Liver and Gastrointestinal Tract Problems in Chronic Kidney Disease

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Before You Start: Facts You Need to Know

- Nonspecific symptoms or signs, such as diarrhea or biochemical liver dysfunction, may in some patients be an important clue to the etiology of CKD.
- The level of some common biochemical tests such as ALT/AST is falsely low in the late CKD stages.
- Infection by the hepatitis B and C viruses is more common in CKD patients than in the general population.

Liver or gastrointestinal (GI) tract disease may sometimes be a cause or a consequence of CKD. In the first section, we discuss the etiologies of liver or GI tract disease that may be a clue to CKD etiology. In the second section, we discuss the liver and GI tract manifestations that are more prevalent or associated with CKD.

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20.1 Liver and Gastrointestinal Tract Disease as Potential Clues to CKD Etiology

20.1.1 Liver Disease

20.1.1.1 Liver and Kidney Disease from the Same Cause

A number of diseases may cause both liver and kidney damage. The detection of biochemical or imaging evidence of both liver and kidney involvement may thus point to specific etiologies of CKD. These include among others amyloidosis (especially of the AL type), as well as autosomal dominant polycystic disease. The latter will easily be diagnosed by imaging, whereas the former should be investigated by the search for a paraprotein, a sign of clonal B cell lineage proliferation, followed by biopsy of an affected organ.

20.1.1.2 Liver Disease as Cause of CKD

Some liver diseases may not infrequently be complicated by significant glomerulonephritis (GN). These include hepatitis B and hepatitis C virus infection.

Hepatitis B virus (HBV) infection is an important cause of membranous nephropathy, especially in children and in emerging countries. A recent case series of biopsy-proven membranous nephropathy from China ascribed the disease to HBV in 12 % of cases [1]. The substantial reduction of the prevalence of HBV-associated membranous GN in several emerging countries since the advent of anti-HBV vaccination strongly supports

M. Arici (ed.), *Management of Chronic Kidney Disease*,
DOI 10.1007/978-3-642-54637-2_20, © Springer-Verlag Berlin Heidelberg 2014

the causal role of HBV. Thus, testing for HBV serological markers should be part of the etiologic investigation of any GN. Successful antiviral treatment is associated with improvement of the associated GN [2].

Similarly, the hepatitis C virus is one of the causal agents of type 1 membranoproliferative glomerulonephritis, with or without circulating cryoglobulins. Testing for HCV should thus be part of the etiologic investigation of a GN and successful antiviral treatment may improve the associated GN [3, 4]. Sometimes, immunosuppressive agents (corticosteroids, cyclophosphamide, rituximab) may be required to treat hyperactive lesions (such as crescents/capillary necrosis), prior to or associated with antiviral treatment or in case of failure of antiviral agents [3, 4].

20.1.2 Gastrointestinal Tract Disease

20.1.2.1 Kidney and GI Tract Disease from the Same Cause

Several diseases may concurrently affect both the GI tract and the kidney. This coexistence may thus be an important clue to the etiology of CKD. Such etiologies include among others Henoch-Schönlein purpura and atheroembolism.

The coexistence of signs of GN (hematuria and proteinuria) together with bouts of abdominal pain, with or without GI tract hemorrhage, not always accompanied by arthritis and/or skin purpura, should prompt consideration of Henoch-Schönlein purpura as a potential etiology of CKD. The diagnosis may ultimately be confirmed by the histological demonstration of IgA deposits in an affected organ. Management is supportive, with temporary steroids for symptomatic treatment of articular or digestive disease. The long-term prognosis is dependent on kidney involvement. A kidney biopsy should be performed if significant albuminuria persists.

Similarly, albeit much less frequently, atheroembolism is a more and more frequent cause or contributor to CKD in elderly patients with coexistent cardiovascular disease. Atheroembolism may affect various abdominal organs, including the bowel, in addition to the kidney. The coexistence of acute episodes of abdominal pain, sometimes with peritoneal irritation, in a patient with a recent potential trigger of atheroembolism (coronary or peripheral angiography, warfarin start, thrombolysis) should prompt, especially if peripheral eosinophilia is present, considering the diagnosis of atheroembolism. The management is supportive, together with withdrawal of warfarin and aggressive statin treatment.

