Prevalence of Abnormal Esophageal Acid Exposure and *Helicobacter pylori* Infection in Patients with Functional Dyspepsia: A Preliminary Report

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ABSTRACT

Background: There were observations in the overlap of symptoms between GERD and functional dyspepsia. Thai GERD patients have symptoms very similar to functional dyspepsia because heartburn or regurgitation is not common. It is unclear whether some patients with diagnosed functional dyspepsia actually have abnormal esophageal acid exposure (AEAE). Prevalence of *H. pylori* infection in dyspeptic patients with or without AEAE is unknown.

Objective: To determine the prevalence of AEAE in functional dyspeptic patients and the prevalence of *H. pylori* infection in patients with and without AEAE.

Patients and Methods: Twenty-seven functional dyspeptic patients (12 male, 15 female, age 20-64 years) diagnosed by Rome II criteria were interviewed by gastroenterologists regarding their upper gastrointestinal symptoms by using questionnaires. *H. pylori* status was detected by rapid urease test. All patients underwent 24-hour pH monitoring. AEAE was diagnosed by fraction time pH below 4 $\geq$4% or composite score $\geq$14.72.

Results: There were 3 patients (11.1%) with AEAE diagnosed by abnormal fraction time pH below 4 and 6 patients (22.2%) by abnormal composite score. *H. pylori* was detected in 6 patients (23%); 2 (66%) and 4 (17%) of patients with and without AEAE by fraction time pH below 4, respectively (p = NS); 3 (60%) and 3 (14%) of patients with and without AEAE by composite score, respectively (p = NS). There was no significant association between symptom details and the presence of AEAE.

Conclusion: Prevalence of AEAE and H. pylori infection in functional dyspeptic patients is low. The correlations between symptoms or *H. pylori* infection and abnormal 24-hour pH monitoring could not be determined precisely due to the too small number of patients with AEAE.

Key words : 24-hour pH monitoring, esophageal acid exposure, gastroesophageal reflux disease, dyspepsia, *Helicobacter pylori*

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BACKGROUND

Dyspepsia is a common problem worldwide. The incidence of dyspepsia is approximately 20-25% in general population[1] and 70-80% of dyspeptic patients have functional dyspepsia. In western countries, common presenting symptoms of functional dyspepsia are bloating, abdominal discomfort, epigastric pain and early satiety.[2] In Thailand, there is no data regarding to this but in general, the common presenting symptoms observed in Thai functional dyspeptic patients are similar to the Western. In clinical practice, when patients have symptoms of heartburn or regurgitation, which are suggestive of gastroesophageal reflux disease (GERD), they are usually diagnosed as GERD and excluded from the studies of functional dyspepsia, since the treatment results of both conditions are different.[3,4] However, almost 20% of dyspeptic patients also have concomitant GERD at the first presentation.[5] A prospective study from Sweden including 1,059 patients with dyspepsia found that major symptoms of this group of patients resemble to GERD[6]. In another study of 99 patients who were followed up for 6 years, the number of patients who had dyspepsia as major initial symptom was decreased from 32% to 30%, while the number with reflux symptom increased from 6% to 11%. In contrast, if patients were initially presented with reflux disease, the number of patients with reflux symptoms was decreased from 61% to 29%[7]. Hauque *et al.*[8] found that 56% of patients with dyspepsia had reflux symptoms and 69% of patients with GERD also had dyspepsia.

Common symptoms of patients with GERD in Western countries are heartburn and regurgitation. In Thailand, study by Leelakusolvong *et al.*[9] revealed that most Thai GERD patients were usually presented with bloating, flatulence and epigastric pain while heartburn and acid regurgitation were only found in 30-40%. Another study by Iamudomkan *et al.*[10] also illustrated that heartburn and acid regurgitation were less specific for GERD in Thai patients than what reported from Western literatures. Thus, it is very difficult to differentiate between these two conditions because they can occur concomitantly and the symptoms may be interchanged.

