

# Clinically Significant Endoscopic Findings in a Multi-Ethnic Population With Uninvestigated Dyspepsia

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## Abstract

**Introduction** The proportion of clinically significant endoscopic findings (CSEF) in dyspepsia affects the initial management of this condition. With the changing epidemiology of organic upper gastrointestinal diseases in Asia, current data on CSEF remains uncertain.

**Methods** A cross-sectional study of consecutive adult patients attending an open access endoscopy list for the primary indication of dyspepsia was conducted. Independent epidemiological and clinical factors for CSEF were determined prospectively.

**Results** Data for 1167/1208 (96.6 %) adults (mean age  $49.7 \pm 15.9$  years, 42.4 % males, ethnic distribution: 30.5 % Malays, 36.9 % Chinese and 30.8 % Indians) were analysed between January 2007 and August 2008. Three-hundred and eight (26.4 %) patients were found to have CSEF, most often those with age  $\geq 45$  years (30.3 vs 19 %,  $P < 0.0001$ ), male gender (34.1 vs 20.7 % female,  $P < 0.0001$ ), lower education levels (i.e. primary or no education), smoking (36.7 vs 24.9 %,  $P = 0.003$ ), *H. pylori* infection (40.6 vs 21.8 %,  $P < 0.0001$ ), and duration of dyspepsia  $\leq 5$  months (32.8 vs 24.4 %,  $P = 0.006$ ). Age  $\geq 45$  years (OR 1.82, 95 % CI = 1.38–2.48), male gender (OR 1.84, 95 % CI = 1.53–2.59), *H. pylori* infection (OR 2.36, 95 % CI = 1.83–3.26), and duration of dyspepsia  $\leq 5$  months (OR 1.44, 95 % CI = 1.13–2.03) were subsequently identified as independent risk factors for CSEF.

**Conclusion** CSEF are found in 26.4 % of Asian adults with uninvestigated dyspepsia. Duration of symptoms

$< 5$  months, among other recognised factors, is predictive of CSEF.

**Keywords** Dyspepsia · Clinically significant endoscopic findings · Peptic ulcer disease · Erosive oesophagitis · Gastro-oesophageal malignancy · Asia · Multi-ethnic population

## Introduction

Uninvestigated dyspepsia is a common global condition with a reported prevalence of 10–40 % [1]. It has a chronic, relapsing natural history [2] and is known to have a significant effect on health-related quality of life of sufferers [3]. The commonest cause of dyspepsia is functional disease; organic diseases, for example peptic ulceration, erosive oesophagitis, and gastro-oesophageal malignancy are known to be less frequent [4]. Treatment response varies substantially between functional and organic dyspepsia, with the latter having a potential for cure, particularly in peptic ulcer disease and erosive oesophagitis.

Guidelines from Europe [5] and the US [6] recommend a “*Helicobacter pylori* test and treat” strategy for uninvestigated dyspepsia in adults without alarm symptoms, while reserving upper gastro-intestinal endoscopy (UGIE) for patients aged  $> 45$  years, with alarm symptoms or who fail to respond to initial empirical therapy. Because erosive oesophagitis has been demonstrated to be the commonest cause of organic dyspepsia in Western patients [4, 7], others have suggested that empirical proton pump inhibitor (PPI) therapy may be more cost-effective [8].

It is uncertain if treatment strategies developed in the West are appropriate for Asians with uninvestigated dyspepsia. Prevalence of peptic ulcer disease, erosive

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oesophagitis, gastroesophageal malignancy, and *Helicobacter pylori* (an important cause of peptic ulcers) are known to vary between East and West [9, 10]. Furthermore, the epidemiology of organic causes of dyspepsia is changing globally [11]. A recent systematic review attempted to pool the prevalence of clinically significant endoscopic findings (CSEF), i.e. organic disease responsible for symptoms of dyspepsia, from both Western and Eastern studies [12]. However, most of the studies from Asia in this review were predominantly from East Asia with populations of ethnic Chinese only. Malaysia, a South East Asian country of some 26 million citizens, has a multi-ethnic population consisting of ethnic Malays, Chinese, and Indians [13]. The distinctly varied proportion of organic disease in these three different Asian ethnic groups [14–16] provides a unique opportunity to determine CSEF in patients with uninvestigated dyspepsia which is of relevance to other regions in Asia.

## Methods

A cross-sectional study was conducted on consecutive adults aged 18 years and above, referred for the primary indication of dyspepsia. Most cases of UGIE were referred from a large, dedicated, primary care unit within the vicinity of the institution. The remainder of cases were referred from the specialist Gastroenterology or General Surgical clinics from this institution. Local institutional ethics committee approval was obtained before conducting the study.