20.1.2.2 Diseases of the GI Tract or Pancreas as a Cause of CKD

Diseases of the GI tract may cause acute, subacute, or sometimes chronic kidney disease (CKD). Indeed significant small bowel disease such as Crohn's disease but also in the postsurgical short bowel syndrome, chronic pancreatitis, as well as orlistat therapy (prescribed with the aim to favor weight loss) all can cause steatorrhea. The consequence of steatorrhea is that calcium binds to free fatty acids in the bowel lumen and there will thus be less calcium available to bind oxalate. Thus, more oxalate will be absorbed by the bowel, leading to hyperoxaluria and the so-called oxalate nephropathy. This is definitely an under-recognized cause of kidney disease. Kidney dysfunction may be partly reversible after etiologic treatment and oral calcium supplementation [5]. Thus, in the presence of unexplained CKD and concomitant diarrhea, oxaluria should be measured.

Preparations rich in sodium phosphate ("Fleet Phosphosoda") given orally are convenient to clean the large bowel prior to colonoscopy but have recently been recognized as a cause of acute kidney injury, sometimes with irreversible (chronic) kidney damage [6]. Their high phosphate content favors substantial phosphate absorption by the bowel, with the risk of renal deposition of calcium phosphate salts, especially in predisposed patients, such as CKD patients, the elderly, those under diuretics, and those with diabetes, hypertension, congestive heart failure, active colitis, etc. The recent KDIGO CKD Guidelines specifically recommend not to use oral phosphate-containing bowel cleaning preparations in patients with an eGFR <60 [7] (Box 20.1).

Box 20.1. What the Guidelines Say You Should Do

Oral phosphate-containing bowel preparations should not be used in people with a GFR <60 ml/min./1.73 m^2 or in those known to be at risk of phosphate nephropathy.

Source: Kidney Disease: Improving Global Outcomes (KDIGO) [7]

20.2 Liver and GI Tract Consequences/Implications of CKD

20.2.1 Liver

Patients with CKD can develop a variety of acute and chronic diseases of the liver. The most common and serious ones in CKD patients remain HBV and HCV infection.

20.2.1.1 HCV as a Cause of Liver Disease in CKD

Several studies, mostly small sized, have suggested that the prevalence of anti-HCV antibodies is high among patients with the late stages (mostly 4 and 5) of CKD non-D, ranging from 3.9 to 14 % [8–12]. These prevalence figures should be interpreted in the light of the known prevalence of HCV in the general population worldwide, known to be highest in Egypt; intermediate in Asia, the USA, and Southern/Eastern Europe; and lowest in Northern Europe [13].

The importance of HCV as cause of liver damage in patients with CKD stage 4–5 non-D has increased with the advent of preemptive kidney transplantation: understanding the characteristics of liver disease is important for the evaluation and management of potential renal transplant candidates. Lemos et al. [12] assessed the epidemiology and clinical significance of hepatitis C in a large cohort of uremic patients not yet receiving dialysis in Brazil. A total of 1,041 patients with a creatinine clearance of 36 ± 18 ml/min were enrolled (49 % had CKD stage 4–5). Forty-one (3.9 %) patients were anti-HCV positive (with viremia in 95 % of them). A population study conducted in the same region reported an anti-HCV prevalence of 1.4 % ($P<0.001$). Moreover, chronically HCV-infected patients presented significantly higher serum alanine aminotransferase (ALT) levels (1.3 vs. 0.4× ULN, $P<0.001$). By logistic regression analysis, a history of blood transfusion before 1992, intravenous drug abuse, and ALT level all had an independent and significant association with chronic HCV.

