Relationship among symptoms, mucosa injury, and acid exposure in Gastroesophageal Reflux Disease

Abstract

Symptoms, endoscopy, and pH monitoring form the basis of diagnosis of gastroesophageal reflux disease (GERD). Their relationship was meaningful for primary care physicians, but still unclear. This study aimed to determine the relationship among symptoms, mucosa injury, and acid exposure in Gasteroesophageal Reflux Disease.

A cross-sectional analytic study was carried out in 48 patients with symptoms of GERD (heartburn or acid regurgitation) after explaining about the study and taking written consent during the one-year period in2015. The patients underwent upper GI endoscopy to assess mucosa injury and 24-hour esophageal pH monitoring to assess pathological acid exposure in Department of Gastroenterology, Yangon General Hospital. The data were then analyzed and their relationships were determined.

Among 48 patients 66.7% were female and 33.3% were male. This study found that the majority (89.5%) of patients did not have mucosa injury on endoscopy and only 10.5% had mucosa injury. Pathological acid exposure (PAE) were seen in 31.3% of patients and 68.7% did not have pathological acid exposure in 24-hour pH monitoring. There were no significant association between symptoms and endoscopic findings and pathological acid exposure. Statistically association was seen among the mucosa injury and PAE. The sensitivity of symptoms was > 80% but specificity was only <10%. Regarding mucosa injury on endoscopy, the sensitivity was low only 26.7% but specificity was 96.9%. Therefore GERD cannot be accurately diagnosed by its typical symptoms alone in a Myanmar population with symptoms suspected of GERD. A definitive diagnosis of GERD still depends on endoscopy or 24-hr pH monitoring.

Introduction

Gastroesophageal reflux disease (GERD) is a disease that develops when the reflux of stomach's contents causes troublesome symptoms and/or complications. Its diagnosis is based on symptoms, endoscopy, pH monitoring, and other new technologies, such as impedance monitoring and high-resolution manometry. GERD can be further classified as the presence of symptoms without erosions on endoscopic examination (non- erosive disease or NERD) or GERD symptoms with erosions present (Erosive Reflux Disease or ERD). GERD is one of the most common conditions that affect the gastrointestinal tract. In Myanmar, the increasing number of patients presenting with heartburn or reflux dominant symptoms were encountered in daily Gastroenterology practice. The relationship between symptoms, endoscopic findings and 24-hour pH monitoring in-patient with GERD has not been studied before. Therefore, the result of this study might be able to contribute the evidence-based data regarding the knowledge of endoscopic findings and esophageal acid exposure in GERD patients of Myanmar population.

Methods

A total of 48 patients with symptoms of GERD (heartburn or acid regurgitation) of both sexes from Department of Gastroenterology in Yangon General Hospital, both in-patients and out patients aged 18 years and above were studied during one year from December 2014 to November 2015. The patients underwent upper GI endoscopy to assess mucosa injury and 24-hour esophageal pH monitoring to assess pathological acid exposure in

Department of Gastroenterology, Yangon General Hospital. Then, the characteristics of different investigations and their relationships were analyzed. The severity of mucosa injury was assessed according to the Los Angeles classification.

Los Angeles Classification of Oesophagitis

Grade A   One (or more) mucosal break no longer than 5 mm that does not extend between the tops of two mucosal folds

Grade B   One (or more) mucosal break more than 5 mm long that does not extend between the tops of two mucosal folds

Grade C   One (or more) mucosal break that is continuous between the tops of two or more mucosal folds but which involve less than 75% of the circumference

Grade D   One (or more) mucosal break which involves at least 75% of the esophageal circumference

Pathological acid exposure (PAE) was defined as the DeMeester score greater than 18.

