

REVIEW

Gastroesophageal Reflux Disease in Asia: A historical perspective and present challenges

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Key words

Asians, Barrett's esophagus, erosive esophagitis, gastroesophageal reflux disease, risk factors.

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Abstract

Gastroesophageal reflux disease (GERD), previously uncommon in Asia, has now become an important disease in the region. Although much variability exists between studies, most endoscopy-based studies show a prevalence of erosive esophagitis of more than 10%. Symptom-based studies also show a prevalence of 6–10%. Two longitudinal follow-up studies on GERD symptoms have shown an increase with time, and several endoscopy-based time trend studies have also shown a significant increase in erosive reflux esophagitis. Studies on Barrett's esophagus have been confounded by the description of short (SSBE) and long segment (LSBE) Barrett's esophagus. Great variation in prevalence rates has been reported. SSBE vary from 0.1% to more than 20% while LSBE vary from 1–2%. Of the putative causative factors, obesity has been the most important. Many studies have linked GERD-esophagitis as well as occurrence of reflux symptoms with an increase in body mass index (BMI), obesity, especially visceral or central obesity, and metabolic syndrome. A decline in *Helicobacter pylori* infection with growing affluence in Asia has been broadly thought to result in healthier stomachs and a higher gastric acid output resulting in reflux disease. However, variable results have been obtained from association and *H. pylori* eradication studies.

Introduction

Historically, gastroesophageal reflux disease (GERD) was considered an extremely uncommon disease in Asia. The first report in the published English medical literature on GERD in Asians was by JY Kang and colleagues in 1993.¹ In a survey of more than 10 000 patients undergoing endoscopy in the Singapore General Hospital, they recorded a very low prevalence of reflux esophagitis of 3.3%. Prior to that, in the late 1970s, two reports from Taiwan in the Chinese language made a passing reference to the presence of esophagitis amongst patients who had undergone gastroscopy.^{2,3} Several papers in the Japanese medical literature had also reported on the occurrence of esophagitis.^{4–6}

Kang *et al.* stated in their paper, that “there was a general impression that reflux esophagitis is uncommon in Asian populations” and commented that “further studies were required to determine why reflux esophagitis should be so much less common than peptic ulcer disease.”¹ In a later study, Kang and Ho showed in an endoscopy-based study carried out simultaneously in the UK and Singapore, the marked differences in prevalence rates of esophagitis and hiatus hernia between Western and Asian patients.⁷

In 2000, the Journal of Gastroenterology and Hepatology published a review on the subject which commented on the low prevalence of GERD in Asia but also projected that, based on sparse published data available at that time, the disease appeared to

be on the increase.⁸ For that review, references were difficult to obtain, with few direct prevalence studies available. Since then, there has been a steady increase in published literature on GERD from the Asia-Pacific region. More recent studies with better defined study methodology are now available and have shown that GERD is in fact, not uncommon in Asia. Two Asian Pacific consensus meeting on GERD have been convened and their proceedings published,^{9,10} and GERD is now considered an important disease in the Asia-Pacific region.

Studies on GERD

The burden of GERD has been measured by determining the frequency of esophagitis in endoscoped patients as well as the prevalence of GERD symptoms in the community or population. The latter has been thought to be a more accurate indicator of the true burden of GERD in a population, especially with the recognition of non-erosive reflux disease (NERD) as the predominant disease subgroup.