Dyspepsia was defined in accordance with the Leeds Dyspepsia Questionnaire (LDQ). The LDQ is an eight-item symptom-based questionnaire relating to the frequency and severity of different upper GI symptoms, namely upper abdominal pain/discomfort, heartburn, regurgitation, dysphagia, belching, nausea, vomiting, and post-prandial distension/early satiety [17]. The questionnaire has previously been translated, and validated for our local population, and shown to be reliable in assessing dyspepsia amongst Malaysians [18]. Exclusion criteria for the study included: previous UGIE or barium meal at any stage, previous documented upper G.I. pathology or surgery, previous empiric *H. pylori* eradication, or PPI use within two weeks of endoscopy. Adults in the latter category were included in the study if they were willing to discontinue PPI use and re-schedule their endoscopy appointment four weeks later.

Informed consent was obtained and a trained research assistant interviewed all patients before endoscopy. Baseline demographical data, BMI, smoking habits, duration of dyspepsia symptoms, and primary care consultation were prospectively collected. Alarm features were defined as the presence of any of the following: dysphagia, significant

weight loss ( $\geq 5$  kg) over the last six months, haematemesis, melaena, and anaemia. The presence of these features was dependent on the patient's perception of symptoms, apart from anaemia. Anaemia was defined as serum haemoglobin (Hb) of less than 11 g/dL for both males and females, confirmed by laboratory results. Data on regular aspirin or NSAID use was obtained from this institution's electronic pharmacy database, because all prescriptions from the primary care unit were dispensed from the hospital's pharmacy. Patients were also asked if they used non-prescribed NSAIDs.

## Endoscopic Evaluation

UGIE was performed with conscious sedation (midazolam) for most patients by trained gastroenterologists or by trainees under supervision of a senior gastroenterologist. Video gastroscopes (GIF 140 or 160, Olympus Optical, Tokyo, Japan) were used in all cases. Biopsies were taken of all suspicious lesions for histopathological evaluation. In addition, two biopsies each were taken from the antrum and body for detection of *H. pylori* by use of a local rapid urease test kit, shown to have 96.6 % sensitivity and 99.2 % specificity for *H. pylori* detection [19].

Gastro-duodenal erosions were defined as superficial mucosal defects ( $< 5$  mm in diameter) with a flat or raised edge and could be either red, white, or yellow [20, 21]. Gastric or duodenal ulcers were defined as mucosal breaks  $> 5$  mm in diameter [22]. Erosive oesophagitis was defined in accordance with the Los Angeles classification [23] and Barrett's oesophagus was diagnosed on the basis of the appearance of columnar-lined distal oesophagus with histological confirmation of intestinal metaplasia. All suspected gastro-oesophageal malignancies were confirmed by histopathological reports. Because the correlation between histological gastritis and endoscopic appearance is recognised to be poor [24], reports by endoscopists with findings of "erythema" or "gastritis" were documented as "normal" for the purposes of this study. Where appropriate, the most clinically significant endoscopic diagnosis was recorded for each patient. For example, a patient with both gastric erosions and duodenal ulcers was documented as having duodenal ulcer alone for this study. The order for the most important endoscopic findings was: gastric/oesophageal malignancy  $>$  peptic ulcer  $>$  reflux oesophagitis  $>$  duodenitis  $>$  gastric erosions. Endoscopists were instructed to digitally record images of reported endoscopic pathology (apart from normal or "gastritis") on the computerised endoscopy reporting software and all such images were subsequently reviewed by the lead investigator (SM) to confirm the reported endoscopic findings. Differences in opinion were discussed with the appropriate senior endoscopists and a consensus diagnosis was made.

## Clinically Significant Endoscopic Findings

Clinically significant findings (CSEF) were defined as any endoscopic pathology that may have accounted for symptoms of dyspepsia. In particular, hiatus hernia and gastric erosions were not thought to be clinically relevant. The significance of the former is uncertain, and several studies have refuted the association of chronic gastritis and erosions with symptoms of dyspepsia [24, 25]. A recent 17-year follow up study has further confirmed that gastric erosions alone (without *H. pylori* infection) had no relationship with dyspepsia symptoms and resulted in no increased risk of peptic ulcer development [26]. In contrast, endoscopic duodenitis/erosions has been shown to have a similar phenotype to peptic ulcer disease [27], with endoscopic resolution correlating with symptom improvement for patients on anti-secretory medication [28]. Clinically significant endoscopic findings in this study were therefore defined as duodenitis/erosions, peptic ulcer disease, reflux oesophagitis, and gastro-oesophageal malignancy.

## Statistical Analysis

On the basis of an estimated 25 % prevalence of CSEF [10], it was calculated that a sample size of 1,200 would have a power of 99.7 % to detect differences between groups at the 0.001 significance level. Data analysis was performed by use of a standard software package (SPSS version 11.5, Chicago, IL, USA). For the purposes of analysis, continuous data were classified into categorical groups, i.e. age, BMI, etc. Univariate comparisons of relevant clinical and demographic data were performed to identify associations for CSEF using  $\chi^2$  or Fisher's exact test where appropriate. Independent risk factors for CSEF were subsequently identified by use of a logistic regression model, with values expressed as odds ratios with 95 % confidence intervals. All *P* values were two-tailed with the level of significance defined at 0.05.

