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Risk factors of erosive esophagitis and barrett's esophagus in patients with reflux symptoms

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Abstract

Background: Gastroesophageal reflux disease (GERD) is a prevalent condition. Erosive esophagitis (EE) and Barrett's esophagus (BE) are the two important complications of GERD. We aimed to study the prevalence of EE and BE in a group of Patients with reflux symptoms who were referred for endoscopy. The relationship between reflux symptoms and endoscopic findings was also examined.

Methods: We enrolled 139 consecutive patients with characteristic symptoms of GERD. Demographic and clinical characteristics of the patients including duration and severity of reflux symptoms, were recorded. Endoscopic findings of EE were identified and classified according to the Los Angeles classification, while BE was confirmed by histopathology examination. The Fisher's exact test and the two-sample *t*-test were used to test the association of esophageal lesions (BE and/or EE) with the patients' clinical and endoscopic data.

Results: Forty seven and 13 patients were found to have EE and BE, respectively. Multivariate analysis showed that older age (p=0.001) and hiatal hernia (p=0.004) was significantly related risk factors for erosive esophagitis and BE. While an increase in BMI (p=0.004) was related to EE, patients with BE were more likely to have severe reflux symptoms than others (p=0.002).

Conclusion: In patients with GERD, the presence of hiatal hernia may be strong risk factor for erosive esophagitis and BE, as does older age. For Barrett's esophagus, severe reflux symptoms are more likely.

Keywords: Barrett's esophagus, Reflex esophagitis

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Introduction

Gastroesophageal reflux disease (GERD) is a condition that develops when reflux of stomach contents causes troublesome symptoms (e.g, heartburn and regurgitation) and/or complications (1, 2). GERD is a common condition, affecting 10% to 20% of the general population (3).

Several factors may predispose patients to GERD; including hiatus hernia, lower esophageal sphincter hypotension, abdominal obesity, gastric hypersecretory states, delayed gastric emptying. Multiple risk factors are often present (4-7).

The most common GERD-related complaints are heartburn and acid regurgitation. Extraesophageal syndromes with an established association to GERD include chronic cough, laryngitis, asthma, and dental erosions. Pulmonary fibrosis, chronic sinusitis, cardiac arrhythmias, sleep apnea, and recurrent aspiration pneumonia have proposed associations with GERD (8).

The diagnostic guidelines for GERD depend on the

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↑What is "already known" in this topic:
Older age, male gender, smoking, duration of reflux symptoms more than 5 years, and the presence of hiatus hernia are considered risk factors for esophagitis and Barrett's mucosa.

→What this article adds:
The presence of severe reflux symptoms, including acid regurgitation, is another risk factor that should be considered. The presence of lax cardia without hiatus hernia is not considering as a significant predictor of esophagitis and Barrett's mucosa.

symptoms with relief obtained empirically with PPI. Poor response to the PPI necessitates further diagnostic workup (gastroscopy, esophageal biopsy, ambulatory esophageal pH monitoring, and impedance monitoring).Treatment without invasive diagnostic testing is recommended unless the presence of dysphagia, weight loss, gastrointestinal blood loss, or anemia is present (9).

Endoscopy is used to identify Barrett's mucosa and erosive esophagitis (which are the two important complications) in patients with long-term symptoms or alarm symptoms. The presence of typical findings of reflux esophagitis on endoscopy (erosions or ulcers at or immediately above the gastroesophageal junction) is diagnostic of GERD with a specificity of 90% to 95 % (10, 11) . At least 50% of patient with reflux symptoms have normal esophageal endoscopic findings nonerosive reflux disease (NERD) (12).

There are several classification systems for grading the endoscopic severity of erosive reflux esophagitis and associated complications. Los Angeles (LA) classification is commonly used in the clinical practice (13).

BE is a condition in which the squamous epithelium of the distal esophagus is replaced by an abnormal columnar epithelium known as specialized intestinal metaplasia, that confers a predisposition to cancer (14). Barrett's esophagus was diagnosed in 1.6% of studied people and 10% to 15% of patients undergoing EGD for GERD (15). The diagnosis of Barrett's esophagus requires findings on endoscopy that columnar mucosa extends above the gastroesophageal junction, lining the distal esophagus, plus esophageal-biopsy results that confirm the presence of columnar metaplasia (16).

Barrett's esophagus is more common in men than in women; it is uncommon in blacks and Asians and is rare in children (17, 18). Other important risk factors include obesity (with a predominantly abdominal type) and cigarette smoking, and positive family history of Barrett's esophagus, which accounts for 7 to 11% of all cases (19, 20).

Endoscopic screening for Barrett's esophagus is recommended in patients with chronic GERD symptoms who have additional risk factors for esophageal adenocarcinomas, such as an age of 50 years or older, male sex, white race, hiatal hernia, abdominal obesity, or smoking (21-23).

