



Original Research

Relationship Among *Helicobacter Pylori*, Lower Esophagus Sphincter Pressure, and Gastroesophageal Reflux: A Single-Center Experience

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Abstract

Objectives: The aim of the study was to evaluate the relationship among lower esophageal sphincter pressure (LESP), *Helicobacter pylori* (Hp), and gastroesophageal reflux (GER).

Methods: The retrospective study included patients with isolated hypertensive or hypotensive lower esophageal sphincter (LES) who underwent esophageal manometry in our gastroenterology motility laboratory and had normal manometry results. Demographic characteristics, complaints on admission, upper endoscopy findings, 24-h esophageal pH monitoring results, and presence of Hp in gastric biopsy were evaluated.

Results: A total of 1226 patients were included in the study, among whom women comprised 54% of all patients. Mean age was 45.4±13.4 years. Most common presenting complaint was pyrosis (85.4%). Pathological reflux was detected in 61.4% of the patients in 24-h esophageal pH monitoring. Reflux esophagitis was detected in 22.9% and LES laxity was present in 17.4% of the patients. In gastric biopsy, Hp was positive in 40% of the patients. The age of patients with hypertensive LES was significantly higher and female gender and body mass index (BMI) were associated with hypertensive LES. Pyrosis was significantly less prevalent in patients with hypertensive LESP. Esophagitis and LES laxity were significantly more prevalent in patients with hypotensive LES. No significant difference was found among the three groups with regard to reflux and Hp positivity. No significant difference was found between Hp-positive and Hp-negative groups with regard to reflux and reflux esophagitis.

Conclusion: No clear relationship was found among LES disorders, GER, and Hp. Moreover, no significant difference was found among LES disorders with regard to GER, while the presence of hypotensive LESP, rather than Hp, was found to be an important factor in the development of reflux esophagitis.

Keywords: Gastroesophageal reflux, *Helicobacter pylori*, Hypertensive lower esophageal sphincter, Hypotensive lower esophageal sphincter

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Gastroesophageal reflux (GER) disease can occur for many reasons, including disruption of the antireflux barrier, esophageal clearance, and esophageal mucosal re-

sistance due to temporary relaxation of the lower esophageal sphincter (LES).^[1] The LES and the crural diaphragm are the main antireflux barriers that protect the esophagus

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against reflux of gastric contents.^[2,3] LES is defined as a zone of high pressure determined by manometry, consisting of both the inner and outer musculature where the esophagus joins the stomach. The relationship between LES and GER is highly complex. GER and erosive esophagitis can be seen in many patients with normal LES pressure (LESP) and crural diaphragm. However, GER may not be detected in some patients with low LESP.^[3]

Although there are many studies reporting on the possible role of *Helicobacter pylori* (Hp) in the pathogenesis of GER, the relationship between GER and Hp remains unclear.^[4,5] Moreover, Hp infection can play both a protective and aggressive role in the development of GER.^[5] On the other hand, studies evaluating the relationship between LESP and Hp are highly limited. In this study, we aimed to evaluate the relationship among LESP, Hp, and GER.

Methods

Patients

The retrospective study included patients with isolated hypertensive or hypotensive LESP who underwent esophageal manometry in our gastroenterology motility laboratory and had normal manometry results. Patients' motility records and digital electronic records were retrieved from hospital database. Demographic characteristics, complaints on admission, upper endoscopy findings, 24-h esophageal pH monitoring results, and presence of Hp in gastric biopsy samples were reviewed for each patient. The study was evaluated and approved by the Local Ethics Committee of our hospital and the study protocol was conducted in accordance with the principles of Declaration of Helsinki (Approval No: 12; Date: November 27, 2019).

Exclusion Criteria

Patients aged below 18 years and those with primary esophageal motor diseases (achalasia, nutcracker esophagus, diffuse esophageal spasm, and non-specific esophageal motility disorder) and patients with secondary esophageal motor diseases (scleroderma, myasthenia gravis, amyotrophic lateral sclerosis, and cerebrovascular event), malignant neoplasms, malignant gastric neoplasms, and malignant lung neoplasms were excluded from the study. Patients with a history of esophageal or gastric surgery for any reason were also excluded from the study.