## Results

### Patient and Dyspepsia Characteristics

Between January 2007 and August 2008, 1,198 of 1,208 patients who were approached agreed to participate in the study. Thirty-one adults were taking regular PPIs at the time and were excluded, leaving a total of 1,167 (96.6 %) patients in the study. Eight-hundred and seventy-one (74.6 %) patients were referred from primary care and 296 (25.4 %) were referred from the hospital's specialist clinics. The baseline characteristics of these patients are listed in Table 1. The mean age of the study cohort was

49.7 ± 15.9 years, with 495 (42.4 %) males, and similar distribution of the three main ethnic groups was observed, i.e. 30.5 % Malays, 36.9 % Chinese, and 30.8 % Indians. A relatively low proportion of patients were regular smokers (12.6 %) or consuming regular alcohol (4.9 %). One-hundred and nineteen (10.4 %) patients had additional cardiovascular co-morbidity necessitating regular aspirin intake. Regular NSAID consumption was observed in 136 (11.9 %) adults, and 15 (1.3 %) patients were consuming a combination of aspirin and NSAIDs.

The median duration of dyspepsia was 24 months. With the LDQ, we were able to characterise predominant dyspeptic symptoms as follows: dysmotility like (i.e. bloating, nausea, belching) *n* = 447 (38.3 %), upper abdominal pain *n* = 487 (41.7 %), reflux-like (heartburn and regurgitation) *n* = 163 (14.0 %), and mixed *n* = 70 (6.0 %). Alarm features were present for 618 (53.0 %) patients. Individual frequency of alarm features/symptoms were: dysphagia *n* = 237 (20.3 %), weight loss *n* = 286 (24.5 %), haematemesis *n* = 35 (3.0 %), passing dark stool *n* = 168 (14.4 %); and anaemia *n* = 203 (17.4 %). Using age ≥45 years as a cut off for increased risk of significant pathology (see below), it was also observed that alarm features were more common for patients ≥45 years of age (*n* = 407, 66.1 %) than for those aged <45 years of age (*n* = 209, 33.9 %). This age “cut off” was based on historical European data [29], which has formed the basis for clinical guidelines in the management of dyspepsia globally [5, 6]. Most patients had been consulting primary care physicians for a median period of 12 months and had been consuming medications (either prescribed or bought over-the-counter) for a similar period of time. Seven-hundred and forty-seven (62.4 %) patients were taking antacids, 239 (19.9 %) had taken H2RAs up to one week before endoscopy, and the remainder were not on medication or consuming traditional/herbal remedies.

### Endoscopic Findings for Study Patients

The endoscopic findings for 1,167 adults with uninvestigated dyspepsia are listed in Table 2. For 632 (54.2 %) patients endoscopic findings were entirely normal. Three-hundred and eight (26.4 %) were found to have CSEF, which included: peptic ulcer disease *n* = 165 (14.1 %), reflux oesophagitis/Barrett's esophagus *n* = 137 (11.7 %), and gastro-oesophageal malignancy *n* = 6 (0.6 %). Ninety-two of 131 (70.2 %) cases of reflux oesophagitis had L.A. Grade A findings. Different opinions regarding endoscopic pathology mainly related to grading of reflux oesophagitis, with initial higher rates of Grade B subsequently revised to Grade A. No significant differences in organic pathology were observed between patients referred from primary or secondary care. Major endoscopic findings were found to

**Table 1** Baseline demography and clinical features of dyspepsia in the subjects

	<i>n</i> = 1,167 ( % )
Age (years)	
Mean $\pm$ SD	49.7 $\pm$ 15.9
(Range)	18–86
Sex	
Male	495 (42.4)
Female	672 (57.6)
Ethnicity	
Malay	356 (30.5)
Chinese	431 (36.9)
Indian	359 (30.8)
Native	21 (1.8)
Education level	
Tertiary	255 (21.9)
Secondary	601 (51.5)
Primary	250 (21.4)
None	61 (5.2)
BMI (kg/m <sup>2</sup> )	
Mean $\pm$ SD	24.9 $\pm$ 5.3
Smoking habit	
None	1,005 (86.1)
<20 cigarettes per day	110 (9.4)
>20 cigarettes per day	52 (4.5)
Alcohol intake	
Regular	57 (4.9)
NSAID/aspirin use	
Aspirin alone	119 (10.4)
NSAID alone	136 (11.9)
Aspirin + NSAID	15 (1.3)
LDQ score	
Mean $\pm$ SD	18.2 $\pm$ 7.8
Duration of dyspepsia (months)	
Median	24
Interquartile range	6–84
Duration of medical consultation (months)	
Median	12
Interquartile range	3–60
Alarm features (any)	
Age < 45 ( <i>n</i> = 405)	209 (51.6)
$\geq$ 45 years ( <i>n</i> = 762)	407 (53.4)

be more common in adults aged >45 years than in those aged <45 years (Table 2). Four dyspeptic patients with chronic hepatitis B, who were not known to have cirrhosis, were found to have incidental oesophageal varices, all of which were Grade 1 in size (varices that can be flattened by insufflation).

