503, p = <0.001).
Conclusion : Liver cirrhotic patient with higher child pugh score has higher grade of esophageal varices.

Abstract #1537

Duration of oral anticoagulation and not severity of the disease correlates with presence of abnormal bone density in Budd Chiari Syndrome

Chauhan Shamshersingh Gajendra[1], Vishwanathan Deepti[1], Kolhe Kailash[1], Khairnar Harshad[1], Chaudhari Vipul[1], Walke Swapnil[1], Jadhav Rahul[1], Pandey Vikas[1], Ingle Meghraj[1], Shukla Akash[2]

[1]Department of Gastroenterology, Lokmanya Tilak Municipal General Hospital & Medical College, Mumbai, [2]Department of Gastroenterology, Seth GS Medical College and KEM Hospital, Mumbai.

Background: Abnormal bone density [ABD] is commonly seen in patients with chronic liver diseases. There is a paucity of data on ABD in patients with primary Budd Chiari syndrome [BCS].
Methods: Forty-two consecutive patients with primary BCS were evaluated with Dual-energy x-ray absorption [DEXA] to calculate the bone mineral density of these patients at the hip and at the lumbar spine along with intact parathyroid hormone and vitamin D. Demographic details, disease severity, and duration of use of anticoagulants were correlated with presence and severity of osteoporosis/osteopenia.
Results: Twenty-two (52.38%) patients had osteoporosis and 15 (35.71%) had osteopenia. Low serum sodium (p-0.003) and high INR (p-0.005) at baseline were associated with the presence of ABD. Patients who were anticoagulated for more than 1 year had a significantly higher prevalence of abnormal bone density (15 v/s 4; p-0.035). The presence of ABD did not correlate with the Rotterdam and Clichy indices.
Conclusion: ABD is common in BCS. Patients with BCS on warfarin therapy for more than 1 year have a higher prevalence of ABD. The presence of severe disease does not correlate with the presence of ABD.

Abstract #1582

Correlation between APRI score and the grade of esophageal varices in liver cirrhosis patients

Nohabrilyanti Intan[1], Wowor Amanda C[1], Supriono[2], Pratomo Bogi[2], Mustika Syifa[2]

[1]Resident of Internal Medicine Department, Saiful Anwar Hospital, Medical Faculty, Brawijaya University, Malang, Indonesia, [2]Gastroenterohepatology Division, Department of Internal Medicine, Saiful Anwar Hospital, Medical Faculty, Brawijaya University, Malang, Indonesia

Introduction: The prevalence of esophageal varices in patients with liver cirrhosis may range from 60% to 80%. Mortality rate because of variceal bleeding is about 17% to 57%. Considering the wide area of Indonesia with more than 260 million citizens, the endoscopic services is still far from ideal. There are 2813 hospitals in Indonesia, and only 313 hospitals provide endoscopic services, with 515 gastroenterologist. In consequence we need to discover a screening methods that can be used in most of health service center. APRI score is a predictor of fibrosis, which is the main cause of portal hypertension in liver cirrhosis, therefore APRI score may be a good methods for esophageal varices screening.
Objectives : To analyzed the correlation between APRI score and the grade of esophageal varices in liver cirrhosis.
Methods: Observational analysis research with cross sectional sampling in liver cirrhosis patients that underwent endoscopy at Saiful Anwar Hospital Malang in 2016–2018. The correlation between APRI score and the grade of esophageal varices was analyzed by using Spearman's test. Then, based on the causes of hepatitis, the data were divided into Hepatitis B groups and hepatitis C groups. We reanalyzed the correlation between APRI score and the grade of esophageal varices in each group.
Results: There were 60 subjects in this study. 4 (7%) subjects with esophageal varices grade I, 17 (28%) subjects with grade II, 18 (30%) subjects with grade III, and 21 (35%) subjects with grade IV. Spearman's test showed there was a strong positive correlation between APRI score and the grade of esophageal varices in liver cirrhosis (r = 0.610; p = 0.000); there was a moderate positive correlation between APRI score and the grade of esophageal varices in liver cirrhosis that caused by hepatitis B (r = 0.526; p = 0.003); there was a strong positive correlation between APRI score and the grade of esophageal varices in liver cirrhosis that caused by hepatitis C (r = 0.707; p = 0.000).
Conclusion: There is a correlation between APRI score and the grade of esophageal varices in liver cirrhosis especially that caused by hepatitis C.

Abstract #1605

Computed tomography imaging has high accuracy in predicting esophageal varices and bleeding risk in cirrhotic patients from systematic review with meta-analysis

Li Yue[1], Li Lei[1], Weng Honglei[2], Liebe Roman[3], Ding Huiguo[1]

[1]Department of Gastroenterology and Hepatology, Beijing You'an Hospital affiliated with Capital Medical University, Beijing 100069, China, [2]Department of Medicine II, Section Molecular Hepatology, Medical Faculty Mannheim, Heidelberg University, Mannheim 68167, Germany, [3]Department of Medicine II, Saarland University Medical Center, Homburg 66424, Germany

Introduction: Liver stiffness measurement (LSM), computed tomography (CT) and magnetic resonance imaging (MRI) are non-invasive diagnostic methods for the prediction of esophageal varices (EV) and high bleeding risk esophageal varices (HREV) in cirrhotic patients. However, clinical using of these methods is controversial.
Objectives: To evaluate the accuracy of LSM, CT and MRI in predicting EV and HREV in cirrhotic patients.
Methods: We performed literature searches in PubMed, Embase, Cochrane, CNKI, and Wanfang databases. Summary sensitivity and specificity, diagnostic odds ratio (DOR) and area under the summary receiver operating characteristic curves (AUSROC) were analyzed. Articles quality was assessed by "quality assessment of diagnostic accuracy studies-2" tool. Heterogeneity was examined by I^2 index. Sources of heterogeneity was explored using meta-regression and subgroup analysis. Publication bias was evaluated using Deek's funnel plot.
Results: Overall, 18, 17 and 7 articles on the accuracy of LSM, CT and MRI in predicting EV and HREV were retrieved. Significant heterogeneity was observed in all analyses with $P < 0.05$. The AUSROC of LSM, CT and MR imaging in predicting EV and HREV were 0.86, 0.91, 0.86, and 0.85, 0.94, 0.83, respectively. Sensitivity was 0.84, 0.91, 0.81, and 0.81, 0.88, 0.80. Specificity was 0.71, 0.75, 0.82, and 0.73, 0.87, 0.72. The DOR was 13.01, 30.98, 19.58, and 11.93, 49.99, 10.00. CT scanner is the source of heterogeneity. There was no significant difference in diagnostic threshold effects and publication bias ($P > 0.05$).
Conclusion: It is suggested that CT is the best choice for diagnosis of EV and predicting HREV in cirrhotic patients comparing with LSM and MRI.

Abstract #1611

The clinical and biological characteristics of spontaneous bacterial peritonitis: mono-center experience in Calmette Hospital, Cambodia

Sann Channa[1], Chea Khang[1]

[1]Liver and GI Unit doctors, Calmette Hospital, Cambodia

Introduction: Spontaneous bacterial peritonitis (SBP) is an acute and serious bacterial infection of ascitic fluid (AF) in advanced cirrhosis. The diagnosis is based on the level of AF polymorphonuclear leukocyte $\geq 250/mm^2$ and/or positive AF culture.
Objectives: The aim of this study was to determine the associated factors of SBP, in order to make an appropriate management in ascitic liver cirrhosis.
Methods: It was a retrospective mono-center study of 259 decompensated ascitic cirrhosis cases between 2005 to 2011, who underwent abdominal paracentesis. We analyzed the prevalence of SBP, causes of cirrhosis, clinical and biological characteristics by comparing the SBP group and the non-SBP group.
Results: SBP presented 25.5% in ascitic cirrhosis, while men were predominant 66.7%. The mean age was 58 years old. HBV and HCV were detected in 50% and 42.4%, respectively. Fever and abdominal pain, Child–Pugh score C, and the cloudy color of AF were significantly associated with SBP as compared with non-SBP group (15.2% vs. 1.6%, 16.7% vs. 4.7%, 74.2% vs. 43%, 48.5% vs. 4.7%, respectively with $p < 0.05$). Whereas the total protein (< 10 g/l) in AF was not significantly different between these two groups.
Conclusion: The prevalence of SBP was high. Fever and abdominal pain might be the associated sign in SBP. SBP mostly appeared in decompensated stage liver cirrhosis (Child–Pugh C). Ascites paracentesis should be done in all decompensated ascitic cirrhosis particularly in patient with fever and abdominal pain. The primary prevention of SBP in patients with protein < 10 g/l in AF still remains questionable.

Abstract #1613

Role of oral zinc supplement in management of hepatic encephalopathy

Dr Abdul Latif[1], DR Riaz Hussain Awan[2]

[1]Avicenna medical college Lahore, Pakistan, [2]Liaquat University of Health science Jamshoro, Pakistan

Introduction: Hepatic encephalopathy is a neuropsychiatric complication of liver disease that affects 20 to 30% of the patients with cirrhosis, Previous studies have demonstrated that a reduction in blood ammonia levels improves hepatic encephalopathy, neuropsychological test performance, cognitive function, and health-related quality of life Zinc deficiency is observed frequently in patients with cirrhosis and hepatic encephalopathy. Zinc supplementation, in addition to standard therapies, may increase the hepatic conversion of amino acids into urea, decrease serum ammonia level, and consequently improve health-related quality of life
Objective: The aim of the present study was to assess the effects of oral zinc supplementation in patients with all grades of Hepatic Encephalopathy.
Setting: Department of Gastroenterology, Liaquat University of health sciences Jamshoro
Duration of study: Six months from 15 Feb 2019 to 15 August 2019
Study design: Descriptive Cross sectional study
Subject and Methods: One hundred and thirty five patients having Hepatic encephalopathy of any Grade were given oral zinc supplements for 2 weeks along with standard lactulose therapy, serum zinc level and ammonia level were obtained at baseline and after 2 weeks of therapy, number connection test was perfomed at 1 week and after 2 weeks
Results A Total of 135 patients, out of which 78 (57.7%) were male; the average age of the patients was 51.04 ± 5.27 years. Child–Pugh class-A, B, C were seen in 40, 65 & 30 patients (29.62, 48.14% & 22.2) respectively Reduction of serum ammonia level were seen 81.48% (110/135) and improved performance in the number connection test were seen in 66.66% 90/135 patients. No complications from oral zinc supplements were observed.
Conclusion: Our results show Oral zinc supplementation (zinc acetate 600 mg/d) in addition to standard therapy normalized the serum zinc levels improves serum ammonia level, number connection test and overall Grades of Hepatic encephalopathy.

Abstract #1625

Correlation between quality of life with the severity of liver cirrhosis

Jefri Pratama Susanto[1], Syifa Mustika[2], Bogi Pratomo[2], Supriono[2]

[1]Resident of Internal Medicine, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia, [2]Gastroenterohepatology Division, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia

Introduction: Liver cirrhosis had negative impact to quality of life and often associated with loss of job, mood swings, anxiety, low self-esteem and depression. Recent treatment of liver cirrhosis mainly focused on clinical manifestation, not the patient's quality of life. By assessing quality of life, one could know emotional, physical and life style impact of the disease and its treatment.
Objectives: To find the correlation between quality of life with the severity of liver cirrhosis
Methods: The study was observational study with cross sectional data collecting. We collected subject of the study from outpatient and inpatient clinic of Saiful Anwar Hospital. The subjects were given chronic liver disease questionnaire to analyze quality of life and, we counted the Child Pugh score to measure severity of liver disease. Data was analyzed using Kruskal Wallis and Rank Spearman test with $p < 0.05$ was considered significant.
Result: There were 54 subjects with average age was 53.71 years and 74% of subject was male. The result was all domains in chronic liver disease questionnaire showed significant difference between Child Pugh A, Child Pugh B and Child Pugh C group ($p = 0.000$). Rank Spearman test showed very strong correlation between quality of life and severity of liver cirrhosis (r: -0.817)
Conclusion: The milder of the severity of liver cirrhosis then the better of the quality of life.

Abstract #1626

Corrrelation between Subjective Global Assessment (SGA) score with Child Pugh in liver cirrhotic patient

Amanda Cininta Wowor[1], Meti Metiani[1], Syifa Mustika[2], Supriono[2], Bogi Pratomo[2]

[1]Resident of Internal Medicine, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia, [2]Gastroenterohepatology Division, Department of Internal Medicine, Faculty of Medicine Universitas Brawijaya, Malang, Indonesia

Introduction: Liver cirrhotic patients have a risk of malnutrition that affects life expectancy. Child pugh score is used to determine the prognosis of them regardless of nutritional states. Therefore a nutritional asessment is needed, one of them is subjective global assessment (SGA) which reflects metabolic and functional changes.
Objective: This study aims to correlate the nutritional states based on SGA scores on child pugh in 36 liver cirrhotic patient.
Methods: Analytic study, cross sectional design with consecutive sampling of 36 liver cirrhotic outpatient gastroenterology clinic at Dr. Saiful Anwar General Hospital Malang in February–May 2017. Nutritional assessments are grouped into SGA A (good nutrition), B (mild and moderate malnutrition), C (severe malnutrition). Prognostic score are divided into child pugh class A (mild), B (moderate), C (severe).
Results: 75% of subject in this study had SGA A. A significant correlation was obtained between the SGA score and the degree of child pugh ($p = 0.001$, $r = 0.978$), child pugh score ($p = 0.001$, $r = 0.576$), and albumin ($p = 0.001$, $r = 0.545$). There was a significant difference between SGA A and B, A and C on child pugh scores ($p = 0.002$).
Conclusion: This study proves that SGA scores affect child pugh and have ability to reflect the severity of liver disease so that it can be recommended for use in assessing the nutritional states of liver cirrhotic patients.

Abstract #1631

Precipitants of hepatic encephalopathy

Samad, A

Introduction: Hepatic encephalopathy is a common manifestation in patients with liver cirrhosis causing significant morbidity and mortality. There are a number of recognized precipitants that leads or worsens encephalopathy and timely management has better outcome.
Objective: To determine the precipitants of hepatic encephalopathy and its impact on outcome and mortality in cirrhotic patients.
Methods: This was a retrospective, cross sectional study of consecutive patients admitted at Patel Hospital Karachi with different grades of hepatic encephalopathy from June 2016 to June 2019. Grading of hepatic encephalopathy, precipitants, hospital stay, outcome and mortality were entered in a designed questionnaire.
Results: Out of total 245 patients, 165 were males and 80 were females.31.83% had Grade I, 34.69% Grade II, 24.48% Grade III and 8.979% Grade IV Hepatic encephalopathy respectively. Etiologies for liver cirrhosis in patients were Hepatitis C (144), Hepatitis B (68), NASH (22), Alcohol (6), Autoimmune Hepatitis (4) and Hemochromatosis (1) respectively. The most common precipitant of encephalopathy was constipation in 82 (33.46%), SBP in 66 (26.93%), GI bleed in 39 (15.91%), hypokalemia in 34 (13.87%) and urosepsis in 24 patients (9.79%). Mean hospital stay was 3 ± 2 days. Majority of patients were Child C cirrhotic (76.73%) followed by Child B (23.26%). 218 patients (88.97%) recovered completely and discharged, whereas 27 patients expired (11.02%). Majority of expired patients had Grade IV encephalopathy. The most common precipitant causing death was GI bleed in 16 patients followed by SBP (8) and urosepsis (3).
Conclusion: Hepatic encephalopathy has an overall better survival, provided the precipitating factors are properly managed.

Abstract #1642

Massive upper gastrointestinal bleeding from a bleeding duodenal varix due to non-cirrhotic portal hypertension secondary to splanchnic vein thromboses in a patient with primary myelofibrosis

Francisco, Carlos Paolo D.[1] Gravador, Emilio Jose S.[2] Cruz, Rachel Maire A.[1] Cua, Ian Homer Y.[1]

[1]Institute of Digestive and Liver Diseases St. Luke's Medical Center-Bonifacio Global City, Taguig City, Metro Manila, Philippines, [2]Department of Medicine St. Luke's Medical Center-Bonifacio Global City, Taguig City, Metro Manila, Philippines

Introduction: Ectopic varices are dilated portosystemic collateral veins of the gastrointestinal mucosa located in unusual sites commonly found in the duodenum. It accounts for 1–5% of all gastrointestinal bleeding in patients with portal hypertension. Extrahepatic portal vein obstruction (EHPVO) including portal vein

thrombosis is a common cause of portal hypertension in developing countries. Ectopic varices are reported in 27–40% of patients with EHPVO. The prognosis from bleeding ectopic varices is poor, with 40% mortality from initial bleed. This report presents an account of a rare cause of gastrointestinal bleeding for which a therapeutic dilemma is confronted.

Clinical Presentation: A case of a 38 year old male with splenomegaly on ultrasound who developed persistent vague epigastric pain. CT angiogram revealed spleno-portal axis thromboses. Patient developed pulmonary embolism and was maintained on Enoxaparin. Patient had episodes of alternating melena and hematochezia; hence, referred to a specialist in our institution.

Management: Upper gastrointestinal endoscopy showed portal hypertensive gastropathy with mild esophageal varix and gastric varices. Bone marrow biopsy revealed primary myelofibrosis (JAK2 positive). Few months on Enoxaparin patient had GI bleeding, repeat upper GI endoscopy revealed a bleeding duodenal varix where multiple hemoclips and N-butyl-2-cyanoacrylate injection were applied which provided complete hemostatic control. On surveillance imaging, splanchnic vein thromboses remained unchanged; hence, anticoagulant was resumed.

Recommendations: The association of myeloproliferative disorder-related splanchnic vein thrombosis with ectopic varices should be taken into consideration when managing patients presenting with gastrointestinal bleeding with portal vein thrombosis. Frequent endoscopic surveillance is important to prevent future massive bleeding.

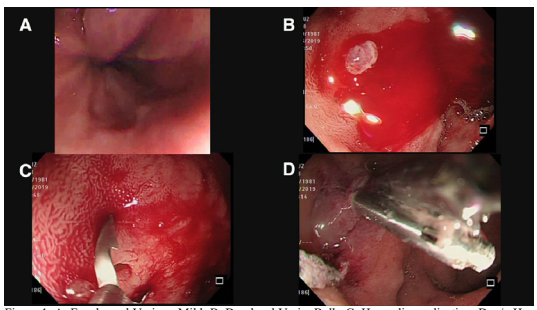


Figure 1. A: Esophageal Varices, Mild; B: Duodenal Varix, Bulb; C: Hemoclip application; D: s/p Hemoclipping and N-butyl-2-cyanoacrylate injection.

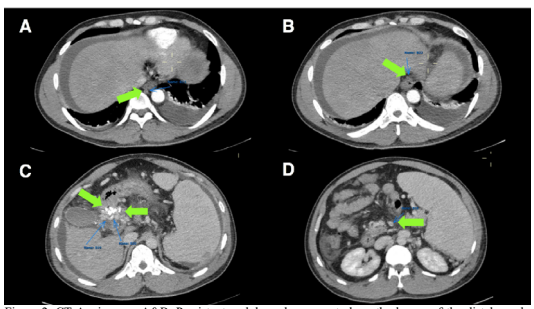


Figure 2. CT Angiogram. A&B: Persistent nodular enhancement along the lumen of the distal esophagus may be from esophageal variceal formation; C: Hyperdensities within the duodenum, region of the gallbladder, porta hepatis and right hepatic lobe parenchyma, which likely relates to post-surgical material; D: Persistent small filling defects at the region of the portal vein suggestive of thrombosis.

Abstract #1647

Decision curve analysis of non-invasive predictive tools for varices needing treatment in patients with chronic liver disease

Agarwal S[1], Sharma S[1], Gunjan D[1], Kaushal K[1], Poudel S[1], Anand A[1], Gopi S[1], Mohta S[1], Saraya A[1]

[1]Department of Gastroenterology and Human Nutrition, All India Institute of Medical Sciences, New Delhi, India 110029

Background and Aims: Detection of varices needing treatment [VNT] in patients with chronic liver disease (CLD) is important for initiation of primary prophylaxis, thus preventing variceal bleeding. Transient Elastography (TE) and non-TE based criteria exist for non-invasively ruling out patients with low incidence of VNT thus avoiding esophagogastroduodenoscopy (EGD). We aimed to validate existing non-invasive criteria and identify best TE and non-TE based criteria for VNT screening at usual risk thresholds.

Methods: Patients with compensated advanced CLD (cACLD) and early CLD without any decompensations who underwent EGD and TE within 3 months were included for retrospective analysis. Diagnostic performance of Baveno-VI, expanded Baveno-VI, platelet-MELD and platelet-albumin (RESIST-HCV) criteria were estimated. Decision curve analysis was conducted for different predictors across range of threshold probabilities.

Results: 1657 patients (cACLD-895 and early CLD-762) with CLD related to HBV (38.2%), HCV (33.4%), NASH (14.7%) and alcohol (11.8%) were included. Mean Liver stiffness measurement was 14.9 kPa, with 16.2% VNT. Patients were followed-up for median duration of 548 (IQR 262–1112) days, over which 84 (5.1%) patients developed variceal bleed. Baveno-VI identified maximum VNT (97.4%), while platelet-albumin criteria had best negative predictive value (97.9%). Expanded-Baveno-VI and platelet-MELD had intermediate performance. At threshold probability of 5%, Baveno-VI criteria showed maximum net-benefit, while platelet-albumin criteria was next best, with need for 257 additional elastographies to detect one additional VNT. Decision curves for variceal bleed showed near similar net-benefit for all predictive models, with slight advantage to Baveno-VI criteria.

Conclusion: Baveno-VI criteria maximizes yield of VNT at threshold probability of 5%. Platelet-albumin criteria is an acceptable alternative in resource-limited settings.

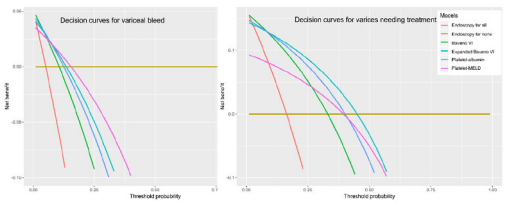


Figure 1. Decision curve plots demonstrating net benefit of different classification criteria for prediction of future variceal bleed (left) and varices needing treatment (right) across range of threshold probabilities

Abstract #1676

Prognosis of secondary IgA nephropathy in liver cirrhosis

Divyaveer S[1], Kumar P[2], Dasgupta S[3], Das Bhattacharya T[3], Bagur V[3], Banerjee A[3], Raychaudhury A[3], Pandey R[3]

[1]Department of Nephrology, Post Graduate Institute of Medical Education and Research, Chandigarh, India, [2]Department of gastroenterology, Institute of Gastrosciences, Apollo Gleaneagles Hospital, Kolkata, India, [3]Department of Nephrology, Institute of Post Graduate Medical Education and Research, Kolkata, India.

Introduction: Prognosis of secondary IgA Nephropathy with cirrhosis on conservative management in relation to (Mesangisal Mesangial cellularity, Endocapillary proliferation, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, Crescents) MEST-C classification is not well known.
Objectives: Change in estimated glomerular filtration rate (eGFR) by Modified Diet in Renal Disease (MDRD) 6 formula and proteinuria (PU) in secondary IgAN in relation to the MEST C.
Methods: All patients with biopsy proven IgAN with MEST C classification and liver cirrhosis were included. All recieved conservative management with Renin angiotensin blockers. Outcomes: eGFR and proteinuria at 6 months in relation to each of M, E, S, T, C component of IgAN classification.
Results: Of 62 IgAN patients, 8 had cirrhosis. All were Child Pugh class A. MEST-C was: M0E1S0T0C0, M1E1S1T1C0, M0E0S1T2C0, M1E0S0T0C0, M0E0S0T0C0, M1E1S0T1C0, M0E0S1T1C0 and M0E0S0T1C0. Baseline: mean eGFR : 54.33 ± 14.3 and median eGFR : 60.4; IQR 44.62 to 68.56 ml/min/m2. Baseline mean Proteinuria was 1.4 and median was 1.2 with IQR 0.77 to 2.4gm/day. eGFR mean and median at 6 months was 50.54 ± 12.33 and median eGFR was 52.34 (IQR 37.54 to 54.46) ml/min/m2; p = 0.03. At 6 months the proteinuria was mean 1.4 gm/day, median 1.3gm/day IQR (1.0 to 2.97 gm/day); p = 0.24. Those with E1 had higher decline in eGFR. Proteinuria did not differ in those with E0 and E1.
Conclusion: In patients with cirrhosis and secondary IgAN there is no significant change in proteinuria but there is significant decline in eGFR at 6 months. E1 is associated with worse decline in eGFR.

Abstract #1685

Effectiveness of antibiotics as secondary prevention of spontaneous bacterial peritonitis in patients with liver cirrhosis: an evidence based case report

Kemal Fariz Kalista[1], R Gantira W Danasasmita[2]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, University of Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Backgrounds: The presence of ascites in cirrhosis patient can cause to infection condition called spontaneous bacterial peritonitis (SBP) and lead to increase mortality. The mechanism of SBP in liver cirrhosis patient was intestinal bacterial colonization, decrease immnune function and bacterial translocation from intestinal to peritoneal cavity. Related to bacterial colonization, antibiotic prophylaxis maybe useful in preventing the recurrence of SBP in cirrhosis patients. In this evidence based case report (EBCR) our PICO was P: liver cirrhosis with history of SBP, I: antibiotic, C: no antibiotic, O: recurrence of SBP.
Methods: Two selected articles are made through Pubmed, EBSCO Host and Cochrane according to clinical questions. The selection of articles is based on inclusion and exclusion criteria.
Result: Saab et al found antibiotics prophylaxis decrease the incidence of SBP by 51%, both in its use as a primary & secondary prevention (RR 0.49; p < 0.0001; 95% CI 0.35–0.69), decrease all mortality by 35% (RR 0.65; p = 0.006; 95% CI 0.48–0.88) and decrease mortality related to SBP by 28% (RR 0.72; p = 0.09; 95% CI 0.48–1.06). Cohen et al found antibiotic prophylaxis decrease mortality by 39% (RR 0.61; 95% CI 0.43–0.88) and decrease SBP with RR 0.20; 95% CI 0.11–0.37 with *number needed to treat* (NNT) 5.9.
Conclusion: Administration of antibiotic as prevention, both primary and secondary, can reduce the incidence of SBP and mortality in cirrhosis patient.

Abstract #1710

Bleeding risk of oral direct anticoagulant in cirrhotic patients with portal vein thrombosis: evidence-based case report

Nabila Hasan[1], Saut Horas H. Nababan[2]

Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, [2] Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia

Introduction: Portal vein thrombosis (PVT) is more likely to be found on cirrhosis patients compared to normal population. Most patients need anticoagulant therapy with low molecular weight heparin (LMWH) or vitamin K antagonist (VKA). The use of direct oral anticoagulant (DOAC) in recent years is increasing for PVT therapy because of the convenience for the patients. But, cirrhosis patients have high risk of bleeding from oesophageal varices or portal hypertension gastropathy especially because DOAC is considered unsafe in cirrhotic patients.
Objectives: To evaluate the bleeding risk of DOAC for PVT therapy in cirrhosis patients compared with traditional anticoagulants.
Method (Subjects/Participants Interventions, Outcome measure): We used literature searching on Pubmed with keywords "cirrhosis"; "portal vein thrombosis"; "DOAC"; "anticoagulant" with restrictions on human study in the last 2 years, in English. We evaluated the validity, importance, and applicability of each study and be given the level of evidence according to Centre for Evidence-Based Medicine (CEBM).
Results: We found two studies comparing DOAC to traditional anticoagulant. One study comparing DOAC (apixaban and rivaroxaban) and traditional anticoagulant (LMWH and VKA) found no significant statistical difference on bleeding event between both groups (p = 0.12). The second study also found no significant difference between both groups on bleeding event (p = 0.9). Both studies are retrospective cohort. No RCT were found regarding this topic.
Conclusion: The risk of bleeding in DOAC on compensated cirrhosis patients is not significantly different compared to traditional anticoagulant. But, the quality of evidence on this topic is still lacking and warrant further research.

Abstract #1728

Demographic characteristics of the cases with liver cirrhosis

Elif Yorulmaz[1], Oguzhan Ozturk[2], Levent Doganay[2], Ilyas Tuncer[3], Hatice Yorulmaz[4]

[1]Bagcilar Education and Research Hospital, Department of Gastroenterology, Istanbul, Turkey, [2]Umraniye Education and Research Hospital, Department of Gastroenterology, Istanbul, Turkey, [3]Goztepe Education and Research Hospital, Department of Gastroenterology, Istanbul, Turkey, [4]Haliç University, School of Nursing, Istanbul, Turkey

Introduction: Liver cirrhosis (LC) is one of the most important causes of morbidity and mortality in the world. The purpose of the study is to determine the demographic characteristics of the patients diagnosed with LC.

Methods: In the study, 155 patients diagnosed with LC were included. The patients were retrospectively evaluated for the etiologic causes of cirrhosis, Child–Pugh scoring (CPS), complications, and comorbid diseases.
Results: One hundred and three male (66%) and 52 (34%) female patients with an average age of 60.8 ± 10.6 were included in the study. When assessed in terms of the etiology of cirrhosis, the reason was hepatitis B in 56 (36.1%) of the cases, hepatitis C in 38 (24.5%), alcohol in 29 (18.7%), cryptogenic in 18 (11.6%), and other reasons in 14 (9%). According to the CPS, 79 (50.9%) of the cases was assessed as C, 63 (40.7%) as B, and 13 (8.4%) as A. Forty two patients (27%) had diabetes mellitus and 17 (10.9%) had hypertension, and 75 (48%) had another concomitant disease. As the complication of cirrhosis, hepatic encephalopathy was detected in 59 (38%) of the cases, infection in 27 (17%), hepatocellular carcinoma in 15 (10%), and upper gastrointestinal system bleeding in 8 (5.2%).
Conclusion: In the study, the most common etiologic causes of LC are viral hepatitis and alcohol. Vaccination, prevention of contamination routes, and taking preventive public health measures for preventing alcohol consumption will significantly reduce deaths related to this disease in our country.

Abstract #1755

Characteristic of hepatic cirrhosis patients at Budhi Asih General Hospital in 2018: a descriptive study

Antariga, Dwi. R,[1] Haerani, Fitri,[1] Simamora, Joshua. P,[1] Wardhana, A. Wisjnu[2]

[1]General Practitioner at Budhi Asih General Hospital Jakarta, Indonesia, [2] Gastrenterohepatologist Consultant at Budhi Asih General Hospital Jakarta, Indonesia

Introductions: Hepatic cirrhosis (CH) is a chronic liver disease characterized by fibrosis, disorganization of the lobes and vascular architecture, and regeneration of hepatocyte nodules. WHO (World Health Organization) data for 2004 states that the prevalence of cirrhosis of the liver in the world reaches 1.3%. This disease is ranked 18th cause of death. CH is one of the most diseases treated in the Internal Medicine ward of Budhi Asih General Hospital (RSBA).
Objectives: The aim of this study is to know the characteristics of CH patients at RSBA in 2018.
Methods: The method used was an observational descriptive study using medical records of CH patients who hospitalized at RSBA from January 1, 2018 to December 31, 2018.
Results: In 2018 total visits of CH patients were 88 visits, consisting of 63.7% male patients and 36.3% female patients. Based on age, the highest age was over 60 years (39.8%). Based on patient complaints, 40.9% of patients present with vomiting blood and/ black stool, 27.2% of patients present with an enlarged abdomen. Based on etiology there were 67% with hepatitis B. Based on laboratory abnormalities there were hypoalbuminemia (65.9%), thrombocytopenia (67.1%), increased creatinine (54.5%), and 84.1% with AST/ALT ratio > 1. There were 14.8% of patients who were re-hospitalized, and 10.1% of patients died.
Conclusions: Most CH patients are male, over 60 years old, with the main complaint being gastrointestinal bleeding, ascites, hypoalbuminemia, thrombocytopenia and creatinine elevation, with hepatitis B being the most common cause.

Abstract #1758

The prevalence of *Helicobacter pylori* infection in liver cirrhosis patients admitted in Chong Hua Hospital: a prospective cross-sectional study

K. C. B. Duenas

Chong Hua Hospital

Significance: Prevalence of H. Pylori infection in cirrhotic patients differs worldwide. The role of *H. pylori* in the pathogenesis of upper gastrointestinal lesions in cirrhotic patients is still unknown, with most studies showing severe lesions with H. Pylori infection. Testing for and treating this infection is important for these patients. This study aims to determine the prevalence of H. Pylori infection in liver cirrhosis patients admitted in the local setting.
Methodology: This is a prospective, cross-sectional, single-center study, conducted in Chong Hua Hospital, Cebu City, from July 2019-December 2019. All admitted liver cirrhosis patients, 18 years and older, who will undergo esophagogastroduodenoscopy were included. Patients below 18 years, and without consent were excluded. Demographic data, endoscopic findings, and H. Pylori test results were documented, compared, and analyzed using chi-square test and Minitab.
Results: Of 139 patients, only 28 (20.14%) tested positive for H. Pylori with a mean age of 63.1 years, were predominantly male (75%), diabetic (46.43%), smokers (78.57%) and alcoholic drinkers (60.71%), had alcoholic liver disease (57.14%), and had Child–Pugh A cirrhosis (71.43%). Gastritis was the most common endoscopic finding (28.26%). There was no significant difference in the findings of portal gastropathy (p-value 0.235) and esophageal varices (p-value 0.702) between H. Pylori positive and negative patients. Baseline characteristics showed no significant difference between the 2 groups
Conclusion: H. Pylori infection is not common in liver cirrhosis patients admitted in Chong Hua Hospital, Cebu City. There is no difference in patient characteristics and endoscopic findings between H. Pylori positive and negative liver cirrhosis patients.

Abstract #1760

Sarcopenia as a prognostic factor in cirrhosis

Nibin Nahaz

Background& Objectives: Studies hasve shown that ultrasound measured thigh muscle thickness is a good parameter of sarcopenia. It is a low cost tool and easily available. So this study assesses the predictive accuracy of sarcopenia as measured by thigh muscle thickness on ultrasound, on patient outcome at 6 months and to compare it with CHILD and MELD scores.
Methods: All patients with cirrhosis were taken and assessed for sarcopenia using thigh muscle based index. Subjects were followed up for 6 months. Their anthropometric measurements, history of decompensation, number of hospital admissions and mortality are noted
Results & Discussion: In our study, out of the 483 patients, sarcopenia was present in 197 patients (40.8%). It was found that sarcopenia was less prevalent in CHILD A (17.03%) and CHID B (37.6%) cirrhotic patients when compared with CHILD C (90.9%) cirrhotic patients. The study also showed that sarcopenia was highest in autoimmune hepatitis related cirrhosis (75.0%), followed by NASH (55.8%), ethanol (37.7%), HCV (29.1%) and HBV (20.2%). Sarcopenia have statistically significant correlation ($P < .001$) with 6 month mortality, number of decompensation and number of

hospitalistion, eventhough less correlation than the MELD or CHILD score.

Conclusion: NASH related cirrhosis were having higher prevalence of sarcopenia than Alcohol related cirrhosis. Sarcopenia was seen even in Child A cirrhosis in NASH. Sarcopenia was less prevalent in HBV and HCV related cirrhosis. Sarcopenia has a statistically significant correlation with 6 month mortality, number of decompensation events and frequency of hospitalization. However MELD and CHILD performed better in predicting 6 month mortality, number of decompensation events and frequency of hospitalization.

Abstract #1784

Antithrombotic treatment for splenic vein thrombosis in liver cirrhosis patients

Husin Thamrin, Iswan Abbas Nusi, Poernomo Boedi Setiawan, Titong Sugihartono, Herry Purbayu

Gastroentero-Hepatology Division, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Hospital, Jl. Prof dr. Moestopo 47 Surabaya 60132, Indonesia

Introduction: Antithrombotic treatment of vein thrombosis was a clinical challenge. Depending on the site of thrombosis, patients are at risk of experience recurrence bleeding. Splenic Vein Thrombosis (SpVT) results in an increase of localized sinistral portal pressure. Most SpVT patients cause left-sided portal hypertension, while can cause gastrointestinal bleeding from the esophagus or gastric varicose. Splenomegaly was followed by thrombocytopenia, pancytopenia and abdominal pain are also manifestations of the disease.

Case description : B was a 28 years old man who admitted to hospital after have abdominal pain, black vomitting, black bowel since 2 days and stomach enlarged since 6 months. He had known liver cirrhosis secondary to chronic alcohol consumption. Laboratory tests revealed an international normalized ratio (Hb : 4.2 g/dl, Platelet: 76000/uL), prothrombin time ratio of 12.8 and activated partial thromboplastin time of 28.1 seconds. SpVT was suspected because of recurrent gastrointestinal bleeding & haematological disorders in the form of pancytopenia. CT scan result found ± 5.8 cm splenic vein thrombus, dilatation of splenic vein, tourtosity of the left gastric vein and the distal esophagus vein. Patients received anticoagulant therapy using warfarin 2 mg sodium clathrate every 12 h orally for 3 months and also given prophylactic therapy for gastrointestinal bleeding.

Conclusion : The decision to administer antithrombotic drugs should be considered for all patients with objectively diagnosed. However, defining evidence-based management of SpVT remains a clinical need and good-quality research is still warranted.

Abstract #1787

The role of endoscopic treatment for recurrent variceal bleeding after transjugular intrahepatic portosystemic shunt (TIPS)

Liyuan Ni[1], Xiaoquan Huang[1], Shiyao Chen[1]

[1]Department of Gastroenterology and Hepatology, Zhongshan Hospital, Fudan University, Shanghai, P. R. China

Introduction: Transjugular intrahepatic portosystemic shunt (TIPS) is suggested as the salvage therapy in variceal bleeding, secondary prophylaxis of re-bleeding and refractory ascites. However, re-bleeding might occur in some patients after TIPS. Evidence still lacks about whether endoscopic treatment can be used in these patients instead of repeating TIPS.

Objective: To evaluate the efficacy of endoscopic treatment in patients with variceal bleeding after TIPS.

Methods: In this single-center study, we included patients receiving endoscopic treatment for prevention of recurrent variceal bleeding after TIPS between January 2017 and August 2019. All the included patients were followed until death or 31th December 2019.

Results: A total of 6 patients were included (male/female: 5/1, median age: 47 years, ranging from 27 to 65 years). They received TIPS at first for HVPG $>$ 15 mmHg (4 in 6) or para-gastric (2 in 6). All of them experienced re-bleeding after TIPS and half were found stent occlusion. Then they chose endoscopic treatment including esophageal variceal ligation (EVL), gastric variceal cyanoacrylate injection, esophageal variceal sclerotherapy (EVS) and balloon-occluded retrograde transvenous obliteration (BRTO) assisted endoscopic cyanoacrylate injection. Among them, 2 patients died shortly after EVL (14 and 19 days) due to re-bleeding. For the other 4 patients, only 1 had re-bleeding episode in 422 days and the median rebleeding-free time is 475 (202.3–873.8)days. For them, median duration of follow-up time is 611 (228.8–915.3)days.

Conclusion: Endoscopic treatment may be a choice of secondary prophylaxis after TIPS in selected patients. Further studies are needed to carefully define the indication and efficacy of this option.

Abstract #1797

The prospective prognostic values of diabetic conditions based on 75gm oral glucose tolerance test in cirrhotic patients

Moon Young Kim

Background and Aims: Disorders of glucose metabolism, such as impaired glucose intolerance (IGT) and diabetes mellitus (DM), occur frequently in cirrhosis. However, DM and IGT have not received enough attention and have been underestimated when fasting plasma glucose (FPG) levels are considered. we evaluated whether abnormal glucose metabolism, estimated by fasting plasma glucose (FPG) and the oral glucose tolerance test (OGTT), influences the prognosis of patients with liver cirrhosis.

Methods: This prospective observational study included 713 patients with either compensated or decompensated cirrhosis; these patients underwent a 75-g oral glucose tolerance test (OGTT). The patients were divided into three groups: patients with normal glucose tolerance (NGT), patients with IGT ($100 \leq$ fasting plasma glucose [FBG] $<$ 126 mg/dL or $140 \leq$ 2-h OGTT $<$ 200 mg/dL), and patients with newly diagnosed DM (126 $\leq$ FBG or 200 mg/dL $\leq$ 2-h OGTT).

