

Gastroesophageal reflux disease is uncommon in Asia: evidence and possible explanations

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DEFINITIONS

Gastroesophageal reflux that predisposes an individual to the risk of physical complications, or produces symptoms leading to significantly impaired quality of life, is termed gastroesophageal reflux disease (GERD)^[1]. Clinically, GERD encompasses a broad spectrum of separate, though related conditions that are sometimes conveniently grouped under two broad categories: endoscopic esophagitis and endoscopy negative reflux disease. Endoscopic esophagitis is considered to be present when there is endoscopically visible breakage of the mucosa^[2], regardless of whether the patient has symptoms. The term "endoscopic negative reflux disease" refers to GERD that is not associated with Barrett's esophagus or esophageal mucosal breaks. It includes such conditions as esophageal mucosal acid sensitivity, which is symptomatic reflux induced by acid reflux and proven by objective means; abnormal esophageal acid exposure, which is excessive acid reflux confirmed by objective measures; and reflux-type symptoms (heartburn and/or acid regurgitation) that clearly dominate the patient's complaints^[3]. Barrett's esophagus is the eponym applied to the columnar epithelium-lined lower esophagus that is acquired as a consequence of chronic gastroesophageal reflux^[4]. Hiatus hernia, on the other hand, has been defined as a displacement of the gastric mucosa 1.5cm or more above the diaphragmatic hiatus^[5].

EVIDENCE FOR A LOW PREVALENCE OF GERD IN ASIA

Prevalence of reflux-type symptoms in general population

Until recently, there has been no systematic study on the prevalence of reflux type symptoms in the general population of Asia. A cross-sectional survey of a race-stratified sample of adults in a Singaporean town provides some of the first evidences, that re-

flux-type symptoms are uncommon in the East^[6]. Of 696 persons evaluated, only 2% had heartburn and/or acid regurgitation for more than once a month. This prevalence is much lower than those (29%-44%) of Western populations^[7,8].

Prevalence of GERD in pregnant women

The individuals with the highest prevalence of heartburn are often said to be pregnant women. A prospective study, using a reliable questionnaire, on a consecutive series of pregnant women in Singapore, provides the second piece of evidence that reflux-type symptoms are uncommon among Asians^[9]. Of the 35 pregnant women evaluated, 23% had heartburn some time during their pregnancy. This percentage is lower than those (48% - 96%) reported previously in the West^[10,11].

Frequency of GERD in outpatient clinics

In a large clinical series from Singapore, Kang *et al* from Singapore noted a 2% frequency of GERD among 2141 consecutive patients investigated^[12]. The diagnosis of GERD was established on the basis of an abnormal endoscopy, a positive acid perfusion test and/or an abnormal 24-hour pH monitoring. The frequency was lower as compared with a similar series from the West^[13].

Prevalence of endoscopic esophagitis

Very few epidemiological data on reflux esophagitis in Asians are available in the literature. However, Chang *et al* found 5% with reflux esophagitis^[14] in an endoscopic series of 2044 patients who underwent self-paid medical check-ups. Esophagitis, when present, was often mild. The prevalence of endoscopic esophagitis among symptomatic subjects has not been well studied and the available data are conflicting. In a study from Taiwan, a 15% prevalence of erosive esophagitis was found in 455 consecutive patients evaluated for various upper gastrointestinal tract symptoms^[15]. Most of the patients presented with mild esophagitis. The expected high frequency of erosive esophagitis is not supported by other endoscopic series from Asia. Erosive esophagitis was uncommon in both indigenous Fijians and Indians, being detected in only 2% of a total of 693 endoscopic examinations^[16]. This contrasts with the higher prevalence (11%) of reflux esophagitis noted by the same author among New Zealanders^[17]. Esophagitis is likewise uncommon in Japan; a prevalence rate of 3% was recorded among 240 consecutive outpatients with dyspepsia^[18]. Our own retro-

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spective series from Singapore showed that of 11943 patients undergoing diagnostic upper endoscopy for various complaints, 4% had esophagitis^[19]. This frequency was lower than those reported from Western centers^[20,21]. Thus, with the exception of the Taiwanese series, the proportion of patients with endoscopic esophagitis in Asian series appears lower than that in reports from Western countries. The severity of esophagitis also appears mild, unlike that in Western populations^[20,21].

Prevalence of hiatus hernia

Hiatus hernia, as seen on barium studies, appears rare in the Far East with a < 1% prevalence^[22]. Recent endoscopic series from Asia confirm this impression. Chang *et al* from Taiwan found hiatus hernia in 2% of patients endoscoped as part of an annual medical examination^[14]. In another Taiwanese study in patients endoscoped for gastrointestinal complaints, hiatus hernia was found in 7% of the cases^[15]. In our retrospective series from Singapore, the proportion of hiatus hernia among patients seen for gastrointestinal complaints was 3%^[19]. Thus, the available data show that the prevalence of hiatus hernia is lower than that in Western series (17%-22%)^[20,21].