Differences in organic disease between the three main ethnic groups were examined (Fig. 1). Peptic ulcer disease was found to be more common among patients of Chinese ethnicity (17.6 %) than among ethnic Indians (11.4 %) and Malays (12.4 %) ( $P = 0.02$ ). In contrast, reflux oesophagitis and gastro-esophageal cancer were more prevalent among ethnic Indians than among the other ethnic groups. *H. pylori* infection was significantly higher among ethnic Indians (35.3 %) and Chinese (27.1 %), and much lower in patients of Malay ethnicity (8.2 %) ( $P < 0.0001$ ).

Six patients with dyspepsia were found to have gastro-esophageal malignancy—gastric adenocarcinoma  $n = 2$ , gastric lymphoma  $n = 1$ , distal oesophageal squamous cell carcinoma (SCC)  $n = 3$ . Five patients were aged  $\geq 45$  years, and they were either of Indian ( $n = 4$ ) or Chinese ( $n = 2$ ) ethnicity. All six patients had at least one alarm feature and 5 of the 6 had disease of stage III or more (based on TNM classification [30]) at the time of presentation of clinical symptoms. The median duration of dyspepsia in this group of patients was five months. The patient with gastric non-Hodgkin's lymphoma was diagnosed with concomitant hepatocellular carcinoma one week later and died a month later with no oncological therapy.

#### Risk Factors for CSEF

Potential clinical and basic epidemiological risk factors for CSEF were examined by use of a univariate model (Table 3). CSEF were more commonly found in patients with the factors: age  $\geq 45$  years ( $P < 0.0001$ ), male gender ( $P < 0.0001$ ), lower education levels (i.e. primary or no education), smoking ( $P = 0.003$ ), *H. pylori* infection ( $P < 0.0001$ ), and dyspepsia duration of  $\leq 5$  months ( $P = 0.006$ ). Of interest was that no particular ethnic group was significantly associated with significant endoscopic findings, although patients with Chinese ethnicity seemed to have more significant pathology than ethnic Malays or Indians. Also, neither regular NSAID/aspirin consumption nor alarm features increased the risk of endoscopic pathology. Independent predictors of significant endoscopic findings were explored by logistic regression (Table 3). Age  $\geq 45$  years (OR 1.82, 95 % CI = 1.38–2.48), male gender (OR 1.84, 95 % CI = 1.53–2.59), *H. pylori* infection (OR 2.36, 95 % CI = 1.83–3.26), and dyspepsia duration  $\leq 5$  months (OR 1.44, 95 % CI = 1.13–2.03) were identified as independent risk factors for significant endoscopic findings. The importance of lower education levels and smoking, identified earlier, were rendered insignificant in the multivariate analysis.

**Table 2** Endoscopic diagnoses in Malaysian adults with dyspepsia, stratified by age and referral source

Diagnosis	Age < 45 n = 405 (%)	Age ≥ 45 n = 762 (%)	Specialist clinics n = 296 (%)	Primary care n = 871 (%)
Normal/Insignificant <sup>a</sup>	327 (80.7)	528 (69.3)	231 (78.0)	640 (73.5)
Peptic ulcer disease	32 (7.9)	133 (17.5)	43 (14.8)	111 (12.7)
Gastric ulcers	13 (3.2)	65 (8.5)	21 (7.1)	55 (6.3)
Duodenal ulcers	6 (1.5)	37 (4.9)	9 (3.0)	33 (3.8)
Gastro-duodenal ulcer	2 (0.5)	1 (0.1)	0	2 (0.2)
Duodenitis	11 (2.7)	30 (3.9)	13 (4.4)	21 (2.4)
Reflux oesophagitis	44 (10.9)	93 (12.2)	20 (6.8)	111 (12.7)
L.A. Grade A	32 (8.0)	60 (7.9)	14 (4.7)	79 (9.1)
L.A Grade B	9 (2.2)	21 (2.8)	5 (1.7)	24 (2.8)
L.A Grade C	3 (0.7)	6 (0.8)	0	3 (0.3)
Barrett’s esophagus	0	6 (0.8)	1 (0.3)	5 (0.6)
Malignancy	1 (0.2)	5 (0.7)	0	6 (0.7)
Oesophageal cancer	1 (0.2)	2 (0.3)	0	3 (0.3)
Gastric cancer	0	3 (0.4)	0	3 (0.3)
Other <sup>b</sup>	1 (0.2)	3 (0.4)	2 (0.7)	3 (0.3)