In a prospective, observational study in 860 US patients, the anti-HCV positivity rate was seven to eight times greater at dialysis start (14.4 %) than in the general population (1.8 %). In these US inner city units, much of the HCV burden (prevalence 16.8 %) was thus acquired prior to starting dialysis, particularly among those who are younger and black or have a history of drug use [10]. The authors concluded that risk factors for HCV infection in patients receiving dialysis now may differ substantially from those identified 20 years ago. Transmission of HCV in the HD setting has clearly decreased because of a now much safer blood supply, at least in developed countries, the availability of erythropoiesis-stimulating agents, and better hygienic precautions. Rather, most anti-HCV (+) dialysis patients may have become infected before the initiation of dialysis.

HCV infection results in an increase in serum aspartate (AST) and alanine (ALT) aminotransferase levels. Unfortunately, the diagnostic value of AST/ALT measurement to assess acute or chronic HCV is rather weak in CKD patients. Lower serum aminotransferase values in dialysis patients than in healthy controls have long been reported [14]. This phenomenon may extend to CKD non-D patients. In a large ($n=407$) cross-sectional survey of consecutive individuals with a serum creatinine >2 mg/dl, Fabrizi et al. [15] reported lower serum aminotransferase activity in comparison with healthy persons. The difference persisted in age-matched comparisons and after correction for viral markers (HBsAg and

anti-HCV), AST 17.9 ± 8 vs. 20.4 ± 6 IU/l ($P = 0.0001$) and ALT 17.5 ± 10 vs. 21.7 ± 11.3 IU/l ($P = 0.0001$). Although this is a single cross-sectional study, it seems reasonable to state that in patients both with and without viral hepatitis, aminotransferase levels are higher in those with normal kidney function, probably intermediate in pre-dialysis, and lowest in patients on dialysis. Although the causes of this lower ALT/AST level in CKD are still disputed, the diagnostic implications are significant.

Regarding the management of HCV infection in CKD, the KDIGO Guidelines [16] recommend that all HCV-infected patients, regardless of treatment, be followed for HCV-associated comorbidities, including the onset of cirrhosis or hepatocellular carcinoma. Patients with clinical or histological evidence of cirrhosis should have follow-up every 6 months, whereas annual follow-up is suggested for patients without cirrhosis. Follow-up should include both alpha-fetoprotein measurement and liver imaging (Box 20.2).

The KDIGO Guidelines further suggest to base the decision to treat HCV infection on the potential benefits and risks of therapy, including life expectancy, candidacy for kidney transplantation, and comorbidities. The KDIGO Guidelines specifically suggest to treat HCV-infected patients accepted for kidney transplantation, but prior to kidney transplantation (Box 20.3).

Until recently, a liver biopsy was required before any antiviral treatment. Since the 2008 KDIGO Guidelines [16], both the APRI index (the ratio of AST level to platelets) and transient elastography (or "Fibroscan") have been shown to be good noninvasive markers of the extent of liver fibrosis [17, 18]. In particular, transient elastography has been validated both in the general population and in dialyzed patients so that despite the absence of large CKD non-D series, it probably works in CKD as well. It measures the velocity of a low-frequency elastic shear wave propagating through the liver. This velocity is directly related to tissue stiffness. The result of transient elastography and/or serum markers may in some cases make a liver biopsy unnecessary.

Finally it should be stressed that the main drugs (pegylated interferon and ribavirin) used hitherto in HCV antiviral treatment are eliminated by the kidney and their dosage should thus be adapted as a function of eGFR or CKD stage, along the general recommendations of Table 20.1.

Box 20.2. What the Guidelines Say You Should Do

All patients with HCV infection, regardless of treatment or treatment response, should be followed for HCV-associated comorbidities. Patients who have evidence of clinical or histological cirrhosis should have follow-up every 6 months. Annual follow-up for patients without cirrhosis is suggested.

Source: Kidney Disease: Improving Global Outcomes (KDIGO) [16]

Box 20.3. What the Guidelines Say You Should Do

It is suggested that the decision to treat CKD patients with HCV infection be based on the potential benefits and risks of therapy, including life expectancy, candidacy for kidney transplantation, and comorbidities. It is specifically suggested to treat HCV-infected patients accepted for kidney transplantation, but prior to kidney transplantation.

