REVIEW ARTICLE

Clinical and epidemiological differences in functional dyspepsia between the East and the West

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Key Messages

- The prevalence of FD appears to be generally higher in the West, regardless of the definitions of FD used (i.e. Rome I, II, or III).
- Eastern patients seem to have more dysmotility-type (Rome II) or PDS-type (Rome III) FD compared with Western FD patients.
- Differences in body mass index, opposing trends in the association between socio-economic status and FD, and variations in the components of dietary intake between West and East are possible contributory factors.
- The magnitude of symptom improvement post H. pylori eradication appears to be greater in Eastern patients with FD.
- The economic impact of FD differs significantly between the East and the West. Variation in healthcare-seeking behavior, management by secondary care clinicians, and work absenteeism are some of the causes.

Abstract

Background Functional dyspepsia (FD) is a common condition, affecting adults in both Western (North America and Europe) and Eastern (Asian) parts of the globe. The prevalence has been reported to range from 5% to 40%, largely due to variation from definition criteria and geographical location. Recent published reports in Western and Eastern populations separately indicate that differences in the epidemiology and clinical patterns of FD may exist. Such differences will have implications for the clinical management of and healthcare strategizing for FD at the local level.

Purpose This review aims to examine the prevalence and clinical patterns of FD in specific groups, namely Western and Eastern populations, based on the Rome criteria. Further differences in the epidemiological associations of FD will be explored between population-based studies in both the East and the West. Finally, the socio-economic consequences of FD, an important measure of the impact of the disease, will be compared between the East and the West.

Keywords Asian, Caucasian, clinical sub-type, East, economic impact, epidemiology, functional dyspepsia, West.

INTRODUCTION

Functional dyspepsia (FD) is defined as the presence of persistent symptoms referable to the upper gastrointestinal (GI) tract, in the absence of a structural organic pathology that would explain these symptoms. Functional dyspepsia is a common condition, affecting...
populations in both the West (North America and Europe) and the East (i.e., South, South-East, and East Asia). A previous systematic review suggested that the prevalence of FD was in the range of 11–15%, but this was largely based on Western data. Although FD does not lead to an increase in mortality, it leads to substantial morbidity, in terms of its impact on health-related quality of life and healthcare resource utilization. Despite its recognition as a global problem, it is uncertain if clinical and epidemiological aspects of FD are similar worldwide, particularly between the West and the East. Various factors known to influence the symptomatology of FD, such as transient lower esophageal sphincter relaxations, pathological acid exposure in the distal esophagus, dietary constituents, and body habitus, are known to differ in White Caucasian and Asian adults. Furthermore, healthcare-seeking behavior and resource utilization, important measures of the impact of FD, may depend on cultural attitudes and healthcare systems globally. This review article aims to compare and contrast the epidemiological associations and clinical characteristics of FD in both Western and Eastern populations. Selected epidemiological factors and the clinical features of FD which are notably different between Eastern and Western populations will be discussed. The observations in this review have been made using data from population-based studies or systematic reviews of population-based studies, published in the English language. In the absence of population-based data, evidence from large-scale (with \( n \approx 1000 \)) clinical studies, randomized clinical trials, or meta-analyses of randomized clinical trials were used instead.

**PREVALENCE OF FD**

Population-based studies in both the West and East have documented the prevalence of FD using various definitions, with the Rome III criteria being the current gold standard used in most recent publications. These consist of the presence of several upper GI symptoms (bothersome postprandial fullness, early satiety during a normal sized meal, epigastric pain or burning) lasting for 3 months or more, without any evidence of structural disease. One of the purposes of the Rome process, among others, was to standardize definitions of functional GI disorders, to minimize diagnostic confusion between them. To meet these criteria for FD in referral populations, upper GI endoscopy must be performed to exclude organic disease. In population-based studies on the other hand, where organic disease is rare, the implicit assumption is that the majority of subjects meeting the Rome criteria will have FD. This is supported by endoscopy-based studies conducted among adults in the community, which have demonstrated consistently that between 70% and 80% of people with uninvestigated dyspepsia will ultimately be labeled as having FD, particularly in the West. Although a concern for gastro-esophageal malignancy still exists for a sub-set of populations in the Far East, reports from other parts of Asia appear to demonstrate a similar rate of functional disease following investigation of patients with uninvestigated dyspepsia as in the West.

Hence, for this review, we have considered data from population-based studies which used any iteration of the Rome criteria (despite some limitations) to contrast the estimated prevalence rates of FD between the East and the West. Table 1 summarizes the prevalence rate ranges across several studies from Western and Eastern populations. Data for this summary have been derived from several review articles and recent original articles. It is clear that the prevalence of FD varies widely within Western or Eastern populations, let alone between them. Although studies using either the Rome I or II criteria appear to demonstrate a higher prevalence of FD, many of these were conducted several years ago. Hence, the differences observed in the prevalence of FD according to the different iterations of the Rome criteria may not only be due to the underlying differences in the definitions used but also additionally to the changing epidemiology of FD over time. Nevertheless, regardless of the definitions of the Rome criteria used, the prevalence rates for FD appear to be generally higher in Western compared with Eastern populations (Table 1).

