

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.⁶ 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 un-

derwent 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 al ⁸	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 al ⁹ Ma et al ⁶⁷	China	919	2009	2005-2006	GERD, heartburn or regurgitation over 1 wk recall period 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
Lee et al ¹⁰	Korea	1,443	2009	2005	Direct interview	GERD, 8.5%; overlap with dyspepsia in 27% and with IBS in 24%
Yang et al ¹¹	Korea	1,044	2008	2004	Telephone survey with random number; GERD, heartburn or acid regurgitation at least weekly	7.1%; risk factors: educational level for heartburn, aging for acid regurgitation
Li et al ¹²	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%) (<i>P</i> < 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 al ¹³	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 al ⁴²	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 al ¹⁴	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 al ¹⁵ Cho et al ⁴¹	Korea	1,417	2008	2000-2001	Direct interview; GERD, heartburn and/or acid regurgitation at least weekly	3.5% (95% CI, 2.6-4.5); GERD exhibited significantly worse HRQOL
Cheung et al ¹⁶	China (Hong Kong)	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)
South Eastern Asia						
Lim et al ²³	Singapore	237 in 1999 696 in 1994	2005	1994 vs 1999	Direct interview: GERD, retrosternal burning or acid regurgitation at least monthly	GERD, 10.5% ± 2.0% in 1999 vs 5.5% ± 1.5% in 1994
Ho et al ⁶⁸	Singapore	696	1998	-	GERD, heartburn or acid regurgitation more than 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 (5.6% vs 1.5%, <i>P</i> < 0.01)

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 al ⁶⁹	Iran	717	2009	2006	GERD, at least weekly any symptoms of heartburn, regurgitation, chest pain, dysphagia, hoarseness and cough	33% (237)
Solhpour et al ¹⁷	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 al ¹⁸	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/m ² (OR, 1.79; 95% CI, 1.03-3.12), less education, smoking, NSAID use and GERD in spouse
Somi et al ¹⁹	Iran	620	2006	2005	GERD, heartburn or acid regurgitation at least weekly	GERD, 6.3%; no gender difference
Nourai et al ²⁰	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 al ²¹	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 al ²²	Iran	700	2007	1999	GERD, heartburn or acid regurgitation	GERD, 39.7% (278)
Western Asia						
Sperber et al ²⁴	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%
Kitapçioğlu et al ⁷⁰	Turkey	630	2007	1998-1999	Direct interview: GERD, heartburn or acid regurgitation at least weekly	GERD, 20%
Bor et al ⁴⁸	Turkey	630	2005	-	GERD, heartburn and/or acid eructation occurring at least weekly	GERD, 20%
		in low-income region				

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.

endoscopic reflux esophagitis is summarized in Tables 2 and 3. Most endoscopy-based studies were conducted with medical check-up participants or patients having upper gastrointestinal symptoms who visited the referral hospitals. Most of the GERD endoscopic studies were consisted of Eastern Asian studies including Japan, China and Korea. The prevalence of endoscopic reflux esophagitis in Eastern Asia was 3.4%-5.0%^{25,26} before 2000, with these 2 studies using the definition of reflux esophagitis by Savary-Miller classification, while other 9 studies showed results of 6.6%-15.0%²⁷⁻³¹ from 2000 to 2005 and 4.3%-15.7%³²⁻³⁵ after 2005, with the definition by LA classification. However, it is quite uncertain why such a wide range of prevalence has been

found for endoscopic reflux esophagitis. There might be some variability in interpreting the endoscopic findings. Furthermore, several studies were conducted in retrospective manner and might have under- or over-estimated the exact prevalence of endoscopic reflux esophagitis.