DeMeester score (Medica, 2012).
This is calculated on 6 classical parameters:

Total Reflux Number:	the number of reflux episodes with a pH less than 4
Long Reflux Number (>5 min):	the number of reflux episodes with a pH less than 4 that last longer than 5 minutes
Maximum Reflux Duration:	the duration of the longest reflux episode in minutes and decimals.
% total time pH < 4:	percentage of the total recording time with a pH less than 4.
% upright time pH < 4:	percentage of the total recording time with a pH less than 4 but calculated over the upright time
% supine time pH < 4:	percentage of the total recording time with a pH less than 4 but calculated over the supine time.

For each parameter a score is computed according to the following formulae:
Score = [Vp-(Vm-SD)]/SD
Where Vp is the patient value
Vm is the mean value of the reference group
SD is standard deviation
Adding up the score of the several parameters, obtained the final score which normal threshold is 18.

Data on each patient were collected in a pre-constructed proforma. SPSS 15.0 Statistical Software was used for data analysis. Descriptive statistics was shown with frequency and percentage. The data was expressed as a mean and standard deviation (SD) for continuous variables and expressed as count and percentage for categorical variable. For the number of acid reflux events and the percentage time spent at pH<4, the analysis of variance (anova) was used to analyze the difference between the groups. Chi-squared test was used to compare the proportion of patients with symptoms, the proportion of patients with a symptom index $\geq$ 50% and the distribution of gender and ethnicity between the groups. All statistical tests utilized a significance level of 0.05.

Results

A total of 48 patients were recruited into the study. 66.7% were female and 33.3% were male. The mean age was 40.69 with SD 14.41. The commonest age group in the study was ≤40 years (48.3%). The mean body mass index in this study was 23.1 ± 3.36.

In evaluation of symptoms, 46 patients (95.8%) presented with symptom of heartburn and only 2 patients did not have heartburn. 42 patients (87.5 %) had symptoms of acid regurgitation and 6 patients (12.5%) did not have acid regurgitation. 40 patients (83.3%) had both symptoms of heartburn and acid regurgitation.

The majority of the patients (89.6 %) had no mucosa injury. 10.4% had evidence of mucosa injury on endoscopy. Pathological acid exposure according to Demesster score >18 were found only in 15 cases (31.3%) and majority of cases did not have pathological acid exposure.

As shown in table (1), Among 46 patients who have symptoms of heartburn, majority (89.1 %) did not have mucosa injury and only 10.9 % had mucosa injury on endoscopy. There was no significant association between symptoms of heartburn and mucosa injury. (Fisher exact p value 0.801).

According to table (2), among 42 patients with symptoms of acid regurgitation, 11.9% had features of mucosa injury on endoscopic finding. There was no association between symptoms of acid regurgitation and mucosa injury with Fisher exact p value 0.497.

Among patients with symptoms of heartburn, only 30.4% had positive pathological acid exposure. Regarding symptom of heartburn and pathological acid exposure, no association was seen between them with Fisher exact p value of 0.532 (Table 3).

28.6% of patients with symptoms of acid regurgitation had a positive 24-hour esophageal pH score. There was no significant association between symptom of acid regurgitation and pathological acid exposure with p value 0.360 (Table 4). The finding indicated that there was significant association between mucosa injury and pathological acid exposure with p value 0.028 (Table 5).

Table (1) Association between symptom of heartburn and mucosa injury

Heart burn	Mucosa injury		Total
	Present	Absent	
Present	5 (10.9%)	41 (89.1%)	46 (100.0%)
Absent	0 (0.0%)	2 (100.0%)	2 (100.0%)
Total	**5 (10.4%)**	**43 (89.6%)**	**48 (100.0%)**

Fisher exact p value = 0.801

Table (2) Association between symptom of acid regurgitation and mucosa injury

Acid regurgitation	Mucosa Injury		Total
	Present	Absent	
Present	5 (11.9%)	37 (88.1%)	42 (100.0%)
Absent	0 (0.0%)	6 (100.0%)	6 (100.0%)
Total	**5 (10.4%)**	**43 (89.6%)**	**48 (100.0%)**

