

# THE ROLE OF GASTRIC LOCALIZATION AND THE GASTRITIS SCORE OF HELICOBACTER PYLORI IN THE DEVELOPMENT OF EROSIVE ESOPHAGITIS

## EROZİV ÖZOFAJİT GELİŞİMİNDE HELICOBACTER PYLORI'NİN GASTRİK LOKALİZASYONUNUN VE GASTRİT SKORUNUN ROLÜ

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### ABSTRACT

**Objective:** The interactions between Helicobacter pylori (Hp) and gastroesophageal reflux disease (GERD) are a complex issue. The aim of this study was to investigate the correlation between Hp infection and the gastric localization of Hp and reflux esophagitis (RE) in adult patients.

**Material and Method:** Two hundred thirty-nine patients with RE were compared with 229 age and sex matched participants in a control group. Biopsy specimens obtained from the gastric antrum and corpus were histologically evaluated.

**Results:** The prevalence of Hp infection was significantly lower in the patients with RE than in the control group (Odds ratio 1.56, 95% CI 1.08-2.27; p=0.02, p<0.05). Hp colonization in the corpus and gastritis scores in the corpus were significantly lower in the esophagitis group (p=0.01, p<0.05), but there was no significant difference in Hp colonization in the antrum and gastritis scores in the antrum. It was found that Hp colonization and gastritis score in the corpus showed a negative correlation with esophagitis development.

**Conclusion:** This study demonstrated that the prevalence of Hp infection and corpus gastritis score were significantly lower in patients with erosive reflux esophagitis than in the control group. Furthermore, it demonstrated that Hp colonization and corpus gastritis score were negatively correlated with esophagitis development.

**Keywords:** Helicobacter pylori, Reflux esophagitis, GERD, Corpus dominant gastritis

### ÖZET

**Amaç:** Helicobacter pylori (Hp) enfeksiyonu ve gastroözofageal reflü hastalığı (GÖRH) dünya çapında yaygın hastalıklardır. Hp ve GÖRH arasındaki etkileşim ise karmaşık bir konudur. Bu çalışmanın amacı erişkin hastalarda Hp enfeksiyonu ve Hp'nin gastrik lokalizasyonu ile reflü özofajit arasındaki ilişkiyi araştırmaktır.

**Gereç ve Yöntem:** Reflü özofajit tanılı 239 hasta, 229 yaş ve cinsiyet uyumlu kontrol grubu ile karşılaştırıldı. Gastrik antrum ve korpus elde edilen biyopsi örnekleri histolojik olarak değerlendirildi. Enflamasyon, aktivite ve Hp kolonizasyonunun ciddiyeti, 0 (hiçbiri) ile 3 (en ağır) arasında skorlandı. Enflamasyon ve aktivite skorları toplandı ve gastrit skoru olarak ifade edildi.

**Bulgular:** Hp enfeksiyonu prevalansı RE'li hastalarda kontrol grubuna göre anlamlı olarak düşüktü (olasılık oranı 1,56 %95 güven aralığı 1,08-2,27; p=0,02, p<0,05). Korpusdaki Hp kolonizasyonu özofajit grubunda anlamlı derecede düşüktü, fakat antrumda Hp kolonizasyonunda anlamlı bir fark yoktu (sırasıyla p=0,01, p<0,05 ve p=0,09, p>0,05). Korpusdaki Hp kolonizasyonu ve gastrit skorunun özofajit gelişimi ile negatif korelasyon gösterdiği, antrum ve gastrit skorundaki Hp kolonizasyonunun özofajit ile korelasyon göstermediği bulundu.

**Sonuç:** Sonuç olarak, bu çalışmada Hp enfeksiyonu ve korpus gastrit skoru sıklığının, eroziv reflü özofajit hastalarında kontrol grubuna göre anlamlı derecede düşük olduğu gösterilmiştir. Ayrıca, Hp kolonizasyonu ve korpus gastrit skorunun özofajit gelişimi ile negatif korele olduğunu göstermiştir.

**Anahtar Kelimeler:** Helicobacter pylori, Reflü özofajit, GÖRH, Korpus dominant gastrit

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## INTRODUCTION

Gastroesophageal reflux disease (GERD) is characterized by the presence of reflux symptoms caused by damage to the esophageal mucosa or abnormal backflow of gastric content into the esophagus. Although it is common in Western societies, in recent years, GERD has become more prevalent in Asian populations, which may be associated with numerous factors such as increased Western dietary habits, advanced age, male gender, obesity, increased gastric acid secretion and reduced *Helicobacter pylori* (Hp) infection (1, 2). The acidity of reflux content (ie pH<4) is a very important risk factor in the development of esophageal mucosal damage (3).

