Epidemiology of Gastroesophageal Reflux Disease in Asia: A Systematic Review

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Ethnic and geographical differences are important factors in studying disease frequencies, because they may highlight the environmental or genetic influences in the etiology. We retrieved the studies which have been published regarding the epidemiologic features of gastroesophageal reflux disease (GERD) in Asia, based on the definitions of GERD, study settings, publication years and geographical regions. From the population-based studies, the prevalence of symptom-based GERD in Eastern Asia was found to be 2.5%-4.8% before 2005 and 5.2%-8.5% from 2005 to 2010. In Southeast and Western Asia, it was 6.3%-18.3% after 2005, which was much higher than those in Eastern Asia. There were robust epidemiologic data of endoscopic reflux esophagitis in medical check-up participants. The prevalence of endoscopic reflux esophagitis in Eastern Asia increased from 3.4%-5.0% before 2000, to 4.3%-15.7% after 2005. Although there were only limited studies, the prevalence of extra-esophageal syndromes in Asia was higher in GERD group than in controls. The prevalence of Barrett’s esophagus was 0.06%-0.84% in the health check-up participants, whereas it was 0.31%-2.00% in the referral hospital settings. In summary, the prevalence of symptom-based GERD and endoscopic reflux esophagitis has increased in Asian countries. However, the prevalence of Barrett’s esophagus in Asia has not changed and also still rare.

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Key Words
Asia; Epidemiology; Gastroesophageal reflux; Prevalence

Introduction

Gastroesophageal reflux disease (GERD) broadly includes the whole spectrum of reflux disease, from intermittent symptoms like heartburn or acid regurgitation to endoscopic reflux esophagitis and Barrett’s esophagus.1 It usually gives a considerable impact on the quality of the patient’s life not only by the symptoms, but also by the following consultation procedures and medical cares. While GERD is a common disease and also the major upper gastrointestinal problem in Western countries, its prevalence amongst Asian has been reported to be relatively low.2-4

During the recent decade, several studies about prevalence of symptom-based GERD and endoscopic reflux esophagitis have revealed generally higher number of patients compared to other previous Asian studies. Time trend studies have also shown the increase of prevalence both in symptom based-GERD and endoscopic reflux esophagitis.5

Heartburn and acid regurgitation are the characteristic symptoms of GERD. Heartburn is defined as a burning sensation at
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the retrosternal area. However, different criteria of GERD have been published from all over the world including Asia, with the frequency of its symptoms differing from once a week to even once a year. Furthermore, it also has been attributed to the lack of the exact word for heartburn in some Asian languages, such as Chinese or Korean. In addition, there has not been any consensus distinguishing GERD from dyspepsia.

In Asia, endoscopic reflux esophagitis is quite commonly diagnosed because the cost of endoscopic examination is relatively inexpensive. Actually, a lot of asymptomatic people get the upper endoscopic examinations for gastric cancer screening and comprehensive medical check-up. The major limitation of studies with individuals in screening program is that it might not represent the general population. However, such studies have advantages of their large sample size and consistent diagnostic manners.

This paper was aimed to review the epidemiologic aspect of GERD and its related disease manifestations, such as endoscopic reflux esophagitis, Barrett's esophagus and extra-esophageal syndrome, according to various definitions, study settings, publication years and geographical regions in Asia.

Methods

Identification and Eligibility Assessment of Relevant Studies

A systematic PubMed search was performed to identify all of the reports written about the prevalence of GERD, published from January 1995 to October 2010, using combinations of the following index terms: “gastroesophageal reflux disease,” “reflux,” “gastroesophageal reflux” or “esophagitis” and “prevalence” or “epidemiology.” Only the papers published in English were reviewed. Included studies had to meet all of these 3 following criteria: (1) including epidemiologic studies performed with at least 200 subjects gathered by population-based or medical check-up settings; (2) having detailed description of GERD definition or its related manifestations and (3) subjecting any sample type, including subjects from tertiary hospitals, to collect data about extra-esophageal symptoms or Barrett’s esophagus.

Data Extraction

Following information was abstracted from each study included: the year of publication, study periods, country of subjects, sample types (the population-based type, subjects who underwent the medical check-up or those from referral hospitals), study design (derived from case-control, cohort or other cross-sectional studies), sample size and prevalence of GERD, reflux esophagitis, Barrett’s esophagus or extra-esophageal syndromes of GERD.

All studies were sub-grouped by each geographical region, based on GloboCan 2008, the project of the International Agency for Research on Cancer which provides contemporary estimates of the incidence, prevalence and mortality from major types of cancers for all countries over the world.7 The Asian geographic area includes these 4 regions of Eastern (China, Japan, Korea and Taiwan), Southeastern (Malaysia, Singapore and Thailand), South Central (India, Iran and Pakistan) and Western (Israel and Turkey) Asia.

Among a total of 3,440 papers searched by those key words, 1,696 papers were excluded from this study because they were not written by English or their subjects were not adults or human. Only 70 studies were included in the final analysis.

Prevalence of Symptom-Based Gastroesophageal Reflux Disease

Details of published studies satisfying the inclusion criteria on the symptom-based GERD (ie, symptoms of heartburn or acid regurgitation occurring at least once a week), in the population-based studies are listed in Table 1. They generally used methods of face-to-face or telephone interviews or the postal questionnaires.

The largest sample group was consisted of Eastern Asia studies, followed by those from South Central Asia (Figure). The prevalence of symptom-based GERD in Eastern Asia was 5.2%-8.5%8-13 from 2005 to 2010, while it was 2.5%-4.8%14-16 before 2005. Most studies in South Central Asia were conducted in Iran. The prevalence of GERD in Iran was 6.3%-18.3%17-20 from 2005 to 2010, which seemed more prevalent than in Eastern Asia. Before 2005, 2 population-based studies from this country with different definitions of GERD also showed similar results.21,22 On the other hand, the time trend of GERD prevalence showed drastic change between 2 cross-sectional surveys of the general population in Singapore in Southeastern Asia. The first survey which was held in 1994 showed the prevalence of GERD by at least monthly symptoms to be around 5.5% ± 1.5%, while it has increased to 10.5% ± 2.0% after 5 years (OR, 2.2; 95% CI, 1.0-5.2; P = 0.05).23 However, the sample size of this study was relatively small and this increased result might also have been
Table 1. Population-Based Study of Gastroesophageal Reflux Disease in Asia