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%,^{31,34,36} 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 ⁷¹	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, a <i>H. pylori</i> 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; <i>P</i> = 0.002)
Yamagishi et al ⁷²	Japan	82,894	2008	2003	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/m ² (OR = 3.3, 95% CI, 1.8-6.1)
Fujiwara et al ⁷³	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 ²⁸	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 in 2002 2,044 in 1995	2009	2002, 1995	RE by endoscopy	RE, 5% in 1995 and 12.6% in 2002 (<i>P</i> < 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, videosophagography; 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 35 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	In patients with GI symptoms, RE, 20.7% at 2000 and 51% at 2007; In screening endoscopy, RE, 14.5% at 2000 and 23.5% at 2007; GERD, 3.4% at 2000 and 12.4% at 2007; NERD 1.8% at 2000 and 2.3% at 2007
Miyamoto et al ⁷⁶	Japan	241 non-GERD patients cohort	2008	1998, 2004	GERD, QUEST questionnaire > 6	Incidence of GERD, 15.4% (37) for 6 years; risk factors: negative <i>H. pylori</i> , constipation and calcium channel antagonists
Mishima et al ⁷⁷	Japan	Referral populations: 2,760	2005	-	GERD, QUEST questionnaire > 6; RE by LA classification	RE, 7.1% (195); GERD, 12.7% (351); NERD, 10.9% (300)
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	RE, 14.9% (1,199) without gender difference; heartburn, 27.7%; dysphagia, 19.0%; odynophagia, 6.1%; acid regurgitation, 18.3%
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 ⁶⁰	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.^{32,34} 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 de-

defined as the presence of classic GERD symptoms in the absence of esophageal mucosal injury which has been detected during the upper endoscopy.³⁷ 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 Goh ⁸¹	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 al ⁸²	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 al ⁸³	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 al ⁸⁴	Pakistan	963	2005	-	GERD	GERD, 24% (228)
Western Asia						
Al-Humayed et al ⁸⁵	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 signifi-

cant 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 al ⁸⁶	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 al ⁴³	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 al ⁴⁴	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 al ⁸⁷	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 al ⁸⁸	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 al ⁸⁹	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	Fujiwara et al ⁴⁵	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 al ²	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 al ⁴⁶	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 (56.5% vs 40.7%, $P < 0.0001$); no difference according to RE
Temporo-mandibular disorder	Gharaibeh et al ⁹⁰	Jordan	Tertiary hospital: 60 GERD vs 60 control	2009	Case-control study	36.6% in GERD vs 18.3% in control ($P = 0.025$); myofascial pain, 31.7% vs 15% ($P = 0.03$)
Dental erosion	Wang et al ⁴⁷	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 al ⁴⁹	Malaysia	Tertiary hospital: 27 NCCP	2009	RE or 48 hr Bravo ambulatory pH monitoring	GERD, 66.7% (18/27) among NCCP
NCCP	Bor et al ⁴⁸	Turkey	Population-based study: 630 in low-income region	2009	GERD, heartburn and/or acid eructation at least weekly	GERD, 20%; NCCP, 37.3%; dysphagia, 35.7%; dyspepsia, 42.1%; odynophagia, 35.7%
ENT symptoms	Toros et al ⁹¹	Turkey	45 ENT outpatients in Tertiary hospital	2008	Symptoms; RE by endoscopy	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 al ⁹²	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.¹ Extra-esophageal syndromes rarely occur with concomitant manifestations of the typi-

cal 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 al ⁴¹	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 al ⁴²	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.

