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A comparison of the clinical, demographic and psychiatric profiles among patients with erosive and non-erosive reflux disease in a multi-ethnic Asian country

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Abstract

AIM: To examine the clinical spectrum of gastroesophageal reflux disease (GERD) and compare erosive (ERD) with non-erosive (NERD) in terms of clinical, demographic and psychiatric profiles.

METHODS: Patients with reflux symptoms were enrolled and stratified to NERD and ERD after endoscopy (LA classification). Patients with ERD presenting with dyspepsia were included. Patients on proton pump inhibitors (PPI) or H_2 receptor antagonists before endoscopy were excluded. Demographic data, *Helicobacter pylori* (*H pylori*) status and presence of minor psychiatric morbidity (based on General Health Questionnaire-28) were analyzed.

RESULTS: Among 690 patients screened, 533 were eligible for analysis (male to female ratio: 3:2; Chinese: 75.4%; Malay: 9.8%; Indian: 14.8%). Clinical spectrum of GERD: N: 40.5%; A: 46%; B: 9.2%; C: 2.1%; D: 0.6%; Barrett's esophagus: 1.7%. Compared to patients with NERD, patients with ERD were significantly older (45 *vs* 39.4 years), more likely to be male (64.4% *vs* 53.7%), tended to smoke (19.6% *vs* 9.7%), less likely to have minor psychiatric morbidity (26.4 *vs* 46.7%) and were more likely to respond to PPI (79.7 *vs* 66.8%). There was also a trend towards a higher BMI (24.5 *vs* 23.5). Race, alcohol consumption and *H pylori* status were not significant. On multivariate analysis, age and presence of minor psychiatric morbidity remained with significant differences.

CONCLUSION: The majority of patients who have typical symptoms of GERD have NERD or mild erosive reflux disease. Compared to patients with erosive reflux disease, patients with NERD were younger and had a higher prevalence of minor psychiatric morbidity.

Key words: Reflux disease; Clinical spectrum; Psychiatric morbidity

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INTRODUCTION

Gastroesophageal reflux disease (GERD) is a common disorder in Western countries and is associated with a huge economic burden. Although it is generally believed to occur less frequently in Asia when compared to the West, recent studies suggest that the prevalence of GERD in Asia is increasing[1]. However, the epidemiology of GERD remains to be fully elucidated, especially in the Asian context. Understanding of the epidemiology and natural history is important because it would facilitate appropriate and timely diagnosis, treatment and allocation of healthcare resources.

In terms of epidemiological profile, it has previously been reported that older age, male gender, white ethnicity are risk factors in the development of severe forms of GERD[2,3]. As Singapore has an ethnically mixed population, it is ideal for a study on the impact of racial differences on the type and severity of reflux disease. In an earlier community based study in Singapore, it was reported that Indians had a higher prevalence of reflux symptoms[4]. In a subsequent study looking at the issue of erosive and non-erosive reflux disease (NERD) in Singapore, the only difference between the groups was gender, with no difference in terms of age or ethnic profile[5]. The role of *Helicobacter pylori* (*H pylori*) in GERD also remains controversial, with several studies showing a protective effect[6,7], whereas others have shown improvement in symptomatology after *H pylori* eradication[8].

There are limited data on the relationship between GERD and the psychosocial profile of a patient, especially with regards to response to treatment and natural history. This is in contrast to irritable bowel syndrome, where studies have shown significant psychopathology[9,10]. In particular, data based on direct comparisons between erosive (ERD) and NERD are lacking. This relationship is important because if significant psychopathology exists, this subgroup of patients may benefit from adjunctive psychotherapy, in addition to standard medical therapy with acid suppression or pro-kinetics.

Traditionally GERD has been regarded as a spectrum of disease. At one end of the spectrum are the patients with symptomatic gastroesophageal reflux but no evidence of esophagitis; at the other end of the spectrum are the patients with complications such as esophageal stricture, Barrett's esophagus and adenocarcinoma. More recently a new conceptual framework dividing GERD into three unique groups of patients (NERD, erosive esophagitis and Barrett's esophagus) has been proposed[11].