| Study        | Country     | Sample size | Publication year | Study year | Definition of study/Methods                                      | Prevalence                                                                 |
|--------------|-------------|-------------|------------------|------------|-----------------------------------------------------------------|---------------------------------------------------------------------------|
| **Eastern Asia** |             |             |                  |            |                                                                 |                                                                           |
| He et al8    | China       | 16,091      | 2010             | 2007-2008  | Self-reported questionnaires                                     | At least weekly, 5.2%; at least twice a week, 3.1% (2.4% in urban and 3.8% in rural area) |
| Wang et al9  | China       | 919         | 2009             | 2005-2006  | GERD, heartburn or regurgitation over 1 wk recall by RDQ         | GERD, 6.2% (95% CI, 4.64-7.76); experienced eating and drinking problems, 47%; sleep impairment, 32%; reduced work productivity, 32%; GERD related with impaired HRQOL |
| Ma et al17   | China       | 1,443       | 2009             | 2005       | Direct interview                                                | GERD, 8.5%; overlap with dyspepsia in 27% and with IBS in 24%              |
| Lee et al10  | Korea       | 1,443       | 2009             | 2005       | Direct interview                                                | 7.1%; risk factors: educational level for heartburn, aging for acid regurgitation |
| Yang et al11 | Korea       | 1,044       | 2008             | 2004       | Telephone survey with random number; GERD, heartburn or acid regurgitation at least weekly | 7.28% (95% CI, 6.87-7.69); men (7.8%) vs women (6.7%) (P < 0.05); risk factors: old age, night-shift work, heavy work burdens, single or divorced people, increase intake of greasy or sweet foods, excessive eating and constipation |
| Li et al12   | China       | 15,283      | 2008             | 2004-2005  | Self-reported questionnaires; GERD, RDQ score > 12               | 7.28% (95% CI, 6.87-7.69), men (7.8%) vs women (6.7%) (P < 0.05); risk factors: old age, night-shift work, heavy work burdens, single or divorced people, increase intake of greasy or sweet foods, excessive eating and constipation |
| Chen et al13 | China       | 3,338       | 2005             | -          | Direct interview; GERD, heartburn or acid regurgitation at least weekly | GERD, 6.2%; no gender difference; risk factors: marital status, heavy burden of work for GERD |
| Wang et al42 | China       | 2,532       | 2004             | 2003       | Symptomatic GER, composite score of following 3 GER symptoms ≥ 3 | Weekly heartburn, 4.1% (103), acid regurgitation, 7.8% (197), food regurgitation, 3.3% (83), SGER, 17.0% |
| Wong et al14 | China (Hong Kong) | 2,209      | 2003             | 2002       | Telephone survey; GERD, heartburn and/or acid regurgitation at least weekly | GERD, 2.5%; risk factors for health care seeking: female gender, depression, social morbidity |
| Jeong et al15 | Korea       | 1,417       | 2008             | 2000-2001  | Direct interview; GERD, heartburn and/or acid regurgitation at least weekly | 3.5% (95% CI, 2.6-4.3); GERD exhibited significantly worse HRQOL |
| Cho et al11  | Korea       | 1,649       | 2007             | 1996       | Telephone survey; GERD, heartburn and/or acid regurgitation at least weekly | GERD, 4.8% (79); IBS, 4% (68); risk factor: overlap of IBS (OR, 3.0; 95% CI, 1.05-6.27) |
| Cheung et al16 | China (Hong Kong) | 1,649      | 2007             | 1996       | Telephone survey; GERD, heartburn and/or acid regurgitation at least weekly | GERD, 10.5% ± 2.0% in 1999 vs 5.5% ± 1.5% in 1994 |
| **South Eastern Asia** |            |             |                  |            |                                                                 |                                                                           |
| Lim et al23  | Singapore   | 237 in 1999 | 2005             | 1994 vs 1999 | Direct interview; GERD, retrosternal burning or acid regurgitation at least monthly | Ethnic-adjusted rate of 1.6% (95% CI, 0.6-2.6): Indians, 7.5% (95% CI, 4.4-11.7), Chinese, 0.8% (95% CI, 0.1-3.0), Malays, 3.0% (95% CI, 1.2-6.1); men > women (1.6% vs 1.5%, P < 0.01) |
| Ho et al44   | Singapore   | 696         | 1998             | -          | GERD, heartburn or acid regurgitation more than monthly          |                                                                           |

attributed to the increased awareness.

The prevalence in Western Asia was found to be the highest among the whole Asian region as represented by 20% in Turkey. One population-based study performed in Israel (2007) also reported the high prevalence of GERD symptoms, including 6.5% of retrosternal burning, 5.2% of retrosternal pain, 10.4% of acid taste in the mouth and 7.9% of the reflux of gastric contents.24

Prevalence of Endoscopic Reflux Esophagitis

The list of studies published regarding the prevalence of en-
### Table 1. Continued

| Study            | Country   | Sample size | Publication year | Study year | Definition of study/Methods                                                                 | Prevalence          |
|------------------|-----------|-------------|------------------|------------|-------------------------------------------------------------------------------------------|---------------------|
| **South Central Asia** |           |             |                  |            |                                                                                           |                     |
| Mostaghni et al69 | Iran      | 717         | 2009             | 2006       | GERD, at least weekly any symptoms of heartburn, regurgitation, chest pain, dysphagia, hoarseness and cough | 33% (237)           |
| Solhpour et al17  | Iran      | 5,733       | 2008             | -          | Direct interview: symptoms of reflux at least once a week                                  | GERD, 9.1%; no association with obesity and GERD |
| Nasseri-Moghaddam et al18 | Iran | 2,057       | 2008             | -          | Direct interview: GERD, heartburn or acid regurgitation at least weekly                      | GERD, 18.2%; risk factors: female gender (OR, 1.55; 95% CI, 1.01-2.41), BMI > 30 kg/m² (OR, 1.79; 95% CI, 1.03-3.12), less education, smoking, NSAID use and GERD in spouse |
| Somi et al19      | Iran      | 620         | 2006             | 2005       | GERD, heartburn or acid regurgitation at least weekly                                         | GERD, 6.3%; no gender difference |
| Nouriaie et al20  | Iran      | 1,202       | 2007             | 2004-2005  | Telephone survey with random number: GERD, heartburn or acid regurgitation at least weekly  | 6.8% (95% CI, 5.4-8.3); no relationship with gender, age or education. |
| Saberi-Firoozi et al21 | Iran | 1,978       | 2007             | 2004       | GERD, heartburn or acid regurgitation at least 3 times a week                                | GERD, 15.4% (304); risk factor: consulting with physicians, 24.8% |
| Ehsani et al22    | Iran      | 700         | 2007             | 1999       | GERD, heartburn or acid regurgitation                                                       | GERD, 39.7% (278)   |
| **Western Asia**  |           |             |                  |            |                                                                                           |                     |
| Sperber et al24   | Israel    | 981         | 2007             | -          | Telephone survey: suffered GERD symptoms at least weekly.                                    | Reported retrosternal burning, 6.5%; retrosternal pain, 5.2%; acid taste in the mouth, 10.4%; reflux of gastric content, 7.9% |
| Kitapçıoğlu et al25 | Turkey | 630         | 2007             | 1998-1999  | Direct interview: GERD, heartburn or acid regurgitation at least weekly                      | GERD, 20%           |
| Bor et al26       | Turkey    | 630         | 2005             | -          | GERD, heartburn and/or acid regurgitation occurring at least weekly                           | GERD, 20%           |

GERD, gastroesophageal reflux disease; RDQ, Reflux Disease Questionnaire, HRQOL, health-related quality of life; IBS, irritable bowel syndrome; SGER, symptomatic gastroesophageal reflux; BMI, body mass index.

The intensity and frequency of reflux induced symptoms are poor predictors for finding the presence or the severity of endoscopic mucosal breaks (erosion or ulcer). In the medical check-up studies, the prevalence of GERD based on symptoms like heartburn or acid regurgitations at least once a week was 5.0%-8.2%, which were similar with those of population-based studies.
### Table 2. Epidemiology of Gastroesophageal Reflux Disease in Asian Medical Check-up People