Fisher exact p value = 0.497

Table (3) Association between symptom of heartburn and pathological acid exposure

Heart burn	Pathological acid exposure		Total
	Present	**Absent**	**Total**
Present	14 (30.4%)	32 (69.6%)	46 (100.0%)
Absent	1 (50.0%)	1 (50.0%)	2 (100.0%)
Total	**15 (31.3%)**	**33 (68.8%)**	**48 (100.0%)**

Fisher exact p value = 0.532

Table (4) Association between symptom of acid regurgitation and pathological acid exposure

Acid regurgitation	Pathological acid exposure		Total
	Present	**Absent**	**Total**
Present	12 (28.6%)	30 (71.4%)	42 (100.0%)
Absent	3 (50.0%)	3 (50.0%)	6 (100.0%)
Total	**15 (31.3%)**	**33 (68.8%)**	**48 (100.0%)**

Fisher exact p value = 0.360

Table (5) Association between mucosa injury and pathological acid exposure

Pathological acid exposure	Mucosal Injury		Total
	Present	**Absent**	**Total**
Present	4 (26.7%)	11 (73.3%)	15 (100.0%)
Absent	1 (3.0%)	32 (97.0%)	33 (100.0%)
Total	**5 (10.4%)**	**43 (89.6%)**	**48 (100.0%)**

Fisher exact p value = **0.028**

Discussion

In this study, majority of patients (89.5%) did not have mucosa injury on endoscopic findings. Only 10.5% had mucosa injury in endoscopic findings.

Similarly, several community-based European studies of NERD patients found a prevalence of 70%.[4]However, early studies reported that about 50% of patients with heartburn were found to exhibit normal esophageal mucosa during endoscopy.[3]

In a population-based study, 1000 subjects with or without GERD-related symptoms from an adult population of 2 Swedish municipalities were randomly selected to undergo an upper endoscopy. Among the patients with gastroesophageal reflux symptoms, only 24.5% were found to have erosive esophagitis.[10]Overall, the result of recent studies has suggested that the prevalence of NERD is higher than what has been previously described and is estimated to affect between 50% and 70% of the GERD population, whereas the rest have erosive esophagitis, excluding 6% to 10% with Barrett esophagus.[2]

The prevalence of erosive esophagitis in subjects undergoing an upper endoscopy for any reason has been reported to be between 1.2% and 2.4%.[1]In contrast, the population-based study from Sweden found that 15.5% of the subjects, regardless of whether GERD symptoms were present or absent, had erosive esophagitis on upper endoscopy.[10] Similarly Kouzu et al

(2007) concluded that 75.5% of patients who had heartburn did not have any endoscopic abnormalities.[7]

In this study, 89.5 % of the study population was found to have no feature of mucosa injury and only 10.5% had mucosa injury with variable severity. This percentage was slightly different from the data of other studies as mentioned above.

Abnormal endoscopic findings are less common these days due to widespread PPI use and gastroenterologists are more commonly faced with the dilemma of patients who are not responding to PPI therapy in the context of a normal endoscopy. There is great variability among endoscopists to recognize the subtle changes in esophageal mucosa manifesting esophagitis. There is no existing epidemiological data with special emphasis on ERD and NERD for Myanmar population. Therefore the high estimation of no mucosal injury on endoscopic finding in this study, though it was not population-based in nature, may be due to different baseline characteristics of patients, genetic and environmental factors, and increasing trend of NERD in Myanmar. Wu et al concluded that Endoscopy-negative GERD patients are more likely to be female, younger, thin, and without hiatal hernia, and they have a higher prevalence of functional GI disorders.[12] In this study, female patients are more predominant than male. This may be the one of contributing factors of higher percentage of NERD in this study.

