

Is there any relationship between *H. pylori* gastritis and mucosal esophagitis?

H. pylori gastriti ve mukozal özefajit arasında bir ilişki var mı?

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Abstract

Background Gastroesophageal reflux disease (GERD) and *H. Pylori* gastritis are common seen in childhood. In the literature, it was found that the incidence of *H. pylori* infection in patients with GERD was between 30-90%. Co-existence of two diseases is one of the topic and controversial issue in these days. In our study; we aimed to assess the prevalence of GERD in pediatric patients with and without *H. pylori* gastritis, and investigate whether *H. pylori* infection is a risk factor for GERD.

Methods The patients undergoing endoscopic examination in Karadeniz Technical University, Faculty of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition clinic between January 2009 - January 2019 included in the study. The data of patients were recorded from the hospital files retrospectively. The patients were divided in two groups according to whether *H. pylori* infection positive and negative. GERD frequency, indication of endoscopy and demographic characteristics were compared.

Results Among the 4337 patients (55.5% female, mean age \pm SD; 9.5 ± 4.4 years, range; 6 months-19 years), 348 patients (8%) had GERD, and 779 patients (18%) had *H. pylori* gastritis. There was no significant difference in gender between patients with *H. pylori* positive and negative ($p > 0.05$). We determined that the age of patients with *H. pylori* gastritis was older ($p = 0.000$). The prevalence of GERD in the *H. pylori* negative patients was 8.4% compared to 6.2% in the *H. pylori* positive patients [OR, 0.71 95% CI (0.52-0.98), $p = 0.030$].

Conclusions Our study showed that *H. pylori* infection had a protector role for GERD. We could not evaluate the patients reflux symptoms after *H. pylori* eradication therapy. Therefore, further prospective studies are needed.

Key words: *Helicobacter pylori*, gastroesophageal reflux disease, child

Özet

Amaç Gastroözofageal reflü hastalığı (GÖRH) ve *H. pylori* gastriti çocukluk çağında sık görülmektedir. Literatürde GÖRH olan hastalarda *H. pylori* enfeksiyonu insidansının % 30-90 arasında olduğu bildirilmiştir. İki hastalığın bir arada bulunması, günümüzde tartışılan konuların başında gelmektedir. Çalışmamızda; *H. pylori* gastriti olan ve olmayan çocuk hastalarda GÖRH prevalansını bulmayı ve *H. pylori* enfeksiyonunun GÖRH için bir risk faktörü olup olmadığını araştırmayı amaçladık.

Yöntem Çalışmaya Ocak 2009-Ocak 2019 arasında Karadeniz Teknik Üniversitesi Tıp Fakültesi Çocuk Gastroen-

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teroloji, Hepatoloji ve Beslenme kliniğinde endoskopik inceleme yapılan hastalar dahil edildi. Hastaların verileri hastane dosyalarından geriye dönük olarak kaydedildi. Hastalar *H. pylori* enfeksiyonunun pozitif ve negatif olup olmamasına göre iki gruba ayrıldı. GÖRH sıklığı, endoskopi endikasyonları ve demografik özellikler karşılaştırıldı.

Bulgular 4337 hastanın (%55.5'i kız, ortalama yaş \pm SD; 9.5 ± 4.4 yıl, yaş aralığı; 6 ay-19 yıl), 348'inde (%8) GÖRH, 779'unda (%18) *H. pylori* gastriti tespit edildi. *H. pylori* pozitif ve negatif olan hastalar arasında cinsiyet açısından anlamlı fark yoktu ($p>0.05$). *H. pylori* gastritinin daha büyük çocuklarda olduğu tespit edildi ($p=0.000$). *H. pylori* negatif hastalarda GÖRH prevalansı %8.4 iken *H. pylori* pozitif hastalarda %6.2 idi [OR, %0.71 95% CI (0.52-0.98), $p=0.030$].

Sonuç Çalışmamız *H. pylori* enfeksiyonunun GÖRH'de koruyucu bir rolü olduğunu göstermektedir. *H. pylori* eradikasyon tedavisinden sonra hastaların reflü semptomları değerlendirilememiştir. Bu nedenle ileriye dönük daha geniş spektrumlu çalışmalara ihtiyaç vardır.

Anahtar kelimeler: *Helicobacter pylori*, gastroözofajial reflü hastalığı, çocuk

Introduction

Gastroesophageal reflux (GER) is a normal physiologic condition and it may happen several times in the postprandial period for less than three minutes in healthy infants, children, and adults and does not need any treatment. However, in the presence of troublesome symptoms and/or complications such as reflux esophagitis (RE), structures, it is defined as gastroesophageal reflux disease (GERD).¹ The development of GERD is multifactorial and factors such as infectious agents, nutrition, physical development, stress, physical exertion, genetic predisposition and anatomical anomalies play role in the development of GERD.² The distinguishing GER from GERD is important for treatment decision. It is based on clinic symptoms, physical examination, endoscopy and pH impedance.³

Helicobacter pylori (*H. pylori*) infection is acquired in childhood, often before the age of five years. It is usually transmitted by fecal-oral, oral-oral or gastro-oral way.⁴