| Study          | Country | Sample size | Publication year | Study year | Definition of study/Methods                                                                 | Prevalence |
|---------------|---------|-------------|-----------------|------------|---------------------------------------------------------------------------------------------|------------|
| **Eastern Asia** |         |             |                 |            |                                                                                              |            |
| Noh et al\(^{35}\) | Korea   | 2,388       | 2010            | 2008-2009  | RE by LA classification; GERD, heartburn at least weekly; Rome III criteria for FGIDs        | RE, 12.0%; NERD, 3.1%; more frequently overlap with FGIDs in NERD than RE |
| Kaji et al\(^{36}\) | Japan   | 2,680       | 2010            | 2008-2009  | Self-reported questionnaires/at least weekly symptoms; Rome III criteria for FGIDs          | GERD, 7.7%; FD, 10.0%, IBS, 14.2%; overlap with FGIDs, 46.9%   |
| Matsuzaki et al\(^{31}\) | Japan   | 2,563       | 2010            |            | NERD, GER symptoms with GER at VE; FH, GER symptoms without GER at VE                     | GER by VE, 11.2% (283); NERD, 12.4% (35/283); FH, 26.5% (75/283) |
| Yamagishi et al\(^{33}\) | Japan   | 6,504       | 2009            |            | RE by LA classification; symptoms (yes/no)                                                 | RE, 6.3%; positive correlation between prevalence of heartburn/dysphagia and severity of RE |
| Kim et al\(^{34}\) | Korea   | 25,536      | 2008            | 2006       | RE by LA classification; GERD, heartburn or acid regurgitation at least weekly; NERD, GERD symptoms without RE | RE, 8% (2,019): LA-A, 6.0% (1,497), LA-B, 2.0% (471), LA-C, 0.2% (47), LA-D, 0.02% (4); GERD, 5% (1,161); NERD, 4% (996); risk factors for GERD: male, \(H. pylori\) eradication history, alcohol and obesity; risk factors for NERD: female, age, low BMI, low monthly income, high fasting sugar, smoking and a stooping posture at work and antibiotic usage |
| Peng et al\(^{32}\) | China   | 2,580       | 2009            | 2006-2007  | RE by LA classification; GERD, heartburn and/or acid regurgitation during the previous 6 mo | RE, 4.3% (110); asymptomatic RE, 33.6% of RE; risk factors: male, alcohol use, hiatus hernia and reflux symptoms. |
| Tseng et al\(^{29}\) | China   | 19,812      | 2008            | 2003-2006  | RE by LA classification; symptom questionnaires                                              | RE, 15.7% (3,129): LA-A, 78.2% (2,446), LA-B, 16.0% (502), LA-C, 5.2% (164), LA-D 0.05% (17) |
| Kang et al\(^{31}\) | Korea   | 2,457       | 2007            | 2004-2005  | RE by LA classification; GERD, heartburn or acid regurgitation at least weekly             | GERD 8.2%; RE, 6.6%; RE according to BMI (5.6%, 8.1% and 15.5% for BMI < 25, 25-30 and > 30, respectively; \(P = 0.002\)) |
| Yamagishi et al\(^{31}\) | Japan   | 82,894      | 2008            |            | Symptom questionnaire; sometimes experienced of heartburn                                   | GERD symptom, 15.8% in men and 20.7% in women |
| Lee et al\(^{30}\) | Korea   | 3,188       | 2008            | 2003-2005  | Erosive esophagitis; RE by LA classification; GERD, heartburn or acid regurgitation at least weekly | Erosive esophagitis, 9.2%: LA-A, 74.7% (218), LA-B, 20.1% (61), LA-C, 4.5% (13), LA-D, 0.7% (2); obesity over BMI ≥ 30 kg/m² (OR = 3.3, 95% CI, 1.8-6.1) |
| Fujiwara et al\(^{33}\) | Japan   | 2,662       | 2005            |            | Symptom questionnaires; GERD, heartburn and/or acid eructation                              | GERD: daily symptoms, 2.1% (124); at least twice a week, 4.6% (275); at least twice a month, 12.8% (773) |
| Fujiwara et al\(^{33}\) | Japan   | 569         | 2003            | 2000-2001  | RE by LA classification                                                                     | RE, 7.7% (42); atrophic gastritis, inversely associated with RE (OR, 0.15; 95% CI, 0.07-0.36) |
| Fujimoto et al\(^{27}\) | Japan   | 6,010       | 2003            |            | Symptom questionnaires; RE by LA classification                                             | RE, 15%; grade A (9.6%), grade B (4.6%) and grade C + D (2.0%); heartburn, 27.0%; dysphagia, 16.9%; odynophagia, 19.2%; acid regurgitation, 7.1% |
| Lien et al\(^{26}\) | Taiwan  | 1,902       | 2009            | 2002, 1995 | RE by endoscopy                                                                              | RE, 5% in 1995 and 12.6% in 2002 (\(P < 0.0001\)); aging related with RE with dose-response manner |
| Lee et al\(^{25}\) | Korea   | 7,015       | 2001            | 1996-1997  | Endoscopy: RE by SM classification                                                          | RE, 3.4% (242); grade 1 (98.3%) and grade 2 (1.7%); hiatal hernia, 9.2%; men : women = 7 : 1 |

RE, reflux esophagitis; LA, Los Angeles; GERD, gastroesophageal reflux disease; FGID, functional gastrointestinal disorder; NERD, non-erosive reflux disease; VE, videoesophagography; FH, functional heartburn; SM, Savary-Miller; FD, functional dyspepsia; IBS, irritable bowel syndrome; \(H. pylori\), *Helicobacter pylori*. 
### Table 3. Epidemiology of Gastroesophageal Reflux Disease in Asian Referral Hospital

| Study             | Country     | Sample size | Publication year | Study year | Definition of study/Methods | Prevalence                                                                 |
|-------------------|-------------|-------------|------------------|------------|----------------------------|-----------------------------------------------------------------------------|
| **Eastern Asia**  |             |             |                  |            |                            |                                                                             |
| Kusano et al 46    | Japan       | 2,426 in 100 consecutive patients at nation-wide institutions | 2009       | 2005        | GERD, heartburn twice weekly or more; RE by LA classification | GERD, 13.7%; NERD, 9.8% (71.7% among GERD)                                  |
| Sakaguchi et al 74 | Japan       | 2,225 in referral hospital | 2008       | 2005-2006   | GER symptoms, heartburn or water brash symptoms twice or more per week; RE by LA classification; GERD including RE and NERD | GERD, 25.9%; RE, 11.1%; NERD, 14.7%; GERD according to BMI: 21.0% in thin patients, 24.4% in normal BMI and 31.9% in obesity |
| Du et al 75        | China       | 10 referral hospitals, 2,231 | 2008       | 2004-2005   | GERD, heartburn, substernal chest pain, acid eructation and food regurgitation; RE by endoscopy | GERD, 31.7% (1,701); RE, 20.8% (464); NERD, 10.6% (237); asymptomatic RE, 37.3% (173); risk factors for RE: old age, male, moderate working burden, divorced/widowed and strong tea drinking |
| Chen et al 39      | Taiwan      | Referral settings: 7,479 in 2000 and 10,195 in 2007 | 2010       | 2000-2007   | GERD, at least weekly heartburn and/or acid regurgitation with RE; NERD, symptoms without RE | Incidence of GERD, 15.4% (37) for 6 years; risk factors: negative *H. pylori*, constipation and calcium channel antagonists |
| Miyamoto et al 76  | Japan       | 241 non-GERD patients cohort | 2008       | 1998, 2004  | GERD, QUEST questionnaire > 6 | RE, 7.1% (195); GERD, 12.7% (351); NERD, 10.9% (300)                     |
| Mishima et al 77   | Japan       | Referral populations: 2,760 | 2005       | -           | GERD, QUEST questionnaire > 6; RE by LA classification | RE, 14.9% (1,199) without gender difference; heartburn, 27.7%; dysphagia, 19.0%; odynophagia, 6.1%; acid regurgitation, 18.3% |
| Okamoto et al 78   | Japan       | Outpatients without taking GI medication (n = 6,166) and health check up (n = 1,865); N = 8,031 | 2003       | 1996-1998   | Direct interview; RE by LA classification |                                                                             |
| Chang et al 79     | China       | Tertiary hospital: 2,044 | 1997       | -           | RE by endoscopy | RE, 5%; gender difference (men : women = 5.6 : 1)                       |
| Haruma et al 80    | Japan       | Tertiary hospital: 6,205 | 2000       | 1995-1997   | RE, presence of hyperemia, erosion or ulcer | RE, 3.7% (229)                                                            |
| Yeh et al 80       | Taiwan      | 464 patients with GI symptoms | 1997       | 1991-1992   | RE by Savary-Miller system | RE, 14.5% (66); gender difference (men : women = 3.1 : 1)                 |

Asymptomatic reflux esophagitis was reported in 33.6%-84.0% among the subjects with reflux esophagitis. This finding might be a true reflection of community or caused by the possible over-diagnosis of endoscopic reflux esophagitis by including mild reflux esophagitis or minimal changes.