In the light of all these observations, we decided to reassess the clinical spectrum of GERD and examine whether erosive (ERD) and NERD were distinct clinical entities in Singapore, a multiethnic urban population. We compared ERD and NERD in terms of clinical, demographic and psychiatric profiles.

MATERIALS AND METHODS

Consecutive patients of both gender aged 21-65 years of either Chinese, Malay or Indian ethnic groups with symptoms of GERD or endoscopic evidence of ERD, seen at the Gastroenterology Division, Changi General Hospital, Singapore, over a period from October 2001 to October 2002 were recruited.

Patients were diagnosed to have GERD on the basis of either frequent complaints of heartburn and/or acid regurgitation for the last 3 mo or the presence of endoscopic evidence of erosive reflux esophagitis based on the Los Angeles (LA) classification[12-14]. Patients who presented with dyspepsia but who were found to have erosive esophagitis were included in the analysis.

Patients were excluded from the study if there was prior use of antibiotics or bismuth containing compounds a month before endoscopy, previous *H pylori* eradication therapy, use of proton pump inhibitors (PPI) or H_2 receptor antagonists a month before endoscopy.

Basic demographic data were recorded. All subjects underwent diagnostic OGD with the presence of erosive esophagitis documented using the LA classification. If Barrett's esophagus was suspected, esophageal biopsy was taken for confirmation. *H pylori* status was determined using a rapid urease test (CLOtest; Delta West, Perth, Australia), which had previously been validated locally[15].

Psycho-emotional assessment

The psycho-emotional profile of patients with reflux disease was assessed using the General Health Questionnaire, 28 questions version (GHQ-28), a brief, subject-administered questionnaire that measured current, non-psychotic, non-organic psychiatric symptoms. This questionnaire had previously been validated in Singapore against ICD-10 psychiatric diagnoses derived from structured psychiatric interview with the Composite International Diagnostic Interview. The optimal cut-off point for the GHQ-28 was determined to be 4/5 for Chinese and 5/6 for Malays and Indians in the Singapore context[16].

Statistical analysis

Parametric data were compared using the Student's *t*-test, while non-parametric data were compared using χ^2 test or Fischer's exact test. Multivariate analysis was performed using logistic regression. *P* value <0.05 was taken as statistically significant.

RESULTS

Patient characteristics and results of endoscopy

A total of 690 patients were screened, and 533 were eligible for analysis. The male to female ratio was 3:2. In terms of racial distribution, 75.4% were Chinese, 9.8% were Malays while Indians and others comprised 14.8%. The clinical presentation of GERD is shown in Table 1. The majority of patients (64.8%) with the typical reflux symptoms of heartburn or acid regurgitation had NERD. The clinical spectrum of GERD, when considering both patients presenting with typical reflux symptoms as well as those presenting with dyspepsia, is shown in Figure 1. Among the cohort, non-erosive or mild erosive reflux disease was present in 95.7%; grade C or D erosive reflux disease was present in just 2.6%, while the prevalence of Barrett's esophagus was only 1.7%.

Table 1 Clinical presentation of patients with GERD

Symptoms	NERD	ERD	Total
Heartburn, acid regurgitation	216	118	334
Dyspepsia	-	199	199
Total	216	317	533

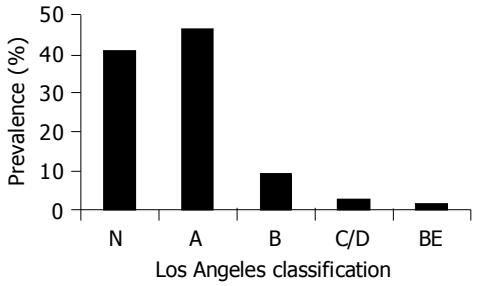

Figure 1 Endoscopic features of GERD.