<sup>a</sup> Includes Hiatus hernia, gastric erosions

<sup>b</sup> Esophageal varices

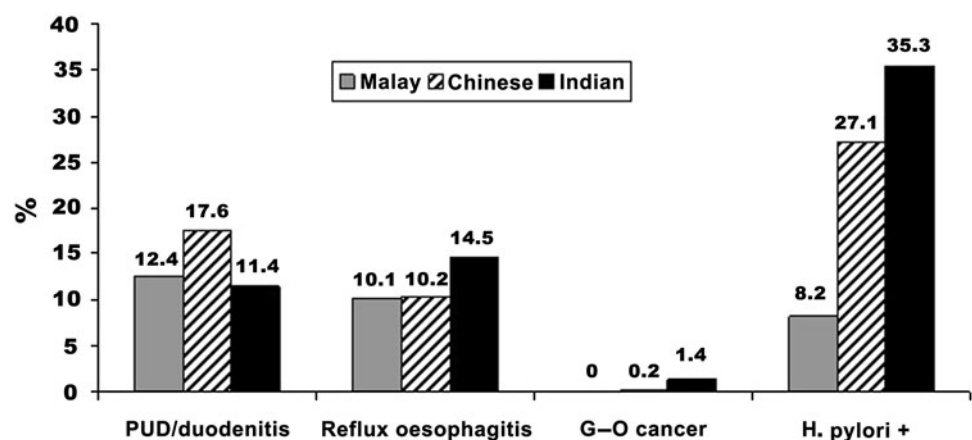
**Discussion**

This large series of 1,167 patients with uninvestigated dyspepsia has provided clinically useful information on the relevance of organic disease in Asian patients with dyspepsia. Despite several limitations, in particular, inter-observer variation of endoscopic findings (limited by single operator review of endoscopic images) and the fact that the study sample was not community-based, there are several strengths to this study. Firstly, 75 % of patients were referred from primary care via an open-access endoscopy list, representing patients who consulted in the community. Secondly, there was a similar proportion of organic disease in both primary and specialist clinic cases referred for UGIE in this series. Due to the structure of the health-care system in urban Malaysia [31] many

patients are able to consult specialists without a prior primary care visit. Third, we used a broad, inclusive, definition of dyspepsia with the Leeds Dyspepsia Questionnaire [18], known to be more representative of patients symptoms in the community [32], unlike previous community-based studies from Asia which used the Rome criteria [33, 34].

The overall prevalence of CSEF (26.4 %) in this multi-ethnic Asian population with uninvestigated dyspepsia was similar to that reported after recent Western community-based studies [4, 7]. However, when examined by type, higher rates of peptic ulcer disease (14.1 %) and a lower frequency of erosive oesophagitis (11.7 %) were observed among our Asian patients compared to Western patients with dyspepsia. A systematic review of nine cross-sectional community-based studies reported that the pooled

**Fig. 1** Differences in endoscopic pathology and *H. pylori* infection among the three major Asian ethnic groups with dyspepsia. (PUD, peptic ulcer disease; G-O, gastro-oesophageal)





**Table 3** Risk factors for clinically significant endoscopic findings

Factors	No CSEF <i>n</i> = 859 (%)	CSEF <i>n</i> = 308 (%)	Adjusted OR	95 % CI	<i>P</i>
<b>Age</b>					
<45	328 (81.0)	77 (19.0)	1.00		
≥45	531 (69.7)	231 (30.3)	1.82	1.34–2.49	<0.0001
<b>Gender</b>					
Female	533 (79.3)	139 (20.7)	1.00		
Male	326 (65.9)	169 (34.1)	1.84	1.40–2.43	<0.0001
<b>Ethnicity</b>					
Malay	276 (77.5)	80 (22.5)	1.00		
Chinese	310 (71.9)	121 (28.1)	1.06	0.73–1.54	0.75
Indian	261 (72.7)	98 (27.3)	0.97	0.67–1.41	0.88
<b>BMI</b>					
<25	506 (75.1)	168 (23.0)	1.00		
≥25	350 (71.4)	140 (28.6)	1.24	0.94–1.63	0.14
<b>Education</b>					
Tertiary	204 (80.0)	51 (20.0)	1.00		
Secondary	443 (73.7)	158 (26.3)	1.26	0.86–1.84	0.24
Primary	171 (68.4)	79 (31.6)	1.41	0.90–2.20	0.14
None	41 (67.2)	20 (32.8)	1.60	0.81–3.16	0.17
<b>Smoker</b>					
No	766 (75.1)	254 (24.9)	1.00		
Yes	93 (63.3)	54 (36.7)	1.27	0.83–1.93	0.27
<b><i>H. pylori</i></b>					
Negative	694 (78.2)	194 (21.8)	1.00		
Positive	164 (59.4)	112 (40.6)	2.36	1.74–3.18	<0.0001
<b>Aspirin/NSAID</b>					
No	657 (72.6)	248 (27.4)			
Yes	182 (75.8)	58 (24.2)	–	–	–
<b>Dyspepsia duration (months)</b>					
>5	677 (75.6)	219 (24.4)	1.00		
≤5	182 (67.2)	89 (32.8)	1.44	1.05–1.97	0.023
<b>Predominant symp</b>					
Dysmotility-like	329 (73.6)	118 (26.4)			
Abdominal pain	361 (74.1)	126 (25.9)			
Reflux-like	115 (70.6)	48 (29.4)	–	–	–
<b>Alarm features</b>					
No	391(71.2)	158 (28.8)	1.00		
Yes	468 (75.7)	150 (24.3)	0.77	0.58–1.01	0.06