Non-erosive reflux disease (NERD) has been commonly defined as the presence of classic GERD symptoms in the absence of esophageal mucosal injury which has been detected during the upper endoscopy. NERD is considered as the major subcategory of GERD, which has been assumed with an increasingly important role. The prevalence of NERD in medical check-up studies was reported from 3.1% to 4.0%, comprising about 70%-
Table 3. Continued

| Study | Country | Sample size | Publication year | Study year | Definition of study/Methods | Prevalence |
|-------|---------|-------------|-----------------|------------|----------------------------|------------|
| South Eastern Asia | Rosaida and Goh81 | Malaysia 1,000 patients with upper abdominal discomfort | 2004 | - | GERD, heartburn and/or acid regurgitation at least monthly; RE by LA classification. | GERD 38.8% (388); RE 13.4% (134); NERD 25.4% (254); Hiatal hernia 6.7% (67); risk factors for GERD: Indian race (OR, 3.25; 95% CI, 2.38-4.45), Malay race (OR, 1.67; 95% CI, 1.16-2.38), obesity, hiatus hernia, alcohol and high education; risk factors for RE: male, Indian race, hiatus hernia and alcohol consumption |
| Ho et al82 | Singapore 16,375 patients who were referred for endoscopy | 2005 | 1992-2001 | RE, presence of erosions and/or ulceration | RE 6.9% (1,128; 95% CI, 6.5-7.3); risk factors: year of endoscopy (OR, 1.99; 95% CI, 1.18-3.36), positive urease test rate (OR, 0.99, 95% CI, 0.983-0.999), male gender (OR, 1.59; 95% CI, 1.01-2.50) |
| South Central Asia | Yarandi et al83 | Iran 6,476 patients with FGID symptoms | 2010 | - | GERD, symptoms or endoscopic finding or pH monitoring; Rome II or III criteria for FGIDs | GERD, 41% (2,658); IBS, 21.9% (1,419); significant overlap with IBS (63.6% in IBS vs 34.7% in non-IBS) |
| Jafri et al84 | Pakistan 963 | 2005 | - | GERD | GERD, 24% (228) |
| Western Asia | Al-Humayed et al85 | Saudi Arabia 1,607 patients with dyspepsia who underwent endoscopy; retrospective review | 2010 | - | GERD symptoms; endoscopic RE | GERD, 15% (242) with or without RE or hiatus hernia |

GERD, gastroesophageal reflux disease; GI, gastrointestinal; FGID, functional gastrointestinal disorder; RE, Reflux esophagitis; LA, Los Angeles; NERD, non-erosive reflux disease; QUEST, questionnaire for the diagnosis of reflux esophagitis; BMI, body mass index; H. pylori, Helicobacter pylori; IBS, irritable bowel syndrome.

80% of GERD.34,35 Most studies using questionnaires might have over-estimated the prevalence of NERD because their questions might have failed to distinguish the functional heartburn.38 More precise data regarding the epidemiology of NERD are needed.

In referral hospital settings, the prevalence of GERD showed wide range results as followings: 12.4%-31.7% of symptom-based GERD, 2.3%-14.7% of NERD and 7.1%-20.8% of endoscopic reflux esophagitis. In a time trend study in Chinese tertiary hospitals from 2000 to 2007, the prevalence of endoscopic reflux esophagitis increased from 20.7% to 51.0% with the increased numbers of undergoing endoscopy secondary to GERD from 4.9% in 2000 to 14.1% in 2007. However, the prevalence of concomitant GERD symptoms did not significantly change (range, 13.0%-15.1%) in screening endoscopic studies with no significant interval change in the prevalence of NERD.39 Therefore, those authors have suggested that the actual increase in the prevalence of endoscopic reflux esophagitis might be the result of the increased demand for endoscopic investigation of GERD symptoms in some populations, or the better recognition of reflux esophagitis by endoscopists.

**Prevalence of Extra-esophageal Syndromes**

Although typical manifestations of GERD are heartburn or acid regurgitation, atypical or extra-esophageal symptoms might also be presented including respiratory symptoms, such as chronic cough, asthma or laryngitis, dental erosions, non-cardiac chest pain (NCCP), sleep disturbance and so on.40 These syndromes
Table 4. Extra-esophageal Syndrome of Gastroesophageal Reflux Disease in Asia

| Symptoms                        | Study                      | Country       | Setting/Sample size | Publication year | Definition of study/Methods | Prevalence/Proportion                                                                 |
|---------------------------------|----------------------------|---------------|---------------------|------------------|-----------------------------|--------------------------------------------------------------------------------------|
| Asthma                          | Takenaka et al86           | Japan         | Tertiary hospital   | 2010             | Self-reported questionnaires | GERD, 27.4% in subjects with persistent moderate to severe asthma treated with anti-inflammatory asthma medication |
| Asthma                          | Bor et al45                | Turkey        | Tertiary hospital: 308 asthma, 133 COPD and 694 control | 2009             | GERD, heartburn/regurgitation at least weekly; case-control study | GERD, 25.4% in asthma, 17.0% in COPD and 19.4% in controls |
| Asthma                          | Shimizu et al44            | Japan         | Tertiary hospital: 78 asthma, 56 non-asthmatic disease control and 150 healthy control | 2006             | Case-control study; RE, LA classification | RE: 39.3% (22), 5.4% (3) and 0.6% (1) in asthma, non-asthmatic disease control and healthy control, respectively |
| Asthma                          | Chunlertrith et al87       | Thailand      | Tertiary hospital: 151 asthma patients and 147 control | 2005             | Case-control study; GERD, heartburn or acid regurgitation | GERD, 12.6% in asthma vs 10.2% in control ($P > 0.05$) |
| Asthma                          | Al-Asoom et al88           | Saudi Arabia  | Tertiary hospital: 50 asthma patients and 22 control | 2003             | Case-control study; GER, a DeMeester score > 14.7           | Pathologic: GER, 44% (22) in asthma; risk factors: hoarseness and nocturnal symptoms |
| Asthma                          | Nakase et al89             | Japan         | 72 asthma patients in tertiary hospital | 1999             | RE by LA classification | RE, 27.8% (20); 67% (43) having one of the followings: heartburn, epigastric pain, water brash, odynophagia and dysphagia |
| Sleep disturbance              | Fujimata et al41           | Japan         | Tertiary hospital: 134 GERD (82 NERD) | 2010             | Self-reported questionnaires | 52.2% in 134 GERD; NERD for sleep disturbance (OR, 2.18; 95% CI, 1.05–4.53) |
| Sleep disturbance              | Chen et al42               | Taiwan        | Health check-up: 3,663 | 2009             | Endoscopy; RE by LA classification | Reflux symptoms for poor sleep quality (OR, 2.05; 95% CI, 1.65–2.54) |
| Sleep disturbance              | Kusano et al46             | Japan         | 35 nation-wide tertiary hospitals: N = 2,426 | 2008             | Sleep disturbance defined by self reported questionnaire classification | Higher sleep disturbance in heartburn compared to no heartburn (36.5% vs 40.7%, $P < 0.0001$); no difference according to RE 36.6% in GERD vs 18.3% in control ($P = 0.025$); myofascial pain, 31.7% vs 15% ($P = 0.03$) |
| Temporomandibular disorder     | Gharaibeh et al90          | Jordan        | Tertiary hospital: 60 GERD vs 60 control | 2009             | Case-control study | |
| Dental erosion                  | Wang et al47               | China         | Tertiary hospital: N = 88 | 2010             | Case-control study | 64.5% in frequent reflux (3-5/wk), 44.4% in occasional (1-2/wk) and 36.7% in control ($P < 0.05$) |
| NCCP                            | Mohd et al49               | Malaysia      | Tertiary hospital: 27 NCCP | 2009             | - | GERD, 66.7% (18/27) among NCCP |
| NCCP                            | Bor et al48                | Turkey        | Population-based study: 630 in low-income region | 2009             | - | GERD, 20%; NCCP, 37.3%; dysphagia, 35.7%; dyspepsia, 42.1%; odynophagia, 35.7% |
| ENT symptoms                    | Toros et al91              | Turkey        | 45 ENT outpatients in Tertiary hospital | 2008             | - | RE, 11%; GERD-related symptoms as sore throat, throat burning, throat clearing, globus, cough, halitosis, dysphonia, dysphagia, postnasal dripping, vocal fatigue and sputum |
| Chronic laryngitis             | Qua et al92                | Malaysia      | 32 chronic laryngitis patients in tertiary hospital | 2007             | GERD, heartburn or acid regurgitation at least once a week | GERD, 65.6% (21) in chronic laryngitis |