Manometry

Drugs that could affect the results of esophageal manometry (calcium channel blockers, nitrates, phosphodiesterase inhibitors, alpha-, and beta-blockers) were discontinued 2 weeks before the procedure and manometric measure-

ments were performed using conventional esophageal manometry (MMS, Dentsleeve, Bel Air, Australia) after 8 h of fasting. The manometry catheter was advanced transnasally into the stomach. After measuring gastric basal pressure, the location of LES was determined by retracting the catheter at 1-cm intervals and requesting the patient to perform deep inspiration, expiration and/or dry swallows. After placing the sleeve of the catheter in the lower esophagus, esophageal motor functions were assessed through 10 wet swallows at 20-s intervals. Patients with normal esophageal body function in 10 wet swallows (along with peristaltic contraction, mean contraction amplitudes ranging between 30 and 180 mmHg) and those with a LES resting pressure of 10–45 mmHg were considered normal. Those who had normal esophageal body functions but had an isolated LES resting pressure <10 mmHg were accepted as having hypotensive LESP and those with an isolated LES resting pressure >45 mmHg were accepted as having hypertensive LESP.^[6-9]

24-h Esophageal pH Monitoring

Drugs that could affect patients' esophageal pH such as antacids, H₂ receptor antagonists, and proton pump inhibitors were discontinued 10 days before the procedure and 24-h esophageal pH monitoring was performed after 8 h of fasting. After determining the location of LES by esophageal manometry, the distal sensor of the PHI15/PHN15 dual pH catheter (Sandhill Scientific Inc.) was transnasally inserted to a location 5 cm above LES and the proximal sensor was inserted to a location 20 cm above LES. Following the insertion of the catheter, the presence of distal and proximal reflux was investigated through 24-h esophageal pH monitoring.^[10-12]

Patients with a total reflux time >5%, standing reflux time >6.3%, supine reflux time in su >1.2%, longest reflux period >9.2 min, total number of reflux episodes >50, number of reflux episodes longer than 5 min >3 in the distal sensor of the 24-h esophageal pH meter, and a DeMeester score ≥15 were accepted as having distal pathological reflux. In contrast, patients with a total reflux time >1%, a standing reflux time >1.5%, longest reflux episode >3 min, and total number of reflux episodes >10 were considered as having proximal pathological reflux.^[7-11]

Statistical Analysis

Data were analyzed using SPSS 26.0 for Windows (Armonk, NY: IBM Corp.). Continuous variables were expressed as mean and standard deviation and categorical variables were expressed as frequencies (n) and percentages (%). Normal distribution of data was assessed using Kolmogorov–Smirnov test, Shapiro–Wilk test, coefficient

of variation, skewness, and kurtosis. Patients were divided into three groups including normal LESP, hypotensive LESP, and hypertensive LESP according to the esophageal manometry results. The three groups were compared using one-way analysis of variance (ANOVA) test for variables with normal distribution, followed by post hoc Bonferroni correction and were compared using Welch's ANOVA and Kruskal–Wallis test for variables with non-normal distribution. Groups were further divided as Hp-positive and Hp-negative, and these groups were compared using Student's t-test for variables with normal distribution and using Mann–Whitney U test for variables with non-normal distribution. All the groups were compared with regard to endoscopic and esophageal pH monitoring findings. A two-tailed $p < 0.05$ was considered significant.

Results

Demographic and Clinical Characteristics

A total of 1226 patients were included in the study, among whom women comprised 54% of all patients. Mean age was 45.4 ± 13.4 years. Most common presenting complaint was pyrosis (85.4%). Mean body mass index (BMI) was 26.96 ± 4.78 kg/m². Pathological reflux was detected in 61.4% of the patients in 24-h esophageal pH monitoring. Esophagitis was diagnosed according to the Los Angeles (LA) Classification.^[13] Reflux esophagitis was detected in 22.9% and LES laxity was present in 17.4% of the patients. In gastric biopsy, Hp was positive in 40% of the patients. Detailed characteristics of all patients are presented in Table 1.