Results: Among 713 patients, NGT was diagnosed in 139 (19.5%), IGT in 252 (35.3%), and DM in 322 (45.2%). During a median follow-up period of 42.0 months (interquartile range 20.5–66.5 months), the cumulative survival rates of patients were as follows: NGT, 75.6%; IGT, 57.6%; and DM, 54.8%. Overall, IGT [adjusted hazard ratio (aHR) = 1.669; 95% CI 1.050–2.653; P = 0.03] and DM (aHR, 1.723; 95% CI 1.101–2.698; P = 0.017) were identified as independent predictors of mortality after adjustment for Child–Turcotte–Pugh (CTP) and MELD scores. In patients with compensated cirrhosis (CTP class A; n = 415), neither IGT nor DM conferred a higher risk for mortality. However, among patients with decompensated cirrhosis (CTP class B and C; n = 298), those with IGT (aHR, 2.279; P = 0.022) and DM (aHR, 2.211; P = 0.022) showed a worse survival rate than those with NGT. In addition, DM was identified as an independent risk factor for acute kidney injury (aHR, 2.247; P = 0.036) and infection (aHR, 2.801; P = 0.034).

Conclusions: Abnormal glucose tolerance in patients with IGT or DM is associated with an unfavorable prognosis in patients with cirrhosis, particularly in the decompensated state. Also, our results demonstrated that AKI and infection were more frequent in patients with DM than in those with NGT.

Abstract #1825

Characteristics of liver cirrhosis patients in Hermina Jatinegara Hospital

Saragih AH, Indriani I, Danneto C

Gastrohepatology Division, Department of Internal Medicine, Hermina Jatinegara Hospital, Jakarta, Indonesia

Liver cirrhosis is a chronic liver disease causing fibrosis and nodule regeneration in liver. The disease causes impairment of liver function due to long-term damage. The purpose of this study is to describe the characteristics of liver cirrhosis patients in Hermina Jatinegara Hospital. The study is an observational descriptive study. Data were collected from medical records of liver cirrhosis patients in Hermina Jatinegara Hospital from January 2019 until December 2019. The total sample in this study is 20 patients. Data collected include the level of hemoglobin, leukocyte, thrombocyte, ALT, AST, albumin, bilirubin, creatinine, pT, aPTT, natrium, potassium, type of hepatitis, esophageal varices grade, ligation of esophageal varices procedure, ascites, and Child–Pugh score. The study showed that 85% of liver cirrhosis patients were male. Based on the type of hepatitis, liver cirrhosis were found 40% on hepatitis B, 30% on hepatitis C, and 30% on non-B non-C hepatitis. Liver cirrhosis were found more often on grade 2 esophageal varices (65%) compared with grade 3 esophageal varices (35%). About 60% of the patients had the Class B Child–Pugh Score, 30% with class A Child–Pugh Score, and 10% with Class C Child–Pugh Score. From the study, we found that majority of liver cirrhosis patients in Hermina Jatinegara hospital were male and the caused of liver cirrhosis were hepatitis B with child pugh score B.

Abstract #1842

The impact of etiology of chronic liver disease on the course and outcome of patients with acute on chronic liver failure

Sunil Taneja

Introduction: Acute-on-Chronic-Liver-Failure (ACLF) leads to higher mortality in patients with chronic liver disease. Whether etiology of chronic liver disease influences the course and outcome of these patients is not well understood.
Aims: To compare the outcome of patients with ACLF with different etiologies of chronic liver disease.
Methods: Retrospective analysis of 3624 patients from APASL-ACLF-Research-Consortium (AARC). Patients were divided into 4 categories according to etiology of chronic liver disease (Group A-Cryptogenic versus others), (Group B—Alcohol versus others), (Group C—Cryptogenic versus NASH) and (Group D-NASH versus others). The clinical, laboratory parameters, organ failure-scores, prognostic models and 28 and 90 day mortality rates were analysed.
Results: 3624 patients predominantly males 3055 (84.3%) with mean age of 44.57 ± 12.3 years were included. The most common etiology of chronic liver disease was Alcohol 1768 (52.7%), Chronic viral hepatitis 596 (16.4%), Cryptogenic 320 (8.85%) and NASH 170 (4.7%). Most common cause of acute deterioration was Alcoholic steatohepatitis in 1631 (48.6%), followed by reactivation of hepatitis B 557 (16.6%), Hepatitis E in 211 (6.3%), Drug induced liver disease in 163 (4.9%) and Anti-tubercular drugs 83 (2.5%), Survival at day 30 was 64.9%, day 60 was 52.9% and day 90 was 46.8%. There was no significant difference in the overall survival except higher mortality in cryptogenic group versus others (at day 7) (16.7% vs 12% p-0.029), in NASH group at day 28 and 90 days (47%vs35% p-0.0008 and 64.8% vs 54.6%, p-0.021, respectively).
Conclusion: ACLF patients with different etiology of cirrhosis behave similarly except higher mortality in patients with NASH cirrhosis.

Abstract #1847

Clinical characteristics, length of stay, and clinical outcome of liver cirrhosis patients hospitalized in Fatmawati General Hospital

Annela Manurung, Nikko Darnindro, Arnold Harahap, Edi Mulyana

Departement of Internal Medicine Fatmawati Hospital Jakarta

Background: Liver cirrhosis is chronic disease that is responsible for causing global public health problem. Cirrhosis mortality rate around the world was estimated at 1.000.000 per year. According to WHO in 2016, mortality rate of cirrhosis in Indonesia in male and female were 51.1 and 27.1 per 100,000 population.
Objective: To know clinical characteristics and mortality rate of hospitalized cirrhosis patients
Method: We retrospectively reviewed the clinicopathologic and virologic records of cirrhosis patients in outpatient clinic whom hospitalized Januari-June 2019. Demographics data, Clinical characteristic, laboratorium and diagnostic examination were obtained
Results: Among 41 patients, the average age was 52.9 ± 13.8 years, 75.6% was male patient, and 12.2% of patients died during hospitalization. The average length of stay (LOS) was 10.8 ± 6.4 days. The most common chief complaint for hospitalization was gastrointestinal (GI) bleeding (46.3%), followed by Hepatic Encepalopathy (22%), and massive ascites (17.1%). The most common physical examination findings in patients was Anemia (73.2%), icteric (29.3%), and shifting dullness (61%). Hepatitis B was found in 53.7% patients while Hepatitis C in 22% patients. Ultrasonography was still needed in 73.2% patients to comfirmed diagnosis or searching for other complication. Esophagogastroduodenoscopy was done in 43.9% patients in order to found and treat varices. Based on Child–Pugh classification, Average Child–Pugh score was 8 ± 2.2. 24.4% of patients classified as Child–Pugh A, and 14.6% Child–Pugh C, and 39% were unclassified due to lack of laboratory data. In Bivariate analysis we found association between mortakity and Child–Pugh classification, mortality rates are significantly related to Child–Pugh classification. The higher the classification the higher the mortality rate (p 0.028).
Conclusion: Hospitalization in liver cirrhosis patients was related to cirrhosis decompensation. Mortality rate in hospitalized cirrhosis patients is still high. Mortlity in cirrhosis is related to Child–Pugh classification.

Abstract #1856

Safety and efficacy of nalfurafine hydrochloride in chronic liver disease patients with pruritus

Tetsuhiro Chiba

Background: Pruritus is frequently observed in patients with chronic liver diseases. Its mechanisms are complicated and appears to be caused not only by chemical mediators but also by endogenous opioids.
Patients and Methods: During 2015–2018, a total of 88 patients (50 *males*, 38 *females*, *median age* 68 years) treated with n*alfurafine* hydrochloride against refractory pruritus in Chiba University Hospital were analyzed. The number of patients in primary biliary cholangitis, viral hepatitis, and others were 24, 32, and 32, respectively. Both safety and efficacy of n*alfurafine* hydrochloride were determined by retrospective medical record review.
Results: Treatment *discontinuation was observed in 11 patients, and sleepiness was the most frequent complication (3/11, 27.3%). However, these symptoms were resolved shortly.* Treatment efficacy *was observed in 33/56 patients (58.9%). Response rate was associated with no clinical factors including, age, sex, cirrhosis,* types of chronic liver diseases, and complication of liver cancer. Among 7 patients who ceased n*alfurafine* hydrochloride treatment because of partial remission of pruritus, 5 recurred eventually.
Conclusion: N*alfurafine* hydrochloride is considered to be a relatively safe drug. Additionally, it appears to be effective in the majority of patients complicated by pruritus. However, the cessation of this frequently causes recurrence.

Abstract #1870

Spur cell anemic in Child C cirrhotic patients have elevated levels of VWF and D-dimer.

Deepika, Sadaf Khan, Radhika Kapil, Chhagan Bihari.

Objectives: To investigate the levels of VWF & D-dimer in cirrhotic patients with spur cell anemia and their relationship between percentages of spur cells.
Method: Blood samples from 27 CLD with Child C score patients were collected in which 20 patients were without spur cells (group 1) & 7 patients (group 2) with spur cell anemia. Sonoclot assay was performed and did ELISA for VWF & d-dimer. Clinical & laboratory parameters including liver dysfunction and MELD-Na score were assessed.
Results: In spur cells $< 10\%$ (group1) & $> 10\%$ (group2), mean plasma levels of VWF (5.98 ± 2.37 vs 7.96 ± 1.82, $p < 0.05$) & D-dimer levels were significantly high (48.92 ± 33.86 vs 65.42 ± 37.00, $p < 0.05$) in group 2. In Sonoclot revealed, Platelet function were significantly better in group 2 (1.05 ± 0.99, 2.07 ± 1.49, $p = 0.05$) whereas clot rate & ACT (26.97 ± 10.12, 24.63 ± 14.18, $p = 051$; 189.33 ± 30.72, 215.86 ± 50.42, $p > 0.05$) showed no significant difference between two groups. Other clinical parameters including Hemoglobin (7.82 ± 1.71, 7.43 ± 1.1, $p > 0.05$), platelets (70.11 ± 23.75, 68 ± 29, $p > 0.05$) also were not significantly different.
Conclusion: Elevated levels of VWF and D-dimers were noted in patients with spur cell anemia in Child C class in comparison to those without spur cell anemia. Both these factors indicates the increased probability of microvascular thrombi in liver cirrhosis patients.

Abstract #1881

Esophageal vein sclerotherapy does not reduce the mortality of patients with esophageal variceal bleeding in type B or C acute-on-chronic liver failure

Sun Yanan[1], Ding Huiguo[1]

[1]Center of hepatic and digestive diseasea, Beijing You'an Hospital Affiliated to Capital Medical University, Beijing, China

Introduction: The 2018 version of liver failure guidelines proposed that patients with liver failure and esophageal variceal bleeding (EVB) can be treated with endoscopic ligation, esophageal varices sclerotherapy (EVS) or tissue glue injection. However, there are few studies on whether EVS can prolong the survival of patients.
Objectives: To identify independent risk factors influencing the survival time of patients with EVB in type B or C acute-on-chronic liver failure (ACLF).
Methods: Retrospective analysis was applied to clinical data of 37 patients with EVB in type B or C ACLF. Each patient was followed up for at least 6 months. Cox regression analysis was used to select the independent risk factors influencing the survival time.
Results: Among 37 patients, 43.2%(16/37) were treated with EVS. The different stages of hepatic encephalopathy, EVS treatment, ascites volume and TBil level were independent risk factors for survival time. The mortality is 45.9%(17/37), 7 cases died of gastrointestinal bleeding, 10 cases died of other causes. According to whether EVS treatment was performed, the patients were divided into EVS treatment group (10 cases) and non EVS treatment group (7 cases). There was no significant difference in gender ($P = 0.485$), etiology ($P = 0.707$), portal vein thrombosis ($P = 1.000$), the type of ACLF ($P = 0.103$), ascites volume ($P = 0.134$), stage of hepatic encephalopathy ($P = 0.222$), cause of death ($P = 0.622$) between the two groups.
Conclusion: EVS did not reduce the risk of death from EVB in patients with type B or C ACLF.

Abstract #1883

Study of prevalence of hepato-pulmonary syndrome and its correlation with CTP/MELD scores

Meher Dinesh, [1] Lamba B. M. Singh, [2] Pandit Neeraj, [3] Singh Shivaram Prasad, [4]

[1]Resident, Department of Gastroenterology, S.C.B Medical College and Hospital, Cuttack, India, [2] Ex-Professor, Department of Medicine, ABVIMS & Dr. RML Hospital, New Delhi, India, [3] Professor, Department of Cardiology, ABVIMS & Dr. RML Hospital, New Delhi, India, [4] Professor & Head, Department of Gastroenterology, S.C.B Medical College and Hospital, Cuttack, India.

Introduction: Hepato-pulmonary Syndrome (HPS) implies severe arterial hypoxemia with significant mortality rates in CLD patients. Literature correlating severity of HPS with severity of liver disease viz; Child Turcotte Pugh (CTP), Model for End Stage Liver Disease (MELD) and MELD-Na scores are scanty.
Objectives: To study the prevalence of HPS in patients of CLD and to correlate the severity of HPS with CTP/MELD/MELD-Na score.
Method: We studied 120 CLD patients (140 enrolled;20 excluded) of various etiology from November 2013 to March 2015. HPS screening was done using arterial O_2 saturation (SaO_2) of $< 96\%$ in pulse oximetry. Diagnosis of HPS was confirmed using ERS Taskforce criteria and further stratified into mild, moderate, severe and very severe category. CTP/MELD/MELD-Na scores were calculated for all and compared with severity of HPS.
Results: 54 (45%) patients were in CTP-C followed by 34 (28.3%) in CTP-A and 32 (26.7%) in CTP-B. HPS was diagnosed in 22 (18.33%) patients and classified as mild in 2 (9.1%), moderate in 10 (45.45%) and severe in 10 (45.45%). All 10 patients in severe HPS belonged to CTP-C whereas 2 patients of mild HPS belonged to CTP-A (< 0.001). 4 from CTP-B and 6 from CTP-C were found to be in moderate HPS. The mean MELD score for HPS positive versus HPS negative patients

was 20.64 versus 14.39 ($p < 0.001$) whereas mean MELD Na score for HPS positive versus HPS negative patients was 27.73 versus 17.37 ($p < 0.001$)
Conclusions: HPS was prevalent in 1/5th of the hospitalized patients of CLD. There was significant correlation between high CTP/MELD/MELD Na scores and severity of HPS.

Abstract #1901

Risk of portal vein thrombosis with use of non-selective beta-blockers in patients with liver cirrhosis

Akhmad Fajrin Priadinata[1], Cosmas Rinaldi A. Lesmana[2]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Hepatobiliary Division, of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Non selective beta-blockers (NSBBs) is recommended as primary and secondary prophylaxis for esophageal variceal bleeding in patients with liver cirrhosis. NSBBs block β1 receptor which decreases heart rate and cardiac output and also block β2 receptor causing splanchnic vasodilatation and decreases portal blood flow. Due to its effect on portal blood flow, the use of NSBBs is suspected to increase risk of portal vein thrombosis (PVT) in patients with liver cirrhosis.
Objectives: This study was done to see if NSBBs increase risk of PVT in patients with liver cirrhosis.
Methods: Online search of PubMed, Cochrane Library, and Science Direct led to two relevant articles. Only articles involving human subjects, published within the last 5 years, available in full-text, written in English, and comparing risk of PVT in patients treated with NSBBs compared to no treatment were included in this study. Critical appraisal was done to assess validity, importance, and applicability using the Evidence-based Medicine Toolkit.
Results: Xiangbo et al found that the use of NSBBs in patients with liver cirrhosis was significantly correlated with PVT (OR 4.62, 95% CI 2.50–8.53, $p < 0.00001$). Nerry et al also found that the use of NSBBs increases risk of PVT in liver cirrhosis patients (HR 10.56, 95% CI 1.35–82.73, $p = 0.025$).
Conclusion: The use of NSBBs may increase risk of PVT in patients with liver cirrhosis.

Abstract #1903

Validation of prognostic 90-days mortality scoring system for liver cirrhosis patients admitted to the Emergency Department of a Tertiary Hospital in Indonesia

Irsan Hasan[1], Andri Sanityoso Sulaiman[1], Cosmas Rinaldi A. Lesmana[1], Juferdy Kurniawan[1], Chyntia Olivia Maurine Jasirwan[1], Kemal Fariz Kalista[1], Saut Horas Hatoguan Nababan[1], Gita Aprilicia[1], Rino Alvani Gani[1]

Hepatobiliary Division, Department of Internal Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia.

Introduction: The number of cirrhotic patients admitted to the emergency department (ED) due to advanced cirrhosis-related complications is increasing. In 2017, study from a single tertiary referral center in Indonesia showed that a scoring system employing patient's age, Child–Pugh score, and leukocyte count can predict 90-days mortality with area under the receiver operating characteristics (AUROC) curve of 0.89.
Objectives: This study was done to validate the prognostic 90-days mortality scoring system.
Methods: A retrospective cohort study of liver cirrhosis patients admitted to the ED of Cipto Mangunkusumo National General Hospital was done from 2015 to 2018. Patients admitted to the ED in 2017 were excluded. All patients with one or more of the following conditions, encephalopathy, ascites, jaundice, and bleeding, were included. Multivariate analysis was done to determine predictive factors of 90-days mortality. Performance of the scoring system was evaluated with the ROC curve.
Results: 178 patients were included in this study. The predominant cause for ED admission was bleeding (39%). 47% of patients died within 90 days. Logistic regression analysis showed that age $\geq$ 60 years old, Child–Pugh score $\geq$ 8, and leukocyte count $\geq$ 12.000 upon ED admission were associated with 90-days mortality and employed into the scoring system. The AUROC curve of this prognostic 90-days mortality scoring system was 0.85 (CI 95%, 0.80–0.91) with p-value < 0.001.
Conclusion: A scoring system employing patient's age, Child–Pugh score, and leukocyte count at ED admission is a validated tool for predicting 90-days mortality of liver cirrhosis patients.

Abstract #1931

The effectiveness of telephonic reinforcement of nutritional counselling in reducing mortality and complications of decompensated chronic liver disease. a randomised control trial

Oommen Tharun[1], Mathew David[1], Varghese Jijo[1], Hareendran Atul[1], Narayanan Premaletha[2], Devadas Krishnadas[2]

[1]Senior Resident, Department of Medical Gastroenterology, Medical College Thiruvanthapuram, Thiruvanthapuram, Kerala, India, [2]Professor, Department of Medical Gastroenterology, Medical College Thiruvanthapuram, Thiruvanthapuram, Kerala, India.

Introduction: Adequate nutrition can reduce mortality and ameliorate the complications of cirrhosis. As physicians, inspite of our knowledge we tend to ignore the role of nutrition in cirrhosis.
Objectives: To assess the effectiveness of telephonic reinforcement of nutritional counselling in reducing mortality and complications of cirrhosis.
Methods: This was a randomized control trial, in which patients with decompensated cirrhosis were randomized based on simple randomization. Patients in the interventional arm received a diet chart based on weight (35–40 kcal/kg/day and 1.2–1.5 gm/kg/day). They were given telephone calls every 2 weeks and counselled. The nutritional goals were reinforced by reiterating the diet chart. The importance of late evening snack was stressed upon. The non-interventional group received the standard care. Mortality, anthropometric variables and complications were compared at the end of 12 months.
Results: 109 patients were analyzed at the end of the study. Mortality at the end of 12 months were comparable in interventional and non-interventional groups (35.1% vs 38.2%, $p = 0.75$). Patients in the interventional group had lesser episodes of infections (35 vs 52, $p = 0.04$) and hepatic encephalopathy (33 vs 51, $p = 0.03$). There was an increment in MAMC (ΔMAMC, + 0.1 vs -0.93, $p = 0.03$), and handgrip (Δhand grip, +0.05 vs -0.7, $p = 0.04$) in CHILD B patients in the interventional arm compared to non-interventional arm.
Conclusion: Telephonic reinforcement of nutritional counselling did not improve mortality rates. However, it significantly reduced

episodes of infections and hepatic encephalopathy. It improved sarcopenia in CHILD B subgroup, but not in CHILD C.

Abstract #1948

Correlation of Child Turcotte Pugh classification and risk of bleeding in liver cirrhosis patients

Tenggara, Riki[1]; Steffanus Mario[2]; Pandy, Louis Putra[3]; Haryono, Christopher[4]

[1]Department of Internal Medicine Atma Jaya Medical Faculty and Health Sciences, Jakarta, Indonesia;

Introduction: Acute variceal bleeding (AVB) is the most dreaded complication of portal hypertension because, although mortality rates have decreased due to improvement in general management, medical treatment, and endoscopic therapy, mortality is still around 15%. AVB is one of the most severe complications of liver cirrhosis (LC) in approximately 30% to 40% of compensated LC patients and 60% of those who present with ascites. Once varices have been diagnosed, the overall incidence of variceal bleeding is 25% within 2 years. One of the predictors for variceal bleeding is severity of liver dysfunction Child-Turcotte-Pugh (CTP) classification. In this retrospective study we hypothesized is there any correlation between risk of bleeding and CTP classification.
Methods: Retrospective data was taken from 2017 to 2019 at Atma Jaya Hospital, and Bivariate analysis to evaluate correlation of CTP classification and risk of bleeding using Chi Square.
Results: Thirty-seven LC patients was retrieved, 62.2% are male, mean age is 57 years old. 29.7% is Hepatitis B, 29.7% is Hepatitis C and 40.6% is non-viral hepatitis etiology. Twenty-three patients (62%) admitted with bleeding and re-bleeding. Eleven patients (30%) admitted for the first bleeding and 12 patients (32.4%) with re-bleeding with mortality of 13.5%. Hemoglobin level at admission is 9.21 g/dL (SD +3.28 g/dL), and median INR 1.19 (0.96–4.12). Most patients (51.4%) have Class B on CTP classification. Chi Square analysis shows no significant relations between CTP classification and variceal bleeding incidence in this study ($p = 0.092$).
Conclusion: Liver cirrhosis bleeding and re-bleeding does not correlate significantly with CTP classification

Abstract #1999

Microvesicle induced monocyte dysfunction is associated with sepsis and high mortality in cirrhosis

Sukriti Baweja[1], Chhagan Bihari[3], Preeti Negi[1], Guresh Kumar[1], Deepanshu Maheshwari[1], Deepika Lal[1], Nidhi Nautiyal[1], Anupam Kumar[1], Gautam Mehta[4], Ashok Kumar Chaudhary[2], Shiv Kumar Sarin[1,2]

[1]Department of Molecular and Cellular Medicine, [2]Department of Hepatology, [3]Department of Pathology. Institute of Liver and Biliary Sciences, New Delhi, India.[4]Department of Hepatology, University College of London, UK.

Background and Aims: Failed and timely immune response to bacterial and fungal infections possibly lies at the base of sepsis and multi-organ failure in cirrhosis. The mechanisms responsible for this are partially understood. We investigated the role of microvesicles (MVs) and immune reserves in cirrhosis with or without sepsis.
Methods: Phenotypic, activation and functional characterisation of microvesicles and immune cells in systemic circulation were performed in alcoholic cirrhosis {Child A, n = 15; B n = 16; C n = 43,}, Child C cirrhosis with sepsis (n = 38), and healthy controls (HC, n = 11). An in vitro model was used to determine the role of MVs in regulating monocyte functions. *In-vivo*, septic MVs infused animal model was investigated the pathophysiological changes.
Results: Monocytes and hematopoietic stem cells (HSCs) in circulation reduced and neutrophils increased with increasing Child score and sepsis ($p < 0.04$) with significant increase in monocyte microvesicles ($p < 0.00$). High monocyte MVs (MV/μl)were predictive of non-survival [AUROC = 0.76, cut-off 53 MV/μl] in sepsis. Healthy monocytes exposed to septic MVs induced the mobilization arrest within 4 h ($p = 0.004$), reduced the basal oxygen consumption rate of monocytes ($p = 0.000$). Whereas, *in-vivo* septic MVs infusion in healthy C57/BL6 mice induced sepsis within 24 h ($p = 0.00$) with significant increase in platelets and low TLC ($p < 0.005$) and severe inflammation in liver with increased CD11b + cells and hyperplasia in bone marrow ($p < 0.005$).
Conclusions: Microvesicles induced functional defects in immune cells contribute to the development of sepsis in Child C cirrhosis and their high levels, are indicative of increased mortality in these patients.

Abstract #2006

Low-dose vs full-dose albumin in prevention of paracentesis-induced circulatory dysfunction following large volume paracentesis in cirrhosis: evidence-based case report

Indahwati N[1], Sitanaya SN[1], Jachja MJ[2]

[1]RSUD Dr. Iskak, Tulungagung, Indonesia, [2]SMF Penyakit Dalam, RSUD Dr. Iskak, Tulungagung, Indonesia.

Introduction: Paracentesis-induced circulatory dysfunction (PICD) may occur following large volume paracentesis (LVP). Studies showed albumin, a plasma expander, can reduce PICD incidences effectively. However, albumin is costly. A 73-year-old woman presented with a 7-day history of abdominal and lower extremity swelling, and dyspnea. Physical examination showed anemic conjunctiva, anicteric sclera, crackles in bilateral lungs, abdominal distention, positive shifting dullness, and pitting edema in lower extremities. Abdominal ultrasound showed chronic parenchymal liver disease, splenomegaly, and > 1000 cc ascites. LVP with full dose albumin transfusion were planned, but her family was concerned about albumin that was not covered by their health insurance.
Objective: To compare low-dose albumin and full-dose albumin in prevention of PICD.
Method: Literature searching from PubMed, Cochrane, ScienceDirect, Ebsco, and manual search from relevant articles. Selected articles were critically appraised based on Central of Evidence-based Medicine (CEBM), Oxford University.
Results: Two RCTs were appraised and considered valid. Study by Alsebaey et al showed PICD occurred equally on both low-dose albumin and full-dose albumin group (ARR = 0; NNT = ∼). They found higher but not statistically significant diuresis in full-dose group compared to low-dose group. Alessandria et al found that low-dose albumin is effective to prevent PICD (ARR = 0.057; NNT 17.5). They also found no significant complications (eg. renal failure, hyponatremia, gastrointestinal bleeding, encephalopathy, and infection) between both groups. Results of both studies may be applied to the patient with consideration of patient's age and financial condition.
Conclusion: Low-dose albumin is comparable to full-dose albumin in prevention of PICD.

Abstract #2070

The prevalence and microbiological profile of spontaneous bacterial peritonitis in cirrhosis of the liver with ascites

Deepak

Background: The microbiological profile of spontaneous bacterial peritonitis (SBP) in Indian patients with cirrhosis of the liver (CL) with ascites is limited.
Objective: To study the prevalence of SBP and its microbiological profile in CL patients with ascites. **Methods**: One hundred consecutive patients with CL and ascites underwent diagnostic paracentesis. SBP was diagnosed when ascitic fluid culture was positive and polymorphonuclear leukocytes (PMN) were $> 250/mm^3$. Two variants were: culture negative neutrocytic ascites (CNNA) when ascitic fluid PMN count was > 250 cells/ mm^3 but culture was negative, and monomicrobial nonneutrocytic bacterascites (MNB) when a single organism was grown but PMN count was < 250 cells/ mm^3.
Results: Of hundred cirrhotic patients with ascites, SBP was found in 36%. Among them, 22% were classical SBP, 72% were CNNA and 6% were MNB. E. coli was the commonest organism isolated; all strains of it were resistant to third generation cephalosporins (cefotaxim, ceftrixone, cefoperazone) whereas 78% were resistant to quinolones (levofloxacin, ciprofloxacin, norfloxacin). All E. coli isolates were sensitive to imipenem, but only 67% were sensitive to a combination of third generation cephalosporin and beta lactamase inhibitor.
Conclusion: SBP is common in patients with CL with ascites and is mostly caused by E coli. A high percentage of E coli are resistant to cephalosporins and quinolones, but sensitive to imipenum or a combination of 3rd generation cephalosporin and beta lactamase inhibitor.

Abstract #2078

Short Physical Performance Battery Frailty Index to predict mortality in chronic liver disease

K A Jinsha

Institute of Medical Gastroenterology, Madras Medical College, Chennai, India

Introduction: Short Physical Performance Battery (SPPB) is a well-established tool to asses physical performance and its ability to predict mortality has conflicting results.
Objectives: The aim of the study is to evaluate SPBB in prediction of mortality in patients with chronic liver disease.
Methods: 128 patients with liver cirrhosis were included for the study. Clinical assessment and routine laboratory tests were performed. SPPB frailty index, Child Score, Model for End Stage Liver Disease (MELD) score were calculated. These variables were compared to assess mortality over a period of 3 months.
Results: The mean age of patients was 52 ± 8 years, mean frailty index score was 7 ± 2. SPPB scores in survivors (6.68 ± 3.8) was significantly higher than in non-survivors ($4.3 + 1.3$) : p value ≤ 0.001, while child score and MELD score showed no significance difference in patient outcomes. Overall 90 days mortality rate was 14.8%. Sensitivity and Specificity of SPPB for predicting mortality were 72% and 74.6% respectively.
Conclusion: SPPB frailty score can be used as a screening tool to predict mortality in patients with cirrhosis.

Abstract #2081

Histoacryl in the management of gastric varices

Raees, Aimun[1], Awan, Safia[2], Abid, Shahab[3]

[1]Post graduate trainee, Section of Gastroenterology, Department of Medicine, Aga Khan University Hospital, Karachi, Pakistan, [2]Statistician, Department of Medicine, Aga Khan University Hospital, Karachi, Pakistan, [3]Professor and Section Head, Section of Gastroenterology, Department of Medicine, Aga Khan University Hospital, Karachi, Pakistan.

Introduction: Histoacryl has been successfully used for the management of bleeding gastric varices (GV). However, its use is debatable in primary and secondary prophylaxis of GV and its efficacy and safety is not comprehensively evaluated.
Objective: To review the efficacy and safety of Histoacryl in management of GV.
Methods: Pubmed, Cochrane and ScienceDirect databases were searched from inception till October 2019 using keywords histoacryl, gastric varices, fundal varices. Peer reviewed articles were included regardless of study design.633 articles were assessed out of which 54 were included based on our inclusion criteria. Seven articles and 34 case reports were added from references. Only English language articles conducted on adult patients were included.
Results: Complications were mentioned in 35 articles among those, 7 were RCTs. Serious complications such as thromboembolization were found to be very low. Common complications were mild fever and abdominal pain. 15 articles discussed technique of histoacryl administration.9 studies used histoacryl diluted in lipoidol using variable ratios (1:1 to 1:3) while undiluted histoacryl was used in 5 studies. Administration of histoacryl under fluoroscopy or EUS-guidance showed better results.
Conclusion: Histoacryl shows promising results in both primary and secondary prophylaxis and acute gastric variceal bleeding. A low rate of serious complications is observed. Technique of administration of histoacryl is variable and requires standardization. RCTs are needed to establish its role further in primary and secondary prophylaxis.

Objective	Number of articles (RCTs*)	Success rate
Primary prophylaxis	9 (1)	93-100%
Secondary prophylaxis	4 (3)	10-51% **
Active Bleeding	30 (4)	87-100%

Abstract #2084

The effectivity of endoscopic histoacryl injection for gastric fundal varices in Cipto Mangunkusomo Hospital in 2016–2019: a retrospective study

Rizka Mutiara

Introduction: Gastric Varices occur in 18–70% of patients with portal hypertension and are classified as a gastro-esophageal varices (GOV1) "esophageal varix extending down to the cardia or lesser curve or (GOV2) "esophageal and fundal varices". Gastric varices located in the fundus tend to cause serious bleeding and are reported to be less responsive to endoscopic treatment. The risk of fundal varices bleeding may range from 55% to 78% with a bleeding-related mortality rate of 45%. The first-line treatment for gastric variceal bleeding is endoscopic obliteration with Histoacryl (N-butyl-2-cyanoacrylate). It has been used to treat fundal variceal bleeding.
Objectives: Our purpose was to evaluate the effectivity of Hystoacryl for gastric fundal varices bleeding
Methods: The clinical records of 33 patients with gastric fundal varices who were seen at PESC "Pusat Endoskopi Saluran Cerna", Cipto Mangunkusumo hospital, and the Department of Internal

Medicine, University of Indonesia during January 2016 to Desember 2019.
Results: 13 patients were GOV1, 20 patients were GOV2 and 11 patients were IGV. The average volume of Histoacryl (® was 1–2 cc/session, mean frequency was (1 session-29 patients, 2 sessions-3 patients and > 3 sessions-1 patient). There was no occurrence of early Fundal Varices rebleeding, procedure-related complications, or bleeding related death.
Conclussion: Histoacryl injection theraphy is an effective treatment for gastric fundal varices and also an effective prophylactic treatment of gastric fundal varices which carry high risk of bleeding

Abstract #2105

The predictive value of exhaled nitric oxide in cirrhotic portal hypertension

Xiaoquan HUANG, Shiyao CHEN

Department of Gastroenterology and Hepatology, Zhongshan Hospital, Fudan University, Shanghai, China

Background and aims: The alteration of intestinal flora and metabolites in decompensated cirrhosis can increase the production of nitric oxide (NO). However, the relationship between the exhaled nitric oxide (eNO) and gastroesophageal varices in cirrhosis is still unknown. We aimed to explore the predictive value of eNO as a non-invasive marker for the development of cirrhotic portal hypertension.
Methods: We performed the measurement of eNO in cirrhotic patients underwent endoscopic intervention for prophylaxis of variceal bleeding.
Results: A total of 94 cirrhotic patients (male/female: 52/42) with gastroesophageal varices were included, and most of them were hepatitis B-related cirrhosis (67%). The eNO level was significantly increased in cirrhotic patients with ascites [15 (14–22) ppb vs 13 (10–18) ppb, P = 0.026]. The eNO level was significantly increased in cirrhotic patients with PVT [19.5 (11.75–22) ppb vs 13.5 (10–17) ppb, p = 0.032]. As for the endoscopic characteristics, eNO was increased in patients with red-color sign of varices [16.5 (10–21.75) ppb vs 13 (10–14.75) ppb (P = 0.041)]. Among patients under hepatic venous pressure gradient (HVPG) measurement. A statistically significant difference in the eNO level was observed between the high-HVPG group and low-HVPG group [15 (11.75–19.25) ppb vs 10 (8–14) ppb, P = 0.011].
Conclusion: eNO level was significantly increased in cirrhotic patients complicated with ascites, PVT, mucosal red-color sign of EGV, and high portal pressure. Further studies with large sample size are needed to further demonstrate the predictive value of the eNO level for the severity of cirrhotic portal hypertension and portal pressure.

Abstract #2112

Prevalence and predictive factors of erectile dysfunction (ED) in cirrhotic patients

Rakesh Kumar Jagdish[1], Ahemad Kamaal[2], Shasthry SM[1], Rakhi Maiwall[1], Ashok Choudhary[1], Ankur Jindal[1], Vinod Arora[1], Rajan V[1], Ankit Bhardwaj[3], Guresh Kumar[3], Manoj Kumar Sharma[1], SK Sarin[1]

[1]Department of Hepatology, ILBS, New Delhi, India, [2]Department of Urology, ILBS, New Delhi, India, [3]Department of Clinical epidemiology and research, ILBS, New, Delhi, India

Introduction: Erectile dysfunction (ED) is considered to be common in cirrhosis; possibly due to endocrine dysfunction and sarcopenia. There is paucity of data on the precise prevalence of and predictive factors for ED in cirrhosis.
Objectives: To find the prevalence and predictive factors of ED in patients with cirrhosis.
Methods: The data was prospectively collected using International Index for Erectile Function (IIEF) questionnaire; Generalized Anxiety Disorder 7 (GAD-7) questionnaire; Patient Health Questionnaire (PHQ-9); Dual-energy X-ray absorptiometry (DEXA) and BIA (bio-electrical impedance) analysis.
Results: A total 400 cirrhotic male patients (age, 43.83 ± 7.13 years; CTP score, 7.23 ± 1.96; MELD, 14.10 ± 4.92, etiology, alcohol 48.8%, NASH, 25.8%, viral, 17%] were included in the study. Prevalence of ED (IIEF score < 25) was 70.3%, which increases with age [59.29% in 21–40 years, 64.80% in 41–50 years and 90.74% in 51–60 years age group, P < 0.001] and severity of liver diseases [63.64% in CTP-A;70.73% in CTP-B and 88.34% in CTP-C patients, P < 0.001]. As compared to patients without ED, patients with ED had low hemoglobin, low albumin, high CRP, high GAD7, high PHQ 9 scores, low free testosterone, high sex hormone binding globulin (SHBG), lower bone mineral density, higher HVPG and low appendicular skeletal muscle index (ASMI). On multivariate analysis age > 40 years, high CTP score, BMI < 18.5 and > 30 kg/m ^{2}were positively associated with ED.
Conclusion: There is a relatively high prevalence (70.3%) of erectile dysfunction in patients with cirrhosis and age > 40 years, high CTP score, BMI < 18.5 and > 30 kg/m^2 were positively associated with ED.

Abstract #2114

A randomized placebo controlled trial of tadalafil for erectile dysfunction in patients with cirrhosis

Rakesh Kumar Jagdish[1], Ahemad Kamaal[2], Shasthry SM[1], Rakhi Maiwall[1], Ashok Choudhary[1], Ankur Jindal[1], Vinod Arora[1], Rajan V[1], Ankit Bhardwaj[3], Guresh Kumar[3], Manoj Kumar Sharma[1], SK Sarin[1]

[1]Department of Hepatology, ILBS, New Delhi, India, [2]Department of Urology, ILBS, New Delhi, India [3]Department of Clinical epidemiology and research, ILBS, New, Delhi, India

Introduction: Tadalafil acts by inhibition of phosphodiesterase 5, increases cGMP levels, which improves erectile dysfunction (ED). There are no placebo controlled randomized controlled trials (RCTs) using Tadalafil for treatment of ED in cirrhotic patients.
Objectives: To evaluate the efficacy and safety of Tadalafil in treatment of ED in patients with cirrhosis.
Methods: A total of 140cirrhotic maleswith ED [age, 45.5 ± 8.2 years; CTP-A (56.4%)/ B (43.6%); etiology, [alcohol 45%, NASH 30%, viral 18.6%] were randomized into Tadalafil 10 mg daily (n = 70) or placebo (n = 70) arm for 12 weeks. ED diagnosed if EF domain score was < 25, in International Index of Erectile Function (IIEF) questionnaire. Other assessments included Generalized Anxiety Disorder 7 (GAD-7) questionnaire; Patient Health Questionnaire (PHQ-9); Karnofsky Performance Score (KPS) and hepatic vein pressure gradient (HVPG). Primary outcome was proportion of patients having an increase in more than 5 points in EF score.
Results: Increase in more than 5 points in EF score was seen in 62.82% in (n = 44/70) in Tadalafil arm compared to 30% (n = 21/70) (p < 0.001) in placebo arm. As compared to placebo, patients taking Tadalafil had significant improvements in orgasmic function,

intercourse satisfaction, overall satisfaction, anxiety (GAD 7) score, depression (PHQ 9) score, functional impairment (KPS) score and HVPG(pre-17.68 ± 2.75, post-14.74 ± 2.74, p = .000). There were no significant differences in adverse event profile between groups (2.7% in Tadalafil vs. 1.7% in placebo, p = 0.154).
Conclusion: Tadalafil significantly improves ED, quality of life and HVPG in CTP-A and B patients with liver cirrhosis, without any major side effects.

Abstract #2120

AST/Platelet ratio index for predicting esophageal varices in cirrhosis: evidence based case report

Panjaitan, Harrison Paltak Bernard[1]

[1]Former Medical Intern, Tanah Grogot, Paser, East Kalimantan, Indonesia

Introduction: Ruptured esophageal varices is one of the severe complications in cirrhosis. Upper gastrointestinal endoscopy is the gold standard for diagnosing esophageal varices (EV). Due to its invasive and expensive nature, several non-invasive methods had been developed.
Objectives: To investigate the role of AST/platelet ratio index (APRI) to predict EV in cirrhotic patient.
Methods: Literature searching was conducted from January, 12th 2020 to January, 15th 2020 in three databases, i.e Pubmed, Sciencedirect and Cochran. Inclusion criteria were article written in English, published within 10 years, and available in full-text. Studies including pediatric population were excluded. Critical appraisal was done by using critical appraisal tools from CEBM.
Results: There were nine articles about APRI and its predicting capability for EV and one of which were meta-analysis. Five articles had been included in the meta-analysis study by Deng *et al.*, hence four articles were selected for critical appraisal. Pooled sensitivity and specificity of APRI from study by Deng *et al.* were 0.60 (0.57–0.63) and 0.67 (0.64–0.70) with significant heterogeneity and various cut-off value. Mandal *et al.* observed the sensitivity and specificity of APRI were 87.3% and 71.4% with cut-off value of 0.908. Khadka *et al.* concluded that APRI with cut-off value of 1.3 could predict EV with sensitivity of 83.2% and specificity of 50%. APRI was not associated with EV in study from Kraja *et al.*
Conclusion: Given the inconsistent diagnostic performance and cut-off value from four studies, APRI was not recommended for predicting EV in cirrhotic patient.