prevalence of peptic ulcer disease and erosive oesophagitis among patients with uninvestigated dyspepsia was 8 and 13.4 %, respectively [12]. However, when studies in the review were examined separately by geographical location, Ford et al. reported that the pooled prevalence of peptic ulcer disease and erosive oesophagitis was 11.0 and 2.7 %, respectively, in Asian studies compared with 6.0 and 25.0 %, respectively in Western studies. This difference in organic disease has been reported elsewhere [10], and

shown to be a result of differences in epidemiology between Asian and Western patients with dyspepsia [9, 35].

The proportion of gastro-oesophageal malignancy amongst this study sample was low (0.6 %). Previous studies in the West have suggested that a search approach for malignancy in adults with uncomplicated dyspepsia was not cost-effective [36]. All patients in our study were aged ≥45 years apart from one female patient who was aged 37 years at presentation. All of these cancers presented at an

advanced stage, indicating that the development of malignancy probably pre-dated the onset of their dyspepsia symptoms, which were fairly short. Furthermore, although most of the patients with gastro-esophageal malignancy had alarm features, this study demonstrated that alarm features were not predictive of CSEF in patients with uninvestigated dyspepsia. Similarly, a recent systematic review demonstrated that alarm features had a low positive predictive value for malignancy [37]. Alarm features had a high negative predictive value for GI malignancy, but this simply reflected the low prevalence of cancer amongst dyspeptic patients, rather than a specific attribute of the absence of alarm features in ruling out malignancy.

Greater age (>45 years), male gender, *H. pylori* infection, and a short duration of dyspepsia symptoms were found to predict significant endoscopic pathology in this study. Increased occurrence of organic disease in adults of advanced age [4, 29, 38–41], male gender [38, 41, 42], and with *H. pylori* infection [4, 38, 40, 42] have been reported in studies conducted largely in secondary care settings. However, the association between duration of dyspepsia symptoms and CSEF is controversial. A shorter duration of dyspepsia with alarm symptoms has been suggested to be associated with poorer prognosis because of the presentation of more advanced gastric malignancy [43]. A recent systematic review, however, was not able to demonstrate a relationship between duration of symptoms and the presence of non-malignant CSEF in patients with dyspepsia [12]. However, there was significant heterogeneity in the definition of dyspepsia used in the nine studies that were included in this review. Dyspepsia is defined with a minimum period of three months in the Rome questionnaire [44] whereas most other definitions usually require a duration of 1 month [17].

Ethnicity alone was not predictive of CSEF in this study. We found that peptic ulcer disease was more prevalent in ethnic Chinese, and erosive oesophagitis was more common in ethnic Indians, similar to previous findings in this region [10, 16]. Furthermore, *H. pylori* infection and gastro-esophageal malignancy were more prevalent among ethnic Chinese and Indians than among ethnic Malays. The different prevalence of *H. pylori* infection among ethnic groups is well recognised in this region [14], mainly because *H. pylori* infection is known to be lower among ethnic Malays. Conversely, whereas prevalence of *H. pylori* infection is highest among ethnic Indians, they have less organic disease than ethnic Chinese, a phenomenon well recognised as the “Indian Enigma” [14]. It is likely, then, that if CSEF outcomes had been stratified into oesophagitis-related or peptic ulcer-related, ethnicity may have proved significant in our analysis.

We have shown that peptic ulcer disease and erosive oesophagitis are the commonest CSEF in a multi-ethnic

Asian population with uninvestigated dyspepsia. It seems possible, then, that an *H. pylori* “test and treat” strategy, i.e. a non-invasive test for *H. pylori* followed by eradication therapy for those testing positive and empirical PPI therapy for *H. pylori*-negative cases, can be used for initial management of Asian patients with uninvestigated dyspepsia. A previous randomised trial conducted among young Asian patients with uninvestigated dyspepsia demonstrated that a *H. pylori* “test and treat” strategy was more cost-effective than immediate endoscopy [45]. Data from our study suggest that such a strategy may be appropriate for older Asian patients also, although further study is required to confirm this.