Hp is a type of bacteria that commonly colonizes the inner surface of the stomach. Hp infection is considered an important risk factor for the development of gastric and duodenal ulcers. Hp infection has also been shown to be associated with the development of chronic active gastritis, gastric atrophy, gastric metaplasia, dysplasia and gastric malignancies (ie gastric carcinoma, gastric mucosa-associated lymphoid tissue (MALT) lymphoma). There is strong evidence that eradication is important for the treatment of Hp-related diseases (4).

Both Hp infection and GERD are common diseases worldwide and the relationship between the two diseases is a very complex issue. There are various pathophysiological factors in the development of GERD and Hp infection may be only one of them. Many studies accentuate the coexistence of Hp infection and GERD. The acidity of reflux content is an important factor in the pathophysiology of reflux esophagitis (RE). Hp infection may increase or decrease acid secretion depending on the type of gastritis caused, so Hp infection can be a factor or protective factor contributing to the development of GERD. Gastritis and inflammation in the corpus cause hypoacidity, while antral gastritis and inflammation have the opposite effect. Hyperacidity caused by antral gastritis can be responsible for the development of duodenal ulcers and GERD, thus an improvement in pre-existing RE may occur after Hp elimination. Hp infection in adults usually causes corpus-associated gastritis, which may result in the development of atrophic gastritis. Atrophic gastritis may provide protection against GERD due to hypoacidity. Pangastritis is usually associated with CagA strains of Hp, causing more severe gastric inflammation. This intense inflammation may also result in gastric atrophy. In the case of Hp-positive corpus gastritis, pangastritis and atrophic gastritis in the stomach, the expectation is that RE is exacerbated if Hp is eliminated (5-12).

The aim of this study was to investigate the correlation between RE and gastric localization of Hp and the score of gastritis caused by Hp infection in adult patients.

## MATERIALS AND METHODS

The records of 3850 patients who underwent endoscopy between December 2017 and March 2019 in the endoscopy unit of territory hospital were retrospectively reviewed. Of the scanned group, there were 284 patients with RE. The inclusion criteria were established to include patients with biopsy specimens taken from the antrum and corpus. The exclusion criteria were determined as follows: those with upper gastrointestinal malignancy, gastric outlet obstruction, previous gastric surgery, hiatal hernia, and obese individuals (BMI>30). The study group was created with 239 patients with RE who met these criteria. The Los Angeles classification system was used to describe the presence and severity of GERD. RE was confirmed by endoscopy according to a 5 grade severity scale. The control group consisted of age- and sex-matched patients (226 patients) randomly selected from the non-esophagitis group who underwent endoscopy.

Ethics committee approval was received for this study from the ethics committee of our hospital.

### Histology

Biopsy specimens acquired from gastric antrum and corpus were evaluated histologically. The intensity of inflammation, activity and Hp colonization was scored from 0 (none) to 3 (severe) according to the updated Sydney system. The gastritis score was found by adding the inflammation and activation scores of the patients (13). The presence of Hp in any specimen in the biopsy reports was considered as positive.

### Statistical analysis

The results were analyzed with SPSS (version 22 SPSS, Chicago, Illinois USA) software. Descriptive statistics were used to report the prevalence of the distribution of age, sex and of endoscopic-pathological findings in the groups. The Student's t test was applied for parametric rates between the independent groups. The Chi-square test or Mann-Whitney U test was used for the statistical analysis between the endoscopic data and pathology findings. Correlation analyses were carried out for the correlation between the results. A p value of <0.05 was considered statistically significant.

## RESULTS

There were 239 patients (138 males (57.7%), 101 females (43.3%)) in the study group and 226 patients (128 males (56.6%), 98 females (43.4%)) in the control group. The mean ages in the study and control groups were 49.37 (SD±14.48 years) and 49.09 (SD±14.85 years) years, respectively. There was no statistically substantial distinction between two groups in terms of age (p=0.22, p>0.05) and gender (p=0.63, p>0.05) (Table 1).

**Table 1:** Descriptive statistics of groups.

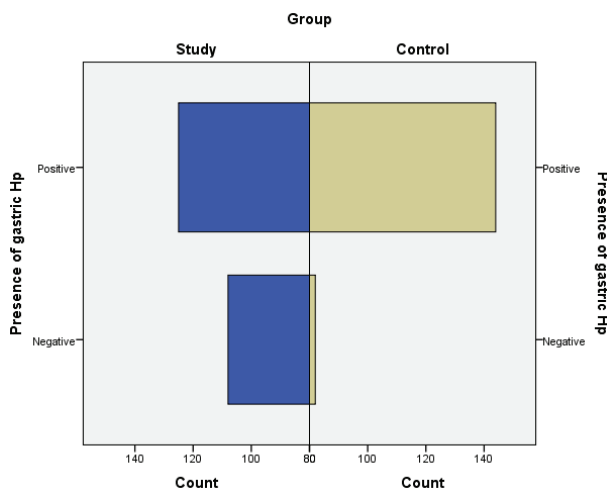
	Study group	Control group	p
n	239	226	
Age	49.37 (SD±14.48)	49.09 (SD±14.85)	(p=0.22, p>0.05)
Gender	138 Male (%57.7) 101 Female (%43.3)	128 Male (%56.6) 98 Female (%43.4)	(p=0.63, p>0.05)
H pylori (+)	131 (%54.08)	147 (%65.00)	(p=0.02, p<0.05)

In accordance with the Los Angeles classification, there were 113 patients (47.3%) with grade A RE, 117 patients (49%) with grade B RE, 6 patients (2.5%) with grade C RE and 3 patients (1.3%) with grade D RE in the RE group.