are usually considered to be multifactorial with GERD as one of the several potential aggravating cofactors. Extra-esophageal syndromes rarely occur with concomitant manifestations of the typical esophageal syndrome. Upper endoscopy and ambulatory pH monitoring were used to diagnose reflux in patients with atypical gastroesophageal reflux symptoms, however, these studies have
Table 4. Continued

| Symptoms | Study | Country | Setting/Sample size | Publication year | Definition of study/ Methods | Prevalence/Proportion |
|----------|-------|---------|---------------------|------------------|------------------------------|----------------------|
| Extra-esophageal symptoms | Cho et al41 | Korea | Population-based study: 1,417 | 2005 | Extra-esophageal symptoms, at least one of chest pain, dysphagia, globus sensation, asthma, bronchitis, pneumonia or hoarseness | GERD, 41.6% in atypical symptoms vs 8.7% in no atypical symptoms; chest pain, 44% in GERD vs 3.6% no-GERD; dysphagia, 16.0% vs 1.0%; globus 14.0% vs 1.1%; asthma, 26.0% vs 3.2%; bronchitis 20.0% vs 3.7%; hoarseness, 10.0% vs 0.6%; all P < 0.001 |
| Extra-esophageal symptoms | Wang et al42 | China | Population-based study: 2,532 | 2004 | SGER, composite score of following 3 GER symptoms ≥ 3 | Snore in SGER vs no-SGER, 28.1% vs 12.3%; laryngitis, 23.7% vs 11.8%; globus, 23.7% vs 5.0%; asthma, 6.5% vs 2.2%; bronchitis, 15.4% vs 8.9%; chronic cough, 21.4% vs 11.0%; all P < 0.01 |

NCCP, non-cardiac chest pain; ENT, ear, nose and throat; COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease; NERD, non-erosive reflux disease; RE, reflux esophagitis; LA, Los Angeles; SGER, symptomatic gastroesophageal reflux.

Figure. The prevalence of gastroesophageal reflux disease in Asian population-based study. Gastroesophageal reflux disease (GERD) is defined as having heartburn or acid regurgitation at least weekly.
*Study conducted in subjects with medical check-up, **GERD, retrosternal burning sensation or acid regurgitation at least once a month.

been proved to have poor diagnostic yield.

Extra-esophageal syndromes of GERD in Asia are summarized in Table 4. These data showed a wide range of prevalence or proportion because of the different definition of disease and different conditions of each study.

Two population-based studies in Asia have demonstrated the association between extra-esophageal syndrome and GERD.41,42 The proportion of GERD was significantly higher in subjects with atypical symptoms than in controls (41.6% vs 8.7%, P < 0.05).41 Symptoms as chest pain, dysphagia, globus, asthma, bronchitis, chronic cough and hoarseness were more frequently associated with GERD than controls.42 Both asthma and GERD are common conditions and they often coexist. However, several Western epidemiologic studies have revealed that asthma had been found more frequently in subjects with GERD than the general population.1 The prevalence of GERD was higher in the asthma group compared with controls in one large scale study (n = 1,135), performed in Turkey (25.4% vs 19.4%, P < 0.05).43 The proportion of endoscopic reflux esophagitis in patients with asthma was also higher than controls.44 There have been several studies demonstrating the association between sleep disturbance and GERD. The proportion of sleep dysfunction was 52.3%-56.6% among the patients with GERD, and GERD increased the OR of sleep dis-
Table 5. Epidemiology of Barrett’s Esophagus in Asia

| Study             | Country       | Setting/Sample size                  | Publication year | Definition of study/Methods                                      | Prevalence of Barrett’s esophagus |
|-------------------|---------------|--------------------------------------|------------------|------------------------------------------------------------------|----------------------------------|
| Xiong et al       | China         | Referral hospital: 2,022 patients with abdominal discomfort | 2010             | BE, ESCE with SIM                                               | BE, 1% (21); risk factors: age (OR, 1.03; 95% CI, 1.00-1.07), RE (OR, 4.44; 95% CI, 1.22-16.17) |
| Lee et al         | Korea         | Referral hospital: 2,048 patients with upper abdominal discomfort | 2010             | BE, a displacement of the squamocolumnar junction more than 1 cm with the presence of SIM | BE, 1% (21); risk factors: typical reflux symptoms (OR, 2.29; 95% CI, 1.16-7.37), RE (OR, 10.28; 95% CI, 4.31-24.50) |
| Chen et al        | China         | Tertiary hospital: 7,479 in 2000 and 10,195 in 2007 | 2010             | BE, SIM                                                         | BE, 0.6% at 2000 and 1.2% at 2007 |
| Peng et al        | China         | Medical check-up: 2,580               | 2009             | BE, SIM containing goblet cells                                 | BE, 1.0% (27); risk factors: reflux symptoms, hiatus hernia and alcohol use |
| Fouad et al       | Egypt         | Tertiary hospital: 1,000 patients with GERD | 2009             | GERD, at least 3 times weekly; BE, columnar-lined esophagus at endoscopy with SIM | 7.3% in chronic GERD; 0.08% (4/502) in NERD; adenocarcinoma, 0.8% |
| Park et al        | Korea         | Medical health check-up: 25,536       | 2009             | BE, ESCE with SIM                                               | 0.84% (215); RE among BE, 33%; having symptoms among BE, 60.1%; risk factors: male sex (OR, 1.82; 95% CI, 1.12-2.50), NSAIDs (OR, 2.02; 95% CI, 1.28-3.20), hiatal hernia (OR, 5.66; 95% CI, 3.70-8.66) and age ≥ 60 yr compared with an age < 40 yr (OR, 1.81; 95% CI, 1.07-3.09) |
| Odemis et al      | Turkey        | Referral hospital: 1,000 consecutive patients | 2009             | BE, ESCE with SIM                                               | 1.2% (12); 14% in hiatal hernia and 0.5% in normal esophago-gastric junction (P = 0.001) |
| Tseng et al       | China         | Medical check-up: 19,812              | 2008             | BE, ESCE with SIM                                               | ESCE, 0.28% (56); BE, 0.06% (12); short segment BE, 91.7% of BE |
| Kim et al         | Korea         | Tertiary hospital retrospective review 70,103 | 2007             | ESCE without SIM; BE, ESCE with SIM                             | ESCE without SIM, 1% (696); BE, 0.22% (151); risk factors: old age, male gender, smoker and having symptoms of acid regurgitation |
| Bafandeh et al    | Iran          | Tertiary hospital: 1,248 patients with heartburn | 2005             | Biopsy on columnar-lined mucosa above the GE junction, at 5 cm above the Z line | RE, 66.3% (960); BE, 2.4% (30); long-segment Barrett’s mucosa, 1/3 of BE |
| Gadour and Ayoola | Saudi Arabia  | Tertiary hospital: 2,572 subjects with endoscopy | 1999             | BE, endoscopic biopsy provided diagnosis                       | BE, 0.31% (8); esophageal adenocarcinoma, 0.62% (16) |
| Rosaida and Goh   | Malaysia      | Tertiary hospital: 1,000 patients with upper abdominal discomfort | 2004             | BE, ESCE with SIM                                               | BE, 2% (20) |
| Yeh et al         | Taiwan        | Tertiary hospital: 464 patients with upper abdominal discomfort | 1997             | BE, ESCE with intestinal metaplasia                            | BE, 2.0% (9) |

GERD, gastroesophageal reflux disease; BE, Barrett’s esophagus; ESCE, endoscopic suspected columnar epithelium; SIM, specialized intestinal metaplasia; RE, reflux esophagitis; NERD, non-erosive reflux disease.

turbance to about twice than controls.2,45,46

Dental erosion is an acid-induced loss of dental hard tissue without the involvement of bacteria. Direct contact of regurgitated gastric acid is considered to be the main mechanism of dental erosion in patients with GERD.47 In tertiary hospitals, dental erosions were found in 64.3% among patients with frequent reflux symptoms (3-5 times/wk), 44.4% among subjects with occasional symptoms (1-2 times/wk) and 36.7% among controls (P
was higher than in Eastern Asia. The prevalence of endoscopic reflux esophagitis in Eastern Asia seemed to increase in participants who have received the medical check-up. In Asia, only few and limited studies have been reported regarding the proportion of extra-esophageal syndromes such as asthma, sleep disturbance, non-cardiac chest pain and dental erosion, which was found to be significantly higher in the GERD patient group than controls. On the other hand, the prevalence of Barrett’s esophagus was found to be relatively low.