Abstract #2126

Defects in energy metabolism impair therapeutic potentials of cirrhotic bone marrow mesenchymal stem cells

Anupam Kumar[1], Dhananjay Kumar[1], Smriti Shubham[1], Deepanshu Maheshwari[1]; Nidhi Nautiyal[1]; Sheetalnath Rooge[1]; Lovkesh Anand[2]; Ashish Vyas[1]; Rekha Kumari[1]; Shvetank Sharma[1]; Chhagan Bihari[3]; Sujata Mohanty[4]; Rakhi Maiwall[2]; Shiv K Sarin[2]

[1]Dept of Molecular and Cellular Medicine, [2]Dept of Hepatology, [3]Dept of Pathology, Institute of Liver and Biliary Sciences, New Delhi, India; [4]Stem Cell Facility, All India Institute of Medical Science, New Delhi India

Background: Autologous bone marrow mesenchymal stem cell therapy in cirrhosis has shown varied clinical responses. Whether cirrhosis *per se* affects the therapeutic properties of bone marrow MSCs is largely unknown. We studied the cirrhotic BM-MSCs for their functionality and therapeutic potentials.
Methods: Functions of cirrhotic (n = 10) and healthy (n = 8) BM-MSCs were assessed *in-vivo* in acetaminophen (APAP) induced animal model of acute liver injury and immunomodulatory, angiogenic and paracrine functions were studied *in-vitro*. The global gene expression profile of MSCs was done by mRNA sequencing to determine the differential therapeutic potentials. The bioenergetic state of the cells was analyzed by XF24-bioanalyzer.
Results: The cirrhotic bone marrow MSCs (cBM-MSCs) showed significant loss of therapeutic functions compared to healthy bone marrow MScs (hBM-MSCs) both *in-vivo (amelioration of APAP induced liver injury, $P < 0.001$)* and in-vitro. mRNA sequencing showed significant up-regulation ($p < 0.05, > 1.5$ fold) of genes associated with insulin resistance and TNFα signaling in these cells compared to hBM-MSCs. Cirrhotic patients showed increased BM plasma level of pro-inflammatory cytokines {TNFα ($p < 0.01$), IL6 ($p < 0.001$), IL1β($P < 0.0001$} and glucose ($p = 0.037$) compared to controls, indicating inflammatory and metabolic milieu induced insulin resistance in cBM-MSCs. Though cBM-MSCs showed up-regulation of genes associated with glycolysis, they showed significant decrease in both glycolysis ($p < 0.001$) and glycolytic reserve ($p < 0.001$) due to poor glucose uptake ($p = 0.002$). Oxidative phosphorylation (OXPHOS) were also compromised in cBM-MSCs along with down-regulation of genes associated with OXPHOS and decreased baseline, maximum and ATP linked respiration ($p < 0.01$) in comparison to hBM-MSCs, suggesting broad defects in energy metabolism. These cells had reduced proton leak ($p < 0.01$), increased mitochondrial ROS ($p = 0.0062$) production, population doubling time ($p < 0.001$), SA-beta-gal positivity ($p < 0.001$) and decreased ($p < 0.001$) colony-forming unit-fibroblast (CFU-F), suggesting mitochondrial dysfunction with early senescence and aging compared to hBM-MSCs.
Conclusions: Compromised energy metabolism due to inflammatory and metabolic stress-induced insulin resistance underlies the abrogation of the therapeutic potential of BM-MSCs in cirrhosis. Bioenergetics of BM-MSCs of cirrhotic patients needs to be evaluated for potential modulation before inclusion in autologous hepatic regenerative protocols.

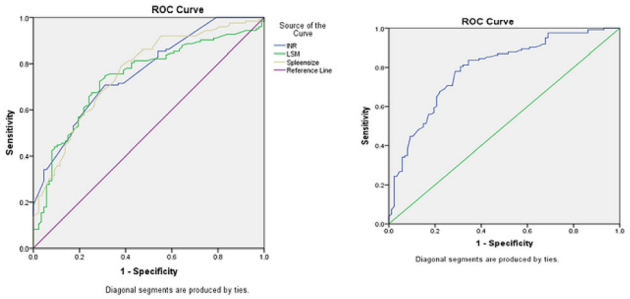
Abstract #2129

Review of efficacy of noninvasive markers of cirrhosis in predicting esophageal varices

Kamran Shafiq, Muhammad Farooq Hanif, Gurdeep Singh, Muhammad Aslam, Bikash Bhattarai, Abdul Nadir

Introduction: A large burden of cirrhosis in Pakistan prompted us to investigate the prediction of esophageal varices based on non-invasive markers. We assessed correlation of Platelets, INR, liver ultrasound and liver stiffness Measurement (LSM) with the documentation of esophageal varices by upper endoscopy (EGD).
Material and Methods: A retrospective study was conducted on patients who underwent ambulatory endoscopy in our hepatitis clinic. Biochemical results, ultrasound findings and liver stiffness measurement using fibroscan within 6 months of EGD were collected. Esophageal varices were graded as F0 = No varices, F1 = Grade I, F2 = Grade II, F3 = Grade III varices. The diagnostic accuracy of all non-invasive markers was estimated by using ROC curve. P value less than 0.05 was taken as significant.
Results: Total number of patients were 209, 128 patients (61.2%) had esophageal varices with different grades while 81 (38.8%) did not have varices. Mean age was 48.50 ± 8.47 years. 113 (54.06%) were

male. Average BMI was 25.9. Mean values of INR, LSM, and spleen size increased with increasing grades of varices while platelets decreased. We noted, Spleen size ≥ 11 cm was significantly associated with presence of esophageal varices, while Platelet count ≤ 177000 predicted varices with sensitivity of 87%, specificity 50.6% & AUC 79% and LSM ≥ 15.1 predicted varices with sensitivity 95%, specificity 96.6% & AUC 73.9%.
Conclusions: We found correlation of progressive increase in grades of varices with falling platelet counts and increasing LSM, and spleen size. An LSM of ≥ 15.1 KP was the most predictive of esophageal varices in our unique population from Lahore, Pakistan.



Abstract #2132

Comparison of GFR determined by using serum cystatin C and serum creatinine concentration alone and in combination for diagnosis of hepatorenal syndrome

Asma Helen Khan[1], Nooruddin Ahmad [1]

Background: Renal dysfunction is common in patients with liver cirrhosis, occurs about 19% of hospitalized patients with cirrhosis which have a huge impact on prognosis. Serum creatinine (Cr) is a widely used but less reliable marker to estimate glomerular filtration rate (GFR). Serum cystatin C (CysC) is a good endogenous marker to determine early renal impairment. Combined cystatin C and creatinine is an effective reflection of GFR.
Objectives: This study aimed to validate renal function by estimation of GFR using serum cystatin C and serum creatinine individually and combinedly.
Methods: This observational cross sectional study conducted in Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka. Thirty cirrhotic patients with hepatorenal syndrome (HRS) and thirty without HRS were included. Serum creatinine and serum cystatin C and estimated GFR [Mdrd 4 variables, CKD-EPI-CysC, CKD-EPI-Cr-CysC] were defined.
Result: Mean value of serum creatinine, serum cystatin C, GFR by creatinine, cystatin C and cre–cys were statistically significant ($p < 0.05$) between two groups. Main causes were HbsAg (60.0%) and Anti HCV (16.7%) in case group.. All the study population were in Child Pugh B and C. Association of mean values of creatinine, cystatin C, GFR by creatinine, GFR by cystatin C and GFR by (cre–cys) with Child Pugh B and C were statistically significant in both groups. Based on ROC curves at cut-off value of 1.29 mg/ml cystatin C had sensitivity 96.7% and specificity 76.7% for detecting HRS. Coefficient of GFR by creatinine was -0.01 (CI -0.01 to 0.00) which was not statistically significant. Coefficient of GFR by cystatin C was -0.02 (CI -0.03 to 0.00) and GFR by (cre-cys) was 0.04 (CI 0.01 to 0.06) which were statistically significant for diagnosis of HRS.
Conclusion: Combined serum creatinine and cystatin C based GFR showed significant association to discriminate early renal impairment in patients with cirrhosis of liver.

Abstract #2147

Thirty-day readmission after esophageal variceal hemorrhage and its impact on outcomes in the tertiary care hospital

Jalpa Devi,[1] Amerta Bai,[1] Saadat Ali,[1] Muhammad Sadik[1]

[1]Asian Institute of Medical Sciences, Hyderabad

Background and aims: Esophageal variceal hemorrhage (EVH) is a potentially fatal Gastro-intestinal emergency. The aim of this study was to evaluate the in-hospital mortality rate, 30-day readmission rate and its impact on mortality and morbidity in EVH patients.
Methods: A descriptive study (prospective) was conducted at the Gastro-hepatology department of AIMS Hyderabad from September 2019 to January 2020. Adults with EVH were included in the study. The clinical characteristics and laboratory data at admission were documented, based on which MELD, and CTP scores were calculated. The surviving patients were then followed via telephone after 30 days and readmission and its reasons, mortality and morbidity within 30-days were determined.
Results: A total of 95 EVH patients were included in the study, out of which 74.7% were males. The mean age of the participants was 49.56 years. The etiology was Hepatitis C in 62 (65.3%) patients. The in-hospital mortality was 5 (5.3%). Of those who survived, 17 (17.5%) had re-admissions with rebleeding as cause in 7 (7.4%) patients. Rest of the patients were admitted with other complications of end-stage liver disease.
Conclusion: The all-cause 30-day readmission rate after EVH was 17.5% with more than one-third of the cases due to re-bleeding. The readmission was not associated with higher rates of mortality (in-hospital mortality rate vs readmission mortality rate).

Abstract #2161

Hyponatremia is prognosis factor of refractory ascites in decompensated liver cirrhosis patients

Obi Shuntaro[1,2], Sato Takahisa[1], Komazaki Shingo[1], Honda Taku[1], Sato Shinpei[1,2], Kawai Toshihiro[2], Kondo Yuji[2]

[1]Gastroenterology, Teikyo Univ. Chiba Medical Center, Chiba, Japan, [2]Gastroenterology and hepatology, Kyoundo hospital of Sasaki institute, Tokyo, Japan

Objective: To evaluate the prognosis factor in decompensated liver cirrhosis patients with or without further complications, such as hepatorenal syndrome and/or hepatocellular carcinoma.
Methods: Twenty-six patients (median age 67 years, males: 20) with decompensated liver cirrhosis and refractory ascites were enrolled. All patients received diuretics (20–80 mg/day of furosemide and 50–100 mg/day of spironolactone). Furthermore, we add tolvaptan (7.5–15 mg/day for 7 days). The etiology of cirrhosis included hepatitis B (19%), hepatitis C (46%) and non-B non-C hepatitis (35%). For analysis of prognosis, we perform multivariate analysis by cox proportional hazard model. Changes in the body weight were assessed. The serum sodium levels were also measured, and adverse events were recorded. A follow-up assessment was conducted 7 days after treatment with tolvaptan.
Results: Median survival time (MST) was 65 days. In multivariate analysis, prognostic factor was hyponatremia (p = 0.037, O.R. 0.278, 95% CI 0.086–0.906). MST was 50 days in hyponatremia group (n = 14), 268 days in normal group (n = 12). The incidence of hyponatremia was 54%. In patients with hyponatremia, the serum sodium levels increase after tolvaptan.

Conclusion: Hyponatremia is prognosis factor of refractory ascites in decompensated liver cirrhosis patients. Tolvaptan is a promising aquaretic for the treatment of hyponatremia in refractory ascites with decompensated liver cirrhosis patients.

Abstract #2173

Table 1. Baseline Clinical and Hemodynamic Characteristics of Patients:

	Statin and propranolol	propranolol	P value
Age (year)	51.50 ± 7.21	49.75 ± 7.86	**.468**
Sex			
Male, n (%)	11 (55)	12 (60)	**.602**
Female, n (%)	9 (45)	8 (40)	
Laboratory Investigation			
Hb (g/dl)	14.22 ± 1.27	14.34 ± 1.13	**.755**
WBCs (g/dl)	6.02 ± 1.81	5.86 ± 2.47	**.817**
RBCs (g/dl)	4.86 ± .45	4.92 ± .29	**.607**
MCV (g/dl)	88.25 ± 6.52	88.55 ± 4.52	**.867**
PLT (g/dl)	131.20 ± 21.38	161.80 ± 73.00	**.08**
Liver function tests:			
Total BIL(mg/dl)	18.37 ± 7.95	13.58 ± 11.35	**.130**
Direct BIL(mg/dl)	9.87 ± 5.57	6.27 ± 4.76	**.034***
Total Protein	72.54 ± 8.15	78.74 ± 5.58	**.008***
Albumin	26.36 ± 17.50	33.02 ± 12.81	**.178**
SGPT	70.88 ± 27.43	67.00 ± 34.94	**.698**
SGOT	72.98 ± 25.30	56.47 ± 20.52	**.029***
GGT	157.40 ± 160.64	118.22 ± 69.66	**.323**
ALP	108.60 ± 43.18	98.45 ± 43.71	**.465**
Prothrombin time	13.87 ± 2.34	12.88 ± 1.06	**.095**
Prothrombin conc	77.52 ± 17.96	81.82 ± 15.66	**.425**
INR	1.18 ± .19	1.09 ± .09	**.053**
Renal function tests:			
Urea (mg/dl)	7.28 ± 5.67	4.87 ± .94	**.069**
Creatinine (mg/dl)	98.63 ± 26.91	87.99 ± 12.08	**.115**

Table 2. Doppler parameters of the studied groups

	Statin and propranolol	propranolol	T	P value
PVD				
Baseline	13.47 ± 2.36	14.35 ± 1.95	1.288	**.206**
2 months after	13.86 ± 2.13	14.46 ± 1.87	.942	**.352**
P value	.039*	.414		
PVV				
Baseline	10.42 ± 1.62	12.42 ± .56	5.178	**.000***
2 months after	12.08 ± 1.21	13.35 ± .66	4.135	**.000***
P value	.000*	.000*		
PVFV				
Baseline	647.59 ± 177.23	882.70 ± 174.73	4.225	**.000***
2 months after	739.66 ± 128.07	920.51 ± 158.71	3.966	**.000***
P value	.000*	.001*		
HARI				
Baseline	.75 ± .07	.72 ± .06	1.407	**.167**
2 months after	.70 ± .05	.69 ± .04	.655	**.516**
P value	.000*	.000*		
HAPI				
Baseline	1.67 ± .29	1.55 ± .24	1.468	**.150**
2 months after	1.51 ± .16	1.45 ± .18	1.173	**.248**
P value	.000*	.000*		
SPARI				
Baseline	.71 ± .05	.71 ± .06	.413	**.682**
2 months after	.67 ± .11	.69 ± .038	.906	**.370**
P value	.126	.175		

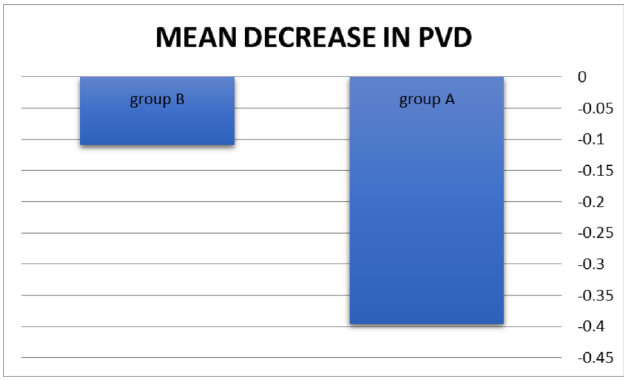


Figure. 1. Comparison of the effects of statin and propranolol on PVD.

Abstract #2201

Effects of exercise on frailty in patients with hepatocellular carcinoma

Takumi Kawaguchi[1], Shunji Koya[2], Keisuke Hirota[2], Jin Tsuchihashi[3], Noboru Koga[4], Hayato Narao[5], Manabu Tomita[6], Dan Nakano[1], Ryuki Hashida[2,7], Hiroo Matsuse[2,7], Taku Sanada[8], Kazuo Notsumata[8], Takuji Torimura[1]

[1]Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine, Kurume, Japan, [2]Division of Rehabilitation, Kurume University Hospital, Kurume, Japan, [3]Division of Rehabilitation, Fukui-ken Saiseikai Hospital, Fukui, Japan, [4]Department of Rehabilitation, Chikugo City Hospital, Chikugo, Japan, [5]Department of Rehabilitation, Yame General Hospital, Yame, Japan, [6]Department of Rehabilitation, Saga Central Hospital, Saga, Japan, [7]Department of Orthopedics, Kurume University School of Medicine, Kurume, Japan, [8]Department of General Internal Medicine, Fukui-ken Saiseikai Hospital, Fukui, Japan

Introduction: Frailty is a geriatric syndrome of physiological decline including physical inactivity. Frailty is recently reported as a prognostic factor for patients with hepatocellular carcinoma (HCC).
Objectives: We aimed to investigate effects of exercise on frailty in patients with HCC.
Methods: This is a multi-center prospective observational study. We enrolled 94 patients with HCC (median age 77 years, female/male 36/58). Patients were classified into the Exercise group (n = 46) or Non-exercise group (n = 48) according to the intention of patients. In the Exercise group, patients performed exercise (2.5–4 metabolic equivalents/20 min/day) during the hospitalization. Frailty was assessed by Liver Frailty Index (LFI). Factors for an improvement of LFI during the hospitalization were examined by multivariate analysis and decision-tree analysis.
Results: There is no significant difference in age, sex, ALBI grade at the baseline between the two groups. BMI and the prevalence of sarcopenia in the Exercise group were significantly lower than those in the Non-exercise group. LFI was significantly improved in the Exercise group (P = 0.0191), but not in Non-exercise group. In multivariate analysis, male was identified as independent factor for the improvement of LFI (HR 2.80, 95% CI 1.067–7.3512, P = 0.0365). In decision-tree analysis, the improvement of LFI was seen in 70% of patients with male and exercise. While, the improvement was seen in 42.9% of patients with male and no exercise.
Conclusion: We demonstrated that exercise improved frailty in patients with HCC. However, the improvement was only remarkable in male, suggesting that exercise program according sex is required for improvement of frailty.

Abstract #2212

Risk of mortality in patients with liver cirrhosis developing QT interval prolongation: a systematic review and meta-analyses of cohort studies

Budiman Fanny[1*], Ivan Ignatius[2*], Ruby Rivaldi[3*], Namretta Lisca[4*]

[*]School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia

Introduction: Previous studies had shown lower survival of liver cirrhosis (LC) patients with QTc prolongation.

Objectives: Our aim is to elucidate the risk of mortality in patients developing both LC and QTc prolongation.
Methods: This systematic review was based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We searched Pubmed, EBSCOhost, and ProQuest for articles published in English from 1995 to 2020. Titles and abstracts extracted were reviewed for relevance. Quality of study was evaluated using Newcastle-Ottawa Scale (NOS) determining quality of selection, comparability and outcome. Moreover, reporting quality in cohort studies also assessed using Strengthening the Reporting of Observational Studies in Epidemiology statement. Between-study heterogeneity was evaluated using Cochran Q test (v2).
Results: Search strategy identified 43 studies. Three relevant full-text articles met our inclusion criteria with adequate reporting qualities and NOS scale of 6–8. Our meta analysis using fixed effect found a significant risk in around 30 months for patients with both liver cirrhosis and QTc prolongation to develop 2% higher risk of mortality (HR, 1.02; 95% CI 1.00–1.04; p = 0.02). Meanwhile, random effect suggested an insignificant result (HR, 1.19; 95% CI 0.88–1.61; p = 0.27) and it may be considered more due to moderate heterogeneity (I^2 = 60%, p = 0.08) and imbalance weight between studies.
Conclusion: Our findings showed an insignificant risk for patients with both liver cirrhosis and QTc prolongation to develop higher risk of mortality based on random effect model. Due to limited studies available, current evidence still lacking and thus further studies with larger sample size need to be conducted.

Abstract #2216

Association between seropositivity of anti-*Helicobacter pylori* (*H. pylori*) immunoglobulin G and platelet counts in liver cirrhosis patients

Mirdania Yaditta[1], Suryadarma I Gusti Agung[2]

[1]Internal Medicine Departement SK Lerik Hospital, Kupang, East Nusa Tenggara, Indonesia, [2]Gastroenterohepatology Division, Faculty of Medicine of Udayana University/Sanglah Hospital, Denpasar, bali, Indonesia

Introduction: H. pylori infection is known to be associated with a decrease in platelets through immune related mechanisms. Several studies found a significant increase in platelet levels after eradication of H. pylori in patients with secondary ITP, but the study among liver cirrhosis patients were limited.
Objectives: This study aimed to determine the prevalence of anti-*H. pylori* immunoglobulin G seropositivity and its association with platelet count in patients with liver cirrhosis.
Methods: This is an observational study with cross-sectional design. Of 58 patients with liver cirrhosis in Sanglah General Hospital who met the inclusion and exclusion criteria were tested for platelet counts and H. pylori serology.
Results: There were 26 patients (44.8%) with H. pylori infection and 32 (55.2%) without H. pylori infection. Patients with H. pylori infection, 6 (23.1%) had normal platelet counts and 77% had thrombocytopenia with composition; 8 (30.8%) mild thrombocytopenia, 6 (23.1%) moderate thrombocytopenia, and 6 (23.1%) severe thrombocytopenia. Analysis using the Mann-Whitney test found that patients with H. pylori infection tended to have platelet counts below normal. In ordinal regression analysis, H. pylori and splenomegaly seropositivity variables significantly influence platelet count. The odds ratio for H. pylori seropositivity was 3.14.
Conclusions: The prevalence of anti-*H. pylori* immunoglobulin G seropositivity in patients with liver cirrhosis was 44.8%, and there was an association between seropositivity of anti-*H. pylori* immunoglobulin G with platelet count in patients with liver cirrhosis.

Abstract #2217

Application of FIB-4 index, MELD-XI, and NFS scoring systems to predict higher risk of mortality for liver dysfunction with heart failure: a systematic review and meta-analyses of cohort studies

Ignatius Ivan[1], Fanny Budiman[1], Rivaldi Ruby[1]

[1]School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia

Introduction: The impact of non-invasive scoring system application on the prognosis of heart failure (HF) patients remains unclear. We investigate the application of fibrosis-4 (FIB-4) Index, model for end-stage liver disease excluding INR (MELD-XI), and non-alcoholic fatty liver disease (NAFLD) fibrosis score (NFS) to predict higher risk of mortality for liver dysfunction with heart failure.
Methods: This systematic review was in accordance with PRISMA guidelines. We searched Pubmed, EBSCOhost, and ProQuest for English articles published between 1990 and 2020. Titles and abstracts were reviewed for relevance. Newcastle-Ottawa Scale (NOS) was used for quality of study assessment. STROBE statement was used to evaluate the quality of reporting from each study. Between-study heterogeneity was evaluated using Cochran Q test (v2).
Results: Search strategy identified 191 articles. 11 relevant full-text articles met our inclusion criteria with adequate reporting qualities and NOS scale of 4–8. Of them, 7 articles included for meta-analyses. Our meta-analysis using fixed-effect found application of FIB-4 index revealed a 31% higher risk of mortality for liver dysfunction with heart failure (HR, 1.31; 95% CI 1.15–1.49; p = <0.0001; I^2 = 0%, p = 0.41) in around 3 years. Using fixed effect, application of MELD-XI revealed a 90% higher risk (HR 1.90; 95% CI, 1.40–2.59; p = <0.0001; I^2 = 0%, p = 0.65) in around 1 year and NFS revealed a 13% higher risk (HR 1.13; 95% CI 1.05–1.22; p = 0.001; I^2 = 0%, p = 0.94) in around 2 years.
Conclusion: FIB-4 index, MELD-XI, and NFS scoring systems significantly predict higher risk of mortality for liver dysfunction with heart failure. As limited study still available, current evidence still lacking and further studies with larger sample size need to be conducted.

Abstract #2218

Portosystemic encephalopathy (PSE) recurrence in cirrhotic patients and its risk factors

Masood Muhammad Karim

Introduction: Recurrence PSE in cirrhotic patient is associated with worse outcome. It is important to assess the risk factors for recurrent PSE so that appropriate prevention and prognostication can be done. Objective: To assess frequency of recurrent PSE in cirrhotic patient after first episode of PSE and its risk factors.
Method: It is a retrospective study done in the section of Gastroenterology, The Aga Khan University Hospital, Karachi, Pakistan from Jan 1, 2019 till December 31, 2019. Patients who were admitted with first time with PSE and admitted within 3 months of index PSE were enrolled in the study. Grading of PSE Grade (I-VI), laboratory tests (Bilirubin, Albumin, Creatinine), ascites with SBP, gastrointestinal

bleeding (GIB), acute kidney injury (AKI) and (CTP, MELD) were collected by chart review and analyzed by SPSS version 20.
Result: Total 61 patients were included in study and 10 were lost to follow up. Mean age was 59 ± 10, male was 58%. Diabetic were (64%) and 54% were hypertensive. As per etiology HCV (59%), HBV (27%), Alcohol (7%), other (7%). Out 51 patients 33 readmitted with PSE, 6 were expired and rest followed in clinic. Risk factors were UTI (19%), AKI (15%), Constipation (15%), Hyponatremia (14%), SBP (12%), Hypokalemia (13%), GIB (8%). Most of patient were in CTP score C,(75%), CTP Score B (25%). MELD > 18 (65%), TB > 3 (41%), > 6 (10%), < 3 (49%) and Albumin > 3.5 (42%), < 2.8 (20%), 2.8–3.5 (38%). PSE Grade 1–2 (42%), PSE-3 (39%), PSE-4 (19%). All patients who were expired were in PSE-4 with raised creatinine > 3.
Conclusion: MELD score > 18, raised TB > 6 mg/dl, decreased sodium and low Albumin significantly associated with PSE recurrence

Abstract #2224

Evaluation of ALBI, Child Pugh, and MELD as predictor 90 days mortality in cirrhotic patients

Gita Aprilicia[1], Krisnawati Bantas[1], Rino Alvani Gani[2]

[1]Department of Epidemiology, Faculty of Public Health Universitas Indonesia, Depok, Indonesia, [2]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia/Dr. Cipto Mangunkusumo National General Hospital, Jakarta 10430, Indonesia.

Introduction: Child Pugh and model for end-stage liver disease (MELD) score are widely used for prognostic mortality among cirrhotic patients. The ALBI (Albumin-Bilirubin) score which initialy used in hepatocellular carcinoma (HCC), nowdays has been studied as simple parameter for assessing liver severity in cirrhotic patients.
Objective: To evaluate performance of ALBI, Child Pugh, and MELD as predictor 90 days mortality in cirrhotic patients.
Method. Cohort retrospective was conducted from hospitalized cirrhotic patients in Cipto Mangunkusumo Hospital during 2017–2019 period. Demographic and baseline laboratory were examined at the admission. Patients were followed-up until 90 days. Performance of ALBI, Child Pugh, and MELD was assesed by receiver operation characteristic (ROC) curve. Cox regression was conducted for analysis predictor factors of 90 days mortality.
Results: Total 275 cirrhotic patients were enrolled. Predominantly male (70.2%). Mean ± SD of ALBI, Child pugh, and Meld score were -1.98 ± 0.76, 9 ± 2.53, and 20 ± 9.65, respectively. Of 47.3% cirrhotic patients died after 90 days follow up. The AUC value of ALBI, Child Pugh and MELD for prognostic 90 days mortality were 0.81 (95% CI 0.76–0.86), 0.83 (95% CI 0.79–88.1), and 0.87 (95% CI 0.83–0.91), respectively. ALBI has a similiar performance with Child Pugh and Meld. Factors that significantly associated with 90 days mortality were ALBI score ≥ -1.9 (HR 1.82, 95% CI 1.13–2.92), Child Pugh score > 9 (HR 1.65, 95% CI 1.08–2.52), and MELD score > 18 (HR 4.07, 95% CI 2.38–6.96).
Conclusion: ALBI can be used for predictor 90-days mortality in cirrhotic patients.

Abstract #2226

Effect of the presence of portosystemic collaterals on hepatic vein pressure measurement

Aya Mohamed

Background: Portal hypertension (PHT) is a common clinical syndrome with pathologic increase in the portal venous pressure. PHT is diagnosed by the increase of the portal pressure > 10–12 mmHg with concomitantly increased wedged hepatic vein pressure (WHVP) > 2–6 mm Hg). Portal pressure is measured by angiography as hepatic vein pressure gradient (HVPG) which is a difference between WHVP and free hepatic venous pressure (FHVP). Difference > 5 mmHg is considered as portal hypertension.
Methods: In this case control study, HVPG measurement was performed in twenty patients using (Siemens Art Zee Pure device). Ten patients were cirrhotic with PHT and portosystemic collaterals and ten were without collaterals, as previously assessed by MDCT. Under local anesthesia, a venous introducer was placed in the femoral using the Seldinger technique. Through the introducer, a 7-French balloon tipped catheter (Swan-Ganz, CORODYNTM P1F7, B. Braun Melsungen, Poland) was advanced under fluoroscopic guidance and hooked into a hepatic vein. The FHVP was measured by keeping the tip of the catheter 'free' in the hepatic vein, and the WHVP was measured after inflating the catheter balloon. The following equation was used [HVPG = WHVP − FHVP]. Aim: find out the effect of the presence of portosystemic collaterals on HVPG through introduction to a new basic technique in our country and university.
Result: There was statistically significant difference in HVPG measurement between patients with and without collaterals (p value < 0.05.)
Conclusion: The presence of portosystemic collaterals reduce portal pressure and hence the HVPG.

Abstract #2249

Study of serum ferritin to predict early mortality in patients with decompensated cirrhosis of liver—a cross sectional observational study

Hossain S, Ahmad N, Mahtab MA, Rahman S, Mamum AA, Karim F, Noor-E-Alam SM, Podder PK, Islam MN

Introduction: Serum ferritin is a known marker of hepatic necroinflammation and has been studied to predict mortality in patients with decompensated cirrhosis of liver.
Objectives: To evaluate serum ferritin level for prediction of early mortality in patients with decompensated cirrhosis of liver.
Methodology: This cross-sectional observational study was carried out in the Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka from April 2017 to October 2017. Blood samples were collected to measure serum ferritin level. Patients were longitudinally followed up of mortality for a period of 30 days. Statistical analysis was done by dividing the patients into two groups (Group A and Group B) according to serum ferritin level > 500 μg/L which was considered, elevated for the study outcome.
Result: Out of total 79 patients majority of patients were in Child–Pugh C. Mean MELD score found 19.0 ± 5.7 in group A and 24.4 ± 6.8 in group B. 1 (1.9%) patient died in group A and 16 (64.0%) in group B. Several factors found significantly associated with mortality in univariate analysis including serum ferritin, serum sodium, ALT, prothrombin time and MELD score. In multivariate analysis, only serum ferritin (OR 0.11, 95% CI 0.01–0.99%, p = 0.001) found significantly associated with mortality within

30 days. ROC curve was constructed using serum ferritin level, which gave a cut-off value 612 µg/L, with 94.1% sensitivity and 91.9% specificity.

Conclusion: Raised serum ferritin level is an independent predictor of early mortality in patients with decompensated cirrhosis of liver.

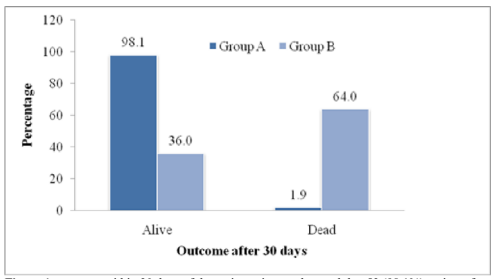


Figure 1. outcome within 30 days of the patients, it was observed that 53 (98.1%) patients found alive in group A and 9(36.0%) in group B. 1 (1.9%) patient found dead in group A and 16(64.0%) in group B. The difference was statistically significant ($p<0.05$) between the groups.

Table1. Univariate logistic regression analysis as predictor of mortality within 30 days (n=79).

	Adjusted OR	95% CI Lower	Upper	P Value
Age	0.018	0.001	1.008	0.893^{ns}
Sex	0.036	0.002	1.280	0.769^{ns}
Hepatitis B	0.66	0.037	1.204	0.626^{ns}
Hepatitis C	0.081	0.053	1.214	0.232^{ns}
Pulse (b/min)	0.043	0.029	1.045	0.327^{ns}
Systolic BP (mmHg)	0.009	0.001	1.222	0.935^{ns}
Diastolic BP (mmHg)	0.016	0.005	1.078	0.604^{ns}
Hb% (g/dl)	0.113	0.42	1.268	0.151^{ns}
TC (x10^9/L)	0.164	0.042	1.950	0.211^{ns}
Platelet count (x10^9/L)	0.243	0.018	1.503	0.067^{ns}
Serum ferritin (µg/L)	0.796	0.613	0.970	0.001^{s}
S. Creatinine (mg/dl)	0.144	0.012	1.356	0.353^{ns}
S. Sodium (mmol/L)	0.269	0.017	0.522	0.037^{s}
S. Potassium (mmol/L)	0.095	0.001	1.152	0.446^{ns}
S. Bilirubin (mg/dl)	0.026	0.001	1.252	0.823^{ns}
AST (U/L)	0.076	0.002	1.134	0.474^{ns}
ALT (U/L)	0.421	0.066	0.830	0.001^{s}
Prothrombin time (Sec)	0.197	0.011	0.383	0.038^{s}
INR	0.122	0.067	2.312	0.201^{ns}
Serum ALP (U/L)	2.01	0.931	14.343	0.746^{ns}
CP score	0.221	0.046	1.250	0.077^{ns}
MELD score	4.01	1.553	7.481	0.024^{s}

OR=odds ratio, CI-Confidence interval, s=significant; ns=non significant
Univariate logistic regression analysis was performed

Table 2. Multivariable logistic regression analysis as predictor of mortality within 30 days (n=79).

	Adjustd OR	95% CI Lower	Upper	P Value
Serum ferritin (µg/L)	0.11	0.01	0.99	0.001^{s}
S. Sodium (mmol/L)	4.73	0.99	22.57	0.51^{ns}
ALT (U/L)	6.28	0.97	20.04	0.521^{ns}
Prothrombin time (Sec)	0.26	0.07	1.98	0.570^{ns}
MELD score	0.53	0.05	6.26	0.533^{ns}

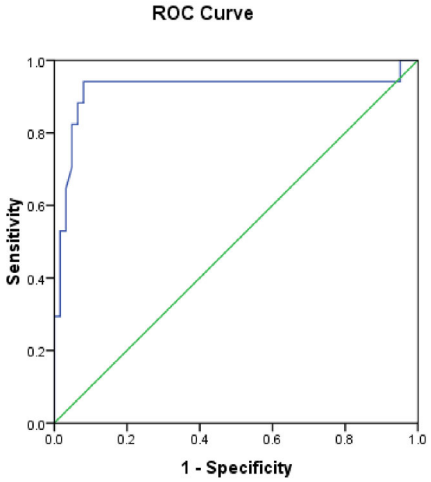


Figure 2. Receiver-operator characteristic curves of serum ferritin level

Pediatric Hepatology

Oral Presentations

Abstract #941

Metformin and mannose inhibit human hepatic stellate cell activation and proliferation: implications for anti-fibrotic therapies in patients with MPI deficiency and chronic liver disease

Bansal M, DeRossi C, Morrison J, and Chu J.

Department of Pediatrics, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Introduction: Children with a genetic disorder of glycosylation characterized by mutations in mannose phosphate isomerase (MPI), an enzyme that converts Mannose-6 phosphate to Fructose-6-phosphate, develop early liver fibrosis that can progress requiring liver transplantation. We have previously found that MPI loss in hepatic stellate cells (HSCs) promotes HSC activation and that mannose supplementation can dampen activation. Metformin can decrease HSC activation and proliferation and promote mannose uptake in dermal fibroblasts. Together, we hypothesized that mannose supplementation suppresses HSC activation through decreased proliferation and would have synergistic anti-fibrotic effects when combined with metformin.

Methods: The immortalized human HSC line (LX-2) or primary human HSCs were treated with increasing concentrations of mannose with and without metformin. RT-qPCR was performed for markers of HSC activation and MPI expression. HSC proliferation was assessed using MTT assays. A stable model of MPI loss was created using CRISPR-Cas9 lentiviral infection.

Results: Both mannose supplementation and metformin significantly decreased HSC proliferation and activation ($p < 0.05$), though synergistic effects with metformin were not pronounced. Decreased MPI was seen both with mannose or metformin alone and may reflect feedback inhibition resulting from increased endogenous intracellular mannose. Decreased MPI activity and HSC activation was seen in CRISPR MPI cells.

Conclusion: Both mannose and metformin can dampen HSC activation and proliferation. Future work focuses on the impact of mannose metabolism on receptor signaling important for HSC

biology, the interplay with metformin, and their potential uses as anti-fibrotics in those with MPI deficiency or other chronic liver disease.

Abstract #1653

Evaluation of the protocol based diagnostic approach for metabolic liver disease

Upadhyay Piyush, Khanna Rajeev, Sood Vikrant, B Lal Bikrant, Alam Seema

Department of Pediatric Hepatology, Institute of Liver and Biliary Sciences, New Delhi

Introduction: high economic burden in evaluation of metabolic liver diseases can be decreased with protocol based approach. This study evaluates the protocol-based diagnostic approach.
Methods: All suspected cases of inborn error of metabolism were suspected, than subjected to clinical exome study, TATA box sequence for Gilbert and suspected Wilson Disease were screened for 5 common mutations.
Result: 492 children and adolescents included: Progressive familial intrahepatic cholestasis suspected in 27: 18 confirmed. Two suspected to have bile acid synthetic defect were confirmed on genomic analyses. Thirteen suspected Glycogen storage disease confirmed. One case of galactossemia and 3 cases of tyrosinemia also confirmed. Among 3 cases of suspected lysosomal storage disease, diagnosis matched in 1 case of Cholestryl ester storage disorder and 1 case of Niemann pick disease. Heriditery fructose intolerance confirmed in 3 of the 5 suspected. Of the 6 cases of PILBD, 5 confirmed Alagille syndrome. Sixty one of 101 cases of Wilson disease found to be harbouring at least one of the 5 common mutations. A total of 333 with unconjugated hyperbilirubinemia: 296 subjects confirmed on TATA box analysis. Of the 492 suspected cases of MLD as analysed by the protocols, 403 were confirmed to have the diagnosis. Table shows the evaluation of the protocol based approach.
Conclusion: The protocol based diagnostic approach have a sensitivity of 100%, specificity of 58% and diagnostic accuracy of 83.72%. Hence we should use screening algorithmic approach which can be confirmed on genetic analyses

Table : Evaluation of the protocol based diagnostic test

Evaluation	Exome sequencing for non Wilsonian MLD	Common Mutations for Wilson Disease	TATA box for Gilbert disease	All 3 types of genetic analysis
Sensitivity	100% (95%CI 92.3-100)	100% (95%CI 94.13-100)	100% (95%CI 98.7-100)	100% (95%CI 99.09-100)
Specificity	94.12% (95%CI 89.9-96.9)	69.4% (95%CI 60.8-77.2)	87.11% (95%CI 82.6-90.76)	50.56% (95%CI 43.02-58.07)
PPV	79.3%(95%CI 68.8-86.9)	60.4%(95%CI 54.0-66.3)	88.89%(95%CI 85.5-91.53)	81.91%(95%CI 79.62-84.0)
NPV	100%	100%	100%	100%
Diagnostic Accuracy	95.2% (95%CI 91.7-97.50)	79.1% (95%CI 72.7-84.6)	93.65% (95%CI 91.3-95.49)	84.73% (95%CI 81.55-87.5)

Abstract #1777

Pancreatic endosonographic changes in portal cavenorma cholangiopathy and effect of portosystemic shunt surgery in children

Sen Sarma M, Ravindranath A, Rai P, Yachha SK

Dept of Pediatric Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, 226014, India.

Backgrounds: Portal cavernoma cholangiopathy (PCC) is a serious complication affecting the hepatobiliary outcome in extrahepatic portal venous obstruction (EHPVO). We aimed to address the concomitant changes in the pancreas in this condition.
Methods: Children with EHPVO (unfit for Meso-Rex bypass) with PCC prospectively underwent endosonography and magnetic resonance cholangiography-portovenography (MRC-MRPV) before and after (at least 6 months of) proximal splenorenal shunt surgery. PCC was graded as per modified Llop classification on MRC.
Results: Of 72 screened EHPVO children, 66 (asymptomatic, n = 61; symptomatic cholangiopathy, n = 5) had PCC changes [grades 1 (18%), II (11%), III (63%)] on MRC. On endosonography (table 1), intrapancreatic collaterals (n = 30) were statistically significant with pancreatic parenchyma changes (n = 33; $p < 0.001$), intracholedochal varices (n = 41; $p = 0.02$) and choledochal perforators (n = 39; $p = 0.03$). All had normal pancreatic duct diameter, serum lipase and fasting blood sugar. Twenty-eight patients with baseline PCC underwent shunt surgery and were reevaluated after 18 (6–54) months with documented shunt patency on MRPV. Pancreatic vascular and parenchymal changes [resolution (n = 11), persistence (n = 17)] correlated with biliary changes [resolution (n = 9), persistence (n = 18)] on endosonography. MRC showed progression (n = 6) and persistence (n = 22) of PCC after surgery. Superior mesenteric vein non-patency [p = 0.003; OR 4.3 (1.8–12.9)] and baseline grade III cholangiopathy [p = 0.01; OR 2.6 (2.0–5.1)] were predictors of persistent pancreatic changes. No progression to chronic pancreatitis was seen in any patient at follow-up.
Conclusions: Portal cavernoma pancreatic vasculopathy may mimic changes of chronic pancreatitis on endosonography in PCC. The pancreatic changes may persist despite shunt surgery due to concomitant superior mesenteric vein block and correlates with advanced cholangiopathy.