Source: Kidney Disease: Improving Global Outcomes (KDIGO) [16]

20.2.1.2 HBV in CKD

Like for HCV, the prevalence rates of HBV in CKD patients are related to the local general population prevalence, with a north-to-south and west-to-east gradient.

Thus, not surprisingly, small reports from India (7 %) or Turkey (10.5 %) showed high HBsAg-positive rates [11, 19], whereas the rate of chronic HBsAg seropositive individuals with pre-dialysis CKD from Spain and Italy was between 0 and 3.7 % [20].

Table 20.1 Recommended treatment of HCV infection in patients with CKD and associated adverse events

Stage of CKD	IFN	Ribavirin	Common adverse events
1 and 2	Pegylated IFN alfa-2a: 180 μg SQ q week	800–1,200 mg/day in two divided doses	IFN: headache, flu-like illness, depression
	Pegylated IFN alfa-2b: 1.5 μg/kg SQ q week		Ribavirin: worsened anemia due to hemolysis
3	Pegylated IFN alfa-2a: 180 μg SQ q week	eGFR 50–60: 400–800 mg/day	IFN: same as above
	Pegylated IFN alfa-2b: 1 μg/kg SQ q week	eGFR 30–50: 300 mg/day (200 mg and 400 mg alternating)	Ribavirin can cause hemolytic anemia, and its use must be supported with increased erythropoietin as needed
4	Pegylated IFN alfa-2a: 135 μg SQ q week	200 mg/day	Same as above
	Pegylated IFN alfa-2b: 1 μg/kg SQ q week		
5 non-D	Pegylated IFN alfa-2a: 90–135 μg SQ q week	200 mg/day	Same as above
	Pegylated IFN alfa-2b: 1 μg/kg SQ q week		

Source: Data from Fabrizi et al. [4]
Abbreviations: *SQ* subcutaneously, *q week* every week

Table 20.2 Dosage adjustment of nucleos(t)ide analogs and interferon according to creatinine clearance (CrCl)

CrCl (ml/min)	Lamivudine	Telbivudine	Adefovir	Entecavir	Tenofovir	Pegylated interferon α-2[a]
≥50	100 mg/day	600 mg/day	10 mg/day	0.5 mg/day	245 mg/day	180 μg SQ/week
30–49	100 mg first dose, then 50 mg/day	600 mg/day 2	10 mg/day 2	0.25 mg/day	245 mg/day 2	135 μg SQ/week
15–29	35 mg first dose, then 25 mg/day	600 mg/day 3	10 mg/day 3	0.15 mg/day	245 mg/day 2–3	
5–14	35 mg first dose, then 15 mg/day	600 mg/day 3	10 mg/day 3[b]	0.05 mg/day[b]	245 mg/week[b]	

Source: Adapted by permission from Macmillan Publishers Ltd: Pipili et al. [2], Copyright 2013
Abbreviation: *SQ* subcutaneous
[a]Recommendations only for nucleos(t)ide analog-naive patients
[b]Recommendation only for CrCl ≥10 ml/min

In a large cohort ($n=405$) of CKD non-D patients, the prevalence of HBsAg positivity was 3.7 % (15), thus lower than in dialysis (8.7 %) but greater than in healthy persons of the same region (0.5 %). Multivariate analysis showed an independent and significant association between AST level and HBsAg positivity.

Numerous risk factors may predispose predialysis patients to HBV and/or HCV infections: these include high-risk behaviors (recreational drug use or unsafe sex), prolonged hospitalizations or frequent health-care utilization potentially increasing nosocomial exposure to blood-borne agents, impaired immune response from chronic uremia, and decreased vaccine responsiveness.

The management of HBV infection in patients with CKD has recently been reviewed extensively [2]. It should be pointed out here again that the dosage of many of the anti-HBV drugs, eliminated by the kidney, should be adapted to eGFR/CKD stage, as detailed on Table 20.2.