In the earlier years studies on GERD were based on the presence of erosive esophagitis at endoscopy. Gastroscopy affords objective visualization of reflux-associated damage to the lower esophagus. The definition of esophagitis used, however, has been variable, and this has led to differences in the rates of esophagitis reported. For example, in the older Savary-Miller classification, erythema was

considered as already Grade 1 esophagitis, whereas in the more recent and now more widely used Los Angeles classification, a breach in the esophageal mucosa must be evident before a diagnosis of esophagitis can be made. Studies based on reflux symptoms have been thought to be a more reliable indicator of GERD but symptom-based diagnosis has also not been easy. Many studies have used predominant symptoms of heartburn and acid regurgitation as a marker of GERD, but there has been great variability in the definition of GERD based on the frequency, and sometimes on the severity, of symptoms. Reflux disease specific questionnaires have now been constructed, and their application has allowed a more consistent and reliable way of measuring the burden of disease.^{11,12}

Disease burden

Prevalence of erosive esophagitis

A summary of the published reports on esophagitis in Asia is shown in Table 1.^{1,13–32} The prevalence of erosive esophagitis ranges from <1.0% to 20.8%. This considerable variability in values could be due to different groups of patients studied: routine health screening patients, patients screened for gastric cancer, patients with dyspepsia or upper gastrointestinal symptoms or all gastroscopied patients. Patients who come for routine health screening and who are not consulters would be thought to have a lower prevalence rate. However, the prevalence rates amongst this group has also been variable, with a prevalence of approximately 10%. In a recent study on asymptomatic subjects from Taiwan, a prevalence rate of 12.0% was reported.³² Large endoscopy-based studies have also been carried out. For example, a nationwide study from Korea involving 40 healthcare centers with a 25 000 patient base, recorded a prevalence of 8.0%.³⁰

In Asian patients the severity or grade of esophagitis remains overwhelmingly mild. In the larger and more recent studies, Du *et al.*²⁹ recorded Grade A esophagitis in 69.4% and Grade B in 23.3%, and Shim *et al.*³⁰ 74.1% of patients Grade A esophagitis and 23.3%, Grade B. In Peng *et al.*'s study from Guangzhou, 91.2% were reported as Grade A or B esophagitis.³¹

Prevalence of GERD: symptom-based studies

Symptom-based studies have been more difficult to perform as reflux symptoms can be highly variable in presentation, frequency and severity. Most studies have used the presence of the cardinal reflux symptoms of heartburn and/or acid regurgitation as an indicator of reflux disease. Some studies have used severity and frequency and a composite score for the diagnosis of GERD. More recent studies have utilized validated structured questionnaires to identify reflux. A summary of published reports is shown in Table 2.^{33–45}

Not all symptom-based studies are true population-based studies; some are clinic or hospital based. These studies have, however, collected large numbers of subjects. Fujiwara *et al.* in survey of more than 6000 patients, recorded a prevalence of GERD in Japan of 12.8%,³⁸ Li *et al.* in a survey of more than 15 000 outpatients attending hospitals in Zhejiang province, China, recorded a prevalence of 7.3% of GERD symptoms.⁴¹ Yamagishi *et al.* in a survey of more than 150 000 patients attending a cancer

screening centre in Miyagi prefecture, Japan, recorded an astounding prevalence rate of more than 20%.⁴⁴

Population-based studies with randomized sampling have been carried out by telephone or household face-to face interviews. In two telephone interview surveys from Hong Kong³⁶ and Seoul, Korea,⁴³ prevalence rates of GERD of 8.9% and 7.1% were recorded. Face-to face interviews have been conducted by Chen *et al.*⁴⁰ and Wang *et al.*,⁴⁵ who reported identical rates of 6.2%, and Cho *et al.*⁴¹ who reported 3.5%. In general, recent population-based studies report prevalence rates of 6–10%.