Based on the distinct genetic characteristics compared from the Western people, and rapid changes of socio-economic environments, this kind of study observing and investigating the epidemiologic changes of GERD in Asia would be a good model to understand the underlying pathogenesis of GERD.

Prevalence of Barrett’s Esophagus

Barrett’s esophagus is histologically confirmed by specialized intestinal metaplasia. It is considered to be one of the most important complications of GERD due to its strong association with adenocarcinoma. However, epidemiologic studies have consistently reported that the prevalence of Barrett’s esophagus-associated adenocarcinoma is very rare in Asia. The prevalence of Barrett’s esophagus was reported as 0.06%-0.84% in medical check-up and 0.31%-2.00% in the referral hospital settings (Table 5). The proportion of Barrett’s esophagus was 7.3% in patients with GERD and 2.4% in those with heartburn symptoms. Importantly, esophageal adenocarcinoma is often found even without any medical history of reflux symptoms. Although GERD symptoms is considered to be one of the most important risk factors of Barrett’s esophagus, only 60.1% of subjects who had received the medical check-up were found to have GERD symptoms.

In the Western world, esophageal adenocarcinoma has become one of the increasing cancers, in parallel with the increased prevalence of GERD and its major determinant, obesity. Such increase in the occurrence of Barrett’s esophagus has not yet been observed in Asia. Epidemiologic changes of GERD in Asia seem to be correlated with economic or environmental effects, Helicobacter pylori infections, nutritional changes, and also the geographic and ethnic differences. The general low-fat diet of Asian, their smaller body mass and also their higher prevalence of Helicobacter pylori might be related with the lower prevalence of GERD compared to Western peoples. However, their rapid economic growth, changes of eating habits and also the growing number of obesity in people would induce many changes in the epidemiology of Barrett’s esophagus and esophageal adenocarcinoma in the future.

In conclusion, many robust studies about GERD in Asia have been published during recent decades. Population-based studies showed that the prevalence of GERD has been increased in Eastern Asia, but still lower than those of the Western population. The prevalence of GERD in Southeast and Western Asia was lower than in Eastern Asia. The prevalence of endoscopic reflux esophagitis in Eastern Asia seemed to increase in participants who have received the medical check-up. In Asia, only few and limited studies have been reported regarding the proportion of extra-esophageal syndromes such as asthma, sleep disturbance, non-cardiac chest pain and dental erosion, which was found to be significantly higher in the GERD patient group than controls. On the other hand, the prevalence of Barrett’s esophagus was found to be relatively low.

References

1. Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R, Global Consensus Group. The Montreal definition and classification of gastro-esophageal reflux disease: a global evidence-based consensus. Am J Gastroenterol 2006;101:1900-1920.
2. Chen MJ, Wu MS, Lin JT, et al. Gastroesophageal reflux disease and sleep quality in a Chinese population. J Formos Med Assoc 2009;108:53-60.
3. Kang JY. Systematic review: geographical and ethnic differences in gastro-oesophageal reflux disease. Aliment Pharmacol Ther 2004;20:705-717.
4. El-Serag HB. Time trends of gastroesophageal reflux disease: a systematic review. Clin Gastroenterol Hepatol 2007;5:17-26.
5. Fock KM, Talley NJ, Fuss R, et al. Asia-Pacific consensus on the management of gastroesophageal reflux disease: update. J Gastroenterol Hepatol 2008;23:8-22.
6. Goh KL, Chang CS, Fock KM, Ke M, Park HJ, Lam SK. Gastrooesophageal reflux disease in Asia. J Gastroenterol Hepatol 2000;15:230-238.
7. GLOBOCAN 2008: Cancer incidence and mortality worldwide in 2008. International agency for research on cancer; 2008. Available from http://globocan.iarc.fr.
8. He J, Ma X, Zhao Y, et al. A population-based survey of the epidemiology of symptom-defined gastroesophageal reflux disease: the Systematic Investigation of Gastrointestinal Diseases in China. BMC Gastroenterol 2010;10:94.
9. Wang R, Yan X, Ma XQ, et al. Burden of gastroesophageal reflux disease in Shanghai, China. Dig Liver Dis 2009;41:110-115.
10. Lee SY, Lee KJ, Kim SJ, Cho SW. Prevalence and risk factors for overlaps between gastroesophageal reflux disease, dyspepsia, and irritable bowel syndrome: a population-based study. Digestion 2009;79:196-201.
11. Yang SY, Lee OY, Bak YT, et al. Prevalence of gastroesophageal reflux disease symptoms and uninvestigated dyspepsia in Korea: a population-based study. Dig Dis Sci 2008;53:188-193.
12. Li YM, Du J, Zhang H, Yu CH. Epidemiological investigation in
outpatients with symptomatic gastroesophageal reflux from the Department of Medicine in Zhejiang Province, east China. J Gastroenterol Hepatol 2008;23:283-289.

13. Chen M, Xiong L, Chen H, Xu A, He L, Hu P. Prevalence, risk factors and impact of gastroesophageal reflux disease symptoms: a population-based study in South China. Scand J Gastroenterol 2005;40:759-767.

14. Wong WM, Lai KC, LamKF, et al. Prevalence, clinical spectrum and health care utilization of gastro-oesophageal reflux disease in a Chinese population: a population-based study. Aliment Pharmacol Ther 2003;18:595-604.

15. Jeong JJ, Choi MG, Cho YS, et al. Chronic gastrointestinal symptoms and quality of life in the Korean population. World J Gastroenterol 2008;14:6388-6394.

16. Cheung TK, Lam KP, Hu WH, et al. Positive association between gastro-oesophageal reflux disease and irritable bowel syndrome in a Chinese population. Aliment Pharmacol Ther 2007;25:1099-1104.

17. Solhpour A, Pourhoseingholi MA, Soltani F, et al. Gastro-oesophageal reflux symptoms and body mass index: no relation among the Iranian population. Indian J Gastroenterol 2008;27:153-155.

18. Nasseri-Moghaddam S, Moftd A, Ghotbi MH, et al. Epidemiological study of gastro-oesophageal reflux disease: reflux in spouse as a risk factor. Aliment Pharmacol Ther 2008;28:144-153.

19. Soni MH, Farhang S, Minirezhad K, et al. Prevalence and precipitating factors of gastroesophageal reflux disease in a young population of Tabriz, Northwest of Iran. Saudi Med J 2006;27:1878-1881.

20. Norouzi M, Razjouyian H, Assady M, Malekzadeh R, Nasseri-Moghaddam S. Epidemiology of gastroesophageal reflux symptoms in Tehran, Iran: a population-based telephone survey. Arch Iran Med 2007;10:289-294.

21. Saberi-Firoosi M, Khademhosseini F, Yousefi M, Mehrbani D, Zare N, Heydari ST. Risk factors of gastroesophageal reflux disease in Shiraz, southern Iran. World J Gastroenterol 2007;13:5486-5491.

22. Ehsani MJ, Maleki I, Mohammadiadeh F, Masihayekh A. Epidemiology of gastroesophageal reflux disease in Tehran, Iran. J Gastroenterol Hepatol 2007;22:1419-1422.