Methods

We conducted a cross-sectional study on 39 consecutive patients with GERD symptoms. Severity and duration of symptoms such as heartburn, regurgitation, and dysphagia; any extra esophageal symptoms were recorded. The severity of heartburn was classified according to frequency into severe (occurs every meal), moderate (occurs every day), and mild (occurs weekly). All patients underwent endoscopy after induction of pharyngeal anesthesia with 10% lidocaine spray. The appearance and location of the squamocolumnar junction, location of gastroesophageal junction GEJ, endoscopic esophagitis and the presence or absence of columnar lined esophagus, its length and morphological types were carefully evaluated, identified and the findings were recorded. Subjects were divided into three groups according to the endoscopic findings, patients with Normal Esophagogastric Junction (NEJ), those with Erosive Esophagitis (EE) and those who had Barrett's esophagus (BE). Endoscopic esophagitis (esophageal mucosal breaks or ulcers), if present, were graded according to the Los Angeles (LA) classification system. Sequamocolumnar junction extends above GEJ (pink tongues of Barrette mucosa extending proximally from the gastroesophageal junction) was described as endoscopic findings consistent with BE that awaited histological evaluation. All Specimens were sent for histopathological examination for the presence of intestinal metaplasia which is defined by the presence of the columnar epithelium in the distal esophagus. Hiatal hernia and lax cardia were also recoded if identified during the procedure. Descriptive analysis was done and frequencies and percentages of the categorical variables were calculated.

Statistical analysis

To summarize quantitative variables, we used means and standard deviations. The Fisher's exact test and the two-sample *t*-test were used to test the association of esophageal lesions (BE and/or EE) with the patient clinical and endoscopic data except for severity of reflux symptoms where Chi-square used. A p-value of <0.05 was considered statistically significant.

Results

A total of 139 patients with a mean age of (40.24±11,12) years and a mean BMI of (25.37±4.37) Kg were included. Seventy two patients were male (51.8%) and 68 were female (48.2%). Heartburn was the most common presenting symptom; it was recorded in 96 patients (69%). Other symptoms were acid regurgitation in 77 patients (55 %), nausea and vomiting in 46 patient (33%), indigestion (dyspepsia like) in 31 patients (22%), dysphagia in 29 patients (20%) and chronic cough in 17 patients (12 %) of the patients.

Endoscopically, seventy nine patients (56.8%) had no evidence of erosive esophagitis (NEJ), while 60 patients (43.2 %) had erosive esophagitis (EE).

Barrett's esophagus (BE) was found in 13 patients (9.3%); none of them had concomitant adenocarcinoma. Hiatus hernia (H.H) was diagnosed in 15 patients (11%).

Demographic characteristics of the patients with NEJ and EE+BE groups (shown in Table 1) showed comparable findings in the gender (p=0.392), but patients in EE+BE group (mean age 46.43±11.95 years and 55.08±15.37 years versus 35.53±11.12 years for NEJ) (p=0.006) were significantly older. Patient with BE showed a high male percentage although it is statistically not significant (p=0.245). Also there was a high body mass index (BMI) in patients with EE (p=0.002) but not in the patients with BE (p=0.146) in comparison to NEJ patients (Tables 1 and 2).

With respect to the clinical symptoms, acid regurgitation (p=0.031) and longer duration of symptoms (p=0.008) were significantly correlated with the endoscopic findings of EE; while in BE, acid regurgitation

(p=0.032) and dysphagia (p=0.029) were the only symptoms appear to be statistically significant. No significant difference was found in other symptoms between these groups. Severe symptoms had a high percentage in patients with EE and BE (p=0.060) but were significant in patients with BE only (p=0.020) as seen in Tables 3 and 4.

In respect to the associated endoscopic findings, hiatus hernia recorded more in EE and BE groups (prevalence of 20 % and 53 %, respectively; and p=0.004 and =0.00, respectively). Endoscopic findings suggestive of a lax cardia seemed to be equal between the patients with NEJ (43%), EE and BE patients (31%) and BE patients (37%). (Tables 3 and 4).

Discussion

The prevalence of EE and BE varies around the world and is higher in western than eastern countries. They are commonly occurring in western patients with the approximate prevalence of 30–60% and 5–15% (24), respectively. In this study, the prevalence of EE was (33.8%) and for BE was (9.3%); this shows that the prevalence of these complications somewhat similar to that seen in western populations. In Eastern countries, lower rates have been reported. For example, in an Iranian study, approximately 43% of patients had erosive esophagitis, and 4.6% had Barrett's esophagus (25).