Complications of esophagitis

Complications such as strictures and bleeding have been uncommonly reported or not noted at all. In the early study by Yeh *et al.* from Taiwan,¹⁴ strictures and bleeding were each found in 3% of patients with GERD. Wong *et al.* reported strictures in only 0.08% of patients.¹⁹

Barrett's esophagus remains the most important complication of reflux disease (see the review by John Dent in this supplement). Prevalence rates are shown in Table 3.^{14,18,46–62} In the earliest study on Barrett's esophagus from Asia, based on biopsy and histological examination, Yeh *et al.* reported a prevalence of 2%. In more recent years, cases have been separated into long segment Barrett's esophagus (LSBE) and short segment Barrett's esophagus (SSBE). The majority of cases reported have been SSBE with rates ranging from 0.04 to >20%. More recent large studies from Korea and Taiwan have yielded prevalence rates of 0.01 and 0.03 for LSBE and 0.14 and 2.4% for SSBE, respectively.^{55,57} The reporting of Barrett's esophagus has been hampered by the variability in diagnostic criteria used: presence of columnar epithelium only without histological examination, presence of intestinal metaplasia or specialized intestinal metaplasia on biopsies. SSBE is particularly difficult to ascertain in Asian patients with a higher prevalence of *Helicobacter pylori* infection and accompanying intestinal metaplasia in the cardio-esophageal junction. It has been commented previously that Japanese studies report a higher prevalence of Barrett's owing to a different definition of the cardio-esophageal junction.⁶³ The Barrett's data from Asia are indeed confusing. What is apparent is the lower prevalence of LSBE compared to the West, and a low prevalence of Barrett's-associated adenocarcinoma reported at the current time in the socio-economic history of the region.⁶⁴ This may change in the future with a possible increase in adenocarcinoma, and close observations of the evolution of the disease are needed.

Is GERD increasing in Asia?

The prevalence rates of both GERD symptoms and erosive esophagitis in the majority of recent reports have, in general, been higher than in earlier studies. This may be due to better diagnosis and recording of cases, but consistently higher rates from many centers in Asia is more likely to reflect a true increase in the prevalence of GERD. Time trend studies for both reflux symptoms and erosive esophagitis have been few but have clearly shown an increasing trend in the prevalence of the disease.

In a longitudinal 5 year follow-up study looking at reflux symptoms, Lim *et al.* from Singapore, reported a rise in the prevalence of reflux symptoms from 1.6% to 9.9%.³⁴ However, only a small