Prevalence of GERD complications

The prevalence of Barrett's esophagus varies, depending on the population being studied. In a series from Taiwan, 2% of patients endoscoped for a variety of upper gastrointestinal symptoms were found to have Barrett's esophagus^[15]. When evaluating only those with erosive esophagitis, this rate increased to 14%. The corresponding figures from the West are 4%-20%^[23,24] and 36%, respectively^[23]. Reports from a Taiwanese center, and our own center showed a frequency of benign (presumably reflux-related) esophageal stricture of only 0.4% and 0.2% respectively, among patients endoscoped for various gastrointestinal indications^[16,19]. These frequencies are lower in comparison with those in reports from the West^[25].

POSSIBLE REASONS FOR THE LOW FREQUENCY OF GERD IN THE EAST

The pathogenesis of reflux esophagitis can be considered in terms of excessive acid load overwhelming mucosal defense. The degree of acid load is in turn determined by the anti-reflux barrier of the gastroesophageal junction^[26], the quantity of acid refluxed^[27], and the ability of the esophagus to clear any refluxate back into the stomach^[28]. The latter depends on the integrity of peristaltic function^[29] and the neutralizing ability of swallowed saliva^[28]. More recently, an inverse relationship between *Helicobacter pylori* (*H. pylori*) and GERD has been suggested^[30]. By examining the potential pathogenetic factors, it is hoped that the lower frequency

of GERD in the East than in the West could be explained.

Anti-reflux barrier

An increase in intra-abdominal and intragastric pressure overcomes the gastroesophageal pressure gradient maintained by the lower esophageal sphincter (LES). Such an increase may occur through obesity^[31] and delayed gastric emptying by fatty meals^[32]. Alcohol, smoking and fat can lower the LES pressure and esophageal peristalsis, thus favoring the occurrence of gastroesophageal reflux^[33-35]. A large hiatus hernia traps gastric contents in its pouch above the diaphragm. This leads to free retrograde flow of acid into the esophagus.

Increased body mass index and presence of hiatus hernia were found to be the most important factors associated with the occurrence of esophagitis in a recent study from Taiwan^[14]. The authors suggested that the lower prevalence of hiatus hernia and smaller body mass index in the Chinese population might account for the lower prevalence of reflux esophagitis in Taiwan. The low prevalence of hiatus hernia in the East has previously been attributed to the consumption of high residue diets in the developing world^[22]. Another report from Taiwan found erosive esophagitis to be associated with smoking, and alcohol consumption^[15]. The authors suggested that the recent increase in smoking, alcohol use, and fat consumption among Taiwanese were contributed to the observed rise in the prevalence of GERD in Taiwan.

Gastric acid output

Since acid secretion correlates with body surface area, Asians in general are characterized by a smaller parietal cell mass and a lower acid output as compared with Caucasians^[36]. Except for the striking example of Zollinger-Ellison syndrome, however, the association between the amount of acid output and the occurrence or severity of reflux disease has remained unproven^[37].

Acid clearance

While evaluating the consecutive Singaporean patients who underwent esophageal manometry, we found that poor esophageal clearance was more common among those with esophagitis than among those without. The results were identical to Western studies^[38]. It is possible that this clearance mechanism has an inherited basis, and is more efficient in Asians than in Caucasians. Data to support this is, however, lacking.

Mucosal defence

Presently, there is no risk factor known to disrupt tissue resistance, except for nonsteroidal anti-inflammatory drugs^[39]. Such drugs cannot be an important factor underlying the geographical variation in the prevalence of GERD, because they are con-

sumed by Asians no more than by Westerners. However, it is possible that inborn differences in tissue resistance, due to yet unrecognized factors, may account for some of the geographical differences.

H. pylori infection

There is circumstantial evidence to suggest that *H. pylori* infection is relatively protective for the occurrence of GERD^[30]. It has been suggested that Hong Kong Chinese are protected against reflux esophagitis by their high prevalence of *H. pylori* associated gastritis^[40]. Such gastritis, when becoming chronic, can lead to gastric atrophy and hypochlorhydria, thereby reducing the likelihood of GERD. If this hypothesis is correct, the effects of *H. pylori* induced gastritis may be an important factor determining the lower prevalence of reflux esophagitis in this part of the world, in which *H. pylori* infection is especially common. No data, however, exists to support this hypothesis.

Genetic factors

It is unlikely that the lower frequency of GERD in Asian populations can be explained simply by the known extrinsic risk factors, such as obesity, smoking habits, and alcohol consumption, being less frequent in Asians as compared with Caucasians. It is likely that genetic factors are involved. If that was the case, the mechanisms through which they confer protection against GERD are poorly understood. It may be that LES function is truly more competent in Asians compared with Westerners. Alternatively, the esophageal mucosa in Asians is inherently more acid resistant. Differences in gastric acid output and esophageal clearance ability between Asian and Western patients are further possibilities. Comparative studies into these parameters in Eastern and Western populations may shed more light on this question, and may lead to formulation of appropriate therapeutic strategies.

In summary, most reports from Asia have suggested that GERD is an uncommon condition in this part of the world. The reasons for the lower frequency compared with the West are not known, and further studies are required.

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