20.2.1.3 Other Causes of Liver Disease in Chronic Kidney Disease

Any therapeutic drug has the potential of causing hepatic damage, although some drugs are far more likely than others to do so. In addition,

susceptibility to developing such injury differs between patients. No firm evidence shows that patients with CKD stage 4 or 5 are more likely to develop drug-induced liver toxicity than other individuals. However, drug interactions have an important role in the pathogenesis of drug-induced liver disease in uremic patients, as these patients frequently receive multiple medications. Drug-induced hepatic injury can be either hepatocellular or cholestatic; a complete list of medications capable of producing hepatic damage is beyond the scope of this chapter. NSAIDs are widely used, although less so in CKD patients, and may, albeit infrequently, cause hepatic damage [21]. Allopurinol and anabolic steroids may be hepatotoxic in CKD patients; numerous antibiotics can also cause hepatic dysfunction, including tetracyclines, macrolides, trimethoprim-sulfamethoxazole, rifampicin, and isoniazid. Some cardiovascular medications are also hepatotoxic; for example, amiodarone and methyldopa cause cholestatic and hepatocellular injury, respectively. Monitoring of serum ALT and AST activity is recommended during treatment with HMG-CoA reductase inhibitors. Another potential cause of hepatic dysfunction is hepatic congestion due to heart failure. The diagnosis of drug-induced hepatotoxicity is made via a process of exclusion.

In the differential diagnosis of acute liver dysfunction in uremic patients, viral infections such as HBV and HCV, herpes simplex virus, Epstein-Barr virus, or cytomegalovirus should be considered, as should adverse effects of drugs. Patients with elevated levels of serum ALT, AST, and/or gamma-glutamyl transpeptidase should be rechecked after the patient has abstained from potentially toxic substances.

Ethanol-induced liver disease is an infrequent condition in uremic patients. Another form of liver disease receiving growing attention is non-alcoholic fatty liver disease. Risk factors include obesity, hyperlipidemia, and diabetes mellitus. All these factors have a growing prevalence and are associated with the prevalence of CKD, too. The diagnosis is a histological one, and disease management involves correcting the predisposing factors.

Box 20.4. What the Guidelines Say You Should Do

- Herbal remedies should not be used in people with CKD.

  Source: Kidney Disease: Improving Global Outcomes (KDIGO) [7]

Another concern that is becoming prevalent is the frequent use of alternative medications, such as herbal and health food store products, by patients on complex medical regimens. The potential toxic effects of herbal products have been understudied, although at least some of these products may cause an elevation of serum levels of ALT, AST, or gamma-glutamyl transpeptidase. The recent KDIGO Guidelines for CKD specifically recommend not to use herbal remedies in CKD [7] (Box 20.4).

20.2.2 GI Tract

20.2.2.1 Upper GI Tract

Upper GI Tract Symptoms

Nausea and vomiting are frequent symptoms in patients with CKD. These may derive from various categories of causes.

- Stage 5 (“terminal”) CKD: Although some degree of anorexia and more rarely nausea, the latter typically in the morning before the breakfast, is common in CKD stage 4, such symptoms should not be ascribed to CKD per se until stage 5 CKD. And even in that late stage, alternative explanations should be searched for nausea/vomiting. Indeed, if symptoms are ascribed to terminal CKD, symptomatic treatment will usually be

relatively unhelpful and renal replacement therapy will be required.

- Role of drugs: Many drugs commonly prescribed to CKD patients may cause nausea. In case of doubt, a short withdrawal (a week) may help clarify the impact of a specific drug. The most frequently incriminated drugs include phosphate binders (calcium based, sevelamer, and lanthanum), numerous antibiotics such as fluoroquinolones, digoxin, iron supplements, morphine derivatives, azathioprine, mycophenolate mofetil, sirolimus, etc. Obviously in patients under immunosuppressive drugs, the suspected causal drug should usually be temporarily replaced by an alternative immunosuppressive agent whenever feasible.