The presence of clinical symptoms or conditions such as duodenal and gastric ulcers, gastric lymphoma, atrophic gastritis with intestinal metaplasia should be treated to eradicate the bacterium.⁵ As a result of studies, it is known that *H. pylori* leads to diseases such as gastric lymphoma, lymphoid nodular hyperplasia and ulcer. However, the role of *H. pylori* infection as a potential protective or / triggering factor in the development of GERD is one of the most controversial issue. There are two opinions according to studies in literature; i) RE occurs because of increased acid secretion due to *H. pylori*, decreased esophageal sphincter pressure, a delay in gastric emptying⁶, ii) the presence of pangastritis or gastritis in the corpus leads to decreased acid secretion with consequent increase in gastrin, increased lower esophageal sphincter pressure, and this opinion explains the inverse relationship between *H. pylori* infection and GERD.⁷ In the literature, it was found that the incidence of *H. pylori* infection in patients with GERD was between 30-90%.⁸

In this study; we aimed to assess the prevalence of GERD in pediatric patients with and without *H. pylori* gastritis, and investigate whether *H. pylori* infection is a risk factor for GERD.

Methods

We included 4893 patients undergoing endoscopic examination in Karadeniz Technical University, Faculty of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition clinic from January 2009 to January 2019. The demographic characteristics, clinical, laboratory, endoscopic and histopathological findings of patients were recorded from the hospital files retrospectively.

The patients, who were not taken biopsy from esophagus, had active gastroesophageal bleeding during the examination, had neurologic disorders, used any medications for *H. pylori* eradication excluded from the study ($n=556$). The endoscopic diagnoses of GERD based on the endoscopic Los Angeles classification (different degrees of erosive esophagitis A, B, C, and D) and/or histopathologic examination (with Giemsa and H&A stain). *H. pylori* gastritis diagnosis based on histopathologic ex-

amination (with Giemsa and H&A stain). The patients were divided in two groups according to whether *H. pylori* infection positive and negative. GERD frequency, indication of endoscopy and demographic characteristics were compared. The study protocol was approved by the institutional Ethics Committee (Ethics Committee no: 2018/284). The study was conducted in accordance with the principles of the Declaration of Helsinki.

At statistical analysis, data were expressed as mean \pm standard deviation (SD) for constant variables and percentages (%) for categoric variables. At comparison of

Table 1. The demographic features, indication of endoscopy, the prevalence of GERD in patients with *H. pylori* positive and negative.

	<i>H. pylori</i> positive n=779, (%)	<i>H. pylori</i> negative n=3558, (%)	p
Gender, female, n, (%)	452 (58.2)	1933 (54.3)	0.060
Age, mean \pm SD	11.1 \pm 3.9	9.2 \pm 4.5	0.000
GERD, n,%	48 (6.2)	300 (8.4)	0.030
Indication of endoscopy			
Abdominal pain	619 (79.7)	2401 (67.4)	0.000
Vomiting	16 (2.1)	205 (5.8)	
Dyspepsia	35 (4.5)	308 (8.7)	
Growth retardation	48 (5.8)	240 (6.7)	
Chronic diarrhea	7 (0.9)	74 (2.1)	
Anemia	28 (3.6)	190 (5.3)	
Dysphagia	5 (0.6)	26 (0.7)	
GIS bleeding	18 (2.3)	94 (2.6)	
Suspect of varice	1 (0.1)	21 (0.6)	

GERD, gastroesophageal reflux disease

group measurement data, Student's t test was used for normally distributed data and the Mann Whitney U test for non-normally distributed data. The chi square test was applied in the comparison of non-measurement categoric data. p values ≤ 0.05 were regarded as significant.

Results

Among the 4337 patients (55.5% female, mean age \pm SD; 9.5 \pm 4.4 years, range; 6 months-19 years), 348 patients (8%) had GERD, and 779 patients (18%) had *H. pylori* gastritis. There was no significant difference in gender between patients with *H. pylori* positive and negative ($p > 0.05$). We determined that the age of patients with *H. pylori* gastritis was older ($p = 0.000$) (Table 1).

The most common indication for endoscopy was abdominal pain and dyspepsia (69.6% and 7.9%, respectively). Among 3020 patients with abdominal pain, 20.5% (n=619) of patients had *H. pylori* gastritis, and 6.3% (n=189) of patients had GERD ($p = 0.000$, $p = 0.000$, respectively).

The prevalence of GERD in the *H. pylori* negative patients was 8.4% compared to 6.2% in the *H. pylori* positive patients [OR, 0.71 95% CI (0.52-0.98), $p = 0.030$] (Fig. 1).