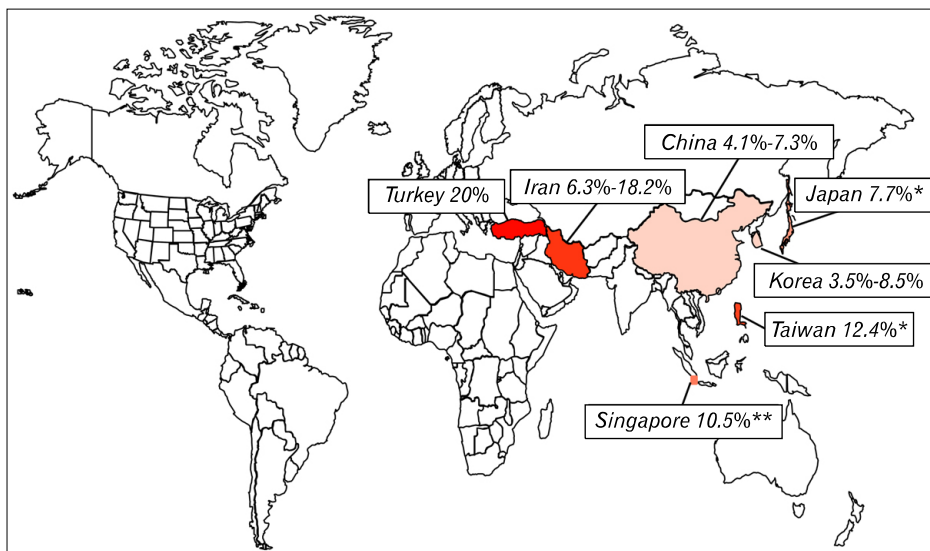


Figure. The prevalence of gastroesophageal reflux disease in Asian population-based study. Gastroesophageal reflux disease (GERD) is defined as having heartburn or acid regurgitation at least weekly. *Study conducted in subjects with medical check-up, **GERD, retrosternal burning sensation or acid regurgitation 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 52.5%-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 ⁵⁵	China	Referral hospital: 2,022 patients with upper 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 ⁵⁶	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 ³⁹	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 ³²	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 ⁶¹	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 ⁵⁷	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, 1.32-2.50), NSAIDs (OR, 2.02; 95% CI, 1.28-3.20), hiatal hernia (OR, 5.66; 95% CI, 3.70-8.66) and age \geq 60 yr compared with an age < 40 yr (OR, 1.81; 95% CI, 1.07-3.09)
Odemiş et al ⁵⁸	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 ²⁹	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 ⁵⁴	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 ⁶²	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, 66.5% (960); BE, 2.4% (30); long-segment Barrett's mucosa, 1/3 of BE
Gadour and Ayoola ⁵⁹	Saudi Arabia	Tertiary hospital: 2,572 subjects with endoscopy	1999	BE, endoscopic biopsy proved diagnosis	BE, 0.31% (8); esophageal adenocarcinoma, 0.62% (16)
Rosaida and Goh ⁸¹	Malaysia	Tertiary hospital: 1,000 patients with upper abdominal discomfort	2004	BE, ESCE with SIM	BE, 2% (20)
Yeh et al ⁶⁰	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 den-

tal erosion in patients with GERD.⁴⁷ In tertiary hospitals, dental erosions were found in 64.5% 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

< 0.05).⁴⁷

NCCP is a heterogeneous and complex disorder with many potential causes including GERD. NCCP has been common in Asia⁴⁸ and GERD has also been frequently detected in NCCP, even though the proportions were different according to the diagnostic modalities.^{48,49}

Prevalence of Barrett's Esophagus

Barrett's esophagus is histologically confirmed by specialized intestinal metaplasia.^{50,51} 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.^{52,53} The prevalence of Barrett's esophagus was reported as 0.06%-0.84%^{29,54} in medical check-up and 0.31%-2.00%^{39,55-60} in the referral hospital settings (Table 5). The proportion of Barrett's esophagus was 7.3%⁶¹ in patients with GERD and 2.4%⁶² in those with heartburn symptoms. Importantly, esophageal adenocarcinoma is often found even without any medical history of reflux symptoms.⁶³ Although GERD symptoms is considered to be one of the most important risk factors of Barrett's esophagus,⁵⁴⁻⁵⁶ only 60.1% of subjects who had received the medical check-up were found to have GERD symptoms.⁵⁷

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.^{64,65} 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.^{53,66} 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.⁵³ 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 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.