Upper GI Tract Disease More Prevalent in CKD Patients

Not surprisingly, in view of the high prevalence of diabetes in patients with CKD, diabetic gastroparesia is very common in CKD patients. Common symptoms are bloating, episodic vomiting, and early satiety. Delayed gastric emptying may adversely affect glycemic control as well as slow absorption of orally administered drugs. The ultimate diagnosis relies on nuclear medicine imaging of gastric emptying. Management is frequently difficult and includes use of prokinetic drugs such as domperidone, keeping in mind that many such drugs prolong the QT interval and should not be combined with other drugs having the same characteristic (such as sotalol, fluoroquinolones, amiodarone, etc.)

20.2.2.2 Lower GI Tract

Bowel Movement Disturbances

Many drugs may cause either constipation or diarrhea or not infrequently alternating constipation and diarrhea in CKD patients. These include the various phosphate binders, both calcium based as well as non-calcium based (sevelamer and lanthanum) and the more recent calcium and magnesium combination. Others are the calcium- and sodium-based potassium-binding resins and oral iron preparations. In a particular patient, a history of irregular bowel movements or constipation or diarrhea should trigger the question: is this drug-induced? A temporal relationship may often be disclosed by careful history taking. In case of doubt, temporary withdrawal of the suspected causal drug(s) may be very helpful.

Lower GI Tract Disease More Prevalent in CKD Patients

1. Ischemic colitis is definitely more prevalent in CKD as a result of the frequent association of CKD with multiple risk factors for atherosclerosis. Thus, this diagnosis should be considered rapidly in a CKD patient with abdominal pain, diarrhea, and bloody stools. Computerized tomography will usually establish the diagnosis.
2. Angiodysplasia is more prevalent too in CKD patients than in the general population. Although the reasons for this higher prevalence are disputed, angiodysplasia is not uncommon throughout the GI tract from the stomach to large bowel thus including the small bowel, much less accessible to investigation.

When managing a lower GI tract hemorrhage, unexplained despite colonoscopy, a small bowel enteroscopy or an angiography (after appropriate preparation to minimize the toxicity of the contrast agent) will be the next step, if bleeding persists.

When facing GI tract bleeding, drugs known to interfere with hemostasis (aspirin, warfarin, NSAIDs, clopidogrel) should be temporarily withdrawn if possible and the search for the causal lesion started. The efficacy of hormone (estrogen-based) therapy for GI tract bleeding due to angiodysplasia is debated. Endoscopic treatment may be possible for some lesions, especially as most patients with angiodysplasia are elderly and surgical resection is associated with a high risk [22].

Before You Finish: Practice Pearls for the Clinician

- The onset of GI tract symptoms/signs (nausea, diarrhea, constipation) in a CKD patient should trigger the suspicion of a drug-related side effect. Numerous drugs may be incriminated, including phosphate binders, K-binding resins, antibiotics, and various analgesics.
- CKD patients have an increased prevalence of GI tract angiodysplasia. This should be kept in mind when investigating GI tract hemorrhage in CKD.
- Testing for both HBV and HCV should be included in the serological assessment of unexplained glomerulonephritis.
- Significant steatorrhea (not always clinically overt) may cause oxalate nephropathy. Thus, when facing unexplained CKD in a patient with diarrhea, oxaluria should be measured.
- The dosage of many drugs used in the treatment of both HBV and HCV infection should be adapted to CKD stage.