**CLINICAL PATTERNS OF FD**

The current Rome III and the previous Rome II criteria categorize FD patients into sub-types, based on symptoms suggestive of specific pathophysiology. The Rome II criteria categorized FD patients broadly into one of three sub-types: reflux-like, ulcer-like, or...
dysmotility-like. The Rome III criteria has simplified this division into either epigastric pain syndrome (EPS) or postprandial distress syndrome (PDS). Although there are no studies directly comparing Western and Eastern FD sub-types, inferences have been made in several published reports. In a meta-analysis of the efficacy of proton pump inhibitors (PPI) in the treatment of FD, Wang et al. were able to compare the sub-types of FD patients in Western and Eastern studies according to the Rome II criteria. It was observed that Western FD patients had a greater proportion of ulcer-like and reflux-like FD sub-types, while Eastern FD patients had a predominance of dysmotility-like subtype. Interestingly, this meta-analysis demonstrated that FD patients with the ulcer-like and reflux-like sub-groups were more likely to have a response with PPI therapy compared to dysmotility-like FD patients.

Recently, two large endoscopy-based studies of dyspepsia, using the Rome III criteria, in secondary care have been published—one from Canada (with a predominant White Caucasian population) and the other from Taiwan (all of Chinese ethnicity). In the Canadian study, investigators reported that 40.8% of 851 adults with FD had a PDS sub-type and 41.2% had an overlap of EPS and PDS. In contrast, the Taiwanese study reported that 71.9% of 491 patients with FD had a PDS sub-type and 34.4% had an overlap of EPS and PDS. Interestingly, the Taiwanese study identified that Helicobacter pylori infection, particularly of the CagA strain (which is more prevalent in Asia) appeared to predict the presence of PDS sub-type among Taiwanese FD patients. This issue is discussed in more detail below. In Japan, a population-based Internet survey using the Rome III criteria reported that 67.3% of 563 adults with FD had a PDS, 11.0% had EPS and 21.7% had an overlap of EPS and PDS. Although the respondents in this survey had not been endoscoped, the low rate of organic disease among Japanese dyspeptics in the community suggests similarities between Japanese and Taiwanese FD patterns.

**BODY MASS INDEX**

An association between body mass index (BMI) and dyspepsia is recognized. A large community-based study based on the general practice research database in various regions in the UK reported a weak association between an increased BMI and dyspepsia (odds ratio [OR] 1.1) among 6913 adult subjects. A longitudinal study of a large British cohort of adults also identified a higher BMI as an independent predictor of the development of dyspepsia over a 10-year period. Furthermore, an increased BMI and obesity are recognized etiological factors for gastroesophageal reflux disease (GERD), a condition that is recognized to overlap with FD in a significant number of patients. In terms of body habitus, White Caucasian adults are well-recognized to have a greater BMI than age and gender-matched Asian adults. In a study comparing age- and gender-matched adults from both the UK and Singapore with uninvestigated dyspepsia, Kang and Ho demonstrated a higher BMI and a greater proportion of reflux-type symptoms among British dyspeptics. A larger scale study was subsequently conducted comparing age- and gender-matched subjects from the UK and Malaysia, the majority of whom had FD. When comparing symptoms alone, White Caucasian patients had a higher prevalence of ‘heartburn’ and ‘regurgitation’ symptoms compared with Malaysian adults, implying that there may be a greater degree of overlap between FD and symptoms suggestive of gastroesophageal reflux among the former (Fig. 1).
SOCIO-DEMOGRAPHY

Several Western population-based studies have reported that uninvestigated dyspepsia is associated with a lower socio-economic status. In a large population-based study in the UK, Moayyedi et al. reported that surrogate markers for a poorer socio-economic status, such as lower educational level, renting accommodation, and absence of central heating, were found to be independent predictors of dyspepsia. Factors such as over-crowding, poorer hygiene, and smoking may predispose to peptic ulcer disease and H. pylori infection, recognized causes of organic dyspepsia. However, other factors related to a lower socioeconomic status, such as obesity, poor dietary habits, and psychosocial disorders are also known to be linked with functional GI diseases. A large, population-based study of >8000 adults in Australia has subsequently shown that dysmotility-like dyspepsia (akin to the PDS sub-type of the Rome III criteria for FD) was more prevalent in adults of a lower socio-economic status, together with other lower GI symptoms. In contrast to these studies in predominantly White Caucasian populations, a recent population-based study in a rural community in Malaysia described the opposite, i.e., that dyspepsia was associated with surrogate markers of a higher socio-economic status, namely a higher education level and better standards of housing.