**Conflict of interest** None.

## References

1. Mahadeva S, Goh KL. Epidemiology of functional dyspepsia: a global perspective. *World J Gastroenterol*. 2006;12:2661–2666.
2. Ford AC, Forman D, Bailey AG, Axon AT, Moayyedi P. Initial poor quality of life and new onset of dyspepsia: results from a longitudinal 10-year follow-up study. *Gut*. 2007;56:321–327.
3. Mahadeva S, Yadav H, Rampal S, Everett SM, Goh KL. Ethnic variation, epidemiological factors and quality of life impairment associated with dyspepsia in urban Malaysia. *Aliment Pharmacol Ther*. 2010;31:1141–1151.
4. Thomson AB, Barkun AN, Armstrong D, et al. The prevalence of clinically significant endoscopic findings in primary care patients with uninvestigated dyspepsia: the Canadian Adult Dyspepsia Empiric Treatment-Prompt Endoscopy (CADET-PE) study. *Aliment Pharmacol Ther*. 2003;17:1481–1491.
5. Malfertheiner P, Megraud F, O’Morain C, et al. Current concepts in the management of *Helicobacter pylori* infection: the Mastricht III Consensus Report. *Gut*. 2007;56:772–781.
6. Talley NJ, Vakil N. Guidelines for the management of dyspepsia. *Am J Gastroenterol*. 2005;100:2324–2337.
7. Zagari RM, Law GR, Fuccio L, Pozzato P, Forman D, Bazzoli F. Dyspeptic symptoms and endoscopic findings in the community: the Loiano-Monghidoro study. *Am J Gastroenterol*. 2010;105:565–571.
8. Delaney BC, Qume M, Moayyedi P, et al. *Helicobacter pylori* test and treat versus proton pump inhibitor in initial management of dyspepsia in primary care: multicentre randomised controlled trial (MRC-CUBE trial). *BMJ*. 2008;336:651–654.
9. Lam SK. Differences in peptic ulcer between East and West. *Baillieres Best Pract Res Clin Gastroenterol*. 2000;14:41–52.
10. Mahadeva S, Raman MC, Ford AC, et al. Gastro-oesophageal reflux is more prevalent in Western dyspeptics: a prospective comparison of British and South-East Asian patients with dyspepsia. *Aliment Pharmacol Ther*. 2005;21:1483–1490.
11. el-Serag HB, Sonnenberg A. Opposing time trends of peptic ulcer and reflux disease. *Gut*. 1998;43:327–333.
12. Ford AC, Marwaha A, Lim A, Moayyedi P. What is the prevalence of clinically significant endoscopic findings in subjects with dyspepsia? Systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2010;8:830–837, 837 e1–e2.
13. Department of Statistics Malaysia. Population distribution and basic demographic characteristics. The 2000 Population and Housing Census of Malaysia. Putrajaya: Department of Statistics 2000.