XU et al stated that among 300 patients, only 85 patients (28.3 %) belonged to group of PAE.[13] According to pH monitoring in this study, only 15 cases (31.3%) were diagnosed as pathological acid exposure and majority of cases had no pathological acid exposure in this study. It is fairly consistent with Xu et al 2013 statement. Whereas Tefera et al revealed that 63 % of patients with grade 2 or 3 heartburn (n=81) and 65 % of patients with grade 2 or 3 regurgitation (n=63) had a positive 24-hour esophageal pH score.[11]

Gastro-esophageal reflux disease (GERD) arises from increased exposure and/or sensitivity of the esophageal mucosa to gastric contents. However, pH monitoring does not detect all gastro-esophageal reflux events even when special pH analysis criteria are used, particularly when little or no acid is present in the refluxate. This is the case in both adults and infants after eating, before the gastric contents have become acidified, and it also applies to reflux in patients taking anti-secretory therapy. Not only the acidity but also the air-liquid composition of the refluxate could be relevant in the pathogenesis of GERD. In this study, the pH metry could detect acid reflux pH<4 and could not detect weaker acid, alkali or gas reflux was used. These factors may lead to different results in different study.

In the present study, symptoms of heartburn and acid regurgitation were not statistically associated with reflux esophagitis on endoscopic findings with Fisher exact p value of 0.801 and 0.497 respectively.

In Chinese study, Xu et al stated that the symptoms including heartburn, acid reflux, and food regurgitation were not statistically associated with reflux oesophagitis.[13]

In this study, symptoms of heartburn and acid regurgitation were poorly correlated with 24-hour esophageal pH monitoring with Fisher exact p value of 0.532 and 0.36 respectively.

Xu et al concluded that symptoms including heartburn, acid reflux, and food regurgitation were not statistically associated with PAE.[13]

According to Tefera et al, individual symptoms of heartburn, regurgitation and dysphagia were poorly correlated with 24-hour esophageal pH monitoring.[11]

Typical symptoms such as heartburn and acid regurgitation could not predict the PAE and reflux oesophagitis. It was the same as a multiple center study in Korea.[6]

In one US study, 149 patients with typical symptoms of heartburn were evaluated 71 (48%) were found to have NERD, 36 (24%) erosive oesophagitis and 42 (28%) Barrett's oesophagus. 75% of erosive oesophagitis demonstrated an abnormal 24-h pH test.[8]

One of the studies from China found that among 300 Chinese patients, 80 patients belonged to the group of reflux esophagitis including 63 (79%) patients with abnormal pH monitoring. Reflux esophagitis was statistically associated with PAE with p value of <0.01.[13] Tefera et al stated that 90% of patients with endoscopic evidence of tissue injury had a positive 24-hour esophageal pH score.[11]

In the present study, among 48 patients, only 5 (10%) patients found to have mucosa injury on endoscopy. 4 (80%) patients with mucosa injury demonstrated an abnormal 24-hr pH test. There was a statistically association between mucosa injury and PAE. This result was consistent with the conclusion of above studies.

In this study 73.3% (n=11) of patients with PAE showed no evidence of mucosa injury in endoscopy. This result supports the recommendation of Kahrilas and Quigley that esophageal pH monitoring is indicated in patients with normal endoscopic findings. [5]

Conclusion

This study described the relationship between symptoms, endoscopy, and pH monitoring in the patients with GERD. There were no significant association between symptoms and mucosa injury and PAE. But it was found that there was an association between mucosa injury and PAE.In this study, symptoms such as heartburn or acid regurgitation could not predict the degree of mucosal injury or PAE. Mucosa injury can predict the presence of PAE.GERD cannot be accurately diagnosed by its typical symptoms alone in a Myanmar population with symptoms suspected of GERD. A definitive diagnosis of GERD still depends on endoscopy or 24-hr pH monitoring.The endoscopy and 24-hour pH monitoring has a role in diagnosis of GERD in Myanmar. However, the use of 24-hour esophageal pH monitoring is not universal as there is no access for appropriate instrumentations for most physicians. Further studies should be done with nationwide multicenter with large sample size.

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