To test this hypothesis further, the investigators of this rural study conducted a similar survey in urban Malaysia, using the same study design and the Rome II criteria for FD. Using a sample size of approximately 2000 adults in both urban and rural studies, investigators were able to demonstrate a higher prevalence of dyspepsia in urban Malaysians (24.5%) with a higher socio-economic status compared with rural Malaysians (14.7%).

Thus, a difference in the socio-demographic association of FD between East and West appears to exist—FD is associated with a lower socioeconomic status in the West, but quite the opposite in the East. Although the exact explanation is unclear, differences in lifestyle habits of the lower socio-economic groups between Western and Eastern populations may account for this observation. For instance, a higher prevalence of obesity due to a sedentary lifestyle among White Caucasians may result in more FD in Western compared to Eastern adults in lower socio-economic classes. Although cigarette smoking (a recognized risk factor for uninvestigated dyspepsia) is more prevalent among adults in lower socioeconomic groups, the lack of difference in smoking behavior between East and West on a global scale suggests that this factor cannot account for FD differences that have been observed. However, differences in alcohol consumption between the West and East, may be a contributing factor to FD differences between these two populations. In Western populations, including those in Russia, alcohol consumption has been reported in the range of 10–12.5 L per capita, compared to 2.5–4.9 L per capita in Eastern nations. Alcohol has a recognized effect on the lower esophageal sphincter, contributing to pathological acid exposure in the distal esophagus, which has been shown to cause more EPS-type FD in Western adults.

HELICOBACTER PYLORI INFECTION

Helicobacter pylori infection may have a role in the etiology of FD, although the exact mechanism is uncertain. The bacterium is a recognized cause of chronic gastritis, which is thought to lead to abnormalities in gastroduodenal motility and sensitivity. Chronic gastritis might also affect a variety of endocrine functions of the stomach, including the production of the GI hormones and neurotransmitters somatostatin, gastrin, and ghrelin, which have also been associated with symptoms in FD. A previous, large, population-based study in the UK suggested that approximately 5% of dyspepsia in the community may be attributable to H. pylori infection.

A recent meta-analysis, of mostly Western-based studies, similarly demonstrated a positive, but modest, association between H. pylori and dyspepsia in the community (OR = 1.18; 95% CI: 1.04–1.33). However, despite these studies linking H. pylori with FD, a systematic review of predominantly Western trials examining H. pylori eradication in patients with FD demonstrated only a 10% improvement in symptoms and no effect on quality of life. In contrast, the findings from several recent randomized trials of H. pylori eradication for FD patients in Eastern studies suggests a greater magnitude of symptom improvement (15–20%). Additionally, a meta-analysis of randomized trials in China, which had only been published in the Chinese literature, demonstrated a threefold (OR = 3.61) chance of symptom improvement following H. pylori eradication in Chinese patients with FD. These reports suggest a possibility for a greater magnitude effect of H. pylori eradication in Asian patients with FD. A greater prevalence of H. pylori together with an increased prevalence of the CagA-positive strain (which is recognized to cause more dyspepsia symptoms) have been proposed as explanations for this observation. Furthermore, a previous study comparing demographically matched British and Japanese dyspeptics with H. pylori-associated gastritis reported a
greater severity of gastric inflammation in the latter [Fig. 2]. Resolution of more intense gastritis with *H. pylori* eradication may be a contributory factor towards greater symptom resolution in East Asian FD patients.

**DIETARY HABITS**

While the majority of patients with FD report meal-induced symptoms, the role of food in the development of FD is not exactly clear. Specific components of a normal diet however, are recognized to contribute to more frequent symptoms of dyspepsia. In the Western diet, foods high in fat have been shown to produce more dyspeptic symptoms, such as early satiety and bloating, compared with a high carbohydrate diet. In the Asian diet, especially that from South and South-East Asia, is known to be particularly spicy with a high chili content. Capsaicin, the active ingredient of chili, can modulate GI sensations of warmth, pressure, cramping, and pain in the gut via TRPV1 receptors, which are found throughout the GI tract. It has been shown to induce symptoms of dyspepsia, more so in FD than non-FD individuals supporting the idea of GI hypersensitivity in the pathogenesis of FD. Furthermore, experimental work in Singapore has previously demonstrated that distal esophageal stimulation is one of the main mechanisms of capsaicin-induced upper abdominal pain. A recent study in urban Malaysia indicated that the amount of chili intake in the person’s diet was strongly associated with the risk of reporting dyspepsia. Adults with a high intake of chili were more than twice as likely to have dyspepsia, compared with those with either a low chili intake or no chili at all. Thus, differences between Eastern and Western diets may explain some of the differences in FD patterns between East and West, although further study in this area is required to elucidate the reasons for this.