14. Goh KL, Parasakthi N. The racial cohort phenomenon: seroepidemiology of *Helicobacter pylori* infection in a multiracial South-East Asian country. *Eur J Gastroenterol Hepatol*. 2001; 13:177–183.
15. Goh KL, Cheah PL, Md N, Quek KF, Parasakthi N. Ethnicity and *H. pylori* as risk factors for gastric cancer in Malaysia: a prospective case control study. *Am J Gastroenterol*. 2007;102:40–45.
16. Rosaida MS, Goh KL. Gastro-oesophageal reflux disease, reflux oesophagitis and non-erosive reflux disease in a multiracial Asian population: a prospective, endoscopy based study. *Eur J Gastroenterol Hepatol*. 2004;16:495–501.
17. Moayyedi P, Duffett S, Braunholtz D, et al. The Leeds Dyspepsia Questionnaire: a valid tool for measuring the presence and severity of dyspepsia. *Aliment Pharmacol Ther*. 1998;12:1257–1262.
18. Mahadeva S, Chan WK, Mohazmi M, Sujarita R, Goh KL. Validation study of the Leeds Dyspepsia Questionnaire in a multi-ethnic Asian population. *J Gastroenterol Hepatol*. 2011;26: 1669–1676.
19. Goh KL, Parasakthi N, Peh SC, Puthuchery SD, Wong NW. The rapid urease test in the diagnosis of *Helicobacter pylori* infection. *Singapore Med J*. 1994;35:161–162.
20. Myren J, Serck-Hanssen A. The gastroscopic diagnosis of gastritis with particular reference to mucosal reddening and mucus covering. *Scand J Gastroenterol*. 1974;9:457–462.
21. Venables CW. Duodenitis. *Scand J Gastroenterol Suppl*. 1985; 109:91–101.
22. Bernersen B, Johnsen R, Straume B, Burhol PG, Jenssen TG, Stakkevold PA. Towards a true prevalence of peptic ulcer: the Sorreisa gastrointestinal disorder study. *Gut*. 1990;31:989–992.
23. Armstrong D, Bennett JR, Blum AL, et al. The endoscopic assessment of esophagitis: a progress report on observer agreement. *Gastroenterology*. 1996;111:85–92.
24. Johnsen R, Bernersen B, Straume B, Forde OH, Bostad L, Burhol PG. Prevalences of endoscopic and histological findings in subjects with and without dyspepsia. *BMJ*. 1991;302:749–752.
25. Cheli R, Perasso A, Giacosa A. Dyspepsia and chronic gastritis. *Hepatogastroenterology*. 1983;30:21–23.
26. Toljamo KT, Niemela SE, Karttunen TJ, Karvonen AL, Lehtola JK. Clinical significance and outcome of gastric mucosal erosions: a long-term follow-up study. *Dig Dis Sci*. 2006;51: 543–547.
27. DeLuca VA Jr, Winnan GG, Sheahan DG, et al. Is gastroduodenitis part of the spectrum of peptic ulcer disease? *J Clin Gastroenterol*. 1981;3:17–22.
28. Danielsson A, Ek B, Nyhlin H, Steen L. The relationship between active peptic ulcer, endoscopic duodenitis and symptomatic state after treatment with cimetidine. *Ann Clin Res*. 1980;12:4–12.
29. Williams B, Luckas M, Ellingham JH, Dain A, Wicks AC. Do young patients with dyspepsia need investigation? *Lancet*. 1988; 2:1349–1351.
30. American Joint Committee on Cancer. Oesophagus & Stomach. In: *AJCC Cancer Staging Manual*. 6th ed. New York, NY: Springer, 2002:91–106.
31. Noor Ghani S, Yadav H. *Health care in Malaysia*. Singapore: University of Malaya Press, 2008.
32. Fraser A, Delaney B, Moayyedi P. Symptom-based outcome measures for dyspepsia and GERD trials: a systematic review. *Am J Gastroenterol*. 2005;100:442–452.
33. Lu CL, Lang HC, Chang FY, et al. Prevalence and health/social impacts of functional dyspepsia in Taiwan: a study based on the Rome criteria questionnaire survey assisted by endoscopic exclusion among a physical check-up population. *Scand J Gastroenterol*. 2005;40:402–411.
34. Zhao Y, Zou D, Wang R, et al. Dyspepsia and irritable bowel syndrome in China: a population-based endoscopy study of prevalence and impact. *Aliment Pharmacol Ther*. 2010;32:562–572.
35. Goh KL, Chang CS, Fock KM, Ke M, Park HJ, Lam SK. Gastro-oesophageal reflux disease in Asia. *J Gastroenterol Hepatol*. 2000;15:230–238.
36. Vakil N, Talley N, van Zanten SV, et al. Cost of detecting malignant lesions by endoscopy in 2741 primary care dyspeptic patients without alarm symptoms. *Clin Gastroenterol Hepatol*. 2009;7:756–761.
37. Vakil N, Moayyedi P, Fennerty MB, Talley NJ. Limited value of alarm features in the diagnosis of upper gastrointestinal malignancy: systematic review and meta-analysis. *Gastroenterology*. 2006;131:390–401; quiz 659–660.
38. Hu PJ, Li YY, Zhou MH, et al. *Helicobacter pylori* associated with a high prevalence of duodenal ulcer disease and a low prevalence of gastric cancer in a developing nation. *Gut*. 1995; 36:198–202.
39. Breslin NP, Thomson AB, Bailey RJ, et al. Gastric cancer and other endoscopic diagnoses in patients with benign dyspepsia. *Gut*. 2000;46:93–97.
40. Sung JJ, Lao WC, Lai MS, et al. Incidence of gastroesophageal malignancy in patients with dyspepsia in Hong Kong: implications for screening strategies. *Gastrointest Endosc*. 2001;54: 454–458.
41. Wai CT, Yeoh KG, Ho KY, Kang JY, Lim SG. Diagnostic yield of upper endoscopy in Asian patients presenting with dyspepsia. *Gastrointest Endosc*. 2002;56:548–551.
42. Hashemi MR, Rahnavardi M, Bikdeli B, Dehghani Zahedani M. *H. pylori* infection among, southern Iranian dyspeptic patients. *World J Gastroenterol*. 2006;1000:5479–5482.
43. Maconi G, Manes G, Porro GB. Role of symptoms in diagnosis and outcome of gastric cancer. *World J Gastroenterol*. 2008; 14:1149–1155.
44. Drossman DA. The functional gastrointestinal disorders and the Rome III process. *Gastroenterology*. 2006;130:1377–1390.
45. Mahadeva S, Chia YC, Vinothini A, Mohazmi M, Goh KL. Cost-effectiveness of and satisfaction with a *Helicobacter pylori* “test and treat” strategy compared with prompt endoscopy in young Asians with dyspepsia. *Gut*. 2008;57:1214–1220.