23. Lim SL, Koh WT, Lee JMY, Ng TP, Ho KY; Community Medicine GI Study Group. Changing prevalence of gastroesophageal reflux with changing time: longitudinal study in an Asian population. J Gastroenterol Hepatol 2005;20:995-1001.

24. Sperber AD, Halpern Z, Silvartzman P, et al. Prevalence of GERD symptoms in a representative Israeli adult population. J Clin Gastroenterol 2007;41:457-461.

25. Lee SJ, Song CW, Jeon YT, et al. Prevalence of endoscopic reflux esophagitis among Koreans. J Gastroenterol Hepatol 2001;16:373-376.

26. Lien HC, Chang CS, Yeh HZ, et al. Increasing prevalence of erosive esophagitis among Taiwanese aged 40 years and above: a comparison between two time periods. J Clin Gastroenterol 2009;43:926-932.

27. Fujimoto K, Iwakiri R, Okamoto K, et al. Characteristics of gastroesophageal reflux disease in Japan: increased prevalence in elderly women. J Gastroenterol 2003;38(suppl 15):3-6.

28. Fujiwara Y, Higuchi K, Shiba M, et al. Association between gastroesophageal flap valve, reflux esophagitis, Barrett's epithelium, and atrophic gastritis assessed by endoscopy in Japanese patients. J Gastroenterol 2003;38:533-539.

29. Tseng PH, Lee YC, Chiu HM, et al. Prevalence and clinical characteristics of Barrett's esophagus in a Chinese general population. J Clin Gastroenterol 2008;42:1074-1079.

30. Lee HL, Eun CS, Lee OY, et al. Association between GERD-related erosive esophagitis and obesity. J Clin Gastroenterol 2008;42:672-675.

31. Kang MS, Park DI, Oh SY, et al. Abdominal obesity is an independent risk factor for erosive esophagitis in a Korean population. J Gastroenterol Hepatol 2007;22:1656-1661.

32. Peng S, Cui Y, Xiao YL, et al. Prevalence of erosive esophagitis and Barrett's esophagus in the adult Chinese population. Endoscopy 2009;41:1011-1017.

33. Yamagishi H, Koike T, Ohara S, et al. Clinical characteristics of gastroesophageal reflux disease in Japan. Hepatogastroenterology 2009;56:1032-1034.

34. Kim N, Lee SW, Cho SI, et al. The prevalence of and risk factors for erosive oesophagitis and non-erosive reflux disease: a nationwide multicentre prospective study in Korea. Aliment Pharmacol Ther 2008;27:173-185.

35. Noh YW, Jung HK, Kim SE, Jung SA. Overlap of erosive and non-erosive reflux diseases with functional gastrointestinal disorders according to Rome III criteria. J Neurogastroenterol Motil 2010;16:148-156.

36. Kaji M, Fujiwara Y, Shiba M, et al. Prevalence of overlaps between GERD, FD and IBS and impact on health-related quality of life. J Gastroenterol Hepatol 2010;25:1151-1156.

37. Hershcovici T, Fass R. Nonerosive reflux disease (NERD) - an update. J Neurogastroenterol Motil 2010;16:8-21.

38. Modlin IM, Hunt RH, Malfertheiner P, et al. Non-erosive reflux disease - defining the entity and delineating the management. Digestion 2008;78(suppl 1):1-5.

39. Chen MJ, Lee YC, Chiu HM, Wu MS, Wang HP, Lin JT. Time trends of endoscopic and pathological diagnoses related to gastro-oesophageal reflux disease in a Chinese population: eight years single institution experience. Dis Esophagus 2010;23:201-207.

40. Koop H, Schepp W, Müller-Lissner S, et al. Consensus conference of the DGVS on gastroesophageal reflex. Z Gastroenterol 2005;43:163-164.

41. Cho YS, Choi MG, Jeong JJ, et al. Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Asan-si, Korea. Am J Gastroenterol 2005;100:747-753.

42. Wang JH, Luo JY, Dong L, Gong J, Tong M. Epidemiology of gastroesophageal reflux disease: a general population-based study in Xi’an of Northwest China. World J Gastroenterol 2004;10:1647-1651.

43. Bor S, Kitapcioglu G, Solak ZA, Ertlalay M, Erdinc M. Prevalence of gastroesophageal reflux disease in patients with asthma and chronic obstructive pulmonary disease. J Gastroenterol Hepatol 2010;25:309-313.

44. Shimizu Y, Dobashi K, Kobayashi S, et al. High prevalence of gastroesophageal reflux disease with minimal mucosal change in asthmatic patients. Tohoku J Exp Med 2006;209:329-336.

45. Fujiwara Y, Kohata Y, Kaji M, et al. Sleep dysfunction in Japanese patients with gastroesophageal reflux disease: prevalence, risk factors, and efficacy of rabeprazole. Digestion 2010;81:135-141.
53. Hongo M, Nagasaki Y, Shoji T. Epidemiology of esophageal cancer.

52. Tu CH, Lee CT, Perng DS, Chang CC, Hsu CH, Lee YC. Esophageal cancer in Taiwan: a higher frequency than in Saudi Arabia. Trop Gastroenterol 2009;20:111-115.

51. Spechler SJ. The columnar-lined esophagus. History, terminology, and clinical issues. Gastroenterol Clin North Am 1997;26:455-466.

50. Hirota WK, Loughney TM, Lazas DJ, Maydonovitch CL, Rholl V, Wong RK. Specialized intestinal metaplasia, dysplasia, and cancer of the esophagus and esophagogastric junction: prevalence and clinical data. Gastroenterology 1999;116:277-283.

49. Mohd H, Qua CS, Wong CH, Azman W, Goh KL. Non-cardiac chest pain: prevalence of reflux disease and response to acid suppression in an Asian population. J Gastroenterol Hepatol 2009;24:288-293.

48. Bor S, Mandiracioglu A, Kitapcioglu G, Caymaz-Bor C, Gilbert RJ. Prevalence of Barrett's esophagus in patients undergoing endoscopy for upper gastrointestinal symptoms. J Dig Dis 2010;11:83-87.

47. Xiong LS, Cui Y, Wang JP, et al. Prevalence and risk factors of Barrett's esophagus and esophageal cancer in Saudi Arabia. Trop Gastroenterol 2009;20:111-115.

46. Kuembo MK, Kouzu T, Kawano T, Ohara S. Nationwide epidemiological study on gastroesophageal reflux disease and sleep disorders in the Japanese population. J Gastroenterol 2008;43:833-841.

45. Wang GR, Zhang H, Wang ZG, Jiang GS, Guo CH. Relationship between dental erosion and respiratory symptoms in patients with gastro-oesophageal reflux disease. J Dent 2010;38:892-898.

44. Bor S, Mandiracioglu A, Kitapcioglu G, Caymaz-Bor C, Gilbert RJ. Gastroesophageal reflux disease in a low-income region in Turkey. Am J Gastroenterol 2005;100:759-765.

43. Mohd H, Qua CS, Wong CH, Azman W, Goh KL. Non-cardiac chest pain: prevalence of reflux disease and response to acid suppression in an Asian population. J Gastroenterol Hepatol 2009;24:288-293.

42. Hirota WK, Loughney TM, Lazas DJ, Maydonovitch CL, Rholl V, Wong RK. Specialized intestinal metaplasia, dysplasia, and cancer of the esophagus and esophagogastric junction: prevalence and clinical data. Gastroenterology 1999;116:277-283.

41. Spechler SJ. The columnar-lined esophagus. History, terminology, and clinical issues. Gastroenterol Clin North Am 1997;26:455-466.

40. Tu CH, Lee CT, Perng DS, Chang CC, Hsu CH, Lee YC. Esophageal adenocarcinoma arising from Barrett’s epithelium in Taiwan. J Formos Med Assoc 2007;106:664-668.

39. Hongso M, Nagasaki Y, Shoji T. Epidemiology of esophageal cancer: Orient to Occident. Effects of chronology, geography and ethnicity. J Gastroenterol Hepatol 2009;24:729-735.

38. Kim JH, Rhee PL, Lee JH, et al. Prevalence and risk factors of Barrett's esophagus in Korea. J Gastroenterol Hepatol 2007;22:908-912.