Table 1: Changes on radial array endosonography in portal cavernoma cholangiopathy

	Overall PCC (n=72)	No PCC (n=6)	Asymptomatic PCC (n=61)	Symptomatic PCC (n=5)	p
Biliary imaging, n (%)					
Intracholedochal varices (ICV)[£]	42 (58)	0	37 (61)	5 (100)	0.009^, 0.002*, 0.2[$]
Choledochal perforators (CPF)[#]	37 (51)	0	32 (52)	5 (100)	0.03^, 0.002*, 0.09[$]
Para-pericholedochal varices (PPCV)[Ω]	65 (90)	3 (50)	56 (92)	5 (100)	0.1[@]
Intramural GB collaterals	31 (43)	0	29 (48)	4 (80)	0.01^, 0.002*, 0.19[$]
GB calculi	5 (7)	0	0	5 (100)	<0.001^*
CBD calculi	8 (11)	0	3 (5)	5 (100)	<0.001^*, 1.0[$]
Pancreatic imaging, n (%)					
Intrapancreatic parenchymal collaterals	30 (42)	1 (17)	27 (44)	2 (40)	0.52[@]
Pancreatic parenchyma changes	33 (46)	3 (50)	28 (46)	2 (40)	0.57[@]
Hypoechoic parenchyma + hyperechoic foci ± hyperechoic strands	29	3	25	1	
Above changes + lobulations	4	0	3	1	
Intraductal collaterals (main pancreatic duct)	4	0	2	2	0.1[@]

Abstract #1852

Non-invasive portal hypertensive indices and portal hemodynamics on Doppler for prediction of clinically significant varices in children with chronic liver disease

Upadhyay Piyush[1], Khanna Rajeev[1], Lal Bikrant Bihari[1], Thapar Shalini[2], Patidar Yashwant[2], Sood Vikrant[q], Alam Seema[1]

[1]Departments of Pediatric Hepatology, Institute of Liver and Biliary Sciences, New Delhi, [2]Departments of Radiology, Institute of Liver and Biliary Sciences, New Delhi

Introduction: Portal hemodynamics (PH) relates to severity of PHT in adults with chronic liver disease (CLD). The present study looked up the association of splenic stiffness and PH with clinically significant varices (CSV) in children with CLD.

Methods: Consecutive children with CLD from January to December 2019 were prospectively enrolled. Transient elastography for liver (LSM) and spleen (SSM), and PH by doppler ultrasonography were measured. Non-invasive indices for PHT (AST-to-platelet ratio index, APRI; clinical prediction rule, CPR; variceal prediction rule, VPR; King's variceal prediction score, KVAPS) were calculated. Varices $\geq$ 2 grade (Japanese classification) were labeled CSV. SPSS version 22.0 was used.

Results: 88 children (58 males) had a mean age of 8.6 years (6 months–18 years). Ascites, variceal bleed and hepatic encephalopathy were present in 31.8%, 14.8% and 10.2%. Presence of CSV(46, 55.4%) was related to SSM, LSM, non-invasive indices of PHT, and splenic vein indices on doppler, but not with platelet count, portal vein indices or APRI. Among the PH parameters, splenic vein peak systolic velocity and congestion index correlated best with SSM, LSM, KVAPS and CPR (Table). On binary logistic regression analysis, SSM was found as the only predictor for CSV[Wald = 19.89, Exp (B) = 1.141, $p < 0.001$] having an AUROC of 0.941 (95% CI = 0.881–1.000, $p < 0.001$), cut-off of 26.0 kPa with a positive likelihood ratio of 12.07.

Conclusion: Presence of CSV and doppler splenic parameters relates to non-invasive markers of PHT in children with CLD. SSM is the best non invasive predictor of CSV in this cohort and can be used for decision making for endoscopy in children with CLD.

Table: Clinically significant varices in children with chronic liver disease and correlation of Doppler parameters with non-invasive indices.

Non-invasive portal hypertension indices and Portal hemodynamic parameters on Doppler in children with and without clinically significant varices (CSV)					
Parameter	CSV Present (mean ± S.D)	CSV Absent (mean ± S.D)	Mean difference	95% CI	p-value
LSM (kPa)	47.2±10.8	20.6±16.8	26.5	(17.1 to 35.9)	**<0.001**
SSM (kPa)	47.5±18.8	20.8±10.8	26.7	(19.7 to 33.6)	**<0.001**
Albumin (g/dL)	2.96±0.88	3.53±0.79	-0.575	(0.182 to 0.938)	**0.002**
Platelet count (X103/cucm)	118±103	153±120	-343	(-83 to +145)	0.166
KVAPS	50.67±26.20	75.06±26.95	-24.39	(-36.0 to -12.7)	**<0.001**
VPR	36.51±31.49	65.39±46.81	-28.88	(-46.0 to -11.7)	**0.01**
CPR	84.75±23.12	106.73±28.65	-21.98	(-33.2 to -10.6)	**0.001**
SV diameter (mm)	7.00±2.23	5.85±1.65	1.15	(0.27 to 2.03)	**0.01**
SVV (cm/s)	15.51±5.24	19.99±3.83	-4.47	(-6.50 to +2.42)	**<0.001**
SVCI (cm.s)	0.032±0.021	0.018±0.013	0.0136	(19.7 to 33.6)	**0.001**
PV diameter (mm)	9.40±3.04	9.06±2.36	0.345	(-0.87 to +1.55)	0.573
PVV (cm/s)	17.89±6.73	20.01±5.93	-2.11	(-4.92 to +0.69)	0.137
PVCI (cm.s)	0.045±0.023	0.038±0.019	0.006	(-002 to +0.016)	0.150
HARI	0.78±0.18	0.72±0.09	0.064	(0.0008 to 0.1291)	**0.047**
Correlation Statistics of Splenic vein velocity with Non-invasive PHT indices (R, p-value)					
	LSM	SSM	KVAPS	CPR	
SVV	R=-0.377, p<0.001	R=-0.400, p<0.001	R=0.255, p=0.001	R=0.226, p=0.002	
SVCI	R=0.165, p=0.025	R=0.285, p<0.001	R=-0.185, p=0.011	R=-0.211, p=0.004	

* CPR = Clinical prediction rule; HARI = Hepatic artery resistive index; KVAPS = King's variceal prediction score; LSM = Liver stiffness measurement; PV = Portal vein; PVCI = Portal vein congestion index; PVV = Portal vein velocity; SSM = Spleen stiffness measurement; SV = Splenic vein; SVCI = Splenic vein congestion index; SVV = Splenic vein peak systolic velocity; VPR = variceal prediction rule.

Abstract #1854

Newer diagnostic biomarkers of acute kidney injury in patient with chronic liver disease in pediatric population

Vijay P, Lal BB, Sood V, Khanna R, Alam S

Department of Pediatric Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: There is limited data on acute kidney injury (AKI) in pediatric liver disease.

Objective: To study the diagnostic value of serum cystatin C, urinary Neutrophil gelatinase-associated lipocalin (NGAL) and Renal Resistive Index (RRI) for AKI in pediatric Chronic Liver disease (CLD).

Methods: Prospective observational study in which all patients of CLD with PHTN with or without AKI were enrolled and followed up for 3 months for development/resolution of AKI as per KDIGO definition.

Results: Of the 247 children with CLD, 54 (21.8%) developed AKI. The most common pathology of AKI was pre-renal (53.4%) followed by renal (46.1%). 40 children (74%) had oliguria. Majority (37, 68.5%) had grade 3 AKI. Mean age at AKI was 8 ± 5.4 years and PELD/MELD of 24 ± 12. Table 1 shows the AUROC, sensitivity, specificity, PPV, NPV & diagnostic accuracy of the markers for diagnosis of AKI. All three markers (Cystatin C, urinary NGAL and RRI) diagnosed AKI with AUROC more than 0.8. On follow up over 6 months 12 (23%) children developed new onset AKI. Complete resolution of AKI was seen in 22 (42%) of patients by 3 months whereas 18 (34%) either died (12) or received LT (6) despite borderline AKI.

Conclusion: AKI developed in 21.8% of pediatric CLD and was associated with poor outcome in one third. Cystatin C, Urinary NGAL and renal resistive index are good markers to identify AKI in pediatric CLD.

Table 1: Evaluation of the New Biomarkers of AKI in Pediatric CLD.

Test	AUROC	Cut-off	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Cystatin-C (mg/L)	0.86	0.9	81.55%	80.4%	83%	78%	81%
Urinary NGAL	0.89	95	79.6%	78.3%	81.1%	76.6%	79%
(ng/ml)							
Renal Resistive Index	0.85	0.8	75.9%	82.6%	83.7%	74.5 %	79%

Abstract #2044

Validation of Indian scoring system for diagnosis of Wilson disease in children

Sen Sarma M, Srivastava A, Seetharaman J, Yachha S K, Poddar U

Dept of Pediatric Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, 226014, India.

Aims: In the diagnosis of Wilson disease (WD), application of Leipzig scoring system (2001) has practical difficulties especially in unknown region-specific genetic mutations. Indian scoring system (modified Leipzig) was introduced in 2019 to increase the yield. We attempted to compare the two scoring systems and validate the Indian Wilson's score for the first time.

Methods: Children with hepatic WD were scored according to the Indian scoring system based on Kayser-Fleischer ring, serum ceruloplasmin, 24-h urinary copper, Coomb's negative hemolytic anemia, liver histology, neurobehavioural symptoms, MRI brain and affected family member. The new system was compared with the original Leipzig scoring system. Non-WD (autoimmune liver disease and cryptogenic cirrhosis) were controls.

Results: 149 hepatic WD were compared with 105 controls (age: 9.1 ± 2.6y vs.10.3 ± 1.3y, p = 0.65; pediatric end-stage liver disease score: 16.5 ± 19 vs. 14.3 ± 12, p = 0.1). Kayser-Fleischer ring (85%), serum ceruloplasmin (< 5: 14%; 6–10: 66%; 11–20: 17%; > 20 mg/dL: 3%), 24-h urinary copper (< 40: 4%; 40–100:16%; > 100mcg: 80%); Coomb's negative hemolytic anemia (19%), compatible liver histology (17%), neurobehavioural symptoms (13%), MRI brain (9%) and affected family member (28%) were the features. 4 of 8 patients with Leipzig score < 4 were reclassfied as established WD by Indian scores. Mean Indian and Leipzig scores were 6.1 ± 1.4 and 5.3 ± 1.3, p = 0.02. The sensitivity, specificity, positive and negative predictive values of the Indian score were 97%, 100%, 100% and 96% respectively. The sensitivity, specificity, positive and negative predictive values of the Leipzig score were 94%, 98%, 98% and 93% respectively.

Conclusions: Indian scoring system of WD has higher yield than Leipzig scores and is applicable even in limited resource settings.

Poster Presentations

Abstract #257

Audit of Hepatology Transition Program Registry in tertiary care hospitals in Singapore

Tan Yi Yuan[1], Tan Hiang Keat[1,] Chiou Fang Kuan[2], Lim Jia Min[2], Lee Hwei Ling[1], Phua Kong Boo[2,] Ekstrom Victoria Sze Min[1], Chia Peh Yuh[1]

[1]Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore.[2]Department of Paediatric Gastroenterology, Hepatology & Nutrition, KK Women's and Children's Hospital, Singapore

Background: Transitioning young adults with paediatric liver conditions to an adult-oriented centre poses unique challenges to both patients and healthcare providers, which can adversely impact disease outcomes. At present, there is no guideline on the transition of care for adolescents with chronic liver diseases.
Aim: To determine if a hepatology transition programme for adolescent patients with chronic liver diseases is feasible.
Methods: A hepatology transition programme was started at the paediatric centre at Kandang Kerbau Women's and Children's Hospital (KKH) and the adult centre at Singapore General Hospital (SGH). Patients aged 18 years and above are selected and seen at transition clinics at KKH and SGH by hepatologists and specialist nurses from both centres with special interest in paediatric-to-adult transition care. A clinical audit was performed on all patients in the programme, from June 2018 to November 2019.
Results: 13 patients (46.2% Malay, 53.8% Chinese) were included. Median age was 19 years; interquartile range (IQR) was 18–24. 61.5% were female. The aetiologies of chronic liver diseases were: biliary atresia (53.8%), autoimmune hepatitis (15.4%), Wilson's disease (7.7%), Alagille syndrome (7.7%), hepatitis C (7.7%) and ischaemic cholangiopathy (7.7%). All patients are still on follow-up at time of audit with two patients on the national liver transplant waiting list. Median follow-up was 233 days (IQR 133–497). A comparison of unscheduled emergency department visits showed improvement in yearly mean unscheduled visits from 0.5 ($\pm$ 0.80) prior to transition and 0.25 ($\pm$ 0.45) after (p-value $<$ 0.19).
Conclusion: A transition period of integrated care with a combined clinic facilitates successful adjustment and management of young adults with paediatric liver disease.

Abstract #1656

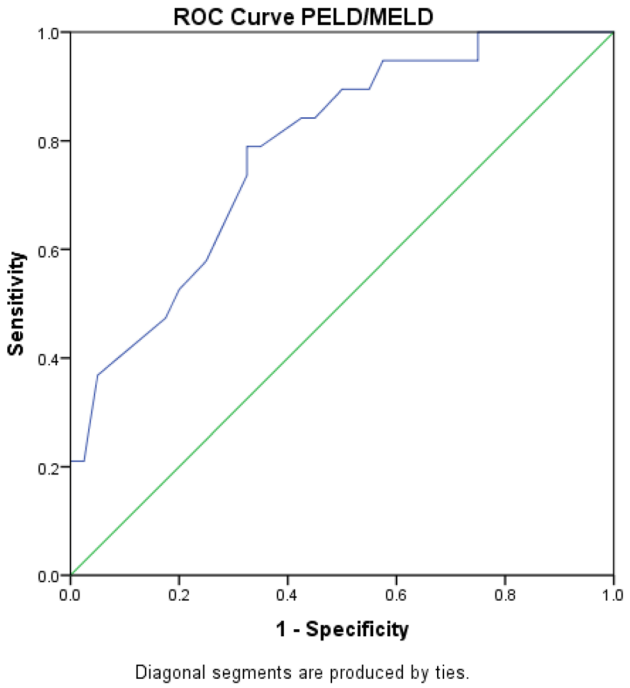
Hyponatremia in childhood chronic liver disease: prevalence, predictors and impact on outcome

Upadhyay Piyush, Khanna Rajeev, Sood Vikrant, B Lal Bikrant, Alam Seema

Department of Pediatric Hepatology, Institute of Liver and Biliary Sciences, New Delhi

Introduction: Prevalence and impact of hyponatremia is unclear. Objective: This study was conducted to examine the prevalence and the impact on outcome of hyponatremia, in children with chronic liver disease (CLD).
Methods: The study evaluated episodes of the hyponatremia ($<$ 130 mmol/L) in CLD of children and adolescents. The clinical and biochemical data was collected from the hospital records. The group comprised children of compensated and decompensated CLD.
Results: There were 390 screening for hyponatremia in 328 cases in the study period. The number of episodes with low serum sodium concentration as defined by a serum sodium levels of $<$ 120 mmol/L and 120–130 mmol/L were 8 (2.1%) and 57 (14.6%). As depicted in the Table 1, on multivariate analysis, high PELD was associated with hyponatremia (adjusted OR 1.05, 95% CI 1.027–1.076, p value $<$ 0.001). Of the 65 patients with hyponatremia 44 survived and 21 either died or were transplanted by 90 days. Hyponatremia ($<$ 130 mmol/L) was significantly associated with death/LT by 90 days (OR 2.56, 95% CI 1.62–4.03, p value $<$ 0.001). Hyponatremia ($<$ 130 mmol/L) with MELD/PELD $\geq$ 30 predicted mortality with senstivity 68%, specificity 70% within 90 days (AUROC 78.4%, p value $<$ 0.001). Each point increase in MELD/PELD was associated with 13% increase in mortality in cases of hyponatremia (OR 1.13, 95% CI 1.05–1.22, p value $<$ 0.001).
Conclusion: The prevalence of hyponatremia is 16.7% in children and adolescent with CLD. High PELD/MELD were independently associated predictors of hyponatremia and mortality in children of CLD with hyponatremia.

Variable	Serum Sodium <130 mmol/l n=65	Serum Sodium ≥130 mmol/l n=325	OR/ Mean Difference (95% CI)	P value
HE	34	132	0.679 (0.436-1.057)	0.099
HE III/IV	11	41	0.71 (0.43-1.35)	0.423
Ascites	45	173	1.301 (1.074-1.575)	0.02
AFI	11	26	2.12 (1.101-4.06)	0.035
Oliguria	20	67	1.49 (0.978-2.277)	0.101
AKI	12	61	0.98 (0.563-1.720)	1.000
Variceal bleed	11	36	1.528 (0.821-2.841)	0.210
PELD	24.92±11.1	16.59±13.6	8.32 (4.61-12.03)	0.000
Serum Creatinine	0.697±0.73	0.51±0.55	0.187 (0.031-0.34)	0.019
INR	2.31±1.20	2.01±1.25	0.30 (0.031-0.63)	0.076
Total Bilirubin	12.9±11.5	85±9.4	4.35 (1.7-6.99)	0.001
Albumin	2.5±0.76	3.29±0.35	0.795 (1.03-2.61)	0.395



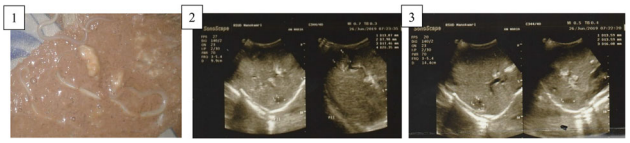
Abstract #1722

A rare case report: intestinal and hepatic ascariasis in infant

Wilona Ida[1]; Widiharso Rio[1]

Manokwari Regional General Hospital, Manokwari, West Papua, Indonesia

Introduction: *Ascaris lumbricoides* is amongst the common helminth disease worldwide. Ascariasis is more prevalent in developing countries especially in communities with poor socioeconomic condition. In endemic areas, ascariasis is more common during the first 2–3 years of age. Despite high incidence of intestinal ascariasis, the hepatic ascariasis is extremely rare.
Objective: To present an infant with hepatic ascariasis as a complication of intestinal ascariasis.
Methodology: Case description.
Results: A 22-month-old girl lived in Manokwari, West Papua, Indonesia admitted to hospital with abdominal pain, difficulty to pass the stool and distended abdomen. She previously had diarrhea and vomiting containing worms in the last 2 days after taking the anthelmintic (albendazole). On the physical examination, she was febrile (39.5 °C), extremely ill, and pale. Her blood test revealed slight anemic and leukocytosis. On fecal examination, adult worms of *Ascaris lumbricoides* were found. The patient's ultrasonography revealed multiple tubular hypoechoic structures, well-defined, with varying hyperechoic edges; accompanied by serpiginous structures with hypoechoic halo in the right and left lobe of liver. Patient was diagnosed with intestinal and hepatic ascariasis. She was treated with standard treatment for ascariasis such as albendazole 200 mg and pyrantel pamoate 100 mg. She also got antibiotics and symptomatic therapies during hospitalization. She went home in good condition.
Conclusion: Although there is very limited data for hepatic ascariasis treatment, albendazole and pyrantel pamoate combined with antibiotics gave a good result for this case. It is important to support this study with a larger group of patients.



Abstract #1835

Ascitic fluid infection and its impact on outcome in childhood chronic liver disease

Mahajan S[1], Lal BB[1], Sood V[1], Khillan V[2], Khanna R[1], Alam S[1]

[1]Department of Pediatric Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India, [2]Department of Microbiology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Ascitic fluid infection (AFI) requires prompt identification of risk factors and treatment for good outcome.
Objectives: The objective was to study the clinico-bacteriological profile of AFI and its impact on outcome in childhood chronic liver disease (CLD).
Methods: Data was collected from hospital records of all patients admitted with CLD between January 2011 to September 2019 who required paracentesis.
Results: Of the 814 children with CLD, 252 [30.9%] received paracentesis on suspicion of AFI. Prevalence of AFI was 31.3% among children with CLD and ascites. Younger age (mean difference: 2.31, 95% CI 0.84–3.75, p value 0.002), male gender (OR 2.36, 95% CI 1.29–4.32, p value 0.007], new onset or rapid increase in ascites [OR 2.58, 95% CI 1.114–5.99, p value 0.032], fever [OR 2.45, 95% CI 1.41–4.27] and higher TLC [mean difference 4.48, 95% CI 1.82–7.13, p value: 0.001] were independently associated with AFI. Twenty three children had positive ascitic fluid culture: 21 gram-negative and 11 (52.3%) multidrug resistant. Hepatic encephalopathy (HE) [OR 2.06, 95% CI 1.29–3.29, p value 0.001], MELD/PELD [mean difference 10.15, 95% CI 5.8–14.4, p value: 0.000] and difficult to treat AFI [OR 2.36, 95% CI 1.29–4.32, p value 0.007 were independently associated with death and/or liver transplant (LT) among those with AFI.
Conclusion: Prevalence of AFI in pediatric CLD with ascites was 31.3%. Abdominal paracentesis should be done in presence of fever, increasing or new onset ascites and/ or increased TLC. Death or LT are more likely due to advanced liver disease and in those with difficult to treat AFI.

Abstract #2076

Portal vein sclerosis is related to cholangitis episodes and affects survival in biliary atresia after Kasai portoenterostomy

Rajeev Khanna[1], Pankaj Kumar[1], Shalini Thapar[2], Bikrant Bihari Lal[1], Vikrant Sood[1], Seema Alam[1]

[1]Department of Pediatric Hepatology Institute of Liver and Biliary Sciences, D-1, Vasant Kunj, New Delhi, [2]Department of Radiology, Institute of Liver and Biliary Sciences, D-1, Vasant Kunj, New Delhi.

Introductions: Portal vein sclerosis (PVS) is common in the setting of biliary atresia (BA) after kasai portoenterostomy (KPE), but its link with cholangitis episodes is not established. We hypothesize that early and recurrent cholangitis episodes lead to PVS with subsequent portal hypertension (PHT) and need for liver transplantation (LT).
Methods: From Jan'2011 to June'2019 all BA children who underwent KPE and screened for portal vein diameter (PVD) were enrolled. Cholangitis episodes were defined with presence of >/=2: fever

(> 100.4F), jaundice or rising bilirubin, acholic stools; and classified as early or late (</= or > 12 months of age) and recurrent (>/=2 episodes/year). Relationship of PVD with cholangitis, presence of PHT (endoscopic varices) and survival with native liver at 1 year post KPE (SNL1y) was studied.
Results: 91 children (59 males) with BA had a median age at KPE of 85 days. Cholangitis was present in 74%—three-fourth were early, 57% were recurrent. PVD was assessed at a median age of 6 (2–204) months. Median PVD was 5.3 (mean 5.7 ± 2.0) mm; 20 had PV size </=4 mm. PHT was present in 67% and SNL1y in 72 (79.1%). Smaller PVD was associated with early (5.2 ± 1.5 vs 7.3 ± 2.2 mm, mean difference, MD = 2.2, $p < 0.001$) and recurrent cholangitis (5.1 ± 1.3 vs 6.0 ± 2.0 mm, MD = 0.98, $p = 0.012$) but not with PHT. Poor outcome (death or transplant) was related to smaller PVD (4.8 ± 1.0 vs 6.2 ± 3.0 mm, MD = 1.4, $p = 0.006$). A cut-off of PVD </=5.6 mm predicted poor outcome with an AUROC of 0.751 with a positive likelihood ratio of 2.34.
Conclusion: Early and recurrent cholangitis lead to PVS which affects their SNL at 1 year.

Abstract #2108

Clinical and laboratory manifestations of intrahepatic and extrahepatic cholestasis in infants in Bali

Ni Nyoman Metriani Nesa[1], A. A. Sagung Dwijayanti P[2], I Gusti Ngurah Sanjaya Putra[2], I Putu Gede Karyana[2]

[1]Pediatric Subspeciality Gastrohepatology Programme, Faculty of Medicine, Airlangga University, Surabaya, Indonesia.[2]Department of Child Health, Faculty of Medicine, Udayana University/Sanglah Hospital, Denpasar, Indonesia

Introduction: Cholestasis is one of the cause of jaundice in in infants. Cholestasis can be classified as intrahepatic and extrahepatic, which are different in etiology and management. It is important to distinguish intrahepatic and extrahepatic in early phase.
Objective: to compare clinical and laboratory examination of intrahepatic and extrahepatic cholestasis.
Methods: It was a cross sectional study in Sanglah Hospital Denpasar Indonesia, on December 2016–2017. There were 85 infants with cholestasis were included.
Results: There were 67 subjects diagnosed with intrahepatic and 18 with extrahepatic cholestatis. There were no differences in gender for both cholestasis. The percentage of acholic stool was 0% vs 56% in intrahepatic and extrahepatic cholestasis, respectively with p 0.00. Low birth weight was higher in intrahepatic cholestasis (37.31% vs 27.78%), with p 0.57. Median of direct bilirubin was higher in extrahepatic cholestatic 7.2 (1.03–12.27) mg/dL vs 6.26 (1.04–32.34) mg/dL with p 0.805. Median of gamma glutamyl transferase was higher in extrahepatic cholestasis 266, 5 (20–1483) U/L vs158 (23–1315) U/L with p 0.174. Subjects with extrahepatic cholestasis had higher Alanin Aminotransferase (ALT) level than subjects with intrahepatic cholestasis, 86.4 (21.7–285.3) U/L vs 48.7 (2.1–1525) with p 0.045. Aspartate Aminotransferase (AST) was higher in extrahepatic cholestasis 158.3 (37.7–477.4)U/L vs 90.77 (17.2–1011.3) with p 0.092. Albumin level of extrahepatic cholestasis was lower with mean 3.18 (0.53)g/dL vs 3.55 (0.58) g/dL with p 0.015.
Conclusion: Significant clinical and laboratory examination that can differ intrahepatic and extrahepatic cholestasis were acholic stool, ALT and albumin.

Abstract #2125

Morbidity due to variceal bleed in cirrhotic children awaiting liver transplantation

Rajeev Khanna, Pankaj Kumar, Vikrant Sood, Bikrant Bihari Lal, Seema Alam.

Department of Pediatric Hepatology, Institute of Liver and Biliary Sciences, D-1, Vasant Kunj, New Delhi.

Introductions: Variceal bleeding (VB) precipitates decompensation and organ failures in adults with chronic liver disease (CLD). There is limited data on morbidity related to VB in infants and children. We aimed to study the organ failures and outcome of cirrhotic children with VB necessitating liver transplantation (LT).
Methods: All children with CLD and variceal bleed presenting between December 2010 and June 2019 were prospectively followed-up. Severity scores, organ failures and mortality at day-90 were analysed.
Results: We identified 101 variceal bleeding episodes in 79 children (30.4% females)—median 1 episode (range 1–8). Commonest aetiologies were biliary atresia (35.4%) and autoimmune hepatitis (21.5%). Sixteen of these episodes were tolerated well without development of second decompensation. One or more organ failure was present in 98 episodes—median Pediatric CLIF-SOFA score was 6 (IQR 4, 10). Seven children developed advance (Grade 3–4) hepatic encephalopathy while stage 3–4 acute kidney injury was seen in 11 children. By 90 days, 12 children received living donor LT, while 11 died. On univariate analysis, mortality at Day-90 was associated with presence of Hepatopulmonary syndrome, hepatic encephalopathy, pneumonia and spontaneous bacterial peritonitis, and with high bilirubin, creatinine, INR, PELD/MELD, Child–Pugh and Pediatric CLIF-SOFA scores and low sodium. On multivariate analysis, Pediatric CLIF-SOFA (Wald 10.593, $p = 0.001$) and Hepatopulmonary syndrome (Wald 4.079, $p = 0.043$) were associated with poor outcome. There was recurrence of VB in 31 children over a median duration of 36 months.
Conclusion: Variceal bleeding in children is associated with organ failures which affect short term prognosis. Hepatopulmonary syndrome also relates to poor outcome in these children.

Abstract #2130

Characteristics and predictors of portal biliopathy in children with extrahepatic portal venous obstruction

Rajeev Khanna[1], Nishu Khemka[1], Shalini Thapar[2], Vikrant Sood[1], Bikrant Bihari Lal[1], Seema Alam[1]

[1]Department of Pediatric Hepatology Institute of Liver and Biliary Sciences, D-1, Vasant Kunj, New Delhi, [2]Department of Radiology, Institute of Liver and Biliary Sciences, D-1, Vasant Kunj, New Delhi.

Introductions: Portal biliopathy (PB) is seen in 70–90% of children and adults with extrahepatic portal venous obstruction (EHPVO). We conducted this study to define the PB characteristics in these children.
Methods: From Jan'2012 to June'2019, children with EHPVO and an MRCP study were enrolled. MRCP was studied blindly by single observer and classified as extrahepatic and intrahepatic. Sarin's and Llop's classifications were used to grade the changes of PB.
Results: 53 children (17 females) presented at a median age of 10 (7.5, 14.3) years. Variceal bleed was present in 34 (66.1%) with median 1 (0, 2) episodes prior to presentation. All of them had >/=1 feature of PB. Overall, 6 patients had clinical or biochemical evidence of PB but only one patient had symptomatic PB at the age of

12 months. Extrahepatic and intrahepatic and combined abnormalities were seen in 45, 37 and 34 children. Indentations, wavy changes, gallbladder varices, pericholecystic collaterals and cholelithiasis were present in 49, 48, 39, 38 and 6 children. Llop grade 3 (stricture with bilobar dilatation) in 29 children was associated with higher ALT (31.4 ± 15.5 vs 21.5 ± 8.7 IU/L, p = 0.005) and alkaline phosphatase (201 ± 98 vs 142 ± 92 IU/L, p = 0.03). There was no difference between Llop grades 3 versus 1/2 with regard to age at presentation, variceal bleed, spleen size, prothrombotic risk profile and angulation of CBD ($p > 0.05$).
Conclusion: Portal biliopathy is universally present, although rarely causes symptoms, in children with EHPVO. Long term follow-up studies are needed to look for the progression of PB in these children.

Abstract #2133

Bile nephrosis is common in pediatric patients with acute-on-chronic liver failure—an autopsy study

Nada Ritambhra [1], Saini Oshan [1], Kumar Ashwani [1], Sekar Aravind [1], Dawman Leza [2], Tiewsoh Karalanglin [2], Lal Sadhna[3], Duseja Ajay[4]

Departments of Histopathology[1], Postgraduate Institute of Medical Education and Research, Chandigarh, India, 160012, [2]Departments of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India, 160012, [3]Departments of Pediatric Gastroenterology, Postgraduate Institute of Medical Education and Research, Chandigarh, India, 160012, [4]Departments of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh, India, 160012.

Introduction: Bilirubin associated renal injuries such as bile cast nephropathy (BCN) and bile nephrosis (BN) are well defined entities in adult patients with limited data in pediatric patients. Objective of the present study was to assess the presence of BCN and/or BN in pediatric patients with liver failure.
Methods: In a retrospective autopsy study presence of BCN and BN were assessed in kidney sections of 14 pediatric patients who died of liver failure. The diagnosis of BCN was based on the presence of pigment casts within the renal tubules and BN was diagnosed based upon presence of bilirubin pigment within proximal renal tubules without any casts.
Results: Of 14 patients (Males 8, Mean age 6.8 years) who died of liver failure, 3 (21.4%) patients had acute liver failure (ALF, Wilson's disease-1, complimentary/alternative medicine -2), 8 (57.1%) had acute-on-chronic liver failure [ACLF, Indian childhood cirrhosis-3, Wilson's disease -1, autoimmune hepatitis -1, Galactosemia-1, cryptogenic-2) and 3 (21.4%) patients had cirrhosis with decompensation (Budd Chiari syndrome-1, Cryptogenic -2) with presence of acute kidney injury (AKI) in 8 (57.1%) patients. Kidney sections showed BN in 6 (42.8%) patients [ALF-1 (16.6%), ACLF-5 (83.3%)] with none of the patients showing BCN. Patients with BN had higher serum bilirubin (mean bilirubin 30.2 Vs 7.7 mg/dl, $p < 0.05$) in comparison to those without BN. Even though higher, difference in serum creatinine (mean creatinine 1.5 Vs 1.03 mg/dl, p = NS) was not significant between those with and without BN.
Conclusion: Bile nephrosis is common in pediatric patients with acute-on-chronic liver failure.

Basic Hepatology Research

Oral Presentations

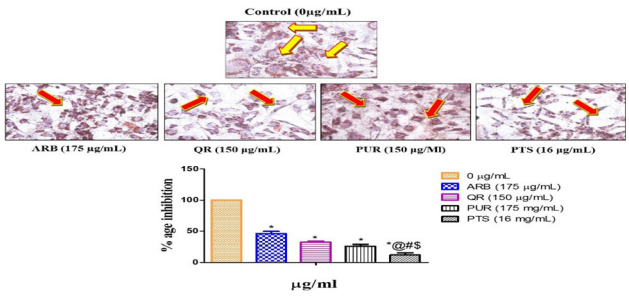
Abstract #27

Anti-adipogenic and attenuation of fatty acid uptake effects of selected pharmacological compounds of stilbene, quinones, and flavonoid on 3T3-L1 pre-adipocytes

Bedi Onkar[1,2,3], Aggarwal Savera[2], Trehanpati Nirupmab Ramakrishna Gayatri[2], Krishan Pawan[1]

[1]Chitkara College of pharmacy, Chitkara University, Punjab, India, [2]Department of Molecular and Cellular Medicine, ILBS, New Delhi, India, [3]Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, Punjab, India.

Introduction: In metabolic disorders like obesity, NAFLD and T2DM, adipocytes are dysfunctional. Hence, pharmacological interventions have importance in preventing differentiation of adipocytes and stimulating lipid uptake.
Objectives: We investigated the effects of Arbutin (ARB), Purpurin (PUR), Quercetin (QR) and Pterostilbene (PTS) on adipocytes differentiation and lipid-uptake using 3T3L-1 adipocytes. Further in-silico docking studies were performed to investigate interactions of ARB, PUR, QR, and PTS with beta-ketoacyl reductase (KR) and thioesterase (TE) domains of fatty acid synthase (FAS) enzyme.
Methods: Mature 3T3-L1 adipocytes were used to investigate the anti-adipogenic effect of selected pharmacological agents by oil red O (ORO) staining and in-vitro fatty acid uptake analysis. Molecular docking studies were performed to predict the binding interactions of selected compounds with KR and TE domains of FAS enzyme.
Results & Conclusion: The LD50 of four pharmacological agents (ARB, PUR, QR and PTS) was 175, 150, 125 and 8 µg/mL respectively. All these agents significantly decrease the adipocytes differentiation & shown the stimulatory effect on fatty acid uptake in 3T3L-1 adipocytes. However, PTS (16 µg/mL;12.05%; $p < 0.05$) and PUR (175 µg/mL;26.21%; $p < 0.05$) proved to be anti-adipogenic whereas ARB (175 µg/mL; 64325.5 RFU; $p < 0.05$) QR (150 µg/mL; 43021 RFU; $p < 0.05$) shown significant effect in fatty acid uptake, compared to others. Similarly, all the compounds displayed significant binding interactions with KR and TE domains of FAS enzyme, supporting the results of in vitro studies.



Abstract #538

Assessing the role of hepatology nurses in the management of patients with advanced liver disease in the outpatient setting.

Soosapilla K[1], Fraser M[1], Stratton E[1], Lama T[1], Xie S[1], Davison S[1], Shackel N[1,2], Prakoso E[1,3]

[1]Gastroenterology Department, Liverpool Hospital, Sydney, New South Wales, Australia, [2]The University of New South Wales, Sydney, New South Wales, Australia, [3]The University of Sydney, Sydney, New South Wales, Australia

Introduction: Patients with advanced liver disease (ALD) are at risk of cirrhosis complications, drug-related side effects and non-adherence. Since July 2016, the hepatology nurses became involved in their management in our hospital.
Objectives: To assess clinician and patient satisfaction with the involvement of nurses in the management of ALD, and to identify factors that require improvement.
Methods: Survey study consisting of two groups, 14 patients and 11 clinicians (doctors, nurses, allied health staff) was conducted between April-May 2019.
Results: Patients found hepatology nurses were helpful (43.8%) and easy to communicate (37.5%). 71.4% stated the nurses adequately explained about their liver condition, nutrition, ascites, and no improvements are required. 42.9% have previously been managed by solely a doctor. The differences seen included increased education (21.4%), support (14.3%), and mood (7.1%). All patients and their families found the "Liver Cirrhosis" booklet helpful, however 85.7% do not use it to record information/appointments.
Clinicians stated the service has improved communication for patient and medication compliance (100%), enhanced management (90.9%), more regular contact/follow-ups (90.9%), improved nutrition knowledge (81.8%), and less patients lost to follow-up (81.8%). Other benefits included multidisciplinary follow-up (42.9%), education and support (35.7%), less hospital admissions and complications (21.4%). The monthly ALD meetings allow for update of patients (30.8%) and education opportunity (23.1%) facilitating quality patient care. 36.36% stated increased nursing resources is needed.
Conclusion: Both clinicians and patients are satisfied with the hepatology nurses involvement in the ALD patients management. An increase in nursing resources would be beneficial to improve the service.

Abstract #826

Deletion of hepatic integrin beta-1 disrupts normal liver microstructure and activates pro-fibrotic signaling

Masuzaki Ryota[1], Kanda Tatsuo[1], Ray C. Kevin[2], Karp J. Seth[2], Moriyama Mitsuhiko[3]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Nihon University School of Medicine, Tokyo, Japan, [2]Department of Surgery, Vanderbilt University Medical Center, Nashville, USA, [3]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Nihon University School of Medicine, Tokyo, Japan

Background: Understanding the basic mechanisms of fibrosis to guide therapy development is a significant unmet need. Our hypothesis is that intact integrin-extracellular matrix (ECM) interactions are essential for normal liver function. We investigated the role of integrin beta-1 both in establishing and maintaining liver microstructure after injury.
Methods: Integrin beta-1 was deleted in utero by crossing albumin-Cre mice with integrin beta-1 floxed mice. Integrin beta-1 was deleted in adult mice by injecting integrin beta1 floxed mice with AAV8-cre to delete integrin beta1 or AAV8-eGFP as controls.
Results: Livers in both integrin beta-1 null and control mice were grossly normal at birth and at 4 weeks of age. In contrast, microscopic examination of the liver demonstrated marked disorganization. Integrin beta-1 null mice contained hepatocytes that varied in size and were arranged irregularly and developed fibrosis in 4 months of age. Transforming growth factor (TGF)-beta1 expression and extracellular signal-regulated kinase (ERK)1/2 phosphorylation was increased in integrin null mice. Integrin beta-1 null mice developed disordered architecture 3 weeks after partial hepatectomy. Histology showed architectural disorder in the hepatocyte-specific integrin beta-1 null mice. Canaliculi were disordered and star-shaped. Sirius Red staining demonstrated extensive fibrosis. In primary sandwich cultures, hepatocytes lacking integrin beta1 were irregularly shaped and were unable to form normal canaliculi. Loss of integrin beta1 led to doubling of the concentration of TGF-beta1 in the conditioned media compared to controls ($P < 0.001$).
Conclusion: These results suggest that interactions between hepatocytes and ECM play a critical role in the development of hepatocyte polarity and to prevent fibrosis.

Abstract #1067

Paneth cells drive microbial induced signals to promote angiogenesis and regulate portal hypertension

Hassan Mohsin[1], Moghadamrad Sheida[1], Sorribas Marcel[2], Muntet Sergi[1], Kellmann Phillp[1], Trentesaux Coralie[4], Fraudeau Marie[4], Nanni Paolo[6,7], Wolski Witold[6,7], Hapfelmeier Siegfried[5], Wiest Reiner[2,3], Shroyer Noah[8], Romagnolo Beatrice[4], Gottardi Andrea. De[1,3]

[1]Department of Biomedical Research, Hepatology, [2]Gastroenterology, [3]University Hospital of Bern and University Clinical Visceral Surgery and Medicine, [4]Switzerland, Institut Cochin, INSERM, Biomedical Research, Oncogenesis of Digestive Epithelia, Paris France, [5]Institut für Infektionskrankheiten, [7]Bern, Switzerland, Functional genomic center-ETH Zurich, [8]Switzerland, Gastroenterology and Hepatology, Baylor College of Medicine, Houston, Texas, USA.