Comparison of Patient Groups according to LESP

The age of patients with hypertensive LESP was significantly higher ($p = 0.013$) and female gender and BMI were associated with hypertensive LES. Among the presenting complaints, pyrosis was the most common complaint in patients with hypotensive LESP (81%) and dysphagia was the most common complaint in patients with hypertensive LESP (48%). Although reflux esophagitis and LES laxity detected on endoscopy were significantly higher in patients with hypotensive LESP ($p = 0.026$ for both), no significant difference was found between the groups with regard to hiatal hernia, Schatzki ring, gastric ulcer, or duodenal ulcer. Moreover, no significant difference was found among the groups with regard to reflux and Hp positivity. A detailed comparison of LES groups is presented in Table 2.

Comparison of Hp-positive and Hp-negative Groups

No significant difference was found between Hp-positive and Hp-negative groups with regard to reflux and reflux esophagitis detected in 24-h esophageal pH monitoring.

Table 1. Demographic and clinical characteristics

Age (years)	45.4±13.4
Gender (%)	Women (54)
BMI (kg/m ²)	26.96±4.78
Presenting complaints (%)	Dysphagia (14.2) Pyrosis (85.4) Chest pain (0.4)
LES pressure on manometry (%)	Normal (57.5) Hypotensive LES (15) Hypertensive LES (27.5)
Esophagogastroduodenoscopic findings	
Esophagitis (%)	Yes (22.9) No (77.1)
Hiatal hernia (%)	Yes (14.8) No (85.2)
Schatzki ring (%)	Yes (1.6) No (98.4)
LES laxity (%)	Yes (27.4) No (72.6)
Gastric ulcer (%)	Yes (1.6) No (98.4)
Duodenal ulcer (%)	Yes (2.8) No (97.2)
24-h esophagus pH Reflux on monitoring	Yes (61.4) No (38.6)
<i>Helicobacter pylori</i> (%)	Positive (39.9) Negative (60.1)

BMI: Body mass index; LES: Low esophageal sphincter.

Patients with LES laxity were found to have significantly less Hp in biopsy (Table 3).

Discussion

In the present study, no significant relationship was found between LESP (normal, hypotensive, or hypertensive) and Hp and between LESP and reflux. Similarly, no significant relationship was found between Hp and reflux. Although no significant relationship was found between the presence of LESP changes and Hp and the development of reflux, low LES resting pressure was found to play a role in the development of reflux esophagitis.

Isolated LES motility disorder was present in 42.5% of the patients included in the study. As we mentioned in the method section, patients with pathology such as achalasia, diffuse esophageal spasm, nutcracker esophagus, non-specific esophageal motor disease were excluded in the manometer test, and only those with normal LES, hypotensive, and hypertensive LES disorders were included in the study, so the rate was determined in these three groups. Majority of these

Table 2. LESP groups

	Normal LES (n=705)	Hipotansif LES (n=339)	Hypertensive LES (n=182)	P
Demographic findings				
Age (year±SD)	45.03±13.12	44.78±13.32	48.12±14.61	0.013
Gender (n/%)				<0.001
Female	382 (54.1)	148 (43.6)	130 (71.4)	
Male	323 (45.9)	191 (56.4)	52 (28.6)	
BMI (kg/m ² ±SD)	27.19±4.72	26.28±4.54	27.31±5.31	0.009
Complaints (n/%)				
Dysphagia	26 (3.7)	62 (18.3)	87 (47.8)	
Pyrosis	679 (96.3)	276 (81.4)	92 (50.5)	
Chest pain	0 (0)	1 (0.3)	3 (1.7)	
Endoscopic findings				
Esophagitis (n/%)	80/337 (23.7)	45/168 (26.7)	14/104 (13.4)	0.026
Schatzki ring (n/%)	6/337 (1.7)	4/168 (2.4)	0/104 (0)	0.31
Hiatal hernia (n/%)	51/337 (15.1)	29/168 (17.2)	10/104 (9.6)	0.21
LES laxity (n/%)	95/337 (28.1)	54/168 (32.1)	18/104 (17.3)	0.026
Gastric ulcer (n/%)	6/337 (1.7)	1/168 (0.6)	3/104 (2.8)	0.33
Duodenal ulcer (n/%)	7/337 (2)	7/168 (4.1)	3/104 (2.8)	0.40
Reflux on 24-h pH meter (n/%)	352/579 (60.7)	127/195 (65.1)	41/73 (56.1)	0.35
<i>H. pylori</i> positivity (n/%)	64/173 (37)	30/66 (45.4)	16/37 (43.2)	0.44

BMI: Body mass index; LES: Low esophageal sphincter; LESP: Low esophageal sphincter pressure.