**PSYCHOLOGICAL DISORDERS**

The gut and the brain are highly integrated and communicate in a bidirectional fashion largely through the autonomic nervous system and the hypothalamic–pituitary–adrenal axis. It is therefore not surprising that psychological disorders have been associated with functional GI disorders such as FD. In a population-based study of almost 1000 adults who had undergone gastroscopy in Sweden, major anxiety, but not depression, was found to be independently predictive of FD (OR = 2.56) and the PDS sub-type (OR = 4.35). In a follow-up study of the same Swedish population, Aro et al. were able to demonstrate that anxiety, but not depression, increased the risk of developing FD by 7.6 times over a 10-year period. However, in an Australian population-based longitudinal study with over 12 years of follow-up, Koloski et al. reported that the association between gut and brain was bidirectional. Furthermore, although anxiety at baseline was predictive of developing various types of functional GI disorders after 12 years, depression was more predictive of FD in this Australian cohort of patients.

In contrast to these population-based studies in the West, most of the published literature from the East examining the association between psychological disorders and FD have been from referral or secondary care patient groups. This, together with the fact that psychological distress is a recognized driver for medical consultation among Eastern patients with FD, indicates that any differences in rates of psychological disorders between Eastern and Western FD patients remain speculative. In a Malaysian single-center study of 839 adults with dyspepsia, the investigators found no significant difference in major anxiety or major depression between patients with FD and organic dyspepsia, although the former appeared to have lower health-related quality of life indices. In another single-center study of 1341 adults from China, Jiang et al. reported that both major depression and major anxiety were more prevalent among patients with FD (60–63%) compared with healthy controls (0–10%). A single-center study from Taiwan of 187 patients meeting criteria for the PDS sub-type, but not the EPS
sub-type, of FD had a greater association with depression, somatization, and phobia, but not anxiety.64

SOCIO-ECONOMIC CONSEQUENCES

The true cost of any disease or condition is known to broadly consist of not only direct medical costs, which are made up of the cost of drug treatments, investigations, medical consultations, and hospitalizations during the management of an individual, but also indirect costs, which include costs to the patient such as traveling to medical facilities, and the costs to employers or society due to sickness-related absence from work or incapacity benefit. In a recent economic study based on FD patients attending a tertiary care center in the US, Lacy et al. estimated the direct and indirect costs of FD at US$ 18.4 billion for the entire US population or US$ 80 000 per 1000 US population for the 2009 financial year.6 Few studies have estimated the economic impact of FD in the East. However, two population-based studies in Malaysia have estimated the annual cost for uninvestigated dyspepsia to be US$ 14 816.00 and US$ 59 282.20 per 1000 population in a rural and urban setting respectively, or an estimated US$ 1.02 billion for the entire Malaysian population.65

As FD is the commonest cause of uninvestigated dyspepsia in this region,15 the Malaysian study suggests significant differences in the economic impact of FD between the West and East. Differences in healthcare systems and costs are recognized between the East and the West, with a higher cost of healthcare in the West.66 Aside from variation in healthcare systems however, other factors seem to contribute to a difference in the economic impact of FD between the East and the West. In the Malaysian study, approximately 70% of adults with dyspepsia were consulting at the primary care level, between 40% and 50% of dyspeptics relied solely on over-the-counter medication (with a significant proportion using traditional Asian medications), and the rate of radiological or invasive investigations in secondary care was low.65 In contrast, the US tertiary care center study reported that 87% of FD patients were on prescription medications, 25% used alternative or complementary medicines, and clinical management was more aggressive (90% had endoscopies, 40% had CT scans, and 23% had abdominal surgeries).6 Hence, differences in healthcare consultation behavior and clinical management by responsible physicians between East and West were major contributors to the economic difference in FD. Furthermore, socio-economic differences between employees (81% in the US study6 vs 27.7% in the Malaysian study65 with >US$ 10 000 annual income) additionally contributed to variation in indirect costs due to work absenteeism.

CONCLUSION

Functional dyspepsia is common globally, but does not have the same epidemiology or clinical features between populations in the East and West. The prevalence of FD appears to be higher in the West compared to the East, although variations within Asian or White Caucasian populations clearly exist. The clinical pattern or sub-type of FD does appear to vary between the East and the West, largely due to a higher prevalence of overlap between FD and GERD symptoms, and greater obesity in the West. Furthermore, variations in socio-demography [and lifestyle habits], dietary habits or preferences, response to H. pylori eradication and economic impact suggest that FD may not be the same condition in Eastern and Western populations.

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AUTHOR CONTRIBUTION

SM conceived the idea for the review article. Both SM and ACF contributed equally to the drafting and final approval of the manuscript.

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