Comparison of NERD with ERD

A comparison was made between patients with NERD and ERD, with the key results from univariate analysis shown in Table 2. Patients with NERD were younger than ERD patients (39.4 years *vs* 45 years) and were more likely to be female (46.3% *vs* 35.6%). The prevalence of minor psychiatric morbidity was significantly higher among NERD patients (46.7% *vs* 26.4%) and the clinical response to PPI was poorer (66.8% *vs* 79.7%). The proportion of smokers was significantly lower among NERD patients and there was a trend towards a lower body mass index.

On multivariate analysis, the association of NERD with a younger age and a higher prevalence of minor psychiatric morbidity remained statistically significant.

There was no significant difference between NERD and ERD patients in terms of racial distribution, *H pylori* status and alcohol consumption.

Table 2 Comparison of NERD with ERD: outcome of univariate analysis

	NERD (n = 216)	ERD (n = 317)	P
Mean age (yr)	39.4	45.0	0.02
Gender:			
female (%)	46.3	35.6	0.015
Ethnic group:			
Chinese:Malay:Indian	165:17:34	237:35:45	NS
BMI	23.5	24.5	NS
Minor psychiatric co-morbidity (%)	26.4	46.7	0.002
Clinical improvement with PPI (%)	66.8	79.7	<0.001
Smoking (%)	9.7	19.6	0.001
H pylori + (%)	24.8	27.5	NS

DISCUSSION

There is limited epidemiologic data on GERD in Asia. In particular, data on a direct comparison of ERD and NERD with respect to demographic and psychiatric profiles are lacking. Although the prevalence of GERD is lower in Asia compared to Western countries, it had been predicted that its incidence and prevalence will rise and become similar to that seen in Western populations. It had been suggested that similar to the change in Western populations that occurred in the last century, in Asian populations, a reduction in the rate of developing corpus gastritis from dietary changes would lead to a change in epidemiology of *H pylori*-related diseases such as atrophic gastritis, gastric ulcer and gastric cancer would be replaced by duodenal ulcer. In addition, improved sanitation would also lead to decreased prevalence of *H pylori*. These changes would lead to patients with asymptomatic gastroesophageal reflux developing gastroesophageal disease because of increased delivery of esophageal acid load[17]. As such, our study is especially relevant in view of this anticipated increased clinical burden of GERD.

Consistent with other published data, the majority of our patients did not have severe erosive reflux disease. In our series, only 2.7% of patients had either LA classification grade C or D reflux esophagitis, while the prevalence of Barrett's esophagus was only 1.7%. Although there are studies that suggest that the majority of patients with GERD actually have NERD[14,18], in our study the overall prevalence of NERD was 40.5% while that of grade A reflux esophagitis was 46%. This may reflect the fact that our data was hospital-based, rather than community-based, and that patients with dyspepsia and ERD were included, with the consequent results that our data were more similar to the results of earlier studies[19]. When only patients with classic symptoms of heartburn or acid regurgitation were considered, the majority (64.8%) had NERD.

We studied ERD and NERD in terms of differences in age, race, gender, BMI, smoking, *H pylori* status and psychiatric profile. These variables may predispose to GERD in terms of an impact on development of gastroesophageal reflux via an effect on the lower esophageal sphincter, the amount of acid refluxate, or the sensory threshold for symptom generation. These factors may lead to more esophageal damage and hence be commoner in ERD. A high BMI had been correlated with GERD in laboratory studies[20,21]. It had been shown that older people were more likely to have symptomatic gastroesophageal reflux, possibly related to a poor esophageal acid clearance and decreased defense mechanisms against reflux of gastric acid contents on the esophageal mucosa[22]. Life-style factors such as smoking[23] and alcohol consumption may have an impact on the lower esophageal sphincter and lead to strain-induced reflux. The role of *H pylori* infection in GERD is controversial. A systemic review of 20 studies[24] found that the prevalence of *H pylori* in subjects with GERD was significantly lower than those without the prevalence. A recent study by Zhang also found a protective role of *H pylori* infection in GERD. However, a post hoc analysis of randomized trials of *H pylori* therapy for peptic ulcer disease found no difference in the likelihood of developing either reflux symptoms or erosive esophagitis in individuals cured of *H pylori* infection compared to those with persistent infection[25]. These disparate observations may be reconciled by different pattern of *H pylori* infection with resultant differences in gastric acid secretion. In patients with corpus predominant gastritis, *H pylori* infection may protect against reflux by decreasing the potency of the gastric refluxate; conversely, in patients with antral predominant gastritis, an increased acid output may be prone to development of GERD[26].