Table 1 Prevalence of erosive esophagitis

| | Period of study | Place of study | Numbers studied | Prevalence % | Grade of Esophagitis | Study sampling |
|---|-----------------|--------------------------|-----------------|--------------|--|--|
| Kang <i>et al.</i> 1993 ¹ | 1981–1991 | Singapore | 11 943 | 3.3 | NA | All endoscoped patients |
| Chang <i>et al.</i> 1997 ¹³ | 1995–96 | Taipei, Taiwan | 2 044 | 5.0 | NA (S-M) | All endoscoped patients |
| Yeh <i>et al.</i> 1997 ¹⁴ | 1991–1992 | Taipei, Taiwan | 464 | 14.5 | NA (S-M) | All endoscoped patients |
| Maekawa <i>et al.</i> 1998 ¹⁵ | 1993–1996 | Japan | 2 278 | 5.2 | LA: A–68.6%, B–22.9%, C–7.1%; D–1.4% | UGI symptoms |
| Yeom <i>et al.</i> 1999 ¹⁶ | 1994–96 | Seoul, Korea | 1 010 | 5.3 | NA | All endoscoped patients |
| Furukawa <i>et al.</i> 1999 ¹⁷ | 1996–98 | Saga Prefecture, Japan | 6 010 | 16.3 | LA: A–59.2%, B–28.2%, C & D–12.6% | All endoscoped patients |
| Lee <i>et al.</i> 2001 ¹⁸ | 1996–97 | Seoul, Korea | 7 015 | 3.4 | S-M: Grade 1–98.3%, 2–1.6% | Health screening |
| Wong <i>et al.</i> 2002 ¹⁹ | 1997–2001 | Hong Kong | 16 606 | 3.8 | LA: A–52%, B–43%, C–2%, D–3% | All endoscoped patients |
| Inamori <i>et al.</i> 2003 ²⁰ | 1999 | Katta, Japan | 392 | 13.8 | LA: A–61.1%, B–29.6%, C–9.3%, D–0 | All endoscoped patients |
| Okamoto <i>et al.</i> 2003 ²¹ | 1996–98 | Saga Prefecture, Japan | 8 031 | 14.9 | LA: A–59.8%, B–28.4%, C & D–11.8% | GI mass survey/hospital outpatients |
| Rosaida & Goh 2004 ²² | 2001–02 | Kuala Lumpur, Malaysia | 1 000 | 13.4 | LA: A–61.2%, B–18.7%, C–13.4%, D–6.7% | Upper GI symptoms |
| Wai <i>et al.</i> 2002 ²³ | NA | Singapore | 10 488 | 5.0 | NA | Dyspeptic patients |
| Rajendra <i>et al.</i> 2004 ²⁴ | 1997–2000 | Ipoh, Malaysia | 1 985 | 6.1 | S-M; NA | UGI symptoms |
| Mishima <i>et al.</i> 2005 ²⁵ | 2001 | Shimane, Japan | 2 760 | 7.1 | LA: | Health screening |
| Lee <i>et al.</i> 2006 ²⁶ | 2003–04 | Taipei, Taiwan | 4 600 | 18.3 | LA: A–72.4%, B–20.8%, C–6.3%, D–0.6% | Health screening |
| Song <i>et al.</i> 2006 ²⁷ | 2005–05 | Seoul, Korea | 224 | 18.8 | LA: A–90.5%; B–7.1% | Upper GI symptoms |
| Chen & Chang 2007 ²⁸ | 1999–2000 | Taipei, Taiwan | 482 | 12.0 | LA: A–53.4%, B–34.4%, C–8.6%, D–3.4% | Health screening; asymptomatic |
| Du <i>et al.</i> 2007 ²⁹ | 2004–05 | Zhejiang Province, China | 2 231 | 20.8 | LA: A–71.8%, B–22.0%, C–4.3%, D–1.9% | Hospital Outpatients |
| Shim <i>et al.</i> 2009 ³⁰ | 2006 | Korea | 25 536 | 7.9 | LA: A–74.1%, B–23.3%, C–2.3%, D–0.2% | Health screening: national multicentre project |
| Peng <i>et al.</i> 2009 ³¹ | 2006–07 | Guangzhou, China | 2 580 | 4.3 | LA: A & B–91.2% | Routine medical examination |
| Wang <i>et al.</i> 2010 ³² | 2008 | Kaohsiung, Taiwan | 572 | 12.0 | LA: A–71.0%, B–29.0% | Asymptomatic subjects |

NA, not available.

Table 2 Prevalence of reflux symptoms

| | Period of study | Place of study | Numbers studied | Prevalence % | Survey method | Questionnaire | Definition of GERD |
|--|-----------------|--------------------------|-----------------|--------------|---------------------|---------------|--------------------|
| Ho <i>et al.</i> 1998 ³³ | 1994 | Singapore | 696 | 1.6% | Population sampling | validated | ≥ 1 per month |
| Lim <i>et al.</i> 2005 ³⁴ | 1999 | Singapore | 237 | 9.9% | Population sampling | validated | ≥ 1 per month |
| Pan <i>et al.</i> 2000 ³⁵ | 1996–97 | Beijing, Shanghai, China | 4 992 | 5.8% | Population sampling | not validated | Symptom score |
| Wong <i>et al.</i> 2003 ³⁶ | 2002 | Hong Kong, China | 3 605 | 8.9% | Population sampling | validated | ≥ 1 per month |
| Rajendra & Alahuddin 2004 ³⁷ | NA | Ipoh, Malaysia | 949 | 9.7% | Population sampling | Not validated | ≥ 1 per month |
| Fujiwara <i>et al.</i> 2005 ³⁸ | 2001 | Kansai, Japan | 6 035 | 12.8% | Clinic based | Not validated | ≥ 2 per month |
| Wang <i>et al.</i> 2004 ³⁹ | NA | Xian, China | 2 789 | 17.0% | Population sampling | validated | Symptom score |
| Chen <i>et al.</i> 2005 ⁴⁰ | – | Guangzhou, South China | 3 338 | 6.2% | Population sampling | validated | RDQ |
| Cho <i>et al.</i> 2005 ⁴¹ | 2000–01 | Asan-si, Seoul, Korea | 1 417 | 3.5% | Population sampling | validated | ≥ 1 per week |
| Li <i>et al.</i> 2008 ⁴² | 2004–05 | Zhejiang, China | 15 283 | 7.3% | Hospital based | validated | RDQ |
| Yang <i>et al.</i> 2008 ⁴³ | NA | Seoul, Korea | 1 044 | 7.1% | Population sampling | Not validated | ≥ 1 per week |
| Yamagishi <i>et al.</i> 2008 ⁴⁴ | 2003 | Miyagi, Japan | 160 983 | 15–20.0% | Hospital based | Not validated | ≥ 1 per month |
| Wang <i>et al.</i> 2009 ⁴⁵ | 2006 | Shanghai, China | 1 034 | 6.2% | Population sampling | validated | RDQ |