Introduction: The number of Paneth cells (PCs) is increased in portal hypertension and in the presence of bacteria. We investigated the mechanisms by which these cells can contribute to the regulation of portal pressure.
Methods: Math-1 $^{Lox/Lox}$VillcreER^{T2} or control mice were injected three consecutive doses of tamoxifen before undergoing PPVL or sham surgery. we studied the effects on hemodynamic parameters, on the proliferation of blood vessels and on the expression of genes regulating angiogenesis. Intestinal organoids were cultured to study the composition of their secreted products by proteomics and their effects on the proliferation and tube formation of endothelial cells (ECs). *In vivo* confocal laser endomicroscopy was used to confirm the findings on blood vessel proliferation.
Results: Portal hypertension was significantly attenuated in PC-depleted mice compared to control mice and was associated with a decrease in portosystemic shunts. Depletion of PCs also resulted in a significantly decreased density of intestinal and mesenteric blood vessels. Tube formation and wound healing responses were significantly decreased in ECs treated with conditioned media from PC-depleted intestinal organoids exposed to intestinal microbial-derived products. Proteomic analysis of conditioned media in presence of PCs revealed the abundance of factors regulating angiogenesis. *In vivo* endomicroscopy showed decreased vascular proliferation in absence of PCs.
Conclusions: The in vivo and in vitro results presented here suggest that intestinal flora and microbial-derived factors positively regulate PCs to secrete not only antimicrobial peptides, but also pro-angiogenic signaling molecules, thereby promoting intestinal and mesenteric angiogenesis and regulating portal hypertension.

Abstract #1246

MIP1β, sEselectin, Fractalkine and HLADR as early prognostic markers to discriminate systemic inflammatory responses syndrome (SIRS) from acute on chronic liver failure patients in 6 h of admission: a single centre prospective study

Rashi Sehgal, Sonal Agrawal, Sadam Hussain Bhat, Mojahidul Islam, Rakesh Kumar, Rakhi Maiwal, Shiv K Sarin, Nirupma Trehanpati

Background and Aim: ACLF is a clinical syndrome of severe liver injury characterised by a release of deregulated pro and anti-inflammatory cytokines presenting systemic inflammatory responses (SIR) leading to multiple organ failure and high short-term mortality. There are no early prognostic or diagnostic markers to discriminate ACLF SIRS from ACLF. We aimed to identify the early marker of ACLF SIRS within 6–24 h.
Methods: A panel of 40 cytokines, chemokines and growth factors were profiled using Procartaplex high sensitivity immunoassay using Luminex 200 technology in plasma of ACLF (Gr.A, n = 15) and ACLF SIRS (Gr.B, n = 25) at the time of admission and following 6 and 24hrs, D3 and D7. Gene expression studies were analysed by qRT PCR and represented with fold change in mRNA levels of cytokines. Wilcoxon signed ranks test was used for correlation analysis with MELD and AARC score.
Results: Enhanced mRNA expression of cytokine storm of pro-inflammatory cytokines; IL-1β, IL-6, IL-12, IL-17, IL-18, TNF-ά and IFN-ϒ differentiated Gr.B from Gr.A at 0 h.
Among all the 40 analytes in immunoassay, significant increase in concentration of 10 analytes including MIP1-β, IL-18, sEselectin, MIF, Fractalkine, CXCL5, CXCL11 ($p > 0.05$) was observed in Gr.B.

In Gr.A, 6 out of 11patients developed increased pulse rate > 90,, respiratory rate < 20, temperature < 37 and TLC < 12 within 6 h of admission leading to ACLF-SIRS.

We have observed increased MIP-1β, sEselectin and Fractalkine (> 100 pg/ml, $p < 0.015$; 60000 pg/ml, < ; 400 pg/ml, $p < 0.035$) with in 6 h in these patients.
Conclusion: This prospective study suggests that MIP-1β, sEselectin, Fractalkine and HLA-DR can be used as the early prognostic markers of SIRS in patients with ACLF.

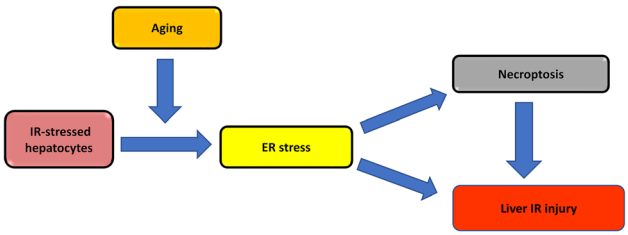
Abstract #2022

Aging aggravated liver ischemia and reperfusion injury by promoting hepatocyte necroptosis in an endoplasmic reticulum stress-dependent manner

Wang Xiaowei[1], Zhong Weizhe[1], Rao Zhuqing[2], Wang Ping[1], Zhou Haoming[1] and Wang Xuehao[1]

[1]Hepatobiliary/Liver Transplantation Center, The First Affiliated Hospital of Nanjing Medical University, Research Unit of Liver Transplantation and Transplant Immunology, Chinese Academy of Medical Sciences, Nanjing, China, [2]Department of Anesthesiology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China.

Introduction: Aggravated liver ischemia and reperfusion (IR) injury has been reported in aged mice. Necroptosis inhibition showed no crucial effect on hepatic IR injury in the young mice.
Objectives: We aimed to determine whether and how necroptosis affected liver IR injury in aged mice.
Methods: The young (8w) and aged (100w) mice were subjected to liver IR model. Liver injury, hepatocyte necroptosis and endoplasmic reticulum (ER) stress were analyzed in different groups.
Results: Significantly increased liver necroptosis was found in aged mice post IR as compared with the young mice. Inhibiting necroptosis by Nec-1 s decreased intrahepatic inflammation, hepatocyte necroptosis and liver injury post IR in the aged mice, with no significant effects in the young mice. Furthermore, IR triggered ER stress activation in both the young and aged mice, and enhanced ER stress was observed in aged mice post IR. Administration of 4-PBA, one of the ER stress antagonists, alleviated liver IR injury both in the young and aged mice. However, ER stress inhibition reduced hepatocyte necroptosis in the aged mice, but not in the young mice. In contrast, ER stress activation by tunicamycin aggravated liver IR injury and increased hepatocyte necroptosis in both the young and aged mice.
Conclusions: Aging increased ER stress in IR-stressed hepatocytes, leading to aggravated necroptosis and liver IR injury. Our study demonstrated a novel mechanism of ER stress in regulating hepatocyte necroptosis in aged livers post IR, which would be a potential therapeutic target to reduce liver IR injury in elderly patients.



Abstract #2028

Three-dimensional tumor models to study crosstalk between hepatoma cells and endothelial cells in hepatocellular carcinoma

Savneet Kaur, Preety Rawal, Dinesh M Tripathi, Vikrant Nain, Shiv K Sarin

Institute of liver and biliary Sciences, New Delhi. Gautam Buddha University, Greater Noida

Background: In our previous studies, we reported that secretory growth factors like VEGF and TGF-β from liver endothelial cells promote epithelial to mesenchymal phenotype in the hepatoma cells.
Methods: In the current study, we developed multicellular three dimensional (3D) tumor models to study the crosstalk between hepatoma and endothelial cells in the progression of hepatocellular carcinoma (HCC). Both scaffold-based and scaffold-free 3D tumor models were developed using hydrogel-based scaffolds and ultra-low-attachment plates respectively. Spheroid morphology was studied by histological staining. The expression of stemness and mesenchymal markers in the spheroids including EpCAM and vimentin was analysed by RT-PCRs and immunoflorescence.
Results: Well-formed and compact mixed-cell tumor spheroids were successfully obtained in both scaffold-based and scaffold-free models over a period of 7 days of culture. The hepatoma-endothelial cell tumor spheroids formed were significantly enlarged in size (> 400 μm) as compared to the spheroids formed by hepatoma cells alone ($P < 0.001$). The histological structure and features of the spheroids closely mimicked the in vivo HCC-like morphology. A significant increase in tumorigenic potential was also seen in hepatoma-endothelial cells spheroids in comparison to that seen alone in the hepatoma cell spheroids. The EMT phenotype was significantly increased in the hepatoma-endothelial cell tumor spheroids as

compared to hepatoma spheroids. The study reports that endothelial cells significantly enhance the stemness and tumorigenicity of hepatoma cells in 3D tumor models.
Conclusion: Our models closely mimic the HCC environment in vivo and thus represent a useful model to study the mechanisms of complex cellular interactions in HCC niche.

Abstract #2036

TGR5/Cathepsin E signaling regulates macrophage innate immune activation in the sterile inflammatory liver injury

Zhou Haoming

Background & Aims: Although the role of plasma membrane-bound G protein-coupled bile acid receptor (TGR5) in regulating liver ischemia and reperfusion (IR) injury has been reported, the underlying mechanism remains to unclear.
Methods: We analyzed the role and underlying mechanism of TGR5 in regulating macrophage migration and M1/M2 polarization in primary murine macrophage cell cultures, IR-stressed livers of mice and peripheral blood mononuclear cells (PBMCs) from patients post IR stress.
Results: TGR5 depletion in myeloid cells aggravated liver injury with increased macrophage infiltration and enhanced inflammation in livers post IR. In vitro, TGR5-deficient bone marrow-derived macrophages (BMDMs) displayed increased mobility and enhanced proinflammatory M1 polarization. INT-777, a TGR5 agonist, enhanced the anti-inflammatory effect of TGR5 both in vivo and in vitro. Microarray profiling of WT and *TGR5*-deficient BMDMs primed with LPS revealed that *TGR5*-deficient BMDMs exhibited enhanced proinflammatory characteristics. Cathepsin E (Cat E) was the most upregulated gene in *TGR5*-deficient BMDMs, and knockdown of Cat E abolished the enhanced mobility and shift of macrophage phenotypes induced by TGR5 depletion. Moreover, Cat E knockdown attenuated liver IR injury and liver inflammation in myeloid TGR5 deficient mice. In patients undergoing partial hepatectomy, IR stress promoted TGR5 activation of CD11b + cells in PBMCs, correlating with the shift in macrophage M2 polarization. Ursodeoxycholic acid administration enhanced TGR5 activation and the trend of macrophage M2 polarization.
Conclusions: TGR5 attenuates proinflammatory immune activation by restraining macrophage migration and facilitating macrophage M2 polarization via suppression of Cat E and thereby protects against liver IR injury.

Abstract #2043

Dexmedetomidine preconditioning alleviated murine liver ischemia and reperfusion injury by promoting macrophage M2 activation via PPARγ/STAT3 signaling

Rao Zhuqing

Background: Although a protective role of dexmedetomidine in liver ischemia and reperfusion (IR) injury has been reported, the underlying mechanism remains to be determined.
Methods: A murine 70% warm liver IR model was used. Mice were randomly divided into dexmedetomidine preconditioning (DEX) and phosphate buffered saline vehicle control (VEH) groups. Bone marrow-derived macrophages (BMDMs) were used for in vitro studies.
Results: Compared to mice observed in the control group, mice in the DEX group showed reduced liver injury and diminished proinflammatory immune responses in livers post IR. In vitro, dexmedetomidine pretreatment promoted BMDMs M2 activation, as evidenced by increased Arg1 and Mrc1 gene induction, decreased iNOS gene induction, much lower levels of proinflammatory TNF-α and IL-6, and higher levels of anti-inflammatory IL-10 cytokine secretion. Signaling pathway analysis revealed that peroxisome proliferator-activated receptor-γ (PPARγ)/signal transducer and activator of transcription 3 (STAT3) activation was upregulated in BMDMs with dexmedetomidine pretreatment. Furthermore, PPARγ knockdown by siRNA not only inhibited STAT3 activation but also abrogated the promotion effects of macrophage M2 activation in BMDMs pretreated with dexmedetomidine. Finally, in vivo PPARγ inhibition in macrophages by siRNA significantly increased liver IR injury and intrahepatic inflammation in mice from the Dex group, with no significant effect in the VEH group.
Conclusions: Our results indicate that dexmedetomidine preconditioning inhibited intrahepatic proinflammatory innate immune activation by promoting macrophage M2 activation in a PPARγ/STAT3 dependent manner. Our results demonstrate a novel innate immune regulatory mechanism by dexmedetomidine preconditioning during liver IR injury.

Abstract #2049

Orphan nuclear receptor NR4A1 impedes hepatic stellate cell activation

Tripathi Dinesh M[1], Kaur Savneet[1], Rawal Preety[1], Garcia-Pagan JC[2] Sarin SK[3]

[1]Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi, India, [2]Barcelona Hepatic Hemodyanimic Lab, Hospital Clínic, IDIBAPS, CIBEREHD, Barcelona, Spain, [3]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Hepatic stellate cell (HSC) activation promotes fibrosis. Orphan nuclear receptors and their role in fibrosis remain unexplored.
Objectives: We evaluated the role of orphan nuclear receptor NR4A1 in HSC activation and liver fibrosis.
Methodology: NR4A1 expression was assessed in healthy and cirrhotic liver tissues from human subjects with different aetiologies and in healthy and cirrhotics rats [thioacetamide (TAA) and carbon tetrachloride (CCl_4)]. HSC were isolated from healthy rats, activated in vitro up to 3 passages (p0, p2, p3) and treated with the NR4A1 agonist, cytosporane B (CsnB;10 μg/ml) or vehicle (Veh; DMSO). HSC activation markers and NR4A1 expression, total NR4A1 and phosphorylated/inactivated (pNR4A1) protein expression was evaluated.
Results: In cirrhotic livers, NR4A1 protein expression was significantly increased as compared to healthy, both in humans (+200 to 350%) and rats (TAA: + 20%; CCl_4: + 49%) with an increase in expression of inactivated (phosphorylated) NR4A1 (pNR4A1, TAA: + 11%; CCl4: + 57%). In vitro data demonstrated significant induction of NR4A1 during HSC activation. NR4A1 mRNA expression was significantly increased from p0 to p2 (> 8 fold) and further up-regulated in p3 (> 30 fold) in comparison to p0 HSC. Increased NR4A1 positively correlated with HSC activation markers (αSMA, Col1a1 and PDGFBR). Pharmacological activation of NR4A1 by CsnB caused down-regulation of HSC activation markers αSMA (-93%,-97%), PDGFRβ (-84%,-86%) and Col1a1 (-49%,-75%) in comparison to vehicle-treated cells.
Conclusion: Our study demonstrates for the first time NR4A1 as a novel modulator of HSC phenotype. Inactive form of this transcription factor is highly expressed in cirrhotic livers, thereby proposing

modulation of NR4A1 activity as a promising avenue to treat chronic liver diseases.

Abstract #2051

Circulatory endothelial progenitor cells from cirrhotics enhances liver fibrosis and angiogenesis in bile duct ligated cirrhotic rats

Tripathi Dinesh M[1], Hasan Mohsin[1], Preety Rawal[1] Kaur Savneet[1], Sarin SK[2]

[1]Department of Research, Institute of Liver and Biliary Sciences, New Delhi, India, [2]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Cirrhotic patient-derived endothelial progenitor cells (EPCs) secrete higher proangiogenic factors in comparison to the control-derived endothelial progenitor cells and lead to greater enhancement of angiogenesis via interaction with resident liver endothelial cells.
Objectives: The effect of cirrhotic and control EPCs on hepatic angiogenesis and fibrosis in vivo was evaluated.
Methodology: Cirrhotic animal models were prepared (n = 10) and circulating EPCs isolated from cirrhotic and healthy human blood were cultured ex vivo and transplanted in control and patient EPC-treated group of BDL rats (n = 5). The untreated group of rats received only saline (n = 5). Rats were sacrificed 1 week after the transplantation of cells. Biochemical parameters were analysed and fibrosis was evaluated by histopathology of the liver tissues, alpha-SMA expression was evaluated by western blotting and immunohistochemistry and angiogenesis was studied by evaluating the expression of CD31 by immunohistochemistry in the treated and untreated animals.
Results: In comparison to the healthy-EPC-treated and saline-treated rats, cirrhotic-EPC-treated rats had higher ALT (204 IU/L) and bilurubin (3.4 mg/dl) ($p < 0.05$ vs both) while lower hepatic glucose (20 mg/dl) and microalbumin (30 mg/dl) low ($p = 0.05$ vs both). An increase in fibrosis (from grade 2 to 4) was observed in cirrhotic-EPC-treated rats as compared to healthy EPC-treated and saline-treated rats. Immunohistochemical data showed an enhancement of both fibrosis and angiogenesis markers, alpha-SMA and CD31 in cirrhotic EPC-treated rats as compared to healthy EPC-treated and untreated rats ($P < 0.05$).
Conclusion: The study suggests that cirrhotic patient-derived circulating EPCs lead to a significant increase in liver fibrosis by enhancing intrahepatic angiogenesis.

Poster Presentations

Abstract #276

Pharmacokinetic studies in patients with hepatic impairment: Child–Pugh Classification versus National Cancer Institute Organ Dysfunction Working Group Criteria

Weith, Ekaterina[1,2], Arold, Gerhard[1]

[1]PRA Health Sciences, Berlin, Germany, [2]Faculty of Medicine, University of Duisburg-Essen, Essen, Germany

Introduction: Hepatic cirrhosis reduces hepatic metabolism and drug clearance capacities by several mechanisms. Pharmacokinetic studies in subjects with hepatic impairment (HI) are conducted if hepatic metabolism is major elimination pathway or if a drug has a narrow therapeutic range. Most commonly accepted classification is Child–Pugh (CP) score, and majority of studies use CP. Recently, National Cancer Institute Organ Dysfunction Working Group (NCI) Criteria were introduced.
Objectives: To compare CP classification to NCI criteria in hepatic impairment studies.
Methods: Nine clinical HI studies using CP classification with a total of 303 subjects were analyzed retrospectively. NCI criteria were applied to the whole population, and shifts in the severity groups were evaluated. Demographics, comorbidities and liver laboratory parameters of subjects with hepatic impairment were analyzed.
Results: Subjects with HI were diagnosed with either cirrhosis alcoholic (52.8%) or cirrhosis of other origin (48.2%). The patients had various comorbidities, most frequently, hypertension, varices esophageal, thrombocytopenia, and portal hypertension. Re-classification according to the NCI criteria, resulted in an impressive shift in subjects with HI towards NCI normal group. The majority (73.6%) of CP mild subjects were classified as normal despite presence of cirrhosis, portal hypertension or esophageal varices.
Conclusion: Subjects with cirrhosis present with multiple comorbidities which may or may not involve liver 942laboratory parameters. Therefore, use of only NCI criteria is concerning as this could underestimate liver dysfunction and potentially put these HI subjects at risk of getting incorrect medication dosage. Despite known limitations, CP score remains the most reliable classification of HI.

Abstract #282

Hsa-miR-637 inhibits human hepatocyte proliferation during liver regeneration by targeting Med1-interacting proteins

Jing Liu[1], Ziying Lei[1], Wenxiong Xu[1], Yihua Pang[1], Bingliang Lin[1], Xiaohong Zhang[1], Yuzhi Jia[2], Zhiliang Gao[1]

[1]Department of Infectious diseases, The third affiliated hospital of Sun Yat-sen university, Guangzhou, Guangdong 501630, China, [2]Department of Pathology, Northwestern University Feinberg School of Medicine, Chicago, IL 60611-3008, USA

Introduction: Mediator complex subunit1 (Med1), a key subunit of the Mediator complex, plays a dominant role in the proliferation and differentiation of hepatocytes. MicroRNA-637 (hsa-miR-637) is a primate-specific miRNA acted as a tumor suppressor in hepatocellular carcinoma, whereas the role of hsa-miR-637 and its target genes in liver regeneration is unknown.
Objective: To illustrate the molecular machanism of Med1 and hsa-miR-637 in liver regeneration.
Methods: In this study, we used co-immunoprecipitation (Co-IP) assay, transfection, Luciferase reporter assay, functional assay by cell counting kit-8 (CCK-8), qPCR analysis of Chromatin immunoprecipitation (ChIP) samples.
Results: We showed that hsa-miR-637 suppressed the expression of peroxisome proliferator-activated receptor α (PPARA) and thyroid hormone receptor α (THRA) which are Med1-interacting nuclear receptors at the transcriptional and translational level in human liver HL-7702 cell line. The Co-IP assay using anti-PPARA and anti-THRA antibodies confirmed the interaction between Med1 and PPARA/THRA in HL-7702 cells. The transcriptional repression of hsa-miR-637 on PPARA and THRA was demonstrated by luciferase assay using hsa-miR-637 and reporter constructs containing the 3'untranslated regions (3'UTR) of PPARA or THRA. Functional assay using CCK-8 revealed that hsa-miR-637 suppressed the proliferation of HL-7702 cells. In addition, transfection of hsa-miR-637 induced cell cycle arrest of HL-7702 cells at the S phase but failed to cause apoptosis. Furthermore, the chromatin IP results indicated that

PPARA directly bound to the promoter of transcription factors β-Catenin, Mdm2 and p53.
Conclusion: This study demonstrates an anti-proliferative role of hsa-miR-637 in liver regeneration and may help understanding the regenerative process of liver.

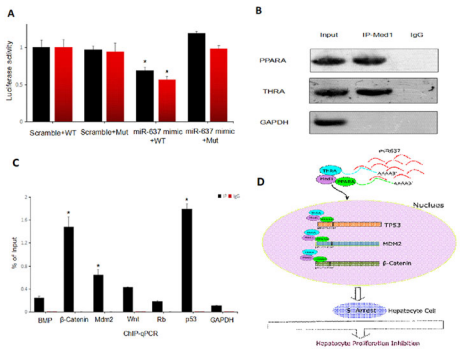


Figure A. Hsa-miR-637 suppresses the translation activities of PPARA and THRA. **B.** PPARA and THRA interacted with Med1 in HL-7702 cells. **C.** Med1/PPARA/THRA complex directly binds to promotes of β-Catenin, Mdm2 and p53. **D.** The summary graph of hsa-miR-637 mechanism in the experiment.

Abstract #311

Total glucosides of paeony decreases apoptosis of hepatocytes and inhibits maturation of dendritic cells in autoimmune hepatitis

Shen, Mengyi[1], Men, Ruoting[1], Fan, Xiaoli[1], Wang, Tingting[1], Huang, Chen[1], Wang, Haoran[1], Ye, Tinghong[2], Luo, Xuefeng[1], Yang, Li[1]

[1]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, Chengdu, China, [2]Laboratory of Liver Surgery, West China Hospital, Sichuan University, Chengdu, China.

Introduction and Objectives: Total glucosides of paeony (TGP) has anti-inflammatory, immune regulatory effects and is widely used for the treatment of autoimmune diseases. However, the role of TGP in autoimmune hepatitis (AIH) is still unknown. Here, we investigate the effect of TGP in concanavalin A (Con A) induced experimental autoimmune hepatitis (EAH).
Methods: TGP was administered before Con A challenge in C57BL/6 mice. The levels of serum liver enzymes including alanine transaminase (ALT), aspartate transaminase (AST), variations of immune cells recruited in liver, liver pathologic examines were determined 12 h after Con A injection. In vitro, we treated the hepatocyte with Con A and TGP. Moreover, we treated the immature bone marrow dendritic cells (BMDCs) with LPS and TGP for 24 h.
Results: In EAH mice, pretreatment with TGP reduced levels of ALT and AST. Moreover, decreased histopathological damage was detected in the TGP-pretreated condition. Importantly, the FCM data showed that pretreatment with TGP reduced the infiltration of mature DCs.
In vitro, pretreatment with TGP ameliorated mitochondrial membrane potential decline and hepatocytes apoptosis stimulated by Con A. The expression of Bcl2 was increased during this process, accompanied with decreased level of Bax and cleaved-Caspase3. In the meantime, the maturation of BMDCs was inhibited by TGP as evidenced by lower levels of MHCII and CD80 as compared with LPS treated cells.
Conclusion: TGP could ameliorate Con A-induced EAH by regulating apoptosis of hepatocytes and maturation of DCs. It might be a potential compound in treating AIH.

Abstract #363

Telomerase reverse transcriptase (TERT) promoter mutation correlated with intratumoral heterogeneous morphology in hepatocellular carcinoma

Effendi Kathryn[1], Kwa Wit Thun[1], Yamazaki Ken[1], Kubota Naoto[1], Hatano Mami[1], Masugi Yohei[1], Sakamoto Michiie[1]

[1]Department of Pathology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan

Introduction: Telomerase reverse transcriptase (TERT) promoter mutations are frequently identified in hepatocellular carcinoma (HCC) and are associated with stepwise hepatocarcinogenesis. However, how TERT promoter mutations (TPMs) affect clinical features and morphological patterns in HCC remains unclear.
Objectives: To elucidate correlations between TPM-positive HCCs and clinical, molecular, and morphological features.
Methods: TERT promoter sequencing was done using DNA extracted from 97 HCC clinical samples. Correlations between TPMs and clinical features and immunohistochemically subclassified HCC subgroups were evaluated. Hematoxylin and eosin-stained slides of the whole tumor cross-sectional area were semi-quantitatively assessed for morphological patterns. The percentages of tumor area occupied by early, well, moderate, and poor histological patterns were calculated as homogeneity index.
Results: TPMs were identified in 53 of 97 (55%) HCCs and were significantly associated with older patient age ($p = 0.018$) and HCV-related etiology ($p = 0.048$). Most TPM-positive cases belonged to the Wnt/β-catenin signaling-related marker-positive subgroup (60%), rather than the billiary/stem cell marker-positive subgroup (29%). Compared with TPM-negative HCCs, TPM-positive HCCs clearly exhibited intratumoral heterogeneity characterized by lower mean homogeneity index (0.800 ± 0.117 vs 0.927 ± 0.096, $p < 0.001$). Two or more heterogeneous histological patterns ($p < 0.0001$), with early or well-differentiated patterns ($p = 0.024$) are more likely seen in the TPM-positive HCCs.
Conclusion: TPM was correlated with HCV-related HCC and was less common in the billiary/stem cell markers-positive HCC subgroup. Moreover, HCC with intratumoral heterogeneity was strongly related to TPM. Our findings indicated comprehensive novel roles for TPMs, particularly in the morphologic intratumoral heterogeneity of HCC, and may inform future treatment strategies.

Abstract #489

Study on the changing of hyaluronic acid concentration in serum cirrhosis patients

Le Thi Thu Hien [1], Le Thi Thai Binh[2], Nguyen Quang Duat[3], Vu Hong Anh[2]

[1]Thai Nguyen University of Medicine and Pharmacy, [2]105 Military Hospital, [3]103 Military Hospital

Introduction: The common pathway leading to liver fibrosis and cirrhosis is growing deposition of extracellular matrix. It results from molecular and histological rearrangement of collagens, glycoproteins and hyaluronans. The main structural role in the formation of extracellular matrix plays hyaluronic acid (HA). Hyaluronic acid (HA) is an important the pathogenesis mechanism on liver fibrosis.
Objectives: Study on the changing of HA concentration in serum cirrhosis patients.
Method: Study cross-sectional descriptive on 60 cirrhosis patients at the Gastroenterology Department of 103 Military Hospital and 20

healthy volunteers, from September 2016 to March 2017. HA concentration was measured by the immunochemical method.
Results: Men accounted for 90%. Age of 40–59 accounted for 65%. Alcoholic cirrhosis accounted for 61.7%; Viral cirrhosis accounts for 26.7%. Mean HA concentration in patients group (224.64 ± 61.45 ng/ml), higher than in control group (36.08 ± 10.11 ng/ml) with $p < 0.01$. HA was associated with the degree of hepatic dysfunction, the more severe hepatic dysfunction, the higher the concentration of HA: Child–Pugh A (171.28 ± 51.89 ng/l); Child–Pugh B (214.78 ± 58.09 ng/l); Child–Pugh C (260.85 ± 42.93 ng/l) with $p < 0.01$. The HA concentration is positively correlated with the Child–Pugh score according to the regression equation: $y = 0.0265 x + 3.3105$, $r = 0.63$.
Conclusion: The concentration of HA changes in liver diseases and is affected by the severity of liver cirrhosis. Serum HA should be considered as a good marker for noninvasive diagnosis of liver fibrosis, but the combination of markers is more useful.

Abstract #491

Development of the hepatic nervous system in the ontogeny of mouse liver

Koike Naoto[1,2], Tadokoro Tomomi[2], Murata Soichiro[2], Sekine Keisuke[2,3], Ueno Yasuharu[2,3], Okamoto Satoshi[2], Uchida Yutaro[2], Takahara Ako[2], Nanjo Kazuki[2], Taniguchi Hideki[2,3]

[1]Department Surgery, Seirei Sakura Citizen Hospital, Sakura, Japan, [2]Department of Regenerative Medicine, Yokohama City University Graduate School of Medicine, Yokohama, Japan, [3]Division of Regenerative Medicine, Center for Stem Cell Biology and Regenerative Medicine, The Institute of Medical Science, The University of Tokyo, Tokyo, Japan.

Introduction: We have previously created functional human micro-hepatic tissue in mouse by coculturing human hepatic endodermal cells with endothelial and mesenchymal cells; however, they lacked portal triads (PTs) in the tissue. The PT consists of branches of the hepatic artery, portal vein, bile ducts (BDs), and autonomic nerves. The role of hepatic nervous system has not been elucidated in the ontogeny of the liver.
Objective: This study evaluated the development of the mouse hepatic nervous system using immunohistochemistry.
Methods: Liver samples of C57BL/6 mice were used at different developmental periods, beginning at E10.5 embryo until P56 of the adult mouse. Thin sections of the surface cut through the hepatic hilum (center) were examined using PGP9.5 and CK19 antibodies, markers of nerve fibers (NFs) and BD, respectively. The number of NFs and BDs were separately counted in a PT around the center and periphery of the liver, with the average values being compared between the center and the periphery at each developmental time period.
Results: NFs and BDs were found in the ductal plate of the center at E17.5. The number of NFs and BDs were significantly larger in the center than the periphery until P5. Their numbers gradually increased in the PTs until P56, with decreased differences and increased growth.
Conclusion: NFs first emerge at the center just before birth and extent toward the periphery with the BD after birth. The addition of nerve cells may support the formation of PTs in hepatic tissue engineering.

Abstract #728

Development of a hepatocyte-like cell differentiation induction method using adipose-derived stem cells (ASCs)

Maiko Koyama[1,2], Shinya Yoshida[2], Haruyo Aoyagi[1], Kosho Wakae[1], Koichi Watashi[1], Masamichi Muramatsu[1], Takaji Wakita[1], Hideki Aizaki[1]

Department of Virology II, National Institute of Infectious Diseases, Tokyo, Japan, [2]Business development department research division, Biomaster, Inc.

Purpose: Although the liver is an organ with high regenerative ability, organ transplantation is the only effective treatment in cases with non-metabolic cirrhosis or progressive liver cancer. Therefore, a treatment that complements the function of the liver or that prolongs life until transplantation is desired. Currently, Induced pluripotent stem cells (iPS), embryonic stem cells (ES), and somatic stem cells are used to generate hepatocyte-like cells in various ways. Among them, somatic stem cells derived from autologous tissue can be expected to reduce various risks. In particular, fat-derived stem cells induce less of a burden on patients. Here, we report a comparison of three major hepatocyte-like cell differentiation induction methods using adipose-derived stem cells (ASCs).
Methods: We compared three methods (three-dimensional culture (1), two-dimensional culture (2), and a patent-pending method (3)) to evaluate the different abilities of the differentiated ASCs, such as the drug metabolizing ability, albumin producing ability, and gene expression of ASCs differentiated into hepatocyte-like cells.
Results: Although (1) was superior in function as a hepatocyte compared to (2) and (3), it was difficult to obtain and evaluate stable spheroids with (1) as compared to (2) and (3).
Discussion: Development of a differentiation induction system for hepatocyte-like cells using ASCs requires acquisition of a large amount of stable cells, development of an evaluation method that provides the results can be used clinically, development of a method that differentiates various types of cells, and sieving techniques based on differentiation of the cells.

Abstract #736

Perception about own HCV and HCV status after national program implementation in Mongolia

Oyuntsetseg D[1], Suvd B[2], Enkhjargal A[3], Tumurbat B[3], Naranzul N[3], Nandintsetseg Ts[3], Erdenebayar N[4]

[1]PhD student of Ach Medical University, Mongolia, [2]National Center for Public Health, Mongolia, [3]Acedamy of Medical professionals NGO, Mongolia, [4]National Center for Blood Transfusion, Mongolia

Background: Mongolia is reporting rapid progress in scaling up hepatitis testing and treatment, adopting ambitious targets and political leadership. The "Healthy Liver" national program was started in 2017.
We aimed to compare awareness about self HCV and HBV status of the general population before and after implementing this program.
Methodology: We used questionnaires for defining the level of own status of HCV and HBV before and after the national program on liver diseases in Mongolia. The first survey was held in 2016 and a follow-up study was held in 2019. There were participated respondents of 8 aimags and 4 districts of Ulaanbaatar. Statistical analysis was done by using an SPSS-23.
Result: In the first survey were attended 3851 respondents and the follow-up survey was attended, 3782 respondents. About 4.2% of

respondents of the first survey knew about own status of HBV, 4.1% of them also knew about HCV status. While during the follow-up survey 3.6% of respondents knew about self HBV status and 8.1% of them were aware of HCV and HBV infection status. After the implementation of the program, screened respondents were raised from 26.0% to 40.2%. People who were undergone to the screening were mainly female (44.2%), residents of Ulaanbaatar city (42.0%), highly educated (master and above) (63.7%) and aged above 35 years old (45.0%).

Conclusion: The national program implementation was improved screening of the HCV and HBV. Mostly women, highly educated, and urban residents were actively involved in the screening program.

Abstract #901

Portal hypertension and myeloproliferative disorders

M. Mahmoudi[1], I. Benelbarhdadi[1], C. Berhili[1], N. Lagdali[1], M. Borahma[1], F-Z. Ajana[1]

[1]Department of Gastroenterology « Medicine C » in Ibn-Sina University Hospital Faculty of Medicine and Pharmacy, University Mohammed V-Rabat

Introduction: Myeloproliferative syndromes (MPS) are a common cause of portal system thrombosis or Budd Chiari syndrome (BC) and hepatic microcirculation. The purpose of our work is to report the clinical, etiological, therapeutic and evolutionary profile of our patients.

Materials and methods: This is a retrospective study, spanning a period of 28 years from January 1991 to May 2019, including 192 patients followed for portal hypertension (PTH) by infra-epic block on portal thrombosis (PT), 114 patients followed for vascular sinusoidal port disease and 19 patients followed for BCS

Results: The average age of our patients was 35.5 ± 14 years old. Sex F/H ratio was 3. The prevalence of MP was 7% during portal thrombosis, 5.3% during MVPS and 2% during BC. The circumstances of discovery were variable: 60.5% of patients were hospitalized for upper gastrointestinal bleeding 25.6% had hematemesis, 6.2% melena, 24% of patients presented for no specific abdominal pain, ascites 18, 6%, 5.4% for anemic syndrome, 3.9% for jaundice, and 3.9% were asymptomatic. he clinical examination showed: signs of HTP in all our patients. All patients had benefited of an abdominal ultrasonography demonstrating PT in 42.6% of cases.5 patients had a normal blood count. Osteomedullary biopsy revealed the presence of idiopathic myelofibrosis in 5 patients; essential thrombocythaemia in 7 patients; Chronic myelogenous leukemia in 3 patients and polycythemia vera in one patient

Conclusion: The prevalence of SMP in our series is 7% for portal thrombosis 5.3% for MVPS of 2% during the SBC. All our patients were in the HTP stage. Our treated patients; treatment including that of HTP, anticoagulants and hydroxyurea; have evolved after an average decline of 10.42 years ± 6.37 years.

Abstract #908

Hepatitis B infection from north-east India with special reference to its genotypes and ethnicity of affected tribal and non-tribal population

Mahanta Bipanchi[1], Das Anup Kr[2], Borkakoty Biswajit[3], Mahanta Jagadish[4]

[1]Dept of Microbiology Jorhat Medical College, Jorhat, Assam, India, [2]Assam Medical College, Dibrugarh, Assam, India, [3]RMRC ICMR, Dibrugarh, Assam, India, [4]RMRC, ICMR, Dibrugarh, Assam, India

Introduction: The prevalence of HepatitisB in India is 2–8%. But certain areas dominated by tribal population show very high prevalence like Andaman & Nicobar Islands and the Northeast India. Study of HBV genotypes help in understanding the epidemiology of HBV infection alongwith influence on disease progression and treatment response.

Objectives: To determine the HBV genotypes in Acute hepatitis, Fulminant hepatitis, Chronic hepatitis, Cirrhosis and Hepatocellular Carcinoma prevalent in Northeast India.

Methods: Cases were included from Assam Medical College, and two districts of Arunachal Pradesh. HBsAg was determined using ELISA kits and HBVDNA was extracted to perform PCR from Positive cases. DNA sequencing and TSP-based PCR was done for genotyping. The S-gene partial sequencing was also performed in approximately 50% of cases. The SHB mutation and partial RT domain, important for lamivudine resistance, was screened with reference genotype A2 and self-genotype.

Results: A total of 638 and 172 subjects were recruited from Assam and Arunachal Pradesh respectively. Most common genotype in Assam was genotype D (79%) and genotype C (13%). However, genotype C (42.9%) and genotype D (35.7%) was common in Arunachal. The difference in the two geographical regions is significant ($p = 0.0001$). Moreover, there was significant difference in distribution genotypes across the clinical categories ($p = 0.0001$). Probable escape mutant (A128V; N131T; G145A or G145P) were detected which needs further confirmation for vaccine escape mutants. Two samples showed mutation V173A in RT polymerase which is related to lamivudine resistance.

Conclusion: HBV shows genotype and clinical differences in tribal and non-tribal areas from Northeastern India and needs further studies.

Abstract #919

Portal thrombosis in normal liver: a university series

M. Mahmoudi[1], I. Ben El Barhdadi[1], H. Boutallaka[1], S. Zertiti[1], N. Lagdali[1], C. Berhili[1], M. Borahma[1], FZ. Ajana[1]

[1]Department of Gastroenterology « Medicine C » in Ibn-Sina University Hospital Faculty of Medicine and Pharmacy, University Mohammed V-Rabat

Introduction: Thrombosis of the portal vein (PVT) is defined as partial or complete occlusion of the lumen of the portal vein and/or its tributaries by a thrombus. Causes seem to be multiple. The objective of our study is to specify the etiological profile of portal hypertension (PHT) by infra-hepatic block on healthy liver.