The key differences between ERD and NERD in our study were an association of a younger age and a higher prevalence of minor psychiatric morbidity with NERD patients when compared to ERD patients. There was a trend towards a lower BMI in NERD patients. Importantly, there was no difference in terms of ethnic group, gender, smoking and prevalence of *H pylori*. These observations suggest that, apart from older age, other demographic and life-style factors are not useful in predicting which patients would tend to have ERD.

Previous studies have shown that the prevalence of reflux symptoms is higher among patients with known psychiatric disorders compared to non-psychiatric patients[27] and that among patients with GERD, a subset may have significant psychological distress[28]. In our study, we took a different perspective and stratified patients into ERD and NERD. We found that the prevalence of minor psychiatric co-morbidity among NERD patients was 46.7%, compared to 26.4% among patients with ERD and this was statistically significant. None of our patients had known psychiatric illnesses. In a previous study which validated the use of GHQ-28 as a screening psychiatric tool in Singapore[16], the overall prevalence of common psychological symptoms (minor psychiatric morbidity) in a community-based study with 3 020 subjects was 16.8%. In that study, a subsequent structured psychiatric assessment showed that affective and anxiety disorders constituted the bulk of psychiatric disorders in individuals who scored above threshold on the GHQ-28. We believe that these types of psychologic disorders would be reflected in our study sample as well. The association of NERD with minor psychiatric co-morbidity suggests that these patients may benefit from adjunctive psychotherapy, in addition to standard medical therapy with acid suppression or pro-kinetics. This is in agreement with the concept that as an entity, NERD may actually be sub-classified into a group with abnormal acid exposure, a group

with normal acid exposure but a hypersensitive esophagus, where a positive relationship exists between symptoms and acid reflux events (symptom index $\geqslant$50%), and a group with negative relationship between symptoms and acid reflux events (symptom index <50%). Patients in the third group may have esophageal perception modulated by peripheral and central neural mechanisms, such as psychological co-morbidity like anxiety, depression and stress, causing these patients to perceive low-intensity intraesophageal events as being painful[29].

Association of an older age with more severe erosive reflux disease had been previously documented[2]. Although Indians were previously shown to have a higher prevalence of gastroesophageal reflux symptoms compared to the Chinese and Malay populations[4], the proportion of patients with ERD and NERD in all three ethnic groups was similar in our study. We also looked at treatment response, and similar to other published data, the clinical response to PPI was lower in patients with NERD compared to ERD[14,30]. A possible explanation for this lower response rate to PPI lies in the previously discussed sub-classification of NERD, whereby a subgroup of patients actually have functional, rather than acid-related, heartburn. Since the role of *H pylori* in GERD is mainly to mask pre-existing gastroesophageal reflux, rather than to cause GERD directly, not surprisingly, no difference was demonstrated between ERD and NERD patients.

In conclusion, in our ethnically diverse population, the majority of patients with GERD had either NERD or mild ERD. NERD was associated with a younger age and a higher prevalence of minor psychiatric co-morbidity. In the management of this group of patients, a formal psychiatric assessment and adjunctive psychological and psychiatric therapy may have a role, especially when refractory to standard medical treatment.

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