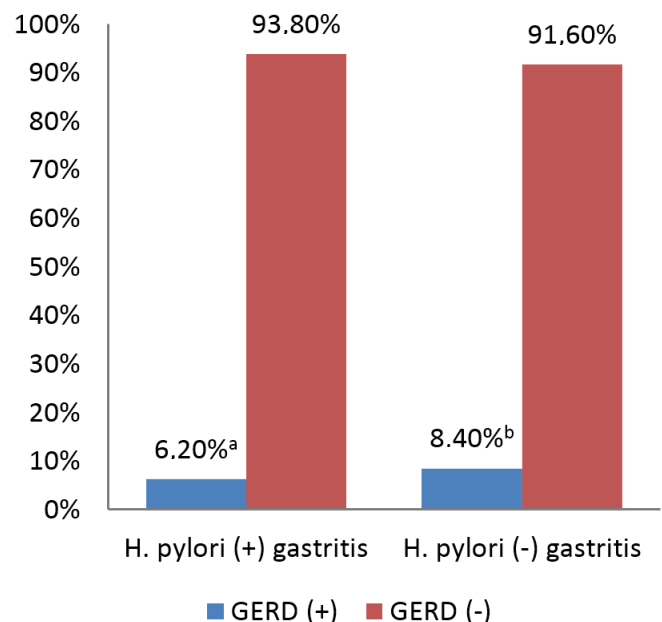


Fig. 1. The prevalence of GERD in the patients with *H. pylori* positive and *H. pylori* negative ($p^{a-b} < 0.05$).

Discussion

In our study, we found that i) *H. pylori* gastritis was more common in older children, ii) there were no significant differences for *H. pylori* gastritis between gender, iii) abdominal pain was higher in the patients with *H. pylori* gastritis, iv) there was a negative relationship between *H. pylori* and GERD.

Helicobacter pylori regulates gastric motility through gastric-regulating gastric hormones such as gastrin, ghrelin and motilin.³⁻⁵ Motilin has a prokinetic role and is secreted by gastrointestinal endocrine cells and increases LES pressure. Ghrelin is secreted by the enteroendocrine cells of gastric mucosa and gastric acid secretion, gastrointestinal motility, and gastric emptying increases due to ghrelin secretion. Gastrin is another hormone which affects gastric motility. It is secreted by antral G cells and affected by *H. pylori*. Release of these hormones may be changed with *H. pylori* infection. The serum levels of gastrin depend on localization of *H. pylori* infection. In *H. pylori* -induced corpus-limited gastritis, hypoacidity develops as a result of parietal cell destruction. Increased gastrin releasing occurs because of rebound hyperacidity after eradication therapy. On the other hand, in antrum-limited *H. pylori* infection leads to destruction of somatostatin secreting cells, hypergastrinemia and hyperacidity occur during the *H. pylori* infection.⁷ So, according to these theories, we can say that the risk of GERD increases in *H. pylori* infection. However, the acidity and therefore the risk of GER are only reduced in atrophic gastritis. Ghrelin decrease GERD by affecting LES pressure, and it has been reported that decreased ghrelin increases GERD development.⁴ Unlike these theories, Eren et al reported that there was no significant relationship between gastric-regulating hormones (motilin, ghrelin, and gastrin) and *H. pylori* infection. They suggested that *H. pylori* has not any role for development GERD.⁷

There have been controversial studies about the relationship between *H. pylori* and GERD until now. According to Nordenstedt et al; *H. pylori* has a protective role for GERD through gastric atrophy and decreased

acid.² Wu et al. reported that there were significant differences in the esophageal sphincter pressure or esophageal peristaltic function between *H. pylori* -positive and negative controls. However, they suggested that esophageal motor abnormalities developed as a result of *H. pylori* and its effects on releasing gastric-regulating gastric hormones.⁶ Additionally, some studies claim that the eradication of *H. pylori* infection leads to erosive esophagitis and GERD relapsing.^{8,9} In a study with adults study; Riberio et al found that there was significant association between *H. pylori*, GERD and gender.¹⁰ On the contrary, Moon et al analyzed 420 endoscopic examination and found positive association between *H. pylori* and GERD.¹¹ In a study on adults; Chourasia et al evaluated 123 patients with GERD and 47.9% had *H. pylori* infection. They reported that *H. pylori* caused less acidity and a decrease in reflux intensity.¹²

When the studies in the literature are examined; it is seen that *H. pylori* gastritis decreases GERD through gastritis and corpus limited gastritis. In general, atrophic gastritis is often seen in adults and is rarely seen in childhood. However in our cases, the biopsy was usually taken from the antrum and there was antral gastritis. There are not atrophic and corpus limited gastritis in our study. So, we could not explain the inverse relationship between *H. pylori* and GERD by this theory. According to another theory; *H. pylori* increases the pH of the stomach by producing ammonia through intragastric urease, and ammonia protects against to GERD¹³. So, increased the reflux symptoms after *H. pylori* eradication may be explained by this theory. In our study; *H. pylori* is protective against to GERD and we suggest that increased ammonia and gastric pH reduce the risk of development GERD. There are some limitations of our study. Firstly, it was a retrospective study. Additionally, gastric biopsies were only taken from antrum. That's why, if there was a *H. pylori* infection on the other gastric area, we could not determine.

In conclusion, our study showed that *H. pylori* infection had a protective role for GERD probably through increased ammonia and gastric pH. Since our study was retrospective, we could not evaluate the reflux symp-

toms of the patients with *H. pylori* after eradication therapy. Therefore, further prospective studies are needed.

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