Table 3. Hp-positive versus Hp-negative groups

	Hp-positive (n=91)	Hp-negative (n=131)	P
Esophagitis (n/%)	19/91 (20.8)	31/131 (23.6)	0.62
LES laxity (n/%)	19/91 (20.8)	48/131 (36.6)	0.009
Hiatal hernia (n/%)	11/91 (12.1)	25/131 (19.1)	0.15
Schatzki ring (n/%)	1/91 (1.1)	2/131 (1.5)	0.78
Reflux on 24-h pH meter (n/%)	44/77 (57.1)	80/131 (61)	0.58

Hp: *Helicobacter pylori*, LES: Low esophageal sphincter.

patients (27.5%) consisted of hypertensive LES cases. We thought that we found this rate high due to the heterogeneous structure of our study group. Dysphagia was present in 47% of patients with hypertensive LES. At the same time, reflux was accompanying in the majority (56%) of patients with hypertensive LES, the presence of reflux explaining the symptoms of pyrosis rather than dysphagia in most of the patients. Perhaps this had a role in increasing LES pressure as a protective reflex. Hypertensive LES is a heterogeneous disorder, and most patients have normal esophageal function despite abnormal LES parameters. Psychological abnormalities are also thought to be related to LES pressure. In addition, many esophageal motility abnormalities, including abnormal LES pressure, were detected in examinations with a high resolution manometer on healthy volunteers. Dys-

phagia is also found in a significant proportion of patients with hypertensive LES. There is no clear data in the literature about how many of these patients who have not been described with a specific motility disorder have dysphagia.^[7,14,15] We identified dysphagia in approximately half of the patients with hypertensive LES.

It is known that the prevalence of Hp in developing countries such as our country is around 70% to 90% in adults. Factors such as geographic region, age, hygiene, and socioeconomic status have an effect on being infected with Hp.^[16] In our study, we detected Hp positivity in approximately 40% of patients. As the reason for this, we thought that some of these patients may have received Hp eradication treatment at their previous admission, as well as the fact that the study was a local study.

Some studies have shown that Hp has a protective role against reflux,^[14-18] while some others showed that there is no causal relationship between Hp infection and GER.^[19-22] A study conducted in China showed that as the prevalence of Hp decreased over time, the frequency of reflux esophagitis increased.^[23] Another study reported that Hp infection is inversely correlated with the risk and degree of reflux esophagitis and that Hp is protective against GER. In the same study, the presence of Hp infection was assessed through serum Hp immunoglobulin G (IgG) antibody positivity and GER was evaluated based on the degree of reflux esophagitis on endoscopy.^[24] A previous study accepted

Hp stool antigen test as the gold standard and reported that Hp IgG positivity had low specificity in detecting the active disease and serology could not detect the active disease.^[25] Shirota et al., in a similar way to our study, evaluated manometry findings and found that reflux esophagitis was significantly more prevalent in patients with low LESP. However, the authors noted that the prevalence of Hp was lower in patients with reflux esophagitis.^[26] In another study, no significant relationship was found between GER patients with and without Hp infection with regard to disease severity.^[27] In the present study, we evaluated the presence of LESP, which is known to affect reflux esophagitis, while investigating the relationship between Hp and reflux and we consider that performing this evaluation is of paramount importance. In addition, we found that LES laxity was significantly less prevalent in Hp-positive patients, but we did not consider it as having a clinical significance since we had already evaluated LES using manometry.

The important limitations of our study were that it had a retrospective design, belonged to a single center, and, therefore, belonged to a single geographical region, and the conditions such as Hp eradication treatment were not known.

Conclusion

In conclusion, no clear relationship was found among LES disorders, GER, and Hp. Moreover, no significant difference was found among LES disorders with regard to GER, while the presence of hypotensive LESP, rather than Hp, was found to be an important factor in the development of reflux esophagitis. Further prospective multicentric studies with larger patient series are needed to provide more substantial findings.

Disclosures

Ethics Committee Approval: The study was evaluated and approved by the local ethics committee of Ankara City Hospital and the study protocol was conducted in accordance with the principles of Declaration of Helsinki (Approval Number: 12; Date: November 27, 2019).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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