37. Xiong LS, Cui Y, Wang JP, et al. Prevalence and risk factors of Barrett’s esophagus in patients undergoing endoscopy for upper gastrointestinal symptoms. J Dig Dis 2010;11:83-87.

36. Lee IS, Choi SC, Shin KN, et al. Prevalence of Barrett’s esophagus remains low in the Korean population: nationwide cross-sectional prospective multicenter study. Dig Dis Sci 2010;55:1932-1939.

35. Park JJ, Kim JW, Kim HJ, et al. The prevalence of and risk factors for Barrett's esophagus in a Korean population: a nationwide multicenter prospective study. J Clin Gastroenterol 2009;43:907-914.

34. Oldemust B, Cicek B, Zengin NI, et al. Barrett’s esophagus and endoscopically assessed esophagogastric junction integrity in 1000 consecutive Turkish patients undergoing endoscopy: a prospective study. Dis Esophagus 2009;22:649-655.

33. Gadour MO, Ayisola EA. Barrett’s esophagus and esophageal cancer in Saudi Arabia. Trop Gastroenterol 1999;20:111-115.

32. Yeh C, Hsu CT, Ho AS, Sampliner RE, Fass R. Erosive esophagitis and Barrett’s esophagus in Taiwan: a higher frequency than expected. Dig Dis Sci 1997;42:702-706.

31. Fouda YM, Maldhoul MM, Tawfiq HM, el-Amin H, Ghany WA, el-Khayat HR. Barrett’s esophagus: prevalence and risk factors in patients with chronic GERD in Upper Egypt. World J Gastroenterol 2009;15:3511-3515.

30. Bafandeh Y, Esmaii H, Aharizad S. Endoscopic and histologic findings in Iranian patients with heartburn. Indian J Gastroenterol 2005;24:236-238.

29. Bytzer P, Christensen PB, Dankier P, Vinding K, Seershølm N. Adenocarcinoma of the esophagus and Barrett’s esophagus: a population-based study. Am J Gastroenterol 1999;94:86-91.

28. Blaser MJ. Hypothesis: the changing relationships of Helicobacter pylori and humans: implications for health and disease. J Infect Dis 1999;179:1523-1530.

27. Ma XQ, Cao Y, Wang R, et al. Prevalence of, and factors associated with, gastroesophageal reflux disease: a population-based study in Shanghai, China. Dis Esophagus 2009;22:317-322.

26. Ho KY, Kang JY, Seow A. Prevalence of gastrointestinal symptoms in a multiracial Asian population, with particular reference to reflux-type symptoms. Am J Gastroenterol 1998;93:1816-1822.

25. Mostaghni A, Mehrabani D, Khademolhosseini F, et al. Prevalence and risk factors of gastroesophageal reflux disease in Qashqai migrating nomads, southern Iran. World J Gastroenterol 2009;15:961-965.

24. Kitapçığlu G, Mandiracioglu A, Caymaz Bor C, Bor S. Overlap of symptoms of dyspepsia and gastroesophageal reflux in the community. Turk J Gastroenterol 2007;18:14-19.

23. Matsuzaki J, Suzuki H, Iwasaki F, Yokoyama H, Sugino Y, Hibi T. Serum lipid levels are positively associated with non-erosive reflux disease, but not with functional heartburn. Neurogastroenterol Motil 2010;22:965-970, e231.

22. Yamagishi H, Koike T, Ohara S, et al. Prevalence of gastroesophageal reflux symptoms in a large unsel ected general population in Japan. World J Gastroenterol 2008;14:1358-1364.

21. Fujiwara Y, Higuchi K, Watanabe Y, et al. Prevalence of gastroesophageal reflux disease and gastroesophageal reflux disease symptoms in Japan. J Gastroenterol Hepatol 2005;20:26-29.

20. Sakaguchi M, Oka H, Hashimoto T, et al. Obesity as a risk factor for GERD in Japan. J Gastroenterol 2008;43:57-62.

19. Du J, Liu J, Zhang H, Yu CH, Li YM. Risk factors for gastroesophageal reflux disease, reflux esophagitis and non-erosive reflux disease among Chinese patients undergoing upper gastrointestinal endoscopic examination. World J Gastroenterol 2007;13:6009-6015.

18. Miyamoto M, Haruma K, Kawabara M, Nagano M, Okamoto T, Tanaka M. High incidence of newly-developed gastroesophageal reflux disease in the Japanese community: a 6-year follow-up study. J Gastroenterol Hepatol 2008;23:393-397.

17. Mishima I, Adachi K, Arima N, et al. Prevalence of endoscopically negative and positive gastroesophageal reflux disease in the Japanese. Scand J Gastroenterol 2005;40:1005-1009.

16. Okamoto K, Iwakiri R, Mori M, et al. Clinical symptoms in endoscopic reflux esophagitis: evaluation in 8031 adult subjects. Dig Dis Sci 2003;48:2237-2241.

15. Chang CS, Poon SK, Lien HC, Chen GH. The incidence of reflux esophagitis among the Chinese. Am J Gastroenterol 1997;92:668-671.

14. Haruma K, Hamada H, Mihara M, et al. Negative association between Helicobacter pylori infection and reflux esophagitis in older patients: case-control study in Japan. Helicobacter 2000;5:24-29.

13. Rosaid MS, Koh 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
82. Ho KY, Chan YH, Kang JY. Increasing trend of reflux esophagitis and decreasing trend of Helicobacter pylori infection in patients from a multiethnic Asian country. Am J Gastroenterol 2005;100:1923-1928.

83. Yarandi SS, Nasseri-Moghaddam S, Mostajabi P, Malekzadeh R. Overlapping gastroesophageal reflux disease and irritable bowel syndrome: increased dysfunctional symptoms. World J Gastroenterol 2010;16:1232-1238.

84. Jafri N, Yakoob J, Islam M, Manzoor S, Jalil A, Hashmi F. Perception of gastroesophageal reflux disease in urban population in Pakistan. J Coll Physicians Surg Pak 2005;15:532-534.

85. Al-Humayed SM, Mohamed-Elbagir AK, Al-Wabel AA, Argobi YA. The changing pattern of upper gastro-intestinal lesions in southern Saudi Arabia: an endoscopic study. Saudi J Gastroenterol 2010;16:35-37.

86. Takenaka R, Matsuno O, Kitajima K, et al. The use of frequency scale for the symptoms of GERD in assessment of gastro-oesophageal reflux symptoms in asthma. Allergol Immunopathol (Madr) 2010;38:20-24.

87. Chunlertrith K, Boonsawat W, Zaeoue U. Prevalence of gastroesophageal reflux symptoms in asthma patients at Srinagarind Hospital. J Med Assoc Thai 2003;86:668-671.

88. Al-Asoom L, Al-Rubaish AM, El-Munshid HA, Al-Nafaie AN, Bukharie HA, Abdulrahman IS. Gastroesophageal reflux in bronchial asthma patients. A clinical note. Saudi Med J 2003;24:1364-1369.

89. Nakase H, Itani T, Mimura J, et al. Relationship between asthma and gastro-oesophageal reflux: significance of endoscopic grade of reflux oesophagitis in adult asthmatics. J Gastroenterol Hepatol 1999;14:715-722.

90. Gharabeh TM, Jadallah K, Jadayel FA. Prevalence of temporomandibular disorders in patients with gastroesophageal reflux disease: a case-controlled study. J Oral Maxillofac Surg 2010;68:1560-1564.

91. Toros SZ, Toros AB, Yüksel OD, Ozel L, Akkaynak C, Nalboglu B. Association of laryngopharyngeal manifestations and gastroesophageal reflux. Eur Arch Otorhinolaryngol 2009;266:403-409.

92. Qua CS, Wong CH, Gopala K, Goh KL. Gastro-oesophageal reflux disease in chronic laryngitis: prevalence and response to acid-suppressive therapy. Aliment Pharmacol Ther 2007;25:287-295.