Dyspeptic patients who had normal upper endoscopic examination may have abnormal esophageal acid exposure (AEAE) when 24-hr pH monitoring was performed. Study by Lauritasen *et al.*[11] revealed that there was AEAE in 53% of patients with dyspepsia who had normal upper endoscopic examination. Similarly, study by Carlsson *et al.*[12] also detected AEAE in 57% of patients who were responded to omeprazole. Prevalence of Helicobacter pylori among patients with dyspepsia are 17% in Western countries[13] and 57% in Thailand[14], corresponding to the higher prevalence of *H. pylori* infection in Thai general population[15]. Prevalence of *H. pylori* infection among patients with GERD is about 0.6 fold lower than those in dyspepsia[16]. However, no study has reported the prevalence of *H. pylori* in dyspeptic patients with AEAE.

Since there has been no study to clarify the relationship between functional dyspepsia and AEAE detected by 24-hr pH monitoring, the objective of this study is to obtain the incidence of AEAE measured by 24-hr pH monitoring in patients with functional dyspepsia and the incidence of *H. pylori* in patients with functional dyspepsia with and without AEAE.

PATIENTS AND METHODS

Patients with dyspepsia who were presented at Siriraj Hospital during March 2004 to February 2005 were asked to complete questionnaires on symptom details, age, underlying diseases and current medications. Upper endoscopic examination, rapid urease test (CLO test®) for *H. pylori* and upper abdominal ultrasonography were performed in all patients.

Inclusion criteria were clinical symptoms compatible with functional dyspepsia by Rome II criteria, age 20-65 years and normal upper endoscopy and ultrasonography. Patients with serious comorbid diseases who might not be eligible for the 24-hr pH monitoring, pregnancy, HIV infection, previous upper abdominal surgery, weight loss, anemia, history of gastrointestinal bleeding and patients receiving calcium channel blockers, nitrates or sedative drugs were excluded. All of the enrolled patients were followed by 24-hr pH monitoring.

24-hr pH Monitoring

Proton pump inhibitor and H_2-receptor antagonist were stopped for at least 7 days before performing 24-hr pH monitoring. After confirming the location of the level 5 cm above the lower esophageal sphincter, the single channel pH probe was placed. Data were analyzed, and acid exposure times were calculated.

Abnormal esophageal acid exposure was defined

by a fraction time of pH below 4 ≥4% and by composite score (calculated from 6 parameters, i.e. % total time pH <4.0, % upright time pH <4.0, % supine time pH <4.0, Number of episodes, Number of episodes >5 minutes and the longest episode) of more than 14.72.[17]

Statistical Analysis

Descriptive data were analyzed by SPSS version 11.0 for window. Values were expressed as number and percentage. Symptoms and results of 24-hr pH monitoring were compared by Fisher exact test. Results were considered statistically significant when p-value was <0.05.

This study was approved by the Siriraj Ethic Committee.

RESULTS

There were 27 patients enrolled in the study, including 12 males (44.4%) and 15 females (55.5%), with a mean age of 39 years. Female patients had longer duration of dyspeptic symptoms (95 months) than male patients (32 months). Body mass index (BMI) was higher in female patients (Table 1).

There were some differences in symptom details between genders. In male, common symptoms were epigastric pain, bloating and epigastric burning, respectively, while in female were bloating, epigastric pain and epigastric burning, respectively (Table 2).

H. pylori status was tested in 26 patients (not done in 1 patient who underwent endoscopy from other hospital). Six patients (23%) had *H. pylori* infection, including 4 males (15.3%) and 2 females (7.6%).

Twenty-four hour pH monitoring demonstrated 3 patients (11.1%) with fraction time pH below 4 ≥4% (1 male and 2 female). Composite score ≥14.72 was found in 6 patients (22.2%), including 2 males and 4 females.