NA, not available.

percentage of the initial cohort of patients participated in the follow-up study. In another study from a small town in Western Japan over a 6-year period, 15.4% of GERD cases were identified as new cases.⁶⁵

More studies on changes in prevalence of reflux esophagitis with time have been carried out. Ho *et al.* from Singapore tracked the prevalence of esophagitis in their endoscopy records over a 9-year period and recorded an increase from 3.9% to 9.8%.⁶⁶ Similar reports have been published by Sollano *et al.* from the Philippines,⁶⁷ Goh *et al.*⁶⁸ from Malaysia, Lien *et al.*⁶⁹ from Taiwan, and Kim *et al.* from Korea.⁷⁰ All these studies have shown a highly significant increase in prevalence of erosive esophagitis over time. (Table 4).

Why is GERD increasing in Asia? Plausible answers

As with many other diseases, the increase in GERD in Asia is the result of the interaction between environmental factors and genetic predisposition. The increase in prevalence occurring over a relatively short period of time (10–20 years) points to the predominant role of environmental factors. The exact reason for this change is difficult to determine but reflects the growing affluence in Asia. Gastric acid secretion would have increased in a “healthier” population. In an interesting and important study, Kinoshita has shown an increase in both basal and maximal acid output in Japanese patients over a 20-year period.⁷¹ Dramatic socio-economic development in Asia has resulted in consequent lifestyle changes. A change in diet and physical activity and an increase in BMI and obesity have often been thought to be putative. Older age and male sex have been shown in many studies to be associated with GERD.^{22,29,31} In a region where life expectancy has now increased markedly, a higher prevalence of GERD could also reflect the ageing of the population.

Risk factors for GERD in Asia

Increase in gastric acid secretion, and *H. pylori* infection

This has often been linked to *H. pylori* infection, but the relationship has not been straightforward. Kinoshita *et al.* showed in their study that acid secretion had increased in both elderly and not elderly patients, regardless of *H. pylori* status, suggesting that *H. pylori* infection did not play a significant role in this change.⁷¹ However, cross-sectional and case-control studies from Asia have shown an inverse relationship between the prevalence of *H. pylori* and GERD.^{72–74} Further support for the role of *H. pylori* infection is shown by the negative association with more virulent strains of *H. pylori*, as has been reported in the Western literature.^{75–77} However, there is an association between *H. pylori* eradication and GERD has been the subject of conflicting reports. Koike *et al.* have shown in two studies, an increase in gastric acid with *H. pylori* eradication and, conversely decreased acid secretion in the presence of *H. pylori*. They proposed that this fall was protective against the development of erosive reflux esophagitis.^{78,79} Wu *et al.* showed that *H. pylori* eradication led to more “difficult-to-treat” cases of GERD.⁸⁰ Hamada *et al.* and Inoue *et al.* have both shown an