Materials and Methods: This is a descriptive and analytical retrospective study, spanning a period of 28 years from January 1991 to May 2019, including 192 patients followed for PHT by infrahepatic block on PV

Results: The average age of our patients was 40.08 ± 16 years old with extremes ranging from 6 to 70 years. The sex ratio M/F was 0.45. 6% of patients had a history of splenectomy prior to the diagnosis of PHT. Regarding functional signs, 60.5% of patients were hospitalized for upper gastrointestinal bleeding, of which 25.6% had haematemesis, 6.2% of melena and 28.7% a combination of both, 24% of patients presented with non specific abdominal pain, 5.4% for anemic syndrome, 3.9% for jaundice, 2.3% for rectal bleeding and 3.9% were asymptomatic. The clinical examination was normal in 11.6% of cases, found ascites in 18.6% and splenomegaly in 85.3%. All

patients had undergone an abdominal ultrasound examination demonstrating a PVT in 42.6%, which was partial in 24%, complete in 6.2% and extended to the spleno-mesaric venous trunk in 12.4%. A portal cavernoma was found in 57.4% of patients, of whom 68% had a portal biliopathy on MRCP performed systematically. Etiologic assessment of thrombosis was performed in all patients, the latter was idiopathic in 45.6% of cases, related to a deficiency of coagulation inhibitors in 32.6%, myeloproliferative disease in 7% (idiopathic myelofibrosis in 5 cases, essential thrombocythaemia in 6 cases, chronic myeloid leukemia in 2 cases and polycythemia vera in 1 case), to a neoplasm in 4.7% (cholangiocarcinoma, mesenteric desmoide tumor, ganglionic lymphoma, poorly differentiated pancreatic mass, gastric adenocarcinoma and hepatocellular carcinoma in 1 case for each one), abdominal surgery in 3.9%, celiac disease in 3%, pregnancy in 1.6%, an antiphosholipid antibody syndrome or prolonged oral contraception in 0.8% for each. 14% of patients with PVT were on anticoagulant therapy because of the acute or symptomatic nature of thrombosis and when the thrombosis was related to myeloproliferative disorder. PVT regressed in 70% in anticoagulated patients, and in 4% in non-anticoagulated patients, stabilized in 30% in anticoagulated and in 96% in non-anticoagulated patients.
Conclusion: Despite a complete etiological assessment, 45.6% of PVT remain idiopathic. When the cause is found, it is in 32.6% of the cases of a deficit in coagulation inhibitors mainly combined deficit in protein C and S. La thrombose de la veine porte (TP) est définie comme une occlusion partielle ou complète de la lumière de la veine porte et/ou de ses affluents par un thrombus

Abstract #925

Prevalence of asymptomatic portal biliopathy during portal cavernoma

M. Mahmoudi[1], I. Benelbarhdadi[1], C. Berhili[1], N. Lagdali[1], M. Borahma[1], F-Z. Ajana[1]

[1]Department of Gastroenterology « Medicine C » in Ibn-Sina University Hospital Faculty of Medicine and Pharmacy, University Mohammed V-Rabat

Introduction: The portal cavernoma (PC) is a network of veins whose caliber, initially millimeter. It is the consequence of a chronic occlusion of the extrahepatic portal system. His diagnosis is mainly based on imaging. The biliary consequences of the cavernoma are related to a compression of the main bile duct. The purpose of our work was to determine the prevalence of portal biliopathy in asymptomatic patients with CP using MRI (PC-MIR).
Patients and Methods: Our prospective monocentric study conducted in a hepatogastroenterology department. We decided to perform PC-MRI in patients followed in our service for cavernoma focused on healthy liver, to determine the prevalence of asymptomatic portal biliopathy.
Results: To date 18 cases have benefited from a PC-MRI in search of a portal biliopathy, they were : 13 women and 5 men with a sex ratio (F/H) of 2.6. The average age of our patients was 47 $\pm$ 10 years old. All patients were clinically asymptomatic ie no jaundice and pruritus or other evidence of cholestasis and biologically with normal liver function in 100% of cases. Estroguodenal Fibroscopy revealed signs of portal hypertension (HTP) in 8 cases (44.4%). The etiology of CP was: a protein C and protein S deficiency in 5 cases (27.78%), a myeloproliferative syndrome with a jack 2 mutation was found in 3 cases. Celiac disease in 2 cases; sinusoidal vascular sinus disease in 2 cases; Biermer anemia in one case. CP-MRI diagnosed portal biliopathy in 10 cases (55%). The anomalies found in our cases: an isolated dilatation of VBIH (Type II) in 7 cases; dilatation of VBIH associated with dilatation of VBP (type III) in one case and lithiasis with dilatation of VBP (type II) in one case. Portal biliopathy was asymptomatic in all our patients.
Conclusion: Portal biliopathy is a common complication in patients with portal cavernoma. PC-MRI is the gold standard for the diagnosis of portal biliopathy. As a result of this examination, the prevalence of asymptomatic portal biliopathy was 55% = 0.55 [95% CI (0.34–0.66)].

Abstract #945

Esophageal varices—the most frequent and rising endoscopic finding in patients with upper GI bleed in Pakistani Population

Talal Khurshid

Objective: To find out the upper GI endoscopy findings in patients presenting with UGIB in relation to age, gender and etiology.
Material and Methods: A retrospective analysis of 3910 patients presented to GI Department from January 2011 to October 2014 for endoscopic evaluation of UGIB. The data was analyzed on SPSS20, descriptive statistics were recorded and results were analyzed as in given table.
Results: The pattern of pathologies on EGD is as shown in the below table. The majority of the patients with UGIB presented with haematemesis alone (n = 3034, 77.6%) followed by combined hemetemesis & malena (n = 540, 13.8%) and malena alone (n = 336, 8.6%). EV were the most frequent finding of UGIB (n = 2998, 76.6%) followed by PUD (n = 381, 9.7%). 93% of the patients with EV were infected by HCV. The bleeding site was accurately identified in 95.8% of patients and re-bleeding was reported in 5.8%.
Conclusions: EV is the commonest cause of UGIB in our territory manifested mainly by hemetemesis and it is due to high endemic nature of HCV infection among the male population in Central Punjab as compared to the western world which is mainly PUD. A good number of patients had normal EGD which warrants us to locate for other causes that mimic UGIB.

No	Endoscopic Finding	Number	%age	Mean Age (yrs)	Male: Female ratio
1	Esophageal varices (EV)	2998	76.6 %	46	1.95:1
2	Peptic ulcer disease (PUD)	381	9.7%	40	1:1
3	Gastritis	298	7.6%	39	1:1.5
4	Normal EGD	165	4.2%	35	1:1.4
5	Portal Gastropathy (PG)	22	0.5%	34	1:1
6	Mallory Weiss	14	0.4%	32	1:1.3
7	Gastric Neoplasm	11	0.3%	45	1.4:1
8	Fundal Varices (FV)	10	0.3%	42	1.3:1
9	Esophageal Neoplasm	10	0.3%	49	1.8:1

Abstract #995

Critical involvement of AP-1 in Hippo signaling for tumor formation and liver size control

Koo, Ja Hyun[1]

[1]Department of Physiology, College of Medicine, The Catholic University of Korea, Seoul, Korea

Yes-associated protein (YAP) and its homolog transcriptional coactivator with PDZ-binding motif (TAZ) are key effectors of the Hippo pathway to control cell growth and organ size, of which dysregulation yields to tumorigenesis or hypertrophy. Upon activation, YAP/TAZ translocate into the nucleus and bind to TEAD transcription factors to promote transcriptional programs for proliferation or cell specification. Immediate early genes, represented by AP-1 complex, are rapidly induced and control later-phase transcriptional program to play key roles in tumorigenesis and organ maintenance. Here, we

report that YAP/TAZ directly promote *FOS* transcription that in turn contributes to the biological function of YAP/TAZ. YAP/TAZ bind to the promoter region of *FOS* to stimulate its transcription. Deletion of YAP/TAZ blocks the induction of immediate early genes in response to mitogenic stimuli. *FOS* induction contributes to expression of YAP/TAZ downstream target genes. Genetic deletion or chemical inhibition of AP-1 suppresses growth of YAP-driven cancer cells, such as *Lats1/2*-deficient cancer cells as well as $G\alpha_{q/11}$-mutated uveal melanoma. Furthermore, AP-1 inhibition almost completely abrogates the hepatomegaly induced by YAP overexpression. These reveal a feedforward interplay between immediate early transcription of AP-1 and Hippo pathway function.

Abstract #1037

Hepatitis B infection from north-east India with special reference to its genotypes and ethnicity of affected tribal and non-tribal population

Mahanta Bipanchi[1], Das Anup Kr[2], Borkakoty Biswajit[3], Mahanta Jagadish[4]

[1]Senior Resident, Dept of Microbiology Jorhat Medical College, Jorhat, Assam, India, [2]Professor of Medicine, Assam Medical College, Dibrugarh, Assam, India, [3]Scientist E, RMRC ICMR, Dibrugarh, Assam, India, [4]Ex-Director and Distinguished Scientist Chair, RMRC, ICMR, Dibrugarh, Assam, India

Introduction: The prevalence of HepatitisB in India is 2–8%. But certain areas dominated by tribal population show very high prevalence like Andaman & Nicobar Islands and the Northeast India. Study of HBV genotypes help in understanding the epidemiology of HBV infection alongwith influence on disease progression and treatment response.
Objectives: To determine the HBV genotypes in Acute hepatitis, Fulminant hepatitis, Chronic hepatitis, Cirrhosis and Hepatocellular Carcinoma prevalent in Northeast India.
Methods: Cases were included from Assam Medical College, and two districts of Arunachal Pradesh. HBsAg was determined using ELISA kits and HBVDNA was extracted to perform PCR from Positive cases. DNA sequencing and TSP-based PCR was done for genotyping. The S-gene partial sequencing was also performed in approximately 50% of cases. The SHB mutation and partial RT domain, important for lamivudine resistance, was screened with reference genotype A2 and self-genotype.
Results:A total of 638 and 172 subjects were recruited from Assam and Arunachal Pradesh respectively. Most common genotype in Assam was genotype D (79%) and genotype C (13%). However, genotype C (42.9%) and genotype D (35.7%) was common in Arunachal. The difference in the two geographical regions is significant ($p = 0.0001$). Moreover, there was significant difference in distribution genotypes across the clinical categories ($p = 0.0001$). Probable escape mutant (A128V; N131T; G145A or G145P) were detected which needs further confirmation for vaccine escape mutants. Two samples showed mutation V173A in RT polymerase which is related to lamivudine resistance.
Conclusion:HBV shows genotype and clinical differences in tribal and non-tribal areas from Northeastern India and needs further studies.

Abstract #1040

Anthocyanin-rich extract of *Clitoria ternatea* flower exacerbates steatohepatitis in BALB/c mice fed a choline deficient high fat diet

Saut Horas H Nababan[1], Seruni T Khairunisa[1], Ening Krisnuhoni[2], Erni Erfan[3], Nafrialdi[4], Irsan Hasan[1], Rino A Gani[1]

[1]Hepatobiliary Division, Internal Medicine Department, Faculty of Medicine, Universitas Indonesia, Indonesia, [2]Department of Anatomy Pathology, Faculty of Medicine, Universitas Indonesia, Indonesia, [3]Department of Oral Biology, Faculty of Dentistry, Universitas Trisakti, Indonesia, [4]Department of Pharmacology and Therapeutics, Faculty of Medicine, Universitas Indonesia, Indonesia.

Backgrounds: Previous studies have shown the anti-inflammation and anti-oxidant effects of *Clitoria ternatae* (CT) flower extracts, which is related to the content of glycosylated anthocyanidins or anthocyanins. However, their potential against nonalcoholic steatohepatitis (NASH) has yet to be determined. Thus, we aimed to study the effects of anthocyanin-rich extract from CT flower on diet-induced NASH mice model.
Methods: Six-week-old BALB/c mice were divided into five groups (n = 8/group) and fed with a standard diet, a choline-deficient L-amino acid defined high-fat diet (CDAHFD) and CDAHFD + anthocyanin-rich extract of CT flower (50, 200, or 800 mg/kg BW) for 6 weeks.
Results: Anthocyanin-rich extract of CT flower induced body weight loss in a dose-dependent manner in CDAHFD-fed BALB/c mice. In groups receiving the combination of CDAHFD + 200 and 800 mg/kg BW of anthocyanin-rich extract of CT flower, two and four mice died, respectively. Histologically, hepatic steatosis and lobular inflammation were induced by CDAHFD in BALB/c mice. Anthocyanin-rich extract of CT flower further aggravated hepatic steatosis and lobular inflammation induced by the CDAHFD.
Conclusion: Anthocyanin-rich extract of *Clitoria ternatea* flower exacerbates steatohepatitis induced by CDAHFD, suggesting its hepatotoxic potential in NASH.

Abstract #1052

Establishing the use of serum mac 2 binding protein glycosylation isomer to provide non-invasive profiling of liver disease

Cao Huu Nghia[1], Nguyen Duc Truc[2]

[1]Medical Microbiology Faculty. Institut Pasteur HCM, Viet Nam, [2]Department of Biomedical, Food Analysis and Health Service. Institut Pasteur HCM, Viet Nam.

Introduction: The gold standard to use liver biopsy to probe possible liver disease is invasive and non-patient friendly. Non-invasive methods of assessing liver disease severity is needed and to fill the critical gaps in disease monitoring.
Objectives: The current study evaluates the concordance of mac 2 binding protein glycosylation isomer (M2BPGi) against commonly used biomarkers in liver disease profiling.
Methods: Archival samples were utilized and spans across patients with different degree of liver disease. Samples were well characterized with accompanying results for FIB-4, APRI and RPR. Linear regression was performed on datapoints derived from these patient samples. Concordance was also established using METAVIR scale for liver disease staging based on cutoff recommended from scientific literature.
Results:A total of 42 unique samples were profiled of which majority were in early stages of liver disease based on FIB-4 measurements.

The Pearson correlation coefficient of datapoints from M2BPGi measurements were 0.68, 0.69 and 0.65 comparing with RPR, APRI and FIB-4 respectively. The concordance among the different markers were 83.8%, 83.8% and 86.5% for RPR, APRI and FIB-4 respectively. Of the dataset, the M2BPGi discrepant results showed more severe liver disease staging. We also observed these patient group were also different in outcomes between RPR, FIB-4 and APRI.
Conclusion:M2BPGi offers significant advantage as a single marker to probe liver disease non-invasively. Blood testing is a common procedure and M2BPGi integrates well into existing management routines. Our results demonstrated excellent concordance with other biomarkers, and this complements existing methods of disease profiling.

Abstract #1245

Low-energy extracorporeal shock wave therapy improves liver fibrosis in a model of liver cirrhosis

Nakano, Toru[1,2], Ujiie, Naoto[1], Yamada, Masato[1], Sato, Chiaki[1], Nakanishi, Chikashi[1], Kamei Takashi[1]

[1]Division of Advanced Surgical Science and Technology, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan. Tel: (81) 22-717-7214, Fax: (81) 22-717-7217, [2]Division of Gastroenterologic and Hepatobiliarypancreatic Surgery, Tohoku Medical and Pharmaceutical University Hospital, Sendai, Miyagi, Japan. Tel: (81) 22-259-1221, Fax: (81) 22-259-1231

Introduction: Current treatment for liver cirrhosis could not improve liver fibrosis. Low-energy extracorporeal shock waves (LESW) have been studied as a new treatment because of its effect on angiogenesis and inhibition of fibrosis such as ischemic cardiovascular disorders and peripheral artery disease. However, the effect of LESW on liver fibrosis has never studied at all.
Objectives: The aim of this study was to verify the amelioration of liver fibrosis by LESW.
Methods: Male Wistar rats aged 7 weeks were injected with carbon tetrachloride intraperitoneally twice a week for 12 weeks. Eight rats underwent LESW therapy (0.25 mJ/mm^2, 4 Hz, 1000 shots) under general anesthesia (shock wave group). Seven rats only underwent general anesthesia (control group).
Results: Quantitative analysis showed that the area of fibrosis in the shock wave group was significantly reduced compared with the control group (11,899.9 vs. 23,525.3 pixels per field, $p < 0.001$). In the shock wave group, the mRNA expression of transforming growth factor (TGF)-β1 was significantly suppressed (0.40-fold, $p = 0.018$) and vascular endothelial growth factor-B was significantly increased (1.77-fold, $p = 0.006$) compared with the control group.
Conclusions: These results suggest that LESW therapy ameliorates liver fibrosis by reducing the expression of TGF-β1 and increasing the expression of angiogenic factors.

Abstract #1256

The effect of hyperbaric oxygen therapy (HBOT) on liver function and fibrosis using a rat model of carbon tetrachloride (CCl_4)-induced liver injury: an experimental study

Navarro, Marc Julius H[1], Bondoc, Edgardo M[1], Cervantes, Juliet G[1], Cua, Ian Homer Y.

[1]Institute of Digestive and Liver Diseases, St. Luke's Medical Center-Quezon City, Philippines

Introduction: Hyperbaric Oxygen Therapy (HBOT) is an intervention in which an individual breathes near 100% oxygen while inside a hyperbaric chamber. Numerous studies supported HBOT as an efficient therapeutic option to improve progress of diseases due to its multi-modal properties. Currently, there is paucity of data with regards to the effect of HBOT on liver diseases.
Objective: To investigate the effect of HBOT on liver function and fibrosis using a rat model of carbon tetrachloride (CCl_4)-induced liver injury.
Methods: Subjects: Fifty-one, adult, Sprague Dawley rats with CCl_4-induced liver injury. Intervention: Rats were randomized into groups: Pilot (sacrificed immediately after liver injury induction), Control (exposed to room air) and Experimental (exposed to HBOT—2.8 ATA, 120 minutes per session, daily, for total of 12 sessions). Outcome Measures: Serological parameters of liver function and histopathological evaluation of liver fibrosis
Results: This study showed that there is a significant difference between control and hyperbaric oxygen treated group in improving AST (p-value less than 0.001) and ALT (p-value less than 0.001) among rats with CCl_4-induced liver injury. On histopathologic evaluation, rats exposed to HBOT revealed very strong evidence in improving degree of hepatic fibrosis (p-value less than 0.001). Majority (94%) of rats exposed to HBOT revealed mild hepatic fibrosis, and on the other hand 76% of the control group revealed moderate fibrosis, with 24% revealing severe fibrosis.
Conclusion: HBOT revealed a very strong beneficial evidence in improving ALT, AST and degree of hepatic fibrosis among adult Sprague Dawley rats with CCl_4-induced liver injury.

Abstract #1364

YAP activation and involvement in the development of ductular reaction in pathogenesis of non-alcoholic steatohepatitis

Liang, Jia-En[2,3], Li, Shi-Ying[2,3], Zeng, Wei-Lan[2,3], He, Cai-Ping[2,3], Wang, Yan[1,2,3]

[1]Guangdong Provincial Research Center for Liver Fibrosis, Department of Infectious Diseases and Hepatology Unit, Nanfang Hospital, Southern Medical University, Guangzhou, China, [2]Biomedical Research Center, Southern Medical University, Guangzhou, China, [3]School of Pharmaceutical Sciences, Southern Medical University, Guangzhou, China.

Introduction: Abnormal expression of Yes-associated protein (YAP) was observed in liver of non-alcoholic steatohepatitis (NASH). Degree of ductular reaction (DR) tracks NASH severity.
Objectives: To characterize YAP activation in early-stage of NASH and possible involvement in DR development.
Methods: Male C57BL/6 mice fed with methionine choline-deficient (MCD) diet, thioacetamide (TAA) diet, western diet (WD), and normal control (NC) diet for modeling NASH were observed at from wk1-wk12. YAP-activity was determined with transcriptional levels of YAP target genes. Expression and location of YAP and grade of DR were measured with immunohistology. Primary mouse hepatocytes treated with palmitic acid (PA) for 24 hrs was used for in vitro analyses.
Results: Increased levels of YAP-activity and YAP protein was observed and preceded DR occurrence in all the NASH-models. In early weeks of MCD and TAA, YAP activity inside hepatocytes distant from portal areas was significantly elevated. Number of YAP-positive hepatocytes first increased but then dropped down along with disease process; meanwhile, YAP-positive ductular cells started to show up in the same area. In WD, YAP-positive ductular cells gradually expanded from portal areas, paralleled by a strong induction

of Ki67. In primary hepatocytes, PA treatment induced YAP activation and an increase of ductular-markers expression and Notch pathway activation. Inhibiting YAP-transcription by verteporfin blocked ductular-markers expression and Notch pathway; but inhibiting Notch signaling activity did not affect YAP-activity but led to downregulation of ductular-markers expression.
Conclusion: YAP activation occurs early in progressing NASH and could contribute to DR even in different pathogenesis of steatohepatitis.

Abstract #1486

Deciphering HBV-related transcription factor profile in in-vitro cell models supporting HBV genotype B replication and transcription

Roxanne Hui-Heng Chong[1], Theresa May-Chin Tan[2], Atefeh Khakpoor[1], Seng-Gee Lim [1,3], Guan-Huei Lee[1,3].

[1]Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, [2]Department of Biochemistry, Yong Loo Lin School of Medicine, National University of Singapore, [3]Department of Medicine, National University Hospital.

Background: Primary human hepatocyte (PHH) is the ideal in vitro infection model for the study of hepatitis B virus (HBV). However, in studies involving HBV genotype B or C, due to lack of high titre producing cell lines, transfection of liver-derived cell models is widely used as a surrogate for PHH infection. As multiple transcription factors, especially liver-enriched transcription factors, regulate the transcription of the virus, it is indispensable to understand the difference in expression levels of HBV-related transcription factors between cell lines and PHH, as well as their relationship to HBV replication.
Methods: We measured mRNA and protein expression of these transcription factors in eight hepatic cell lines (HepG2, HuH-7, HuH-6, JHH-4, THLE-2, L02, HC-04, and HepG2-hNTCP) and compared them with three different batches of PHHs.
Results: Liver-enriched transcription factors such as HNF1α, HNF3β, and HNF4α were undetectable or significantly lower only in L02, THLE-2, and JHH-4 cells. To further decipher the effect of transcription factors expression level on HBV genotype B replication, cells were transfected with linear HBV genotype B DNA monomer.
Conclusions: Our results demonstrate that among these cell lines, HUH-7 and HC-04 have the highest transfection efficiency for HBV genotype B variants due to the high levels of the transcription factors which support HBV replication, especially HNF4 α. JHH-4 and L02 cells which lack HNF4 α in their transcription factor profile, could not support HBV replication. This further explains the hepatotropic nature of HBV.

Abstract #1553

Detection and quantification of covalently closed circular (CCC) DNA in primary tupaia hepatocyte from *Tupaia javanica* infected with human hepatitis B virus

Kalista Kemal F[1]

Introduction: Hepatitis B virus (HBV) remains a major health problem in the world because of its complications such as cirrhosis and hepatocellular carcinoma. Lack of animal model is an obstacle for researching human HBV. Previous study showed Tupaia belangeri can be infected by human HBV. In this study we want to study capability of Tupaia javanica as an animal model for human HBV.
Methods: Primary tupaia hepatocyte (PTH) was isolated from wild adult T. Javanica. Human HBV was taken from human with HBsAg (+) and detected HBV-DNA. When PTH reached its confluence, PTH was infected by human HBV. Observation was done until day-20 post infection. Microscopic examination was done to observe cytopathic effect (CPE). Detection of HBsAg was done using ELISA. Detection and quantification of HBV-DNA and CCC-DNA was done using RT-PCR.
Results: Cytopathic effect was detected during observation. HBsAg, HBV-DNA and CCC-DNA was detected during observation. HBV-DNA was detected until the end of observation period with the peak level at D-12 post infection. CCC-DNA was detected until the end of observation period with the peak level at D-16 post infection. HBV-DNA level has same pattern like CCC-DNA level.
Conclusion: Detection of CPE, HBsAg, HBV-DNA and CCC-DNA showed PTH from T. javanica can be infected by human HBV and T. javanica can be a promising model for human HBV research.

Abstract #1621

Macrophage Nogo-B promotes acute inflammatory liver injury by MST1-mediated Hippo/YAP signaling

Rao. Jianhua[1], Yang. Wenjie[1], Qiu. Jiannan[1], Cheng. Feng[1], Lu. Ling[1], Wang. Xuehao

[1]Hepatobiliary Center, the First Affiliated Hospital of Nanjing Medical University; Key Laboratory of Liver Transplantation, Chinese Academy of Medical Sciences; NHC Key Laboratory of Living Donor Liver Transplantation, Nanjing 210029, China. Tel.: +86 025-83718836; Fax: +86 025-84670769.

Objectives: Nogo-B is an endoplasmic reticulum-residential protein with distinctive functions in different diseases, yet its function in regulating local acute sterile inflammation and liver ischemia reperfusion injury (IRI) remains unclear.
Methods: The role of Nogo-B was systematically accessed in biopsy/serum specimens from 36 patients undergoing ischemia-related hepatectomy, and in a mouse model of liver IRI. Human liver specimens were harvested before ischemia and after 15–30 minutes ischemia and 1.5–2 h post-reperfusion. In the mouse model, we created Nogo-B knockout (Nogo-B^{KO}) and myeloid-specific Nogo-B knockout (Nogo-B^{MKO}) mice to study the function and mechanism of Nogo-B.
Results: In human specimens, post-hepatectomy high Nogo-B expression was correlated with higher transaminase and severe pathological injury at postoperative 1 day. Western blot, qRT-PCR and fluorescent staining displayed Nogo-B is highly expressed on kupffer cells (KCs) in human and mice liver tissues. Compared with controls, Nogo-B^{KO} and Nogo-B^{MKO} mice were protected from IRI, with reduced reactive oxygen species (ROS), inflammatory responses in ischemic liver. In vitro, Nogo-B deficiency inhibited proinflammatory cytokines and enhanced anti-inflammatory cytokines expression on TLR4 stimulation in macrophages. Mechanistic study showed Nogo-B combined MST1, and increased MST1 phosphorylation, then promoted phosphorylation of LATS1 and YAP, and inhibited YAP activity. Interestingly, YAP inhibition or knockdown abolished anti-inflammatory effects of Nogo-B deficiency in vitro and in vivo. Thus, Nogo-B promoted inflammatory responses of macrophages that appeared dependent on MST1-mediated Hippo/YAP pathway.
Conclusion: Nogo-B is a novel adverse factor in liver IRI that promotes innate inflammation and hepatocellular damage by activating MST1-mediated Hippo/YAP pathw

Abstract #1699

Impact of transforming growth factor-beta1 gene polymorphism on the development of cirrhosis in chronic hepatitis C patients in Bangladesh.

Khan Hasan Nazia[1], Jahan Munira[1], Rahmat Raad[1], Tabassum Shahina[1]

[1]Department of Virology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka-1000, Bangladesh

Introduction: Clinical outcomes of chronic hepatitis C virus (HCV) infection may be affected by host genetic factors. TGF-β1 is one of the important mediators playing crucial role in liver injury through inflammation and fibrosis to cirrhosis and HCC.
Objectives: Present study was designed to assess whether TGF-β1 gene polymorphism is associated with cirrhosis in chronic HCV patients from Bangladesh.
Methods: Sixty HCV RNA positive patients including 30 non-cirrhotic and 30 cirrhotic patients were enrolled in this study. TGF-β1 gene SNP at position -509 bp (C/T) was carried out by polymerase chain reaction followed by restriction fragment length polymorphism (PCR-RFLP) method. Plasma TGF-β1 levels were measured by ELISA method.
Results: Among non-cirrhotic group, the distribution of CC, CT and TT genotypes were 6 (20%), 18 (60%) and 6 (20%) respectively. It was 8 (26.7%), 16 (53.3%) and 6 (20%) respectively for the cirrhotic group. In healthy controls, genotype frequencies were, CC in 9 (30%), CT in 15 (50%) and TT in 6 (20%) individuals. There was no significant difference of prevalence of CT, TT or CC genotypes or C and T allele frequencies in cirrhotic or non-cirrhotic group when compared to control group ($p > 0.05$).
Plasma TGF-β1 levels (ng/ml) were 17.49 ± 7.16, 9.98 ± 5.64 and 6.22 ± 3.49 in cirrhotic, non-cirrhotic and healthy controls groups respectively. All 60 HCV infected patients showed significantly higher plasma TGF-β1 levels compared to healthy controls ($p < 0.001$). Moreover plasma TGF-β1 was considerably higher in cirrhotic group than non-cirrhotic group ($p < 0.001$).
Conclusions: It may be concluded that there may not be significant relationship between TGF-β1-509 (C/T) polymorphism and cirrhotic conversion in chronic HCV patients. However, plasma TGF-β1 levels may be used as a biomarker in chronic HCV patients.

Abstract #1788 **"A", a standardized herbal formula, ameliorates colon-liver metastasis via alteration of host microenvironment in a mouse model**

Sung-Bae Lee[1], Jing-Hua Wang[1], Chang-Gue Son[1]

[1]Institute of Bioscience & Integrative Medicine, Daejeon University

Objective: The most harmful behavior of cancer is metastases that make a difficulty to complete cure up to now. In colon cancer, liver metastasis is most commonly observed, and its colon-liver metastatic rate is approximately 30 to 40% worldwide. Herbal formula "A" generally shows the positive pharmacological actions on colon cancer, either stage of development or patients' survival. It however did not reveal how coffee affects to colon-liver metastasis yet.
Method: This study conducted four experiments: 1) effects of "A" on tumor metastasis in "seeding phase", 2) effects of "A" on tumor metastasis in "soiling phase", 3) fluorescence tracking assay for chase of "early seeding phase" and 4) effects of "A" on "host microenvironment". C57BL/6 male mice were divided into 3 groups: Control, "A" 0.2 g/kg, and "A" 1 g/kg, respectively. The colon-liver metastasis animal model adapted spleen injection of MC38, a mouse colon cancer cell line.
Results: The pre-administration of "A" (seeding phase) significantly decreased the nodule numbers of tumor, liver weight and the fluorescence cancer cells in hepatic tissue comparing to the control ($p < 0.01$). The post-administration of "A" (soiling phase) slightly reduced the nodule numbers of tumor and liver weight but was not statistically significant comparing to control ($p > 0.05$). In addition, "A" administration suppressed adhesion molecule (VCAM1) significantly comparing to the control ($p < 0.01$).
Conclusion: Taken together, coffee administration evidently inhibits liver metastasis of colon cancer via modulations of hepatic microenvironments, likely reductions of adhesion molecules.

Abstract #1826

MiRs-21 and -29a in liver cirrhosis of viral etiology

Musabaev Erkin[1], Ibadullaeva Nargiz[1], Joldasova Elizaveta[1], Egamova Intizor[1], Khodjaeva Malika[1]

[1]Research institute of Virology, Tashkent, Uzbekistan

Introduction: Impaired regulation of miRNA expression may be one of the pathogenic factors associated with viral hepatitis in case of liver fibrosis and cirrhosis. The potential of miRNAs is huge and the study of a specific spectrum of miRNAs of importance in liver fibrosis and cirrhosis is an important area.
Objectives: We studied the expression of miRs-21 and -29a in liver cirrhosis of HBV, HCV, and HDV etiology.
Methods: Plasma specimens were collected from 24 patients with liver cirrhosis HBV, HCV and HDV etiology and 20 healthy individuals. The patients were divided into two groups according to Child Pugh score, Class A—13 patients and Class B—11 patients. Total RNA was isolated using the MiRNeasy Serum/Plasma Kit and reverse transcription followed by real-time PCR was performed using the MiScript II RT Kit and the MiScript SYBR® Green PCR Kit (QIAGEN, Germany).
Results: The average level of miRNA-21 expression in group of patients with cirrhosis was slightly elevated compared to the control group. Studying the expression of miRNA-21 showed a significant increase in group with liver cirrhosis Child Pugh Class A ($p = 0.03$) than in group with Class B. Analysis of miRNA-29a expression in these groups of patients showed undetectable level, in comparison with healthy group.
Conclusion: Improving the methods for diagnostics of liver fibrosis and cirrhosis will allow the timely detection of these conditions and may be diagnostic, prognostic for the formation of risk groups.

Abstract #1843

Ontogenic profile of NTCP in the human fetal liver: NTCP glycosylation initiating from the second trimester

Lai Pingping

Background & Aims: Sodium taurocholate co-transporting polypeptide (NTCP) plays important roles in hepatocytes, which functions as the viral entry receptor for HBV as well as the bile acid transporter. After glycosylation, NTCP matures, it then can be transferred to the plasma membrane. Notwithstanding the confirmation of NTCP expression profiles in human livers of different age groups spanning from infancy to adulthood in the previous studies, its ontogenic development, especially posttranslational modifications

such as glycosylation, in prenatal stage still remains elusive. In the current study, we aimed to uncover the expression features of NTCP during human fetal liver development and drew a comparison to its counterparts in postnatal stages.
Methods and Materials: NTCP expression in post-mortem fetal (from therapeutic abortions or stillbirths or voluntary pregnancy termination), surgical infantile (biliary atresia or non-biliary atresia pediatric patients) and adult (HBV infected or non-HBV infected or HBsAg spontaneous seroclearance patients) liver specimens were qualitatively measured via immunohistochemical (IHC) staining and then confirmed by immunofluorescent assay. Among which, liver samples from fetuses aged over 18 gestational weeks were quantified for NTCP protein expression via immunoblotting as well as NTCP mRNA expression by RT-PCR. We also performed de-glycosylation assay with PNGase-F to remove the possible carbohydrate chains of NTCP, thus exploring the extent of glycosylation of NTCP and its maturity during fetal development.
Results: In total, we analyzed NTCP expression in human liver specimens from 30 fetuses at the gestational age of 13–38 weeks, 15 infants aged between 20 days and 2 years, 45 adults aged between 25 and 81 years. IHC staining showed that NTCP was mainly found on the hepatocyte cytoplasm during fetal and infantile periods, in adult liver samples it was otherwise predominantly expressed in the plasma membrane. Also, NTCP mRNA expression in the fetal stage was not positively correlated with age whereas NTCP protein expression and glycosylation were revealed as age-dependent starting from 18 gestational weeks. Interestingly, a few examples showed no or faint NTCP staining and little NTCP protein expression compared to its counterparts at the same gestational age, while some presents in a reverse way.
Conclusions: The protein expression level and location of NTCP altered in an age-dependent manner in the fetal stage and the following postnatal period. The glycosylation of NTCP was initiated as early as 18 gestational weeks, which indirectly consolidates the HBV-NTCP-hepatocyte route of early intrauterine infection. Also, the individual heterogeneity of NTCP expression in the fetal development might also decipher the code of different immunoprophylaxis outcomes of infants born to high HBV viremia mothers.

Abstract #1880

Cathepsin L inhibitor accelerates liver regeneration in pro-fibrotic liver

Shunhei Yamashina[1], Toshifumi Sato[1], Eisuke Nakadera[1], Hiroo Fukada[1], Akira Uchiyama[1], Kazuyoshi Kon, Kenichi Ikejima[1]

[1]Department of Gastroenterology Juntendo University School of Medicine, Tokyo, Japan.

Introduction: It is clinically well-known that liver regeneration is severely impaired in fibrotic liver. Previously, we reported that CTSL-deficiency enhances liver regeneration after partial hepatectomy (PH).
Objectives: We investigated if CTSL-inhibitor can improve liver regeneration in pro-fibrotic liver.
Methods: 70% of PH was performed in C57BL/6 male mice injected with or without 10 mg/kg/day CTSL inhibitor (Z-FY-CHO) intraperitoneally for 3 days. Mice were sacrificed and restituted liver mass was calculated. To evaluate the effect of cathepsin L inhibitor on hepatic regeneration in pro-fibrotic liver, mice were treated with CCl4 intraperitoneally for 2 weeks, and subsequently injected with or without cathepsin L inhibitor for 3 days. Bromodeoxyuridine (BrdU)-immunostaining of liver sections was performed. Expression of CTSL, microtubule-associated protein IA/IB light chain 3 (LC3), p62 and cyclin D1 in the liver was evaluated by western blot analysis.
Results: Restituted liver mass at 5 days after PH in mice treated with CTSL inhibitor was higher than control mice significantly. BrdU incorporation rate was increased from $14.86 \pm 0.9\%$ to $23.74 \pm 0.8\%$ of hepatocytes 48 h after PH by treatment with CTSL inhibitor. Moreover, CTSL inhibitor enhanced increase in cyclinD1, LC3-II and p62 expression after PH more than control. In pro-fibrotic mice model, treatment with CTSL inhibitor for 3 days also augmented BrdU incorporation rate and CyclinD1 expression significantly.
Discussion: CTSL-inhibitor accelerates regenerating response in the liver after PH. Furthermore, CTSL inhibitor increased in hepatocyte proliferation in pro-fibrotic liver. Taken together, CTSL might be a new therapeutic target on disorder of liver regeneration in hepatic cirrhosis.

Abstract #1950

Changes in claudin 2 expression mediates increased gut permeability in patients with acute variceal bleed due to alcohol related cirrhosis

Kaushal K[1], Gupta V[1], Sharma S[1], Agarwal S[1], Poudel S[1], Gunjan D[1], Goswami P[1], Anand A[1], Gopi S[1], Mohta S[1], Vajpai T[1], Saraya A[1]

[1]Department of Gastroenterology and Human Nutrition, All India Institute of Medical Sciences, New Delhi, India-110029

Objectives: Changes in gut barrier with increased permeability has been recently found to have role in onset of liver disease, its progression and complications associated with cirrhosis. The study aimed at evaluating the changes in Tight Junction proteins and endotoxinemia in different Child stages of cirrhosis and change in these parameters with g.i. (gastro intestinal) bleed
Methods: A total of 76 patients with alcohol related cirrhosis (17 with variceal bleed; 59 without) and 20 controls were included. In patients with g.i. bleed, endoscopy was performed at the time of endoscopy for variceal bleed and three weeks later. IgG anti-endotoxin antibody was measured by Endocab ELISA kit (Hycult Biotechnology, Netherlands).
Results: Patents with variceal bleed had significantly lower claudin2 on IHC in both crypts and villi ($p = 0.022$ and 0.026) in comparison to those without variceal bleed. Patients with cirrhosis had overall lower claudin2 and claudin4 on IHC in both crypts and villi ($p = 0.004$, 0.004, 0.044, 0.011). Claudin2 expression improved significantly after 3 weeks of resolution of bleed ($p = 0.003$, 0.001) to baseline levels as in those without bleed. There was concomitant increase in serum endotoxinemia with bleed, but statistical significance was not achieved. Patients with cirrhosis had higher serum endotoxin levels than controls irrespective of present/ past bleed.
Conclusion: Acute changes in claudin2 in duodenal mucosa may be key mediator of changes in gut permeability associated with variceal bleed.

Abstract #2002

Herb medicine ingredient formula Danhongqing alleviates BDL-induced hepatic fibrosis by bile acid (BA) /FXRα signaling pathway in rats

Zhu Hui[1,2], Li Meng[1,2],Ping Jian[1,3,4,5],Xu Lieming[1,2,3,4,5]

[1]Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China, [2]Institute of Liver Diseases, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China, [3]Key Laboratory of Liver and Kidney Diseases, Ministry of Education, Shanghai 201203, China, [4]Shanghai Key Clinical Laboratory of Traditional Chinese Medicine, Shanghai 201203, China, [5]Key Laboratory of State Administration of Traditional Chinese Medicine, Shanghai 201203, China

Introduction: Hepatic fibrosis is a progression of chronic liver disease, which lacks effective therapies in the world. Attractively, more and more evidences show that natural products are safe and effective in the prevention and treatment of hepatic fibrosis. Danhongqing formula (DHQ)is made of Salvianolic acid B, salidroside and artesunate.
Objectives: The aim of the present study was to explore the antifibrotic effects of Danhongqing formula in rats, and its possible mechanism.
Methods: Cholestatic liver fibrosis was established by common bile duct ligation (BDL) in rats. At second day, the rats were randomly divided into a model group (BDL) and a DHQ group. The rats were treated for 26 days. Hepatic fibrosis was determined by hydroxyproline(Hyp) detection and Sirius red staining in the liver tissue. The liver function was tested in serum. The level of mRNAs encoding of collagen I (col I), the farnesoid-X-receptorα(NR1H4)or α-smooth muscle actin (α-SMA) were determined using reverse transcription-quantitative polymerase chain reaction (RT-qPCR).
Results: Danhongqing formula significantly reduced the deposition of collagen and the Hyp content in the liver tissue, efficiently inhibited the serum level of ALT, AST, TBA, TBiland DBil, ALP, γ-GT, and increased the serum level of Alb. Danhongqing formula also markedly downregulated the mRNA expression of α-SMAand collagen I, and upregulated the mRNA expression of NR1H4 in rats.
Conclusion: Danhongqing formula might be a prospective therapeutic drug for hepatic fibrosis. It may alleviate BDL-induced liver fibrosis by prompting FXRα(NR1H4)pathway.

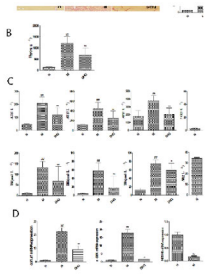


Fig.1. Danhongqing formula(DHQ) significantly alleviates BDL-induced hepatic fibrosis.The rats were grouped as follows: group 1, normal(no BDL); group 2, model group (BDL); group 3, DHQ treatment group (BDL and Salvianolic acid B 10mg/kg, salidroside 436mg/kg and artesunate 32mg/kg). (A) Hepatic fibrosis was determined by Sirius red staining in the liver tissue. Red indicated the deposition of collagen . (B) Hepatic fibrosis was determined by hydroxyproline （Hyp） detection in the Liver tissue. (C) The liver function was tested in the serum level of ALT,AST,TBA,Tbil and DBil,ALP, γ-GT,and Alb. (D) The mRNA expression of α-SMA, col1.a1,NR1H4 in liver tissue. ##$p < 0.01$ vs.normal group, **$p < 0.01$ vs. model group.*$p < 0.05$vs.model group.