No symptom was found to correlate significantly with the presence or absence of AEAE, either diagnosed by fraction time pH below 4 (Table 3) or by composite score (Table 4). However, it might be limited due to the very few numbers of patients with AEAE.

Figure 1 illustrates the prevalence of *H. pylori* infection in patients with and without AEAE diagnosed by fraction time pH below 4 or composite score. No association was found between *H. pylori* infection status and the presence or absence of AEAE defined by either fraction time pH below 4 (p = 0.123) or com-

Table 1 Baseline characteristics

Parameters	Male (n = 12)	Female (n = 15)	Total (n = 27)
Age (yr)	39.6 (21-58)	39.8 (20-64)	39.52 (20-64)
Duration of symptoms (mo)	32 (4-120)	95 (6-360)	67 (4-360)
Weight (kg)	59.7 (47.5-71.4)	60.8 (41.8-89.9)	60.34 (41.3-89.9)
Height (cm)	167.5 (154-175)	156.5 (138-172)	161.4 (138-175)
BMI (kg/m^2)	21.4 (15.8-25.7)	24.8 (17.1-33.5)	23.31 (15.8-33.5)

Table 2 Clinical presentation

Parameters	Male (n = 12)	Female (n = 15)	Total (n = 27)
Epigastric pain	12 (100%)	12 (80%)	24 (88.8%)
Bloating	7 (58.3%)	14 (93.3%)	21 (77.7%)
Epigastric burning	6 (50%)	11 (73.3%)	17 (62.9%)
Early satiety	1 (8.3%)	10 (66.6%)	11 (40.7%)
Retching	2 (16.6%)	4 (26.6%)	6 (22.2%)
Acid regurgitation	3 (25%)	3 (20%)	6 (22.2%)
Heartburn	3 (25%)	3 (20%)	6 (22.2%)
Globus sensation	1 (8.3%)	1 (6.6%)	2 (7.4%)
Nausea	4 (33.3%)	4 (26.6%)	8 (29.6%)

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Table 3 Comparison between symptoms and the fraction time pH below 4

Clinical symptoms	Fraction Time <4% (n = 24)	Fraction Time ≥4% (n = 3)	p-value
Epigastric pain	22 (91.7%)	2 (66.7%)	0.308
Bloating	19 (79.2%)	2 (66.7%)	0.545
Epigastric burning	16 (66.7%)	1 (33.3%)	0.535
Early satiety	10 (41.7%)	1 (33.3%)	1.000
Retching	4 (16.7%)	1 (33.3%)	0.115
Acid regurgitation	6 (25%)	0 (%)	1.000
Heartburn	6 (25%)	0 (0%))	1.000
Globus sensation	2 (8.3%)	0 (0%)	1.000
Nausea	8 (33.3%)	0 (0%)	0.532

Table 4 Comparison between symptoms and composite score

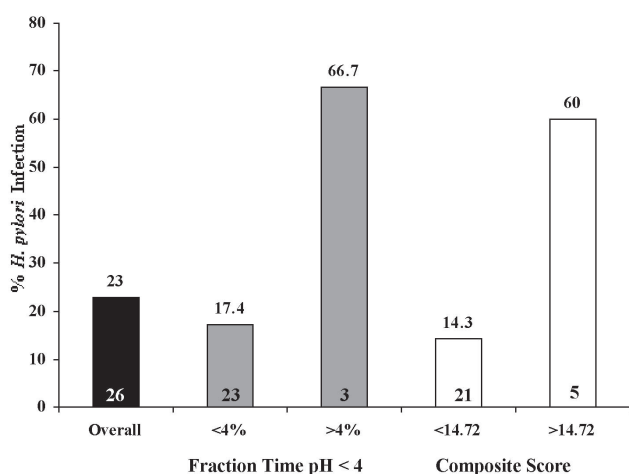| Clinical symptoms	Composite Score <14.72 (n = 21)	Composite Score ≥14.72 (n = 6)	p-value
Epigastric pain	20 (95.2%)	4 (66.7%)	0.115
Bloating	16 (76.2%)	5 (83.3%)	1.000
Epigastric burning	13 (61.9%)	4 (66.7%)	1.000
Early satiety	9 (42.9%)	2 (33.3%)	1.000
Retching	4 (19%)	2 (33.3%)	0.588
Acid regurgitation	4 (19%)	2 (33.3%)	0.588
Heartburn	5 (23.8%)	1 (16.7%)	1.000
Globus sensation	2 (9.5%)	0 (0%)	1.000
Nausea	7 (33.3%)	1 (16.7%)	0.633