Table 3 Prevalence of Barrett's esophagus

| | Place of Study | Study Period | Number studies | Prevalence % | | |
|---|------------------------|--------------|----------------|---------------------------------|------|----------------------|
| | | | | LSBE | | SSBE |
| Yeh <i>et al.</i> 1997 ¹⁴ | Taipei, Taiwan | 1991–1992 | 464 | 1.98 (not specified SS or LSBE) | – | IM |
| Amarapukar <i>et al.</i> 1998 ⁴⁶ | Mumbai, India | 1997 | | 2.6 (not specified SS or LSBE) | | SIM |
| Azuma <i>et al.</i> 2000 ⁴⁷ | Sapporo, Japan | 1996–98 | 650 | 0.6 | 15.1 | Endoscopic diagnosis |
| Lee JI <i>et al.</i> 2002 ⁴⁸ | Seoul, Korea | 2000 | 1 553 | 0.32 (not specified SS or LSBE) | | SIM |
| Choi DW <i>et al.</i> 2002 ⁴⁹ | Seoul, Korea | 2002 | 847 | 0.5 | 16.5 | Endoscopic diagnosis |
| Wong <i>et al.</i> 2002 ¹⁹ | Hong Kong | 1997–2001 | 16 606 | 0.02 | 0.04 | SIM |
| Fujiwara <i>et al.</i> 2003 ⁵⁰ | Kansai, Japan | 2001–03 | 548 | 0.2 | 12.0 | Endoscopic CLE |
| Rosaida & Goh, 2004 ²² | Kuala Lumpur, Malaysia | 2001–02 | 1 000 | 2.0 (not specified SS or LSBE) | | IM |
| Zhang <i>et al.</i> 2004 ⁵¹ | Xian, China | 2001–02 | 391 | 6.6 | 24.0 | SIM |
| Rajendra <i>et al.</i> 2004 ⁵² | Ipoh, Malaysia | 1997–2000 | 1 985 | 1.6 | 4.6 | SIM |
| Kim JY <i>et al.</i> 2005 ⁵³ | Seoul, Korea | – | 992 | 0.1 | 3.5 | SIM |
| Amano <i>et al.</i> 2006 ⁵⁴ | Izumo, Japan | 2003–04 | 1 668 | 0.2 | 19.7 | SIM |
| Kim JH <i>et al.</i> 2007 ⁵⁵ | Seoul, Korea | 1997–2004 | 70 103 | 0.01 | 0.14 | CLE and SIM |
| Okita <i>et al.</i> 2008 ⁵⁶ | Izuma, Japan | 2005–07 | 5 338 | 0.2 | 37.4 | Endoscopic CLE |
| Tseng <i>et al.</i> 2008 ⁵⁷ | Taipei, Taiwan | 2003–06 | 19 812 | 0.03 | 2.4 | SIM |
| Peng <i>et al.</i> 2009 ³¹ | Guangzhou, China | 2006–07 | 2 580 | 1.0 (not specified SS or LSBE) | – | SIM |
| Park <i>et al.</i> 2009 ⁵⁸ | Korea, nation-wide | 2006 | 25 536 | 0.84 | – | SIM |
| Chang <i>et al.</i> 2009 ⁵⁹ | Kaoshiung, Taiwan | 2007–08 | 4 797 | 0.27 | 1.67 | SIM |
| Lee <i>et al.</i> 2010 ⁶⁰ | Korea, multicentre | 2006 | 2 048 | 1.0 (not specified SS or LSBE) | – | SIM |
| Xiong <i>et al.</i> 2010 ⁶¹ | Guangzhou, China | 2007 | 2 022 | 0.05 | 0.99 | SIM |
| Kuo <i>et al.</i> 2010 ⁶² | Taoyuan, Taiwan | 2007 | 736 | 1.8 (not specified SS or LSBE) | – | SIM |

SIM, specialized intestinal metaplasia; IM, intestinal metaplasia.