References

1. Zeng CH, Chen HM, Wang RS, Chen Y, Zhang SH, Liu L, et al. Etiology and clinical characteristics of membranous nephropathy in Chinese patients. Am J Kidney Dis. 2008;52(4):691–8.
2. Pipili CL, Papatheodoridis GV, Cholongitas EC. Treatment of hepatitis B in patients with chronic kidney disease. Kidney Int. 2013;84(5):880–5.
3. Feng B, Eknoyan G, Guo ZS, Jadoul M, Rao HY, Zhang W, et al. Effect of interferon-alpha-based antiviral therapy on hepatitis C virus-associated glomerulonephritis: a meta-analysis. Nephrol Dial Transplant. 2012;27(2):640–6.
4. Fabrizi F, Aghemo A, Messa P. Hepatitis C treatment in patients with kidney disease. Kidney Int. 2013; 84(5):874–9.
5. Cartery C, Faguer S, Karras A, Cointault O, Buscail L, Modesto A, et al. Oxalate nephropathy associated with chronic pancreatitis. Clin J Am Soc Nephrol. 2011;6(8):1895–902.
6. Markowitz GS, Perazella MA. Acute phosphate nephropathy. Kidney Int. 2009;76(10):1027–34.
7. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int. Suppl. 2013;3:1–150.
8. Iwasa Y, Otsubo S, Sugi O, Sato K, Asamiya Y, Eguchi A, et al. Patterns in the prevalence of hepatitis C virus infection at the start of hemodialysis in Japan. Clin Exp Nephrol. 2008;12(1):53–7.
9. Fabrizi F, Marcelli D, Bacchini G, Guarnori I, Erba G, Locatelli F. Antibodies to hepatitis C virus (HCV) in chronic renal failure (CRF) patients on conservative therapy: prevalence, risk factors and relationship to liver disease. Nephrol Dial Transplant. 1994;9(7): 780–4.
10. Bergman S, Accortt N, Turner A, Glaze J. Hepatitis C infection is acquired pre-ESRD. Am J Kidney Dis. 2005;45(4):684–9.
11. Sit D, Kadiroglu AK, Kayabasi H, Yilmaz ME, Goral V. Seroprevalence of hepatitis B and C viruses in patients with chronic kidney disease in the predialysis stage at a university hospital in Turkey. Intervirology. 2007;50(2):133–7.
12. Lemos LB, Perez RM, Lemos MM, Draibe SA, Silva IS, Silva AE, et al. Hepatitis C among predialysis patients: prevalence and characteristics in a large cohort of patients. Nephron Clin Pract. 2008;108(2): c135–40.
13. Lavanchy D. The global burden of hepatitis C. Liver Int. 2009;29 Suppl 1:74–81.
14. Yasuda K, Okuda K, Endo N, Ishiwatari Y, Ikeda R, Hayashi H, et al. Hypoaminotransferasemia in patients undergoing long-term hemodialysis: clinical and biochemical appraisal. Gastroenterology. 1995; 109(4):1295–300.
15. Fabrizi F, Lunghi G, Finazzi S, Colucci P, Pagano A, Ponticelli C, et al. Decreased serum aminotransferase activity in patients with chronic renal failure: impact on the detection of viral hepatitis. Am J Kidney Dis. 2001;38(5):1009–15.
16. Kidney Disease: Improving Global Outcomes. KDIGO clinical practice guidelines for the prevention, diagnosis, evaluation, and treatment of Hepatitis C in chronic kidney disease. Kidney Int. 2008;73 (Suppl 109):S1–S99.
17. Liu CH, Liang CC, Huang KW, Liu CJ, Chen SI, Lin JW, et al. Transient elastography to assess hepatic fibrosis in hemodialysis chronic hepatitis C patients. Clin J Am Soc Nephrol. 2011;6:1057–65.
18. Castera L. Noninvasive methods to assess liver disease in patients with hepatitis B or C. Gastroenterology. 2012;142:1293–302.
19. Chandra M, Khaja MN, Hussain MM, Poduri CD, Farees N, Habeeb MA, et al. Prevalence of hepatitis B and hepatitis C viral infections in Indian patients with chronic renal failure. Intervirology. 2004;47(6):374–6.
20. Lopez-Alcorocho JM, Barril G, Ortiz-Movilla N, Traver JA, Bartolome J, Sanz P, et al. Prevalence of hepatitis B, hepatitis C, GB virus C/hepatitis G and TT viruses in predialysis and hemodialysis patients. J Med Virol. 2001;63(2):103–7.
21. Risser A, Donovan D, Heintzman J, Page T. NSAID prescribing precautions. Am Fam Physician. 2009;80(12):1371–8.
22. Chalasani N, Cotsonis G, Wilcox CM. Upper gastrointestinal bleeding in patients with chronic renal failure: role of vascular ectasia. Am J Gastroenterol. 1996;91(11):2329–32.