Figure 1 Prevalence of *H. pylori* infection in the studied patients. Overall prevalence was shown by the black bar. No statistically difference was found between the prevalence in patients with fraction time pH below 4 <4% and ≥4% (grey bar, p = 0.123) or patients with composite score <14.72 and ≥14.72 (white bar, p = 0.062). Numbers at the bottom of the bars indicated number of patients.

posite score (p = 0.062).

Discussion

In the present study, we found that dyspeptic patients could have many different presenting symptoms. Majority of patients have epigastric pain and/or bloating, but 20-25% also had heartburn. Patients who manifested predominantly with reflux symptoms were not included in this study because they could not be diagnosed as GERD. The median duration of symptoms before enrollment to this study was quite long (67 months or 5.5 years). Interestingly, duration of symptoms in female patients was longer than male patients.

The prevalence of *H. pylori* infection in this study is 23%, which is closed to the prevalence in Western countries (17%).[13] However, this result is much lower than that from the previous study in Thailand, by Kachintorn et al in 1999, which reported the prevalence of 57.4%[14]. This may be related to the improvement in sanitation in Thailand. Furthermore, patients

in this study had very long duration of symptoms, thus they might have received *H. pylori* eradication before entering the study. Finally, the limited numbers of patients in this study may prone to the selection bias.

The results of AEAE measured by 24-hr pH monitoring in our patients were surprising very low; 3 patients (11.1%) with abnormal fraction time pH below 4. This number is much different from the previous studies mentioned above, which found abnormal fraction time pH below 4 53%-57%[11,12]. Our study also tried using composite score, the more delicate score, which is calculated from 6 parameters including % total time, % upright time, % supine time, number of episodes, number of episodes >5 minutes and the longest episode to detect abnormal esophageal pH. At present, the composite score has gained acceptance to be more reliable than the fraction time pH below 4[17] because it minimizes the confounding factors that may affect interpretation, such as gender, nationality and dietary habit[18]. We found more patients (6 patients, 22.2%) with AEAE detected by composite score. Unfortunately, this study can not demonstrate any relationship between clinical symptoms and fraction time pH below 4 or composite score due to the very few patients with AEAE.

In addition, when focused on the correlation between AEAE and *H. pylori* infection, there were a positive trend between the presence of *H. pylori* and the chance of having AEAE, although it was not statistically significant. This result is contrast to the results from meta-analysis[19], which illustrated that *H. pylori* infection reduces the prevalence of GERD, especially in Asian countries. One of the reasons may be because the most common type of *H. pylori* infection in Asian patients is antral predominate gastritis and patients mostly infected by more virulent subtype (CagA- or VacA S1-positive strain).[20]

CONCLUSION

Prevalence of AEAE by mean of abnormal 24-hr pH monitoring in patients with functional dyspepsia by using fraction time pH below 4 is 11.1% and abnormal composite score is 22.2%, which are lower than those from Western studies. *H. pylori* infection may increase prevalence of AEAE, but the small number of patients with abnormal 24-hr pH in this study limited the impact of data analyses in establishing the correlations between patient symptoms or *H. pylori* status with the presence of AEAE. Further study with larger patient number is necessary.