Abstract #2008

Determination of a liver biochemical profile and liver ultrasonographic findings in patients with leptospirosis in a tertiary hospital

Cuaño, Carlos Rolando G.[1,a], Cuaño, Patricia Maria Gregoria M.[1], Torres, John Mark K.[1], Hernandez, Aylmer Rex B.[1], Chua, Alfredo Jr., V. [1], Ong, Janus P. [1,a]

[1]Department of Medicine, University of the Philippines Manila-Philippine General Hospital, Manila, Philippines. [a] Division of Gastroenterology, Department of Medicine, University of the Philippines Manila-Philippine General Hospital, Manila, Philippines

Introduction: Leptospirosis is an important zoonotic disease commonly found in tropical or sub-tropical countries. The most severe form is Weil's Syndrome which presents with jaundice, renal failure, and bleeding diatheses. Although jaundice occurs in 5–10% of patients with leptospirosis, no studies in Asia have focused on the liver profile of these patients. Characterization of liver function tests and ultrasonographic findings that portend a poorer diagnosis may allow for earlier recognition and intervention.
Objective: To describe the liver biochemical profile and liver ultrasonographic findings in adult patients with leptospirosis.
Methods: This retrospective correlational study reviewed all available cases of adult patients with leptospirosis admitted in the Philippine General Hospital from January 2009 to August 2018. The clinical features, liver biochemical profiles, and ultrasound findings were recorded and analyzed.
Results: Serum aminotransferases were only mildly elevated, with an AST:ALT ratio greater than 1. Mortality is associated with elevated ALT levels, which connote hepatocyte injury and subsequent apoptosis. Total and direct bilirubins, on the other hand, were significantly elevated (5.58 times and 24.89 times elevated, respectively). Alkaline phosphatase and coagulation parameters were only mildly elevated. Abdominal ultrasound showed typically unenlarged livers with normal parenchymal echogenicity, normal spleens and non-dilated biliary trees. Although jaundice was present in 57.5% of patients, this was not associated with mortality.
Conclusion: To date, no local studies have fully described the liver profile of patients with leptospirosis. Our findings are compatible with previous studies showing that leptospirosis typically presents with predominantly elevated direct bilirubin from cholestasis and systemic infection. Contrary to previous literature, however, our study found no association between jaundice and mortality.

Abstract #2066

Combined preconditioning of ischemic and rapamycin restored autophagy and alleviated liver ischemia and reperfusion injury in aged mice

Zhong weizhe[1], Zhou haoming[1], Jiang tao[1], Wang xuehao[1]

[1]Hepatobiliary/Liver Transplantation Center, The First Affiliated Hospital with Nanjing Medical University; Research Unit of Liver Transplantation and Transplant Immunology, Chinese Academy of Medical Sciences, Nanjing, China.

Introduction: Ischemic and pharmacological preconditioning has been shown to effectively protect organs against IR injury in many studies. However, controversial results have been reported regarding the role of ischemic and pharmacological preconditioning in aged animals or humans. The aim of this study was to investigate the effects of ischemic and rapamycin preconditioning on IR injury in old livers.
Objectives: we investigated the synergistic effects of ischemic and rapamycin preconditioning on regulating liver IR injury.
Methods: Mice were subjected to IR or a sham control procedure. The aged mice were randomly divided into six groups: IR (CON), IR with ischemic preconditioning (IPC), IR with rapamycin preconditioning (RAPA), IR with combined ischemic and rapamycin preconditioning (IPC + RAPA), IR with 3-methyladenine (3-MA),

IR with combined ischemic and rapamycin preconditioning with 3-MA pretreatment (IPC + RAPA + 3-MA).
Results: Aged mice had aggravated liver IR injury as compared to young mice. In aged mice following IR, IPC + RAPA but not IPC or RAPA alleviated liver injury, as evidenced by lower levels of serum ALT, improved preservation of liver architecture with lower Suzuki scores, and decreased caspase-3 activity compared with CON. In addition, increased LC3B II but decreased p62 protein expression levels in the IPC + RAPA group indicated that autophagic flux was restored by combined ischemic and rapamycin preconditioning. Furthermore, autophagy inhibition by 3-MA abrogated the protective role in the IPC + RAPA group, while no significant effects were observed in the CON group.
Conclusion: Our results demonstrated combined ischemic and rapamycin preconditioning protected old livers against IR injury through restoring autophagy activation.

Abstract #2254

Zinc compounds enhances the effects of interferon on HAV replication

Tatsuo Kanda[1], Reina Sasaki[1], Hiroshi Takahashi[1], Mariko Fujisawa[1], Ryota Masuzaki[1], Mitsuhiko Moriyama[1]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Nihon University School of Medicine, Tokyo 173-8610, Japan

Backgrounds: Outbreak of hepatitis A have recently been reported from Japan and Korea. As well as spread of HAV vaccination is important, therapeutic options to prevent the severe hepatitis A should be needed in the developed and developing countries. We recently reported the effects of zinc sulfate on HAV replication. In the present study, we focused on the effects of zinc compounds on HAV replication with or without interferon.
Methods: We examined whether HAV genotype IIIA HA11-1299 strain, which was provided by Prof. Hiroaki Okamoto, could be inhibited by the treatment of zinc compounds with or without interferon in Huh7 cells. HAV RNA was measured by real-time RT-PCR assay. Cell viabilities were evaluated by MTS assay.
Results: (1) After 72 h of treatment, 5–10 μM ZnSO4 and 5–10 μM ZnCl2 did not have cytotoxicity in HepG2 and Huh7 cells. (2) HAV replication was reduced by the treatment of 10 μM ZnSO4 or 5 μM ZnCl2 (32.3% or 62.3%, respectively). (3) HAV replication was reduced by 0.05 μg IFN with or without 5 μM ZnSO4 (16.5% or 25.1%, respectively; $p = 0.067$). (4) HAV replication was reduced by 0.05 μg IFN with or without 5 μM ZnCl2 (20.2% or 25.2%, respectively; $p < 0.067$).
Conclusion: ZnSO4 and ZnCl2 have inhibitory effects on HAV replication. Combination of these compounds with IFN has a stronger inhibition of HAV replication. Further studies about zinc compounds on IFN signaling pathways should be needed.

Infections in Liver Disease

Oral Presentations

Abstract #657

Circulating transcriptome profiles reveal distinct gene expression in patients with leptospirosis-induced acute liver failure

Limothai U.[1], Srisawat N.[2], Tangkijvanich P.[1], Chuaypen N.[1]

[1]Center of Excellence in Hepatitis and Liver Cancer, [2]Excellence Center for Critical Care Nephrology, Faculty of Medicine, Chulalongkorn University, Bangkok, 10330 Thailand

Introduction: Leptospirosis, an acute bacterial septicemic febrile disease, can present with various clinical manifestations ranging from mild self-limiting illness to life threatening with multi-organ damage including liver involvement.
Objectives: This study was aimed at identifying gene expression profiles in patients with leptospirosis-induced acute liver failure.
Methods: Whole blood samples were collected from patients with definite diagnosis of leptospirosis. Among these patients, two groups were divided based on clinical severity, including the non-severe group and the severe group with acute liver failure. Transcriptomic analysis was performed using the NanoString® nCounter® PanCancer IO 360. Genes with > 1 (log2) fold-change and p-value < 0.05 were considered statistically significant.
Results: Based on the Nanostring analysis, our data revealed that transcriptome of the severe group was significantly different from that of the non-severe group. Among these profiles, there were significant up-regulations of several genes in the sever group, which included ENO1, PTGS2, IL1R2, CD19 and NKG7. In contrast, MB21D1, CCL5, LTB, TGFB1 and EOMES were found to be down-regulated in the severe group. In addition, the severe group differed from the non-severe group in specific transcriptional pathways such as hypoxia, metabolic stress, cytokine and chemokine signaling and myeloid compartment.
Conclusion: Our data provides the first evidence that leptospirosis-induced acute liver failure is transcriptionally different from the non-severe group. These findings indicate that leptospirosis may induce acute liver failure through modulating several gene expression profiles.

Abstract #766

Prevalence and natural history in end stage of liver disease complicated with infections: a multicentral study in Central China

Zhongyuan Yang[1], Youqin Yan[2], Xiaolin Zhou[3], Yi Li[4], Wei Hu[5], Zhongji Meng[6], Xiuji Chen[7], Lvye Xu[8], Ying Zhou[9], GuodongWu[10], Zhongwei Zhang[1], Qiuyu Cheng[1], Tao Chen[1], Qin Ning[1]

[1]Department and Institute of Infectious Disease, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, [2]Department of Infectious Disease, Wuhan No.7 Hospital, Wuhan, China, [3]Department of Liver Disease, Central People 's Hospital of Yichang, Yichang, China, [4]Department

of Infectious Disease, Puren Hospital, Wuhan University of Science and Technology, Wuhan, China, [5]Department of Gastroenterology, Wuhan No.1 Hospital, Wuhan, China, [6]Department of Infectious Disease, Taihe Hospital, Shiyan, China, [7]Department of Gastroenterology, Xiangyang Central Hospital, Xiangyang, China, [8]Department of Infectious Disease, General Hospital of The Yangtze River Shipping, Wuhan, China, [9]Department of Liver Disease, The Third Hospital of Hubei Province, Wuhan, China, [10]Department of Infectious Disease, JingzhouNO.2 People's Hospital, Jingzhou, China

Background: Bacterial or fungal infection is one of the most common complications of cirrhosis, which associated with high mortality. The aim of study was to investigate the prevalence of infections, their clinical characteristics, disease progression and the short-term mortality in patients with end stage of liver disease (ELSD).

Methods: Patients with ELSD admitted for acute on chronic liver failure (ACLF), acute decompensation of liver cirrhosis (ADC), chronic liver failure (CLL) and hepatocellular carcinoma (HCC) were enrolled in the present study retrospectively from 16 centers of central China. Infectious episodes occurring on admission and in hospital were evaluated.

Results: A total of 1520 hospitalized patients with ELSD were enrolled, among which 730 (48%) patients had evidence of infections with components of 29.5% in ACLF, 65.3% in ADC, 3.7% in CLF and1.5% in HCC. Spontaneous bacterial peritonitis (50.7%, 43.6% on admission; additional 7.1% in hospital) was the most common type of infection followed by pneumonia (44.4%, 30.6% on admission; additional 13.8% in hospital), urinary tract infection (8.9%, 7.8% on admission; additional 1.1% in hospital), bacteremia (2.2%, 1% on admission; additional 1.2% in hospital) and others (1.6%, 0.8% on admission, 0.8% in hospital). 64 samples had positive culture results, candida albicans was isolated in 13 of 36 patients in pneumonia, enterococcus faecium was isolated in 4 of 13 patients in spontaneous bacterial peritonitis, and Escherichia coli was isolated in 8 of 11 patients in bacteremia. Ascites was the most common complication in the ELSD patients with infections (100% in spontaneous bacterial peritonitis; 51.9% in pneumonia; 33.8% in urinary tract infection, 43.8% in bacteremia). Mortality in patients with infections (28 days, 21.8%; 90 days, 39.2%) was higher than those without infections (28 days, 11.7%; 90 days, 21.4%, $p < 0.001$). Mortality in patients with spontaneous bacterial peritonitis (28 days, 22.5%; 90 days, 42.7%) was higher than those with pneumonia (28 days, 19.4%; 90 days, 37.2%) and urinary tract infection (28 days, 15%; 90 days, 25%).

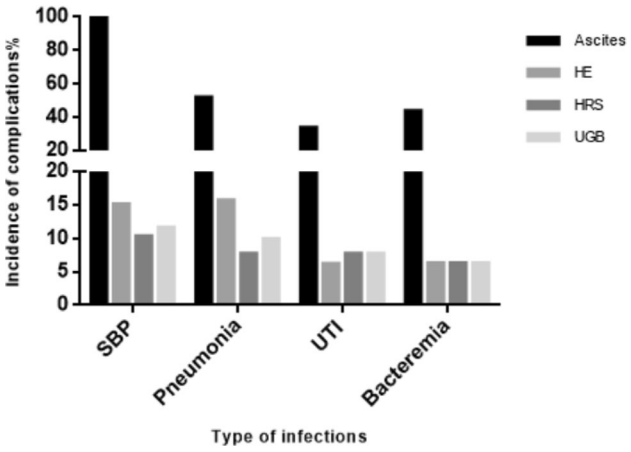
Conclusion: Spontaneous bacterial peritonitis is the most common infection in patients with ELSD on admission and pneumonia is the most common nosocomial infection. Infections were associated with poor prognosis and significantly higher mortality.

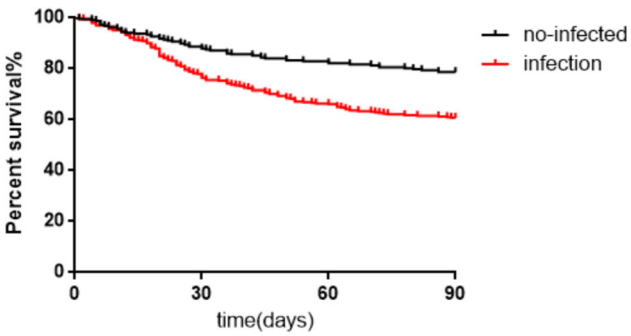
Variates	No-infection(n=790)	Infection(n=730)	P value
Age (years)	57±12	57±12	0.814
Male (%)	512(64.8)	519(71.1)	0.01
Components			
ACLF (%)	198(25.1)	215(29.5)	0.057
ADC (%)	543(68.7)	477(65.3)	0.156
CLF (%)	39(4.9)	27(3.7)	0.259
HCC (%)	10(1.3)	11(1.5)	0.827
Etiology			
HBV (%)	405(51.3)	404(55.3)	0.123
HCV (%)	80(10.1)	72(9.9)	0.932
Alcohol (%)	71(9.0)	70(9.6)	0.724
HBV + Alcohol (%)	41(5.2)	24(3.3)	0.076
AIH (%)	25(3.2)	15(2.1)	0.201
PBC (%)	40(5.1)	22(3.0)	0.051
Schistosomiasis japonica (%)	28(3.5)	30(4.1)	0.594
Others (%)	100(12.6)	93(12.7)	1.000
MAP（mmHg）	89±11	90±13	0.637
ALT(U/L)	36(22-82)	44(23-105)	0.012
AST(U/L)	61(36-128)	75(43-153)	<0.001
ALB (g/L)	32.2±10.3	29.4±5.7	<0.001
TBIL (μmol/L)	44.0(12.6-99.9)	77.1(33.2-218.1)	<0.001
Cr (mg/dl)	66(56-82)	71(56-94)	0.002
Na (mmol/L)	137.6(134.3-140.4)	136.3(132.4-139.1)	<0.001
INR	1.4(1.2-1.7)	1.7(1.4-2.2)	<0.001
WBC ($\times 10^9$/L)	5.07(3.42-7.34)	5.51(3.79-8.15)	0.002
N (x10 ^{9} /L)	3.26(2.04-5.32)	3.79(2.27-6.20)	0.001
L (x10 ^{9} /L)	0.95(0.62-1.41)	0.90(0.58-1.30)	0.067
Hb(g/L)	111(91-130)	110(90-125)	0.029
Plt ($\times 10^9$/L)	84(51-130)	76(49-113)	0.100
CRP (mg/L)	12.1(4.4-27.2)	15.1(6.8-36.6)	<0.001
PCT	0.27(0.10-0.79)	0.45(0.15-1.35)	0.001
Ferritin	153.4(69.0-648.1)	502.4(157.0-1951.2)	<0.001
ESR	10(3-32)	10(3-29)	0.484
Complications			
Ascites	221(27.9)	517(70.8)	<0.001
HRS	51(6.4)	66(9.0)	0.067
HE	73(9.2)	201(27.5)	<0.001
UGB	45(5.7)	74(10.1)	0.002
HPS	0	5(0.7)	0.025
MELD	11(6-16)	16(11-21)	<0.001
MELD-NA	13(8-19)	19(15-23)	<0.001
Transplant-free mortality			
28 days	30/257(11.7%)	81/372(21.8%)	0.001
90 days	55/257(21.4%)	147/372(39.2%)	<0.001

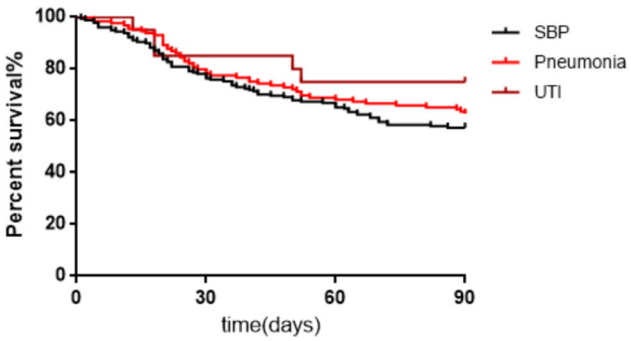
	On admission	In hospital	Total
SBP	318(43.6%)	52(7.1%)	370(50.7%)
Pneumonia	223(30.6%)	101(13.8%)	324(44.4%)
Urinary tract infection	57(7.8%)	8(1.1%)	65(8.9%)
Bacteremia	7(1%)	9(1.2%)	16(2.2%)
Biliary tract infection	4(0.5%)	1(0.1%)	5(0.6%)
Others infection	2(0.3%)	5(0.7%)	7(1%)

	Pneumonia	SBP	Bacteremia	Biliary tract infection	total
Gram-negative organism					
Escherichia coli	2	3	8	1	14
Acinetobacter baumannii	2	2	0	1	5
Klebsiella spp	2	0	2	0	4
Gram-positive organism					
Coagulase negative Staphylococi	2	3	0	2	7
Staphylococcus aureus	4	1	0	0	5
Enterococcus faecium	0	4	1	0	5
others	7	0	0	0	7
Fungus					
Candida albicans	13	0	0	0	13
Aspergillus fumigatus	4	0	0	0	4

	Ascites	HE	HRS	UGB	HPS
Pneumonia (324)	168	51	25	32	1
SBP (370)	370	56	38	43	4
UTI (65)	22	4	5	5	0
Bacteremia (16)	7	1	1	1	2
Biliary tract infection (5)	2	1	0	1	0
Others infection (7)	1	1	0	0	0







Abstract #1347

Early percutaneous catheter drainage reduces hospital stay but not mortality in patients with pyogenic liver abscess

Lee Chang-Hun[1], Kim In-Hee[1], Yang Hee-Chan[1], Yim Sung-Kyun[1], Seo Seung-Young[1], Kim Seong-Hun[1], Kim Sang-Wook[1], Lee Seung-Ok[1], and Lee Soo-Teik[1]

[1]Department of Internal Medicine, Jeonbuk National University Medical School and Research Institute of Clinical Medicine of Jeonbuk National University Hospital-Jeonbuk National University Medical School, Jeonju, Korea

Introduction: Hepatic abscess is one of the most common intra-abdominal infection with poor outcome especially in elderly patients, and the prevalence of disease has been increasing.
Objectives: To investigate the factors associated with prolonged hospital stay and mortality among patients with pyogenic liver abscess (PLA) who underwent percutaneous drainage (PCD).
Methods: We retrospectively reviewed a data from PLA patients admitted from 2005 to 2018 at Jeonbuk University Hospital. We selected patients who underwent PCD during admission period and early PCD was defined whether the procedure was done within 3 days of admission.
Results: Among 482 patients diagnosed with PLA, 250 patients who underwent PCD were enrolled for the study. The patients had a mean age of 63.6 ± 14.6 years, and mean maximal diameter of the hepatic abscess was 6.3 ± 2.7 cm and 70.8% of the lesion was single. Next, two groups were divided depending on the time period of PCD and 179 patients (71.6%) underwent PCD within 3 days of hospitalization. In baseline characteristics, abscess number and maximal abscess diameter were not different. Hospitalization period was significantly lower in the early PCD group though in-hospital mortality was not different. We checked laboratory results at 1 week after the admission and CRP and procalcitonin levels were significantly lower in the early PCD group. We further analyzed the factors related to the long-term hospitalization more than 14 days. In multivariate analysis, underlying hypertension, higher total bilirubin and lower albumin levels, and PCD inserted after 3 days of admission were independent factors associated with prolonged hospital stay.
Conclusion: Early PCD facilitated improvement of inflammatory laboratory markers and shortened the hospital stay. Early PCD may be beneficial in patients with PLA.

Table. Factors associated with prolonged hospital stay (> 14 days)

	Univariate analysis				Multivariate analysis			
	P value	HR	Lower CI	Upper CI	P value	HR	Lower CI	Upper CI
Age	0.0638	1.02	1.00	1.04				
Male sex	0.1407	0.65	0.36	1.14				
Malignancy	0.0128	4.73	1.61	20.25	0.1055	6.20	0.98	124.44
Biliary disease	0.6612	1.15	0.63	2.14				
DM	0.0425	1.87	1.04	3.49	0.5520	1.27	0.58	2.86
HTN	**0.0254**	**2.06**	**1.11**	**3.99**	**0.0451**	**2.40**	**1.04**	**5.83**
Chronic liver disease	0.1131	0.34	0.08	1.31				
Previous liver abscess history	0.6477	0.66	0.11	5.06				
Significant alcohol consumption	0.3644	0.69	0.31	1.58				
Decreased mentality at admission	0.2236	0.22	0.01	2.36				
Shock at admission	0.7051	1.17	0.54	2.68				
WBC, /mm^3	0.0058	1.08	1.02	1.14	0.0517	1.08	1.00	1.17
Hb, mg/dL	0.1637	0.90	0.76	1.04				
Na, mmol/L	0.6096	0.98	0.92	1.05				
ALT, IU/L	0.0129	1.01	1.00	1.01	0.0837	1.01	1.00	1.02
Total bilirubin	**0.0257**	**1.51**	**1.08**	**2.24**	**0.0425**	**1.93**	**1.07**	**3.84**
Albumin	**0.0001**	**0.31**	**0.16**	**0.55**	**0.0068**	**0.28**	**0.11**	**0.68**
Creatinine	0.1148	1.77	0.99	3.89				
LD	0.0307	1.00	1.00	1.00	0.9507	1.00	1.00	1.00
hsCRP, mg/L	0.0286	1.01	1.00	1.01	0.5369	1.00	1.00	1.01
PCT, ng/mL	0.1034	1.01	1.00	1.03				
Number of abscess, single vs multiple	0.4040	1.30	0.71	2.44				
Maximal abscess diameter, cm	0.0029	1.23	1.08	1.42	0.2467	1.10	0.94	1.31
PCD within 3 days of admission	**0.0111**	**0.42**	**0.20**	**0.80**	**0.0219**	**0.35**	**0.14**	**0.83**
Culture positive (blood or pus)	0.0498	1.76	1.01	3.11	0.8547	1.07	0.50	2.34

DM, diabetes mellitus; HTN, hypertension; WBC, white blood cells; Hb, hemoglobin; CRP, C-reactive protein; PCT, procalcitonin; PCD, percutaneous catheter drainage

Poster Presentations

Abstract #21

Injection practices in 2011–2015: a review using data from the Demographic and Health Surveys (DHS)

Tomoyuki Hayashi[1,2], Yvan J-F Hutin[1], Marc Bulterys[1], Arshad Altaf[3], Benedetta Allegranzi[4]

[1]Global Hepatitis Programme, World Health Organization, Geneva, Switzerland, [2]Department of Gastroenterology, Kanazawa University Hospital (WHO Collaborating Centre for Chronic Hepatitis and Liver Cancer), Kanazawa University, Kanazawa, Ishikawa, Japan, [3]ntegrated Service Delivery, World Health Organization, Western Pacific Region, Manila, Philippines, [4]Infection Prevention and Control, World Health Organization, Geneva, Switzerland.

Introduction: Reuse of injection devices to give healthcare injections decreased from 39.8% to 5.5% between 2000 and 2010, but trends since 2011 have not been described.

Objectives: We reviewed results of Demographic and Health Surveys (DHS) to describe injection practices worldwide from 2011 to 2015.

Methods: We searched the DHS for data published on injection practices conducted in countries from 2011 to 2015, extracted information on frequency (number of healthcare injections per person in the last 12 months) and safety (proportion of syringes and needles taken from a new, unopened package). We compared gender groups and WHO regions in terms of frequency and safety. We compared injection practices 2004–2010 and 2011–2015.

Results: Since 2011, 40 of 92 countries (43%) that conducted DHS surveys reported on injection practices. On average, the frequency of injection was 1.64 per person per year (from 3.84 in Eastern Mediterranean region to 1.18 in African region). Among those, 96.1% of injections reportedly used new injection devices (from 90.2% in Eastern Mediterranean region to 98.8% in Western Pacific region). On average, women received more injections per year (1.85) than men (1.41). Among countries with data in 2004–2010 and 2011–2015, the annual number of unsafe injections reduced in 81% of countries.

Conclusion: Injection practices have continued to improve in most countries worldwide, although some regions still faces unsafe practices that are not improving. Further efforts are needed to eliminate unsafe injection practices in health care settings, including through the use of reuse-prevention devices.

Abstract #84

Association of parenteral viral hepatitis with surgical pulmonary tuberculosis

Shugaeva Svetlana [1,2], Suzdalnitskiy Aleksey[1], Savilov Evgeniy[2,3], Malov Sergey[1,2], Malov Igor[1], Zarudnev Evgeniy[2]

[1]Irkutsk State Medical University, Irkutsk, Russia, [2]Irkutsk State Medical Academy of Post-Graduate Education, Irkutsk, Russia, [3]Scientific Center for Family Health and Human Reproduction Problems, Irkutsk, Russia

Background: Parenteral hepatitis can contribute to create a problem radical TB surgery.

Methods: A retrospective study included 573 full-sample adults (18–70 years; 175 women) who received surgical TB treatment between January 2017 and July 2019 at the Irkutsk Regional TB Hospital (Eastern Siberia, Russia).

Results: The association of TB with hepatitis was recorded in 151 patients (26.4%). Hepatitis C prevailed (110/72.8%) compared with hepatitis B (25/16.6%) ($p < 0.0001$) and co-infection B + C (16/10.6%) ($p < 0.0001$). HIV infection was registered in more than one third of TB patients and viral hepatitis (151/39.1%) and much less often in non-hepatitis patients (32/7.6%) ($p < 0.0001$). In the hepatitis patients group, chronic TB were more often detected (55/36.4%) compared with non-hepatitis patients (109/25.8%) ($p = 0.013$). In the same group, multidrug-resistant forms of TB were more often recorded (55 out of 103 bacterial isolators, 53.4%) than in non-hepatitis patients (98 out of 238, 41.2%) ($p = 0.037$). Radical surgeries were less often performed with the association of TB with hepatitis (74/49.0%) compared with TB without hepatitis (304/72.0%) ($p < 0.0001$).

Conclusion: The association of TB with viral hepatitis contributes to the widespread occurrence of chronic and especially contagious TB, leading to an increase in contraindications for radical surgical intervention among this cohort of patients.

Abstract #278

Pyogenic liver abscesses in the elderly: a single medical center experience in Asia

Chia-Wen Lu[1], Tsang-En Wang[2,3,4], Ching-Wei Chang[2,3,4], Zong-Sian Cai[2,3,4]

[1]Division of Gastroenterology, Department of internal medicine, MacKay Memorial Hospital, Taipei, Taiwan, [2]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan, [3]MacKay Junior College of Medicine, Nursing and Management, Taipei, Taiwan, [4]Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan

Introduction: Liver abscesses are the most common type of visceral abscess, and pyogenic liver abscess accounts for more than half 50% of liver abscess in developed country. It is a critical disease without urgent intervention and could be fatal especially for elder patients.

Objectives: To discuss the real world experience for pyogenic liver abscess in the elderly.

Methodology: From Oct 2008 to Aug 2019 in MacKay Memorial Hospital, Taipei and Tamsui branch, we retrospectively reviewed 129 elderly patients with pyogenic liver abscess.

Results: The demographic is listed in table 1, with age of 76.51 ± 8.02 years old. Days from onset of symptoms to diagnosis are 5.09 ± 4.21 days, and days of hospitalization are 23.39 ± 19.34 days. Most patients had co morbidities of DM (49.6%) and Hypertensions (52.88%). The most common symptoms include fever and chills (75%), abdomen pain (39.53%), nausea and vomiting (27.34%) and hypotension (24.22%). For blood culture, Klebsiella pneumonia (34.8%) and E. coli (7.75%) are most common, followed by viridans streptococci and Staphylococcus coagulase (-). For pus culture, most common virulent pathogens are also Klebsiella pneumonia (31.0%) and E. coli (8.53%), followed by Enterococcus and Staphylococcus coagulase (-).

Conclusion: Pyogenic liver abscess are still common in the elderly especially those with DM, hypertension or other immune compromised condition. Klebsiella pneumonia and E. coli are the most common virulent pathogen both in blood and pus culture. Early recognition and intervention is important for survival.

	Clincal charateristics of patients (N=129)		
Sex (Male:Female)	68:61	Hb (g/dL)	11.5 ± 2.12
Age (Years)	76.51 ± 8.02	WBC (10^3/uL)	33.63 ± 8.14
Time of Hospitalization (Days)	23.39 ± 19.34	Platelet (10^3/uL)	175.16 ± 97.47
Time from symtpoms to diagnosis (Days)	5.09 ± 4.21	Glucose (mg/dL)	165.61 ± 95.03
Smoking (%)	7.70%	Albumin (g/L)	2.79 ± 1.28
Alcohol usage (%)	3.70%	GOT (U/L)	107.67 ± 85.71
DM (%)	49.60%	GPT (U/L)	96.298 ± 40.22
Hypertension (%)	52.88%	Total Bilirubin (mg/dL)	1.78 ± 1.68
CAD (%)	22.00%	BUN (mg/dL)	28.75 ± 32.8
Liver cirrhosis (%)	6.30%	Creatinin (mg/dL)	1.46 ± 1.67
HIV and AIDS (%)	1%		
Biliary tract stones (%)	13.30%		
GI and biliary tract cancer (%)	11.80%		
Gastroenteritis (%)	4.80%		
abdomen surgery history (%)	12.60%		

Initial signs and symptoms	%
fever and chills	75.00%
Epgastalgia	39.53%
Right upper abdomial pain	31.25%
Nausea and vomiting	27.34%
Hypotension with SBP<90mmHg	24.22%
Dyspnea	20.16%
Cough	17.05%
Chest pain	5.51%
Diarrhea	6.98%
GI bleeding (Mild to severe)	3.13%
Right lower abdominal pain	1.55%
Chest pain	0.78%

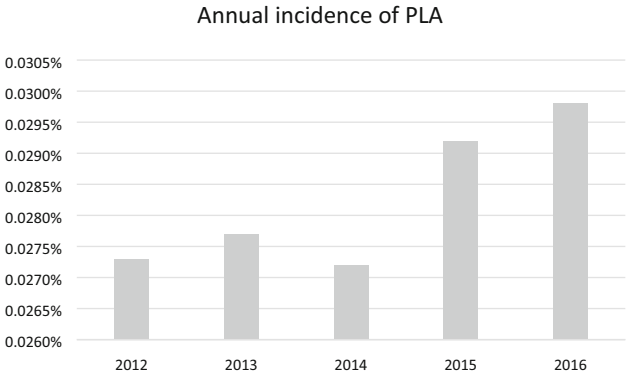
Abstract #331

Increased annual incidence of pyogenic liver abscess and its risk factors: an analysis from HIRA-NPS of South Korea, 2012–2016

Jeong-Ju Yoo[1], Sang Gyune Kim[1], Young Seok Kim[1], Soung Won Jeong[2], Jae Young Jang[2], Sae Hwan Lee[3], Hong Soo Kim[3], Baek Gyu Jun[4], Young Don Kim[4], Gab Jin Cheon[4]

[1]Department of Internal Medicine, SoonChunHyang University School of Medicine, Bucheon, Korea, [2]Department of Internal Medicine, SoonChunHyang University School of Medicine, Seoul, Korea, [3]Department of Internal Medicine, SoonChunHyang University School of Medicine, Cheonan, Korea, [4]Department of Internal Medicine, Gangneung Asan Hospital, Gangneung, Korea

Background: The epidemiology of pyogenic liver abscess (PLA) continues to change but few population-based studies have been conducted in Korea. This study investigated the epidemiology and clinical outcomes of PLA patients in current 5 years.
Methods: We used the Health Insurance Review and Assessment Service-National Patient Samples (HIRA-NPS) between 2012 and 2016. The HIRA-NPS, including approximately 1.4 million individuals, is a stratified random sample of 3% of the entire Korean population. The annual incidence rates, demographic data, underlying diseases, complications, and mortality rates were analyzed using the data.
Results: The annual incidence of PLA for all age groups increased gradually in Korea from 0.0273% (388 cases) in 2000 to 0.0298% (438 cases) in 2016. It occurred more commonly in male sex, and older age (> 65 years). Among the 2042 adult patients with PLA, 998 (48.9%) patients had diabetes mellitus, 108 (8%) patients colon cancer, and 346 (16.9%) patients biliary disease. Surgery due to PLA was in 44 (2.2%) patients, and 1 (0.05%) patient received enucleation due to endogenous endophthalmitis. The mortality rate was 8.2%. In particular the mortality rate was 13.4% in patients aged over 65 and 19.3% over 85.
Conclusion: The incidence of PLA is increasing and the number of patients with comorbidity is also increasing. Especially, the mortality of PLA tend to increase in the old age. Further surveillance of epidemiology using National Health Insurance data is needed.



Abstract #351

Diagnostic value of eosinophils and γ-glutamyltransferase (GGT) in clonorchiasis

Jiahui Lu[1], Mingxing Huang[1]

[1]Department of Infectious Diseases, The Fifth Affiliated Hospital of Sun Yat-Sen University (SYSU), Zhuhai, Guangdong, China

Introduction: Clonorchiasis, caused by Clonorchis sinensis (*C. sinensis*), is an essential food-borne parasitic disease. Nowadays, it is predicted that more than 200 million people are at risk of C. *sinensis* infection, and people that are infected with *C. sinensis* are closely related to cholangiocarcinoma, fibrosis and other human hepatobiliary diseases. Clonorchis sinensis is easy to neglect diagnosis.
Objectives: We aim to find out the diagnostic biomarkersin clonorchiasis.
Methods: In this study, we retrospectively evaluated 12 patients of clonorchiasis patients without other disease; and 13 patients with hepatitis B were selected as controls. We exclude clonorchiasis patients that have biliary tract disease such as choledocholithiasis, cholecystolithiasis etc. We evaluated the biomarkers such as Eosinophils, Eosinophis ratio and GGT of clonorchiasis patients and patients with hepatitis B.
Results: The mean value of eosinophils are 1.87*10^9/L in clonorchiasis patients and 0.14*10^9/L in patients with hepatitis b ($p < 0.001$), and maximum value in clonorchiasis patients and patients with hepatitis B are 5.65*10^9/L, 0.36*10^9/L respectively. The mean value of eosinophils ratio in clonorchiasis patients and patients with hepatitis B are 17.95%, 2.82% respectively ($p < 0.005$), and maximum value in clonorchiasis patientsand patients with hepatitis B are 47.4%, 7% respectively. The mean value of GGT in clonorchiasis patients and patients with hepatitis B are 256.1U/L, 25.69U/L respectively ($p = 0.023$), and maximum value in clonorchiasis patients and patients with hepatitis B are 1140U/L, 66U/L respectively.

Conclusions: In conclusion, higher Eosinophils, Eosinophils ratio and GGT levels in clonorchiasis patients are important predictors of clonorchiasis and they contribute to the diagnosis of clonorchiasis.

Abstract #726

Prevalence of HBV and HCV in the 40–64 age population of Mongolia

Uranbaigali Enkhbayar[1], Davaalkham Dambadarjaa[2], Bira Namdag[3], Otgonbayar Radnaa[4]

[1]Department of Clinical Laboratory, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [2]Department of Epidemiology and Biostatistics, School of Public Health, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [3]Department of Gastroenterology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [4]Deparment of Pediatrics, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia

Introduction: Mongolia is the highest prevalent of hepatitis B and C virus infections. Viral hepatitis is still decreasing when observing its movements, but the disease will remain highly prevalent until 2030.
Objectives: Using high-sensitivity test results of CLEIA we aimed to investigate the prevalence of hepatitis B and C virus, and compare levels of AST, ALT, M2BPGI in the Mongolian population in the age between 40 and 64.
Methods: In order to reflect the administrative and geographical features of Mongolia, the sampling was done at three levels: urban, province center, and rural. Immunological test was measured by chemiluminescence enzyme immunoassay (CLEIA). The statistical package for the social sciences (SPSS) version 25 was used for the statistical analyses.
Results: The survey covered 3196 people. 71.8 percent of the patients surveyed had a negative in hepatitis test. 10.1 percent had a positive HBsAg test. 17 percent had a positive anti-HCV test. 1.1 percent had both a positive both HBsAg and anti-HCV (< .0001). AST and ALT increased more frequently during co-infection. M2BPGI protein average level in the non-infected group was 1.00 C.O.I, in the HBsAg positive group 1.65 C.O.I, in the anti-HCV positive group 1.83 C.O.I, and in the co-infection group 1.87 C.O.I (< .0001).
Conclusion: 10.1 percent of 40–64 year-olds in Mongolia were infected with hepatitis B virus, and 17 percent had Hepatitis C virus and 1.1 percent had hepatitis B and C virus co-infections. Serum M2BPGi is increasing in hepatitis C virus infection and in co-infection.

Abstract #742

Clostridium difficile infection in liver transplant recipients is uncommon and does not impact long-term survival: a case-control study

Kortt, Nicholas.[1], Santhakumar, Positha.[1,2], Davis, Rebecca.[2,4], Strasser, Simone I.[1,2], McCaughan, Geoffrey W.[1,2,3], Liu, Ken.[1,2,3], Majumdar, Avik.[1,2]

[1]AW Morrow Gastroenterology & Liver Centre, Royal Prince Alfred Hospital, Sydney, Australia, [2]Australian National Liver Transplant Unit, Royal Prince Alfred Hospital, Sydney, Australia, [3]Centenary Institute of Cancer Medicine & Cell Biology, University of Sydney, Sydney, Australia, [4]Department of Infectious Diseases, Royal Prince Alfred Hospital, Sydney, Australia

Introduction: Data are conflicting on whether *Clostridium difficile* infection (CDI) in the first year after liver transplantation (LT) is associated with increased mortality.
Objectives: Determine the prevalence, risk factors and patient survival associated with CDI in LT recipients.
Method: Consecutive patients who underwent deceased-donor LT 2007–2017 were studied retrospectively. CDI was defined by positive EIA for *C. difficile* toxins A/B on diarrhoeal stool. CDI cases were matched by age, sex, LT indication and LT year to uninfected controls (ratio 1:2)
Results: 676 patients underwent LT, of which 32 (4.7%) were diagnosed with CDI: 71.8% male, median age 55 years and mean pre-LT MELD 23. Among CDI cases, the most common LT indications were HCC (28.1%), HCV (25.0%) and NASH (18.8%) cirrhosis. Baseline characteristics were similar between cases and controls. The median time to CDI post-LT was 28 days with most diagnosed in hospital (ward 56.3%, ICU 12.5%, community 31.3%). There were 3 cases of severe CDI but no CDI-related deaths or colectomies. Most responded to oral metronidazole (71.9%) with single recurrence occurring in 4 patients. Patient survival was similar between CDI cases and controls (median follow-up 6.3 years). CDI cases were more likely to have returned to theatre (34.4%vs15.6%, p = 0.04) and have longer hospital stays post-LT (35.0vs26.3 days, p = 0.03). Length of hospital stay after LT was associated with CDI on binary logistic regression (OR 1.03, 95% CI 1.00–1.06, p = 0.02).
Conclusion: CDI within 12 months post-LT is uncommon, of low severity and associated with longer hospital stay after LT.

Abstract #759

Etiology and clinical features of end-stage liver disease in Central China

Zhongyuan Yang[1], Youqin Yan[2], Xiaolin Zhou[3], Yi Li[4], Wei Hu[5], ZhongjiMeng[6], XiujiChen[7], LvyeXu[8], Ying Zhou[9], GuodongWu[10], Zhongwei Zhang[1], QiuyuCheng[1], Tao Chen[1], Qin Ning[1]

[1]Department and Institute of Infectious Disease, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, [2]Department of Infectious Disease, Wuhan No.7 Hospital, Wuhan, China, [3]Department of Liver Disease, Central People 's Hospital of Yichang, Yichang, China, [4]Department of Infectious Disease, Puren Hospital, Wuhan University of Science and Technology, Wuhan, China, [5]Department of Gastroenterology, Wuhan No.1 Hospital, Wuhan, China, [6]Department of Infectious Disease, Taihe Hospital, Shiyan, China, [7]Department of Gastroenterology, Xiangyang Central Hospital, Xiangyang, China, [8]Department of Infectious Disease, General Hospital of The Yangtze River Shipping, Wuhan, China, [9]Department of Liver Disease, The Third Hospital of Hubei Province, Wuhan, China, [10]Department of Infectious Disease, JingzhouNO.2 People's Hospital, Jingzhou, China

Objective: End-stage liver disease (ESLD) exhibits heterogeneous clinical phenotypes by etiologies, which has not been fully elucidated. This current study aims to investigate etiology and clinical features of ESLD in a multi-center cohort from Central China.
Method: A total of 1425 cirrhotic patients diagnosed of ESLD from ten tertiary hospitals in January 2013 to December 2018 were retrospectively enrolled. Infectious episodes occurring on admission and in hospital were evaluated.
Results: Of all 1425 patients, 328 were ACLF, 908 were ADC and 190 were CLF. Hepatitis B virus infection was the most common etiology (51.52%, 49.89% and 38.95%, respectively) among all the groups. Hepatitis C virus infection (8.54% and 8.23%) and alcohol

assumption (10.57% and 7.05%) were the second and third etiologies of ACLF and ADC, while alcohol assumption (17.37%) was the second in CLF. Patients with ACLF were more likely to occur in male individuals. Compared to the ADC and CLF, these patients also possessed higher levels of ALT, TBIL, Cr, INR, PCT, Ferritin and occurring of bacterial or fungal infection, hepatorenal syndrome, hepatic encephalopathy, upper gastrointestinal bleeding, and MELD score, Child–Pugh score and SOFA score, but with a lower serum sodium and PLT. Significant differences were observed in the 28-day and 90-day transplant-free mortality rate (ACLF, 29.71%, 51.23%; ADC, 9.66%, 17.97%; CLF, 8.16%, 24.49%) among all entities ($p < 0.0001$). In addition, patients with CLF showed a higher incidence of primary hepatic carcinoma compared to ACLF and ADC (24.21% vs 15.24%/17.17%).
Conclusion: ESLD exhibited heterogenous etiology profiles and clinical phenotypes, in which ACLF manifested higher incidence of SIRS, complications or extra-hepatic organ failures, and lower transplant-free short-term survival.