Table 1. Comparison of demographic characteristics between NEJ and (EE and BE) patients

Characteristics		NEJ patients n=79 (56.8%)	EE+BE patients n=60 (43.2%)	p	Odds Ratio
Age (years)		35.53±11.12	46.43±11.95	0.001	-
Gender	Male	38 (48.1%)	34 (56.6%)	0.392	1.41
	Female	41 (51.9%)	26 (43.4%)		
BMI		24.1±4.37	27.05±3.48	0.002	-
smokers		20 (25.3%)	23 (38.3%)	0.131	1.83
Alcoholic		0 (0%)	2 (3.3%)	0.181	-

Table 2. Comparison of demographic characteristics between Barrette and NEJ patients

Characteristics		Barrett patients		p	Odds Ratio
		Yes n=13 (9.4%)	No n=126 (90.6%)		
Age (years)		55.08±15.37	38.71±11.36	0.001	-
Gender	Male	9 (69.2%)	63 (50%)	0.245	2.25
	Female	4 (30.8%)	63 (50%)		
BMI		27.02±5.27	25.2±4.12	0.146	-
Smoking		5 (38.5%)	38 (30.2%)	0.542	1.44
Alcohol		0 (0%)	2 (1.6%)	1	-

Table 3. Comparison of clinical and endoscopic characteristics between NEJ and (EE and BE) patients

Presenting Symptoms		NEJ n=79 (56.8%)	EE+BE n=60 (43.2%)	p
Heartburn		57 (72.1%)	39 (60%)	0.451
Acid Regurgitation		50 (63.2%)	27 (45 %)	0.031
Dysphagia		15 (19%)	14 (23.3%)	0.534
Nausea and Vomiting		26 (33%)	20 (33.3%)	1
Indigestion		17 (21.5%)	14 (23.3%)	0.830
Chronic cough		10 (12.6%)	7 (11.7%)	1
Duration of symptoms(yrs)		2.59±1.78	4.16±3.31	0.008
Severity of symptoms	Severe	24 (30.3%)	30 (50%)	0.060
	Moderate	20 (25.4%)	11 (18.3%)	
	Mild	35 (44.3%)	19 (31.7%)	
The endoscopic findings	Hiatus Hernia	3 (3.8%)	12 (20%)	0.004
	Lax Cardia	34 (43%)	19 (31.7%)	0.210

Table 4. Comparison of clinical and endoscopic data between NEJ and BE patients

Presenting symptoms		Barrett patients		p	Odds Ratio
		Yes n=13 (9.4%)	No n=126 (90.6%)		
HeartBurn		11 (84.7%)	85 (67.4%)	0.341	2.63
Acid Regurgitation		11 (84.7%)	67 (53.2%)	0.032	4.84
Dysphagia		6 (46.2%)	23 (18.3%)	0.029	3.83
Nausea & Vomiting		6 (46.2%)	40 (31.2%)	0.355	1.84
Chronic cough		3 (23.1%)	14 (11.1%)	0.192	2.4
Indigestion		5(38.5%)	20.6%)/26	0.232	
Duration of symptoms (years)		2.53±2.19	2.84±3.23	0.740	-
Severity of symptoms	Severe	8 (61.5%)	46 (36.5%)	0.020	-
	Moderate	2 (15.3%)	29 (23.1%)		
	Mild	3 (23.2%)	51 (40.4%)		
Endoscopic findings	Lax Cardia	6 (46.2%)	47 (37.3%)	0.551	1.44
	Hiatus Hernia	7 (53.8%)	8 (6.3%)	0.000	17.2

Different studies have shown different risk factors for EE and BE. For instance, in the Labenz et al. study, male gender, overweight, regular alcohol consumption, GERD symptoms for more than one year, and smoking were the reported risk factors (26).

In another study, conducted by Rosaida and Goh, the risk factors for EE were male gender, Indian race, hiatal hernia, and alcohol use (27). In our study, the prevalence of EE and BE did not differ significantly between women and men, although the number of male patients was higher than women. Probably, men have more reflux symptoms or seek medical advice and do endoscopic evaluation compared to women.

In accordance with previous studies, the mean age of patients with EE and BE in our study was significantly older than in those with NEJ. On the other hand, EE and BE patients had a mean BMI higher than NEJ and a significant association was found compared with EE with but it was not significant in comparison of BE and NEJ (p=0.14).

Although the number of smokers was high in both groups, no significant difference was found regarding smoking (25.3% versus 38.3%, p value = 0.131) and alcohol consumption (0% versus 2%, p=0.181)

The presenting symptoms shows that acid regurgitation is a significant risk factor for EE and BE. In addition, dysphagia also shows to be a significant risk for BE, as these symptoms indicate severe GERD, while heartburn is a common symptom (69%) in all patients. The duration of symptoms before endoscopy was significant for patients with EE but not for patients with BE. The study by Sharma N. et al. (28) showed an increased risk of BE with increasing duration of GERD symptoms. This may be explained by the fact that the majority of our patients had GERD for less than 5 years which may not be sufficient to cause Barrette mucosa (mean of duration of symptoms : 2.53 versus 2.84 years, p=0.74).

With respect to endoscopic findings, the presence of hiatal hernia is a strong risk factor for EE and BE (3.8% versus 20%, p=0.004) which is correlated to many other studies like Avidan et al. (29), who found that there is an increased risk of BE in patients with hiatus hernia and the size of hiatus hernia had a linear correlation with the length of BE.

Conclusion

In conclusion, we have shown that the prevalence of GERD complications such as BE and EE are equal to that seen in western countries. In addition, the presence of hiatal hernia is a strong risk factor for EE and BE. Similarly, older age and severe reflux symptoms could be considered significant risk factors for the development of BE in patients with GERD.

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Conflict of Interests

The authors declare that they have no competing interests.

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