Table 4 Time trend studies for erosive esophagitis in asian regions

| Study | Time Interval | Prevalence rates of Erosive esophagitis (first-second, %) |
|--|--------------------------------|---|
| Singapore; Ho <i>et al.</i> ⁶⁶ | 9 years (1992–2001) | 4.3 to 10.0 |
| Philippines; Sollano <i>et al.</i> ⁶⁷ | 6 years (1994/7–2000/3) | 2.9 to 6.3 |
| Malaysia; Goh <i>et al.</i> ⁶⁸ | 10 years (1989/1990–1999/2000) | 2.0 to 8.4 |
| Taiwan; Lien <i>et al.</i> ⁶⁹ | 7 years (1995–2002) | 5.0 to 12.6 |
| Kim <i>et al.</i> 2009 ⁷⁰ | 10 years (1995–2005) | 1.8% (1995), 5.9% (2000), 9.1% (2005) |

increase in incidence of erosive esophagitis after *H. pylori* eradication.^{81,82} However, Kim *et al.*⁸³ reported no association with *H. pylori* eradication, and Tsukuda only found an association only in patients with hiatus hernia.⁸⁴

H. pylori infection especially with the antral-predominant or duodenal ulcer phenotype, is associated with an increase in gastric acid secretion. This would normalize with *H. pylori* eradication. On the other hand, the pangastritis phenotype of *H. pylori* infection is associated with a decrease in gastric acid secretion, so that a rebound of acid secretion would occur with *H. pylori* eradication unless irreversible atrophic gastritis has already occurred.⁸⁵ This difference in the phenotype of *H. pylori* infection likely underlies the variable outcomes of *H. pylori* eradication that have been reported.

Changes in diet, smoking and alcohol consumption

Dietary change has been inevitable with growing affluence in most parts of Asia. An increase in the consumption of dietary fat and protein amongst Asian populations is well documented.^{86–89} The role of diet in the causation of GERD has been widely discussed.

In a cross sectional survey, El-Serag *et al.* reported an association between high dietary fat and increased risk of reflux disease.⁹⁰ Fox *et al.* showed a high fat and energy rich diet increased the severity and frequency of reflux symptoms.⁹¹ In an older study from China, Pan *et al.* implicated eating “greasy and oily” foods.³⁵ However, other studies have not found an association with fat intake.⁹² Dietary studies remain difficult to perform in terms of measurement of food intake.

Smoking and alcohol consumption are well recognized risk factors for erosive esophagitis and GERD^{22,28,29,31}. Consumption of carbonated drinks have been shown previously to be associated with reflux symptoms, but a recent systematic review showed no correlation with GERD.⁹³ Lifestyle changes are difficult to measure. Zheng *et al.* showed that increased physical activity at work was a risk factor for GERD, while, conversely, recreational physical activity was protective.⁹⁴

Increases in BMI, obesity and metabolic syndrome

Perhaps the most important factor in the emergence of GERD in Asia has been the marked increase in prevalence of obesity and

metabolic syndrome in the region.⁹⁵ Obesity has indeed become a major problem in Asians. Recent surveys from China, have shown that overweight and obesity affect a significant proportion of the population.^{96–98} A recent report from India has also reported a marked increase in BMI in that population.⁹⁹ Obesity and its associated diseases, such as cardiovascular disease, diabetes mellitus and non-alcoholic fatty liver, have been reported to be on the increase in the Asia-Pacific region.^{100–102} In a meta-analysis of published studies, Hampel and colleagues have shown that obesity is associated with increased reflux symptoms, erosive esophagitis and esophageal adenocarcinoma.¹⁰³ Many studies from Asia correlating obesity,^{104,105} metabolic syndrome^{106–110} and reflux disease have now been published. In particular the association between visceral adiposity and central obesity has been consistently significant.^{106,111–113} The “epidemic” of obesity in Asia portends a similar exponential increase in obesity related disease such as GERD.