References

1. Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R; Global Consensus Group. The Montreal definition and classification of gastroesophageal 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, Fass 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. Gastroesophageal 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, Lam KF, 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 KF, 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-esophageal reflux symptoms and body mass index: no relation among the Iranian population. *Indian J Gastroenterol* 2008;27:153-155.
 18. Nasseri-Moghaddam S, Mofid 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. Somi MH, Farhang S, Mirinezhad 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. Nouraei M, Razjouyan 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-Firoozi M, Khademolhosseini F, Yousefi M, Mehrabani 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, Mohammadzadeh F, Mashayekh A. Epidemiology of gastroesophageal reflux disease in Tehran, Iran. *J Gastroenterol Hepatol* 2007;22:1419-1422.
 23. Lim SL, Goh WT, Lee JM, 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, Shvartzman 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 gastroesophageal 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 reflux. *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, Ertlav 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.

46. Kusano M, 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.
47. 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.
48. 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.
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.
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;116:277-285.
51. Spechler SJ. The columnar-lined esophagus. History, terminology, and clinical issues. *Gastroenterol Clin North Am* 1997;26:455-466.
52. 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.
53. Hongo 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.
54. 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.
55. 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.
56. Lee IS, Choi SC, Shim 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.
57. 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.
58. Odemiş B, Çiçek 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.
59. Gadour MO, Ayoola EA. Barrett's oesophagus and oesophageal cancer in Saudi Arabia. *Trop Gastroenterol* 1999;20:111-115.
60. 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.
61. Fouad YM, Makhlof MM, Tawfik 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.
62. Bafandeh Y, Esmaili H, Aharizad S. Endoscopic and histologic findings in Iranian patients with heartburn. *Indian J Gastroenterol* 2005;24:236-238.
63. Bytzer P, Christensen PB, Damkier P, Vinding K, Seersholm N. Adenocarcinoma of the esophagus and Barrett's esophagus: a population-based study. *Am J Gastroenterol* 1999;94:86-91.
64. Blot WJ, Devesa SS, Kneller RW, Fraumeni JF Jr. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA* 1991;265:1287-1289.
65. Devesa SS, Blot WJ, Fraumeni JF Jr. Changing patterns in the incidence of esophageal and gastric carcinoma in the United States. *Cancer* 1998;83:2049-2053.
66. Blaser MJ. Hypothesis: the changing relationships of *Helicobacter pylori* and humans: implications for health and disease. *J Infect Dis* 1999;179:1523-1530.
67. 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.
68. 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.
69. 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.
70. Kitapcioglu 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.
71. Matsuzaki J, Suzuki H, Iwasaki E, 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, e251.
72. Yamagishi H, Koike T, Ohara S, et al. Prevalence of gastroesophageal reflux symptoms in a large unselected general population in Japan. *World J Gastroenterol* 2008;14:1358-1364.
73. 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.
74. Sakaguchi M, Oka H, Hashimoto T, et al. Obesity as a risk factor for GERD in Japan. *J Gastroenterol* 2008;43:57-62.
75. 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.
76. Miyamoto M, Haruma K, Kuwabara 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.
77. 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.
78. 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.
79. Chang CS, Poon SK, Lien HC, Chen GH. The incidence of reflux esophagitis among the Chinese. *Am J Gastroenterol* 1997;92:668-671.
80. 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.
81. Rosaida MS, Goh KL. Gastro-oesophageal reflux disease, reflux esophagitis and non-erosive reflux disease in a multiracial Asian population: a prospective, endoscopy based study. *Eur J Gastroenterol*

- Hepatol 2004;16:495-501.
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, Nasser-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. Chunertrith K, Boonsawat W, Zaeoue U. Prevalence of gastroesophageal reflux symptoms in asthma patients at Srinagarind Hospital. *J Med Assoc Thai* 2005;88:668-671.
 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. Gharaibeh 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, Naiboglu 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.