Abstract #944

Risk of failure and complications of endoscopic retrograde cholangiopancreatography; comparison of elderly and young Pakistani patients

Talal khurshid[1], Mashood Ali[1], Muhammad Umar[2], Tayyab Saeed Akhtar[2], Madeha Irfan[2]

[1]Department of Gastroenterology, Pims Islamabad, [2]Department of Medicine, Holy Family Hospital/Rawalpindi Medical College, Rawalpindi.

Background: Endoscopic Retrograde Cholangiopancreatography (ERCP) is an effective diagnostic and therapeutic procedure, widely performed in patients, irrespective of age. The objective of the study was to compare the risk of failure and procedural complications in young and elderly patients.
Methods & Materials: This cohort study was conducted at Holy Family Hospital, where all 362 patients who underwent the therapeutic or diagnostic ERCP performed, in the year 2014 were included and categorized as 276 young (aged 20–59 years) and 86 elderly (60 years and above) patients. The procedural and post procedural records of both study groups were followed up prospectively to compare the risk of failure of procedure and the complications during and after procedure. Chi square test was applied at 5% level of significance and Relative risks (RR) along with 95% confidence intervals (CI) were also determined through SPSS.
Results: Successful therapeutic intended procedures were observed in 95.08% of elderly and 97.32% of young patients. (RR of failure 0.64, CI 0.19–2.85, p value 0.47). Similarly Successful diagnostic intended procedures were performed in 88% of elderly and 91.1% of young patients. (RR of failure 1.35, CI 0.37–4.84, p value 0.64). At least one or more Procedural and post procedural complications were observed in 9.3% and 8.3% of elderly and young patients respectively (p value 0.77), where risk of complications was also observed to be the same with relative risk of 1.11 (CI 0.51–2.40)
Conclusion: The success rates, risk of failure and complications of the procedure in elderly was same as that of young, providing evidence that it is an equally safe procedure for elderly too.

Abstract #957

Infected hepatic cyst in patient with polycystic liver disease as extra renal manifestation of polycystic kidney disease

Dedy G. Sudrajat[1,2]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia, [2]Department of Internal Medicine, Grha Kedoya Hospital, Jakarta, Indonesia

Introduction: Polycystic liver disease (PLD) is the most manifestation of extra kidney cysts in patients with autosomal dominant polycystic kidney disease (PKD). In one study even showed 83–94%.
Case Presentation: a 75-year-old female patient, with right upper abdominal pain since 7 days, VAS is 7–8. Fever is sometimes felt. Since 20 years ago she diagnosed to have PKD. She had a kidney transplants 5 years before, but failed. The patient undergo haemodialysis for the past 2 years. Liver function showed abumin 2.8 g/dL and normal aminotransferase, PT 12.5 sec (13.9), INR 0.91, Hb 8.4 mg/dL, WBC 15.400 /uL, Thrombocytopenia (45,000/uL). Bilirubin direct 8.2 mg/dL and indirect 1.6 mg/dL. Procalcitonin 2.14 ng/mL. Abdominal CT showed polycystic kidney and liver. There is a cystic lesion in the left lobe of the liver with a size of 12x11x7cm seen as an infected cyst. The patient refuses to undergo percutaneus drainage. She given meropenem 0.5 g/12 h on the first day then 0.5 g/24 h. Two weeks after hospitalization showed good clinical outcome and normal infection parameters.
Discussion: This case is a PLD related to polycystic kidney. Infected liver cysts occur in more than 3% end-stage renal failure of PKD, but only occur in less than 1% in patients who have not end-stage. Antibiotics fail in 64–70% of cases. *E. coli* and Klebsiella are the most common species found in liver cysts. Percutaneous drainage is the best therapeutic choice. In kidney transplant patients, 46% occur recurrent cases.

Abstract #959

A comparative analysis of radical and non-radical surgical treatment of hydatid liver echinococcosis: a single-center analysis

Kaniyev Shokan[1,2], Baimakhanov Zhassulan[1], Serikuly Erbol[1], Doskhanov Maxat[1], Skakbayev Aidar[1], Medeubekov Ulykbek[1], Seisembaev Manas[1], Kausova Galina[2], Baimakhanov Bolatbek[1]

[1]Department of HPB surgery and liver transplantation, Syzganov's National Scientific Center of Surgery, 62 Zheltoksan, Almaty 050004, Kazakhstan, [2]Kazakhstan's Medical University "KSPH", Almaty 050060, Kazakhstan

Background: The aim of this study was to compare the postoperative outcome and long-term results after management of LHC by radical and non-radical surgeries.
Methods: From January 2015 to December 2017, 86 patients were treated with various surgical interventions for LHC. These patients were retrospectively divided into two groups according to the surgical method for treatment: radical methods (e.g. liver resection [LR] and pericystectomy [PCE]) and non-radical methods (e.g. echinococcectomy [EE]). Of the 86 patients, 50 (58%) underwent radical treatment, and 36 (42%) underwent non-radical treatment. The clinical data and outcomes were retrospectively analyzed.
Results: Eighty (93%) patients were considered to have been complete cured of their hydatid disease. The surgery duration in the non-radical treatment group was significantly shorter than in the radical treatment group ($p < 0.01$). There were no cases of biliary leakage in the LR patients during the postoperative period. In contrast, among

the EE patients, biliary leakage occurred in 6 (16.7%), which was significantly higher than with other modalities ($p < 0.05$). Recurrence occurred at a median of 32 months after surgery. Recurrent liver hydatid disease occurred in 6 cases (7%): radical group, 1 (2%); non-radical group, 5 (13.9%). There were no mortalities in either group in the postoperative period. The postoperative hospital stay was significantly shorter in the LR patients than in the other patients ($p < 0.01$).
Conclusion: Radical surgical treatment of LHC is more effective than non-radical surgery, resulting in a reduced recurrence rate, reduced postoperative complication rate and early recovery of patients.

Abstract #1181

Successful management of refractory multiple liver abscess by medicine and surgery joining hands

Billy Siahaan[1], Tambar Kembaren[1]

[1]Fakultas Kedokteran Universitas Sumatera Utara-RSUP. H. Adam Malik Medan

Liver abscess is a major tropical disease in Gastrointestinal Hepatology Disease. A liver abscess often occurs in low-middle income countries such as Indonesia. Two most common liver abscesses are amoebic and pyogenic liver abscess. In Medan, North Sumatera, the prevalence increases in male population especially with habitual alcoholic (tuak) consumption history.

The primary management of amebic liver abscess is with medical approach. Somehow, 15% of this condition can be refractory if treated by medical approach alone. Therefore, in some refractory cases we should work with digestive department for surgery drainage. Sometimes the secondary bacterial infection also makes this course of the disease more complex to manage, so the conjunction between two disciplined should work simultaneously to reach the optimal result.

We report a case of 40 years male with refractory Multiple liver abscess that gave incomplete response after two times being managed by medical approach with metronidazole and paramomycin as a standard treatment in combination with percutaneous aspiration of the pus. There phase CT scan showed Multiple mass in right liver lobus with hepatomegaly. After two times of incomplete response within last 1 year, we referred the patient to digestive surgeon and did Laparascopic liver abscess drainage. Escherichia Coli was found from the culture as secondary bacterial infection and we give Ceftriaxone as the antibiotic sensitivity test clue confirmed. After 2 weeks, the patient was discharged with good condition and there is no recurrence recorded in 1 year follow up from outpatient unit in our hospital.

Abstract #1225

Liver abscess, severe anemia, and spleen enlargement, medical aspect encounter biopsychosocial factor in isolated area: a case report

Rakhmad Ramadhan [1]

[1]Internist, Agats General Hospital, Asmat, Papua, Indonesia

Introduction: Liver abscess can be develop from intraabdominal infections of amoebic, pyogenic, parasites, and fungal. The dis-balancing of protective liver cells can be getting infections or abscess formation (Akhondi, 2019). The anemia etiology are complex and range from nutritional deficiencies, inflammatory process, to chronic infections (Stauder R, 2019). Spleen plays a significant role in immunosurveillance and hematopoiesis (Chapman, 2019). The combination of liver abscess, severe anemia, spleen enlargement became a challenge for diagnostic and therapeutic in isolated area.
Case Report: Male, 30 year old, came to Agats general hospital, Asmat, with chief complaint abdominal enlargement since 2 months ago, accompanied with fever. He presented anemic. Liver span 16 cm, spleen schuffner 4/8. Hemoglobin level was 4.6 g/dl. Abdominal ultrasound show hypoechoic appearance, various echogenicity, 9 cm x 10 cm diameter, at liver. He treated with ciprofloxacin and metronidazole, PRC transfusion, sulfas ferrous. The abscess size was shrinking. The abdominal pain was decrease but fullness sensation still persist.
Discussion: The abscess can develop from intraabdominal infection disseminated from the portal vein. Anemia in isolated area related to iron and nutritional deficiency, geographic factor related mud area, helminthes and malaria infection, poor hygiene, etc. Spleen enlargement can be related hematopoiesis. Due to isolated area, diagnostic and therapeutic procedure became difficult related to low education level, socio economic, and primitive thinking about healthy.
Conclusion: Liver abscess, severe anemia, and spleen enlargement have a diagnostic and therapeutic challenge in isolated area. Treat possibilities and education have an important role.

Abstract #1343

Falciform ligament abscess in adult, resolving without surgical treatment

Wijaya, Natalia Sisca[1] and Salim, Sidharta[1]

[1]Internal Medicine Department, Mitra Kemayoran Hospital, Jakarta-Indonesia

Introduction: Only few cases of falciform ligament abscess have been reported. Most cases occurred in childhood following omphalitis. Several cases of falciform ligament abscess in adult following cholecystitis and one case following a ventriculoperitoneal shunt infection have also been reported. In our review of literature, this is the first case of falciform ligament abscess without preceding omphalitis or cholecystitis; which resolved without surgical procedure.
Case Presentation:A 59 year old female presented with a 1 month history of abdominal discomfort, nausea, vomiting, weight loss and a palpable mass on her epigastrium area. Initial history, physical examination and work up lead to a diagnosis of gastric malignancy. However; discharge of purulent secretion from the biopsy site and biopsy results of PMN infiltration later on leads to a diagnosis of abscess. Culture subsequently showed E. coli infection. The patient was not amenable to surgical procedure hence she was treated with third generation cephalosporin antibiotic as guided by culture results. After 1 month of antibiotic treatment, the abscess was completely resolved.
Conclusion: Falciform ligament abscess should be considered as a rare but important illness. It presents a difficult and perplexing problem clinically and is often misdiagnosed. A soft tissue mass beneath the abdominal wall, even though not preceded by any umbilical infection, liver or gallbladder disease should lead physicians to a suspicion of falciform ligament abscess. Radiologic confirmation with ultrasound and CT scan should then be performed. Though less established, successful non-surgical treatment was applied to this case because the patient did not consent to surgical procedure.

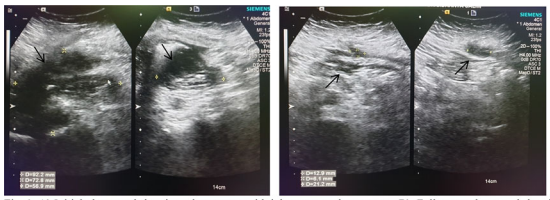


Fig. 1. A) Initial ultrasound showing a large mass with inhomogen echostructure. B) Follow up ultrasound showing reduced size of the mass 3 weeks after antibiotic therapy

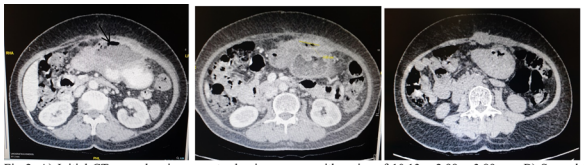


Fig 2. A) Initial CT scan showing an extra luminary mass with a size of 10.13 x 2.98 x 3.89 cm. B) Second CT scan showing reduced size of the mass to 3.02 x 1.45x 0.8 cm. C) Latest CT scan showing a complete resolution of the mass.

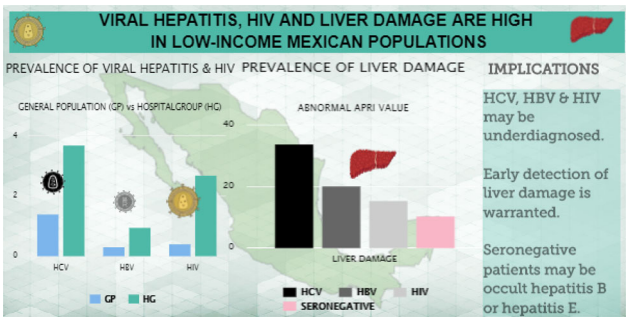
Abstract #1440

High prevalence of viral hepatitis B and C, and human immunodeficiency virus, and liver damage in seronegative patients in a low-income population in West Mexico

Laguna-Meraz S[1], Roman S.[1], Jose-Abrego A.[1], Panduro A.[1]

[1]Department of Molecular Biology in Medicine, Civil Hospital of Guadalajara-Fray Antonio Alcalde and Health Sciences University Center, University of Guadalajara, Guadalajara, Jalisco, Mexico

Introduction: The World Health Organization has sought to eliminate viral hepatitis C and B (HCV/HBV), and human immunodeficiency virus (HIV) by 2030; hence, it is important to search for populations who have the highest risk factors and potential liver damage. One such population is people who live in poverty which represents 41.9% of the population of Mexico. This subpopulation is treated at the "Civil Hospital of Guadalajara-Fray Antonio Alcalde", a large facility located in West Mexico.
Objectives: To determine the seroprevalence of HCV, HBV, and HIV, and potential liver damage in seropositive and seronegative patients.
Methods: In a cross-sectional study, 10,884 serum samples from March 1, 2016 to March 1, 2017 were retrospectively analyzed using the laboratory´s database. Repeated serologies belonging to a same patient were excluded. Stage of liver damage was determined by the indirect biomarkers APRI and FIB-4 indexes.
Results: Out of 10,884 patients, 50.1% (5454) were men and 49.9% (5430) women, the average age was 32.9 years. HCV seroprevalence was 3.7% (n = 304/8248), HBV in 0.96% (n = 80/8200) and HIV in 2.7% (n = 210/7735). Liver damage (F3-F4, APRI/FIB-4) in HCV patients was 34% (53/156), 20.4% (11/54) in HBV and 15.5% (16/103) in HIV; while 10.3% (n = 185/1804) seronegative patients had altered APRI values.
Conclusion: In low-income patients, the seroprevalence for HCV, HBV and HIV are higher than in the general population. The high rate of abnormal APRI values in seronegative patients suggests that occult HBV or hepatitis E virus could be underdiagnosed.



Abstract #1461

Predictive factors for rupture of patients with liver abscess

Ulfa Kholili[1], Herry Purbayu[1], Poernomo Boedi Setiawan[1], Iswan A Nusi[1]

GastroenteroHepatology, Internal Medicine Deparment, Airlangga University/dr Soetomo Hospital, Surabaya-Indonesia

Introduction: Rupture is the most frequent complication of liver abscess (LA) that resulted high morbidity and mortality rate.
Objectives : To analyze predictive factors for abscess rupture in patients with LA who admitted at dr Soetomo Hospital-Surabaya for period 2011–2017
Methods : Analytic observational retrospective study, consecutive sampling, secondary data from medical record. The variables were analyzed with respect to rupture of LA. Univariate analysis using chi-square test ($p < 0.25$). Multivariate stepwise logistic regression analysis was performed to identify predictive factors for rupture.
Result : Involved 138 patients that consist of 40.6% amoebic LA and 59.4% pyogenic LA. Men more dominant than women (4.3:1) with mean of age 44.80 ± 14.98 y.o. The rate of rupture was 26.81% with clinical manifestations as emphyema, peritonitis, pneumonia, and peripancreatic abscess. The overall mortality rate of LA was 5.8% where 5 cases within rupture and 3 cases without rupture. By using univariate analysis, it was revealed that pleural effusion presence, leukocytosis (> 20,000/mm^3), hyperbilirubinemia (> 4 mg/dl), hypoalbumine (< 2 gr/dl), size of lesion (> 10 cm) were associated with rupture of LA. Multivariate stepwise logistic regression analysis revealed these factors of size of lession (> 10 cm), pleural effusion presence and hyperbilirubinemia (> 4 mg/dl) as significant predictive factors respectively $p = 0.007$ with 3.08 (1.35–7.00) of 95% CI, $p = 0.020$ with 2.68 (1.17–6.13) of 95% CI, and $p = 0.031$ with 3.32 (1.12–9.83) of 95% CI.
Conclusion : Size of lesion, pleural effusion presence and hyperbilirubinemia were independent predictive factors for rupture of liver abscess.

Abstract #1467

Incidence and characteristic of liver abscess in Indonesian General Hospital from July to December 2019

Jonathan Kent Setiawan[1], Margono Jacqueline Tasha[1], Kurniawan Andree[2]

[1]Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia, [2]Internal Medicine, Faculty of Medicine, Pelita Harapan University, Tangerang, Indonesia

Introduction: Liver abscess (LA) is defined as a collection of pus surrounded by a fibrous layer of tissue in the liver. Reported incidence

in the literature ranges from 2 to 86 cases per 100,000 hospital admittances/year. The microorganisms most commonly responsible for pyogenic LA are Klebsiella pneumoniae, Escherichia coli and Entamoeba Histolytica for amebic LA. Sepsis, empyema, and peritonitis are the most common complications of LA.
Objectives: To report the incidence and characteristic of liver abscess in Indonesian General Hospital.
Methods: The study was done using a cross-sectional method retrospectively from our abdominal CT scan database in Siloam Hospital Lippo Village in Tangerang, Banten, Indonesia from July 2019-December 2019, from patients with the diagnosis of liver abscess and we describe the characteristics based on the age, gender, diameter, segmental location, lobular location, and characteristic of abscess.
Results: Out of 880 datas provided, 5 cases of liver abscess are found. Out of those 5 cases, we've obtained demographic data of; two patients 59 of age, two patients 56 of age, and one patient 26 of age. Three of them are male, and two of them are female. The biggest diameter has the measurement of 8.25 cm whereas the smallest diameter has the measurement of 4 cm. Based on the location of the liver segments, segment 4 and segment 5 happen to be the location with the most frequent liver abscess. The right lobe of the liver is the most common location as three patients have liver abscess on their right lobe. Based on the characteristics of the abscess we found 1 multilocular abscess, 1 multifocal abscess, and 3 unilocular abscess.
Conclusion: Liver abscess is still an ongoing problem in developing countries such as Indonesia, and if not handled properly, varieties of complications, for instance, sepsis or empyema might arise. Based on the CT scan database of Siloam Hospital Lippo Village with a number of 880 datas provided, 5 cases of abscess hepar (0.56%) are obtained, with an average diameter of 6.83 cm ± 1.68.

Abstract #1468

Effectiveness comparison of intravenous antibiotics transition therapy to oral antibiotics compared to Intravenous antibiotics monotherapy in patients with pyogenic liver abscess

Dania Mirza Ramadhanty[1], Kemal Fariz Kalista[2]

[1]Medical Education Study Program, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia, [2]Division of Hepatobiliary, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Background: Pyogenic liver abscess is suppurative process that occurs in liver tissue due to bacterial invasion through direct penetration, blood flow, or the biliary system. The empiric use of parenteral or intravenous antibiotic with the combination of percutaneous drainage are the main treatment for this disease. Meanwhile, oral antibiotic usually given after initial stabilization. The duration of antibiotic administration is at least 2 weeks for intravenous antibiotic, followed by oral antibiotic for 6 weeks.
Objectives: Determine the effectiveness of intravenous antibiotic transition therapy to oral antibiotic therapy compared with intravenous antibiotic in patients with pyogenic liver abscess
Methods: Online article searches were performed on three databases: PubMed, EBSCO, and Cochrane Library. Therapeutic study articles were selected through inclusion and exclusion criteria, then critically examined using Centre Evidence-Based Medicine Guidelines, University of Oxford.
Results: Critical review was carried out on 2 selected articles. Both articles stated that administration of intravenous antibiotic transition therapy to oral antibiotic was more effective significantly to abbreviate hospital length-of stay ($p = <0.001$). Whereas intravenous antibiotic is more effective significantly to decrease readmission rate in 30 days ($p = 0.03$), 60 days ($= p<0.01$), and 90 days ($p = 0.02$).
Conclusion: The administration of intravenous antibiotic transition therapy to oral antibiotic therapy has a higher effectiveness to abbreviate hospital length-of-stay in pyogenic liver abscess patient than intravenous antibiotic monotherapy. Meanwhile, intravenous antibiotic transition therapy to oral antibiotic is less effective to decrease the rate of readmission than the administration of intravenous antibiotic as a monotherapy.

Abstract #1591

Comparison of mortality in sepsis patients with hypoalbuminemia conditions between those given intravenous human albumin and not in the high care unit room

Marzuki Mochammad Jalalul[1], Supriono[2], Pratomo Bogi[2], Mustika Syifa[2]

[1]Internal Medicine Department, Medical Faculty, Brawijaya University, Saiful Anwar Hospital, Malang, Indonesia, [2]Gastroenterohepatology Division, Department of Internal Medicine, Medical Faculty, Brawijaya University, Saiful Anwar Hospital, Malang, Indonesia

Introduction: Hypoalbuminemia is a strong predictor of mortality in nonoperative and operative patients. The administration of exogenous Human Serum Albumin (HSA) in hypoalbuminemia conditions is still controversial with varying outcomes. Research related to albumin in Indonesia is also still very rare.
Methods: An observational study with a case control design approach involved 75 research subjects aged > 18 years with sepsis accompanied by hypoalbuminemia (< 2.5 g/dL) treated in the High Care Unit of RSUD dr. Saiful Anwar Malang during the period 1 September 2018–31 August 2019 was divided into two groups namely albumin and nonalbumin groups. Both groups were followed during hospitalization until they discharged or died. Differences in mortality between the two groups were analyzed by Chi Square bivariate test. The most influential factors on mortality were analyzed by multivariate binary logistic regression tests.
Results: There were 39 people (52%) from the albumin group and 36 people (48%) from the non-albumin group. Difference in mortality between albumin and nonalbumin groups {25 (64.1%) vs 16 (44.4%) with OR 2, $p = 0.138$}. factors that influence mortality included: SOFA
score (OR 34.27, $p < 0.001$), MAP value (OR 8, $p < 0.001$), septic shock (OR 4.31, $p = 0.03$), diabetes mellitus (OR 0.28, $p = 0.009$), respiratory failure (OR 8.02, $p < 0.001$), decreased of consciousness (OR 64.75, $p < 0.001$), cardiovascular failure (OR 6, $p < 0.001$), hematological failure (OR 3.05, $p = 0.027$). The most dominant factor affecting mortality in sepsis patients is decreased of consciousness (OR 2.67, $p = 0.001$).
Conclusion: The administration of albumin transfusion did not make a significant difference in the incidence of mortality in sepsis patients with hypoalbuminemia. The most influential factor on mortality of sepsis patients is decreased of consciousness.

Abstract #1719

An uncommon multiple left lobe liver abscess with left pleural effusion and loculated ascites

Yogi Umbarawan[1], Chris Tanto[1], Kemal Fariz Kalista[1], Leonard Nainggolan[1]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia/Cipto Mangunkusumo General Hospital

Introduction: Left lobe liver abscess is an uncommon type of liver abscess (10–15%). In contrast with right lobe abscess which has right upper quadrant pain as well-known clinical presentation, epigastric pain in left lobe abscess often causes misdiagnosis leads to delay treatment. Untreated abscess caused by delayed treatment may result in serious complication such as abscess rupture, pericardial effusion, pleural effusion, ascites, and sepsis which are fatal if left untreated.
Case presentation: A 43-year old male was admitted to our emergency department with epigastric pain, high spiking fever, nausea, and loss of appetite started 2 weeks before admission. No diarrhea or diabetes. For his complaint, 2 weeks before admission he received antacid and proton pump inhibitor from primary physician without any sign of improvement, then he was referred to our hospital 2 weeks later. There was epigastric pain on palpation. Laboratory findings showed leukocytosis, neutrophilia, and increase in C-reactive protein. Abdominal ultrasonography revealed left lobe liver abscess, complex ascites, and right lobe cyst. Abdominal CT scan contrast showed multiple left lobe abscess with largest size 8.5 x 11.5 x 10.4 cm, loculated fluid collection at perisplenic area, and left pleural effusion. He underwent abscess aspiration, received antibiotics and analgetic which alleviated the clinical symptoms.
Conclusion: We highlight left lobe abscess with loculated ascites and left pleural effusion as an uncommon type of liver abscess. Careful assessment need to be done to prevent delay treatment since the clinical presentation is different with right lobe liver abscess.

Abstract #1838

Association of liver function parameters and the level of CD4 count in HIV patients at Haji Adam Malik Hospital

Kumalasari Carissa[1], Barimbing Morris Lintong[1], Sopacua Andre[1], Mardianto[2], Ginting Franciscus[1,3]

[1]Antimicrobial Stewardship Program Haji Adam Malik Hospital, [2]Director of Haji Adam Malik Hospital, Medan, Indonesia, [3]Division of Infectious Disease, Department of Internal Medicine, Faculty of Medicine, University of North Sumatera, Haji Adam Malik Hospital, Medan, Indonesia

Introduction: In 2018, there were 54% newly diagnose of human immunodeficiency virus (HIV) infection in global, while approximately 640.000 Indonesians were living with HIV. HIV can infect cells in the liver leading to enhanced intrahepatic apoptosis and fibrosis.
Objectives: To determine association of liver function parameters with level of CD4 count in patients with newly diagnose HIV.
Methods & Materials: This was a retrospective study including 525 HIV inpatients collected from the medical record data and hospital information system, which were diagnosed in their first admission to Haji Adam Malik Hospital, Medan, Indonesia, during period January 1, 2018–December 31, 2019. Data was analyzed using SPSS version 17.0.
Results: One-Hundred and eighty patients were analyzed, predominantly male (75%) and the age group was 35–44 years old, 101 patients (61.7%) with CD4 count < 50 cell/mm^3, in these, 68 patients (68.6%) and 44 patients (68.7%) with higher AST and ALT respectively. HIV patient that associated with HBV infection were 24 patients (13.3%) and HCV infection was 1 patient (0.6%). The median of CD4 count, AST and ALT serum in HIV patients were 32.5 cell/mm^3, 44U/L, 28U/L respectively. The significant level of CD4 count with AST level and ALT level were $p = 0.09$ and $p = 0.39$.
Conclusions: Even though there was no association between the parameter of liver function and the level of CD4 count in HIV patients, proper management of HIV patients required recognition of liver injury conditions for effective treatment.

Abstract #2245

A confusing clinical presentation of rupture liver abscess and appendicitis: a case report

Christy, Kezia[1], Noviyanti, Mellisa[2]

[1]Faculty of Medicine and Health Science, Atma Jaya Catholic University of Indonesia, [2]Faculty of Medicine and Health Science, Atma Jaya Catholic University of Indonesia.

Background and aims: Most of pyogenic liver abscess cases are caused by cholangitis. Other causes are appendicitis, diverticulitis, and inflammatory bowel disease which are smaller percentage. Clinical presentation of liver abscess is often non-specific and confusing with other diagnose. This case is to introduce you other clinical presentation that thought to be perforated appendicitis but actually was a rupture liver abscess.
Methods: A retrospective chart review was performed on a single patient
Results: A 32-year-old man who presented to the emergency department with a week history of right lower abdominal pain. The patient was febrile and severe abdominal pain on presentation. The first thought of diagnose was perforated appendix. Laboratory test was found to have a leukocytosis 22.000. Liver function were slightly elevated but less than two times. Computed tomography of the abdomen showed a slightly dilated appendix and multiseptated right hepatic lobe lesion that thought to be liver abscess. Emergency laparotomy was performed with intraoperative findings of rupture liver abscess. Irrigation, suctioning and placing drain was performed to clean the abscess. We also do an appendectomy of a slightly inflamed appendix. Postoperatively the patient was continued on broad-spectrum antibiotics. The patient was discharged after receiving 2 weeks of intravenous antibiotics and continue oral antibiotics for 6 weeks.
Conclusions: Ruptured liver abscess has a similar symptoms to other perforation organ including perforated appendix. Further imaging would help to diagnose.

Liver Disease in Pregnancy

Poster Presentations

Abstract #535

Pregnancy and fetal outcomes after interferon exposure: a meta-analysis

MengMeng Zhang[1], Shan Fu[1], NaiJuan Yao[1], YaLi Feng[1], Yingren Zhao[1], Jinfeng Liu[1]

[1]Department of Infectious Diseases, First Affiliated Hospital of Xi'an Jiaotong University, 710061 Xi'an

Background: The safety of interferon during pregnancy is unknown and limited data exists regarding the potential harm of interferon exposure during pregnancy. A meta-analysis was performed to evaluate the outcome of pregnancy and fetus.

Methods: A systematic search of PubMed, EMBASE, Cochrane Library, Web of Science, CBM, CNKI, and WanFang Data was conducted from database inception to October 1st 2019 for studies that pregnant women were exposure to interferon with outcome of fetus reported. The primary outcomes were live birth, spontaneous abortion, induced abortion or stillbirth during pregnancy. We used a random-effects model to calculate a pooled estimate.
Results: Eight cohort studies were included with pregnancies exposure to interferon initiated from pregestation. 1409 pregnant women and 1104 live births were included for final analyze. The majority of outcomes were normal live birth, the estimate rate was 79% (95% CI 72–86%). The overall rate of pregnancy complication (16%, 95% CI 0–45%) was comparable with that in common population. The rate of spontaneous abortion was 13% (95% CI 9–17%), which is consistent with the rate reported in the general population. In addition, the rate of stillbirth was 1% (95% CI 0–2%), and the rate of induced abortion, birth defects, and preterm birth was 1% (95% CI 5–18%), 3% (95% CI 1–4%), and 4% (95% CI 0–1%) respectively.
Conclusion: Our meta-analysis highlighted a comparable outcome in pregnancy and fetus exposure to interferon, may help guide decision-making for the pregnant women with intentional exposure.

Abstract #683

Stopping antiviral therapy for prevention of perinatal transmission in chronic hepatitis B pregnant women in immune-tolerant phase is not associated with more increased hepatitis postpartum

Chunrui Wang[1], Qian Zhang[1], Xiaoqing Liu[1], Zhiwei Chen[1], Li Zhang[1], Huimin Wang[1], Yunan Chang[1], Peng Hu[1]

[1]Department of Infectious Diseases, Institute for Viral Hepatitis, The Key Laboratory of Molecular Biology for Infectious Diseases, Chinese Ministry of Education, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China

Introduction: Antiviral therapy withdrawal in chronic hepatitis B patients may increase the risk of hepatitis. Though treatment at the end of pregnancy can effectively prevent perinatal transmission, hepatitis B virus (HBV) DNA increased after drug withdrawal. Research on the hepatitis flare in pregnant women is insufficient.
Objectives: This study aimed to observe the incidence of hepatitis in pregnant women after drug withdrawal.
Methods: 211 chronic hepatitis B pregnant women in one Chinese centers between 2012 and 2019 were enrolled in this study. Concerned information was obtained from outpatient records.
Results: 121 pregnant women were included in the analysis eventually. Among the 71 patients with drug withdrawal and 30 with continued treatment postpartum, the baseline HBV DNA was (4.82 ± 3.23) and (6.82 ± 1.24) $\log_{10}$IU/ml, baseline ALT was (32.59 ± 26.75) and (62.00 ± 54.94) U/L, HBsAg values were (4.55 ± 4.51) and (4.33 ± 4.39) $\log_{10}$IU/ml respectively. 8 of drug withdrawal group developed hepatitis. 2 patients had ALT increased to 5ULN and 6ULN at 21 and 18 weeks respectively. 3 patients's HBV DNA is negative, and 1 developed HBeAg clearance at 86 weeks postpartum. The group including 22 patients with elevated ALT caused by other reasons has lower, earlier appeared peak ALT value, and higher HBVDNA compared with the hepatitis group. There was no significant difference in HBsAg and HBeAg values between two groups.
Conclusion: Postpartum hepatitis is uncommon in pregnant women after drug withdrawal. Stopping antiviral therapy for prevention of perinatal transmission in hepatitis B pregnant women in immune-tolerant phase would not increase more postpartum hepatitis.

Abstract #692

Liver diseases in pregnancy: trends and their consequence in mother and child

Soomro sabir ali[1], Butt nazish[2], Awan ushna jawwad[1], Rasheed mehrab[1], Yasmin haleema[2], Channa riaz hussain[1], Rai lajpat[1], Khemani hanisha[1], Abbasi amanullah[3]

[1]Department of Gastroenterology, Medical unit IV, Ward 23, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Sindh, Pakistan, [2]Department of Gynecology and Obstetrics, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Sindh, Pakistan, [3]Medical Unit II, Dow University of Health Sciences, Ojha Campus, Karachi, Pakistan.

Introduction: Liver diseases in pregnancy are associated with complications and sometimes worse outcome for both mother and baby. It occurs in approximately 3% of all pregnancies, and may lead to various maternal and perinatal morbidities, some of them with fatal consequences for both mother and child.
Objective: To determine the trends and consequences of liver diseases in pregnancy
Methods: This prospective study was conducted at Gastroenterology department, ward 23 and Gynecology & Obstetrics department, JPMC, Karachi, Pakistan. All the pregnant women having concomitant liver disease were included in this study. Baseline characteristics and clinical data entered and analyzed by using SPSS version 21.
Results: Total 105 patients were evaluated in the study. Seven patients were lost to follow up and excluded from the study. Mean age was 27.49 ± 6.02 years. Among 98 patients the most common cause was acute hepatitis E virus (HEV) 32 (32.7%) followed by acute hepatitis C virus 24 (24.5%), pre-eclampsia & eclampsia 8 (8.2%), and HELLP syndrome 7 (7.1%). Fortunately, most of the women survived and discharged without any complication 60 (61.2%) while 15 (15.3%) were died. Fetal mortality occurred in 40 (40.8%). Poor socioeconomic status, non-primary education, low BMI, and HELLP syndrome were associated with poor maternal outcome. HELLP syndrome, low BMI, low systolic blood pressure of mother, and presence of altered level of consciousness were associated with poor fetal outcome.
Conclusion: Liver diseases in pregnancy increases maternal and fetal morbidity and mortality.

Abstract #1193

Acute fatty liver of pregnancy with hepatitis B viral infection complicated by twins

Maimunah U[1], Windradi C[2]

[1]Division of Gastroenterology & Hepatology, Internal Medicine Department, Universitas Airlangga, Dr.Soetomo General Academic, Surabaya, Indonesia, [2]Resident of Internal Medicine Department, Universitas Airlangga, Surabaya, Indonesia

Introduction: Acute fatty liver of pregnancy (AFLP) is rare and life threatening disorder and its relevance to hepatitis B viral infection remains unknown. Prompt suspicion, early recognition, and emergent careful delivery of the baby remain the cornerstones of management of patients with AFLP.
Case Illustration: A 42 years old woman came to hospital with chief complaint yellow discoloration of the skin, nausea and abdominal pain. The patient is 35–36 weeks pregnant with the fourth child known to be a twin. Unknown history of hepatitis B before. Her laboratory findings showed seropositive of HbsAg, SGPT 106 U/l, total bilirubin 21.56 mg/dl, creatinin 2 mg/dl, blood sugar 60 mg/dl and aPPT 70 second. The Swansea criteria defined AFLP was 6 while

still being concerned about suspicion fulminant hepatitis B. To control coagulopathy, she received 4 units of fresh frozen plasma (FFP), vitamin K injection and emergency cesarean section. Entecavir is given after the patient gave birth. Both baby has received HbIg and hepatitis B vaccination.
Discussion: Viral hepatitis patients generally have higher levels of serum transaminases while incidences of coagulopathy, and digestive tract hemorrhage are less common in patients with viral hepatitis than in those with AFLP. Emergency management cesarean section is needed, without accurate diagnosis, can be considered reasonable and necessary.

Abstract #1495

Histopathology analysis on a liver core biopsy specimen as a diagnosis modality for hemolysis, elevated liver enzyme, and low platelet (HELLP) syndrome: a case report

Alif Gilang Perkasa[1], Ening Krisnuhoni[2]

[1]Anatomical Pathology Residency Program, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia, [2]Department of Anatomical Pathology, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Introduction: Haemolysis, elevated liver enzyme, and low platelet (HELLP) syndrome is a rare liver disease in pregnancy. It's develops in about 1 case per 1000 pregnancies. The existence of its, increasing the maternal mortality and morbidity, therefore rapid diagnosis and therapies is needed.
Objective: We describe the role of histopathology and histochemistry staining from liver core biopsy in a severe preeclamptic woman to assure the diagnosis.
Case Description: A 35 year old woman, under abdominal pain and severe headache presented with elevated blood pressure of 200/120 mmHg and 3 + proteinuria at 27th week of pregnancy. Laboratory test showed AST level = 2089, ALT level = 789, LDH = 15.235, thrombocytes = 36.000. A 1640 g female was delivered by emergency caesarean section. Following the delivery, the patient's clinical condition deteriorated. Five days after delivery the patient experience seizures. The clinical finding and laboratories result suggests eclampsia with HELLP syndrome with differential diagnosis hemolytic uremic syndrome (HUS) and acute fatty liver of pregnancy (AFLP). A liver core biopsy performed 16 days postpartum showed area of hemorrhage, periportal hepatocellular necrosis, collapse of trabecular frame and perivenula hepatic loss with fibrin deposits. Based on findings, a final diagnosis of HELLP syndrome was made. After carrying out intensive care the patients slowly recovered eventually discharged home after 20 day of remission.
Conclusion: Similar clinical and laboratories finding can be a challenge to diagnose the liver disease in pregnancy. Well prepared liver biopsy procedure need to be considered to assure the diagnosis.

Abstract #2233

Comparison of HBIG administration to pregnant women with antiviral therapy in preventing transmission of hepatitis B virus from mother to infant

Andri Sanityoso Sulaiman[1,2]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [2]Klinik Hati Prof. Ali Sulaiman. Jakarta, Indonesia

Backgrounds: At present, the most effective mother–infant blockade is to perform active–passive double immunization with HBV vaccine combined with hepatitis B immunoglobulin (HBIG) within 24 h after birth. Therefore, more and more scholars recommend application of antiviral drugs in the third trimester to block MTCT in pregnant women with high HBV DNA load.
Aim: To compare the effectiveness of HBIg (hepatitis B immunoglobulin) administration and antiviral treatment in pregnant women to interrupting mother-to-child transmission (MTCT) of hepatitis B virus (HBV)
Methods: Literature searching was conducted using database Pubmed. The keywords, inclusion criteria were also applied. The articles were appraised to discuss validity and applicability of HBiG and antiviral therapy for pregnant women.
Result: Zhao, et al (2019) studied 728 pregnant women and and 170 of them get HBIG after 2 h of birth without being injected with the mother first. And the results shows a low ALT dan HBV DNA levels ($p = 0.023$ and $p = 0.55$). In Jyoti (2017) study enrolled 60 HBsAg-positive pregnant women treated with antivirals, lamivudine/tenofovir treatment in HBV carrier mothers from 28 weeks of gestation along with active and passive immunization of new born. And the results showed Tenofovir, category B drug, is more effective in preventing transmission of HBV infection to infants ($p = 0.004$)
Conclusion: Both HBIG injection in 2 h after birth infants and Antivirals therapy in pregnant women can effectively decreasing the transmission of Hepatitis B from mother to child.