REFERENCES

1. Simren M, Tach J. Functional dyspepsia: evaluation and treatment. Gastroenterol Clin North Am 2003; 32: 577-91.
2. Tach J, Caenepeel P, Fischler B, *et al*. Symptoms associated with hypersensitivity to gastric distention in functional dyspepsia. Gastroenterology 2001; 121: 526-35.
3. Talley NJ, Stanghellini V, Heading RC, *et al*. Functional gastroduodenal disorders. Gut 1999; 45 (Suppl 2): 37-42.
4. Dent J. Definition of reflux disease and its separation from dyspepsia. Gut 2002; 50 (Suppl 4): 17-20.
5. Agreus L, Svardsudd K, Nyren O, *et al*. Irritable bowel syndrome and dyspepsia in the general population: overlap and lack of stability over time. Gastroenterology 1995; 109: 671-80.
6. Agreus L. The abdominal symptom study. An epidemiology survey of gastrointestinal and other abdominal symptoms in the adult population of Osthammer, Sweden. In: acta Universitalis Upsaliensis, Comprehensive summaries of Uppsala dissertations from the Faculty of Medicine, 434. Uppsala: Uppsala University; 1993.
7. Agreus L, Svardsudd K, Tally NJ, *et al*. Natural history of gastroesophageal reflux disease and functional abdominal disorders: a population-based study 2001; 96: 2905-14.
8. Haque M, Wyeth JW, Stace NH, *et al*. Prevalence, severity of gastrooesophageal reflux and dyspepsia: a population-based study. N Z Med J 2000; 113: 178-81.
9. Leelakusolvong S, *et al*. World Congress of Gastroenterology, 2002.
10. Iamudomkan A, Gonlacchanvit S, Thong-ngam D. Upper Gastrointestinal symptoms in Thai patients with GERD diagnosed by 24-hour pH monitoring. Thai J Gastroenterol 2004; 5: 146-50.
11. Lauritsen K, Aalykke C, Haveland T, *et al*. Effect of omeprazole in functional dyspepsia: a double-blind, randomized, placebo-controlled study. Gastroenterology 1996; 110 (Suppl): A702.
12. Carlsson R, Dent J, Bolling-Sternevald E, *et al*. The udefullness of a structured questionnaire in the assessment of symptomatic gastroesophageal reflux disease. Scand J Gastroenterol 1998; 33: 1023-9.
13. Locke GR, Talley NJ, Nelson DK, *et al*. *Helicobacter pylori* and dyspepsia: a population-based study of the organism and host. Am J Gastroenterol 2000; 95: 1906-13.
14. Mahachai V, Kositchaiwat C, Kachintorn U, *et al*. Epidemiology of *Helicobacter pylori* infection in Thailand. Helicobacter Research 2000; 4: 25-9.

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15. Stomach Research Group (SRG), the Gastroenterology Association of Thailand (GAT). Guideline for the management of dyspepsia and *Helicobacter pylori* infection: Thailand consensus, 1999.

16. Raghunath A, Hungin AP, Wooff D, *et al*. Prevalence of *Helicobacter pylori* in patients with gastro-oesophageal reflux disease: systematic review. Br Med J 2003; 326: 737-44.

17. Wang JH, Lou JY, Dong L, *et al*. Composite score of reflux symptoms in diagnosis of gastroesophageal reflux disease. World J Gastroenterol 2004; 10: 3332-5.

18. Streets CG, Demeester TR. Ambulatory 24-hour esophgeal pH monitoring (why, when and what to do). J Clin Gastroenterol 2003; 37: 14-22.

19. Cremonini F, Di Carco S, Delgado-Aros S, *et al*. Meta-analysis: the relationship between *Helicobacter pylori* infection and gastro-oesophageal reflux disease. Aliment Pharmacol Ther 2003; 18: 279-89.

20. Xia HHX, Yang Y, Wong BCY. Relationship between *Helicobacter pylori* infection and gastroesophageal reflux disease. Chin J Dig Dis 2004; 5: 1-6.