Amongst the mechanism of disease causation, increased intra-abdominal pressure, impaired gastric emptying, decreased lower esophageal sphincter tone and an increase in the number of transient lower esophageal sphincter relaxations have been demonstrated in obese subjects.^{114–118} In a study employing sophisticated manometry techniques, Pandolfino and colleagues showed an increase in intragastric pressure as well as in gastro-esophageal pressure gradients in obese individuals.¹¹⁹

Ethnic differences: role of genetic predisposition?

Genetic predisposition to GERD amongst different ethnic groups would mean that such an increase would be more prominent amongst certain racial groups. High prevalence for GERD symptoms amongst Chinese, Japanese and Koreans indicate that these races may be predisposed to develop GERD. In a multiracial country like Malaysia, where we can compare the changes between different Asian races, Rosaida and Goh, in an earlier study identified Indian race as a risk factor for GERD and erosive reflux esophagitis.²² In a time trend study by the same group, Goh *et al.* recorded a significantly higher rise in esophagitis over a 10-year interval amongst Indians (2.4%–8.1%) compared to Chinese (1.7%–6.4%) and Malays (1.5%–3.7%).⁶⁸ In another study, Rajendra *et al.* showed a distinct predisposition to develop Barrett’s esophagus in Indian patients and further showed a predominance of HLA B7 subtype amongst Indians with Barrett’s esophagus.⁵² While environmental influence would remain fairly consistent across all races, these differences identify Indians as a genetically susceptible race to the influence of environmental factors in the development of GERD. Interestingly a study from the UK lends support to this notion by identifying South Asian race (Indian) versus White Caucasians as a risk factor for GERD.¹²⁰

Clinical presentation and diagnosis of GERD in Asian patients

While heartburn is the cardinal symptom of GERD and is well recognized in the West, the situation is distinctly different in our part of the world. For example, there is no word in the Chinese vernacular language to describe this symptom. Spechler *et al.*¹²¹ in a survey of outpatients attending clinics in the Boston area, USA,

discovered that the majority of patients of East Asian origin did not understand the symptom of heartburn. In the Asian setting many patients complain of chest discomfort which has been loosely classified as non-cardiac chest pains.^{121–124} “Wind” is also a predominant complaint of many patients with reflux disease.¹²⁵ In many Southeast Asian countries, Malay patients use vernacular terms which do not translate exactly to the original terms of heartburn and acid regurgitation.¹²⁶

Endoscopy is a widely used tool for diagnosis of upper gastrointestinal complaints and will continue to be so. More Asian centers are now utilizing pH measurements as an adjunct to clinical and endoscopic diagnosis. The advent of the “catheterless” Bravo capsule has allowed more tertiary centers throughout the region to utilize pH measurements. Bilitic and impedance measurements are also more readily available nowadays in many Asian centers.

Present challenges

The past 20 years has seen the emergence of reflux disease as an important disease in Asia. Although, it generally remains a mild disease in Asian patients, we know from the Western experience that serious complications can arise, chiefly Barrett’s esophagus and associated adenocarcinoma of the cardio-esophageal junction. Continued efforts must be made to ensure an accurate description of the disease burden and to track the evolution of the disease over time and across the whole region. In particular, translated and validated questionnaires should be utilized for surveys of GERD symptoms in the population. Broad agreement should be made with standardized definition of Barrett’s esophagus, including histological description. A broader understanding of the disease will inevitably translate to clinical practice for the benefit of patients in the region.

In the past 10 years since the original review in the *Journal of Gastroenterology and Hepatology*,⁸ was published, many publications on GERD have emanated from Asia. High quality research in GERD is now carried out in Asia, and, in the new decade, Asian research and publications on GERD could lead in a field that was erstwhile considered a Western disease.

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