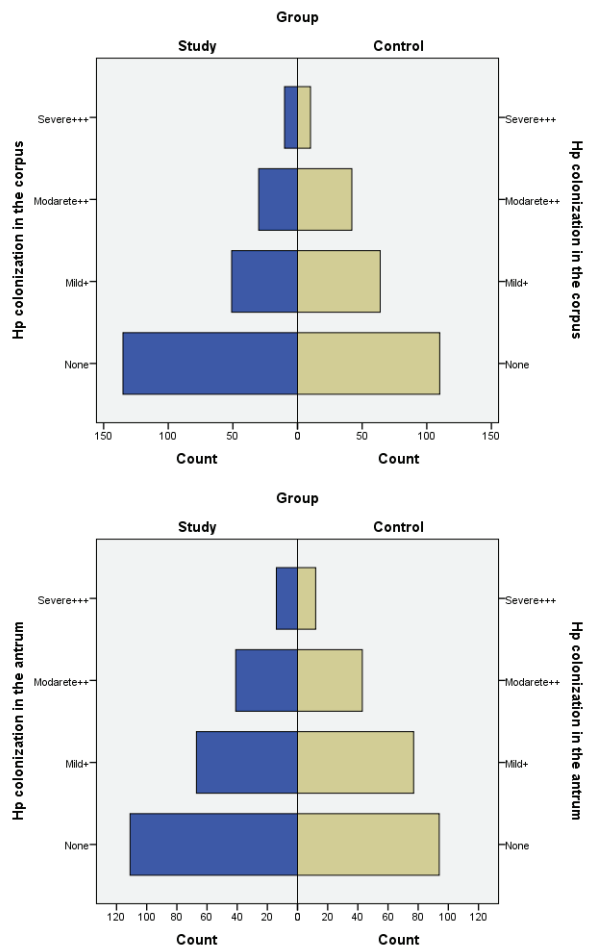
Hp infection was defined in 131 (54.80%) of 239 patients with the diagnosis of RE and in 147 (65.00%) of 226 matched subjects in the control group. The prevalence of infection was significantly lower in the patients with RE than in the control group (Odds ratio 1.56, 95% confidence interval 1.08-2.27; p=0.02, p<0.05, Chi square test) (Figure 1).

According to the Sydney classification, the groups were categorized for Hp colonization in the corpus and antrum. In the study group, Hp colonization in the corpus was as follows: None 142 patients (59.4%), mild + 54 patients (22.6%), moderate ++ 33 patients (13.8%), severe +++ 10 patients (4.2%). In the control group, it was as follows: none 106 patients (46.9%), mild + 67 patients (29.6%), moderate ++ 41 patients (18.1%), severe +++ 12 patients (5.3%). Hp colonization in the corpus was significantly different in the esophagitis group (p=0.01, p<0.05; Mann-Whitney U test). In the study group, Hp colonization in the antrum was as follows: None 111 patients (46.4%), mild + 68 patients

(28.5%), moderate ++ 45 patients (18.8%), severe +++ 15 patients (6.3%). In the control group, it was as follows: none 86 patients (38.1%), mild + 75 patients (33.2%), moderate ++ 48 patients (21.2%), severe +++ 17 patients (7.5%).



**Figure 1:** Presence of gastric Hp. The prevalence of infection was significantly lower in the patients with reflux esophagitis than in the control group (Odds ratio 1.56, 95% confidence interval 1.08-2.27; p=0.02, p<0.05, Chi square test). (Hp: Helicobacter pylori).



**Figure 2:** H pylori colonization in corpus and antrum. Hp colonization in the corpus was significantly different in the esophagitis group, but there was no significant difference in Hp colonization in the antrum (p=0.01, p<0.05 and p=0.09, p>0.05 respectively, Mann-Whitney U test). It was found that Hp colonization in the corpus showed a weak negative correlation with esophagitis development, whereas Hp colonization in the antrum was not correlated with esophagitis development ( $r_s=-0.12$ , p=0.01, p<0.05 and  $r_s=-0.54$ ; p=0.19, p>0.05 respectively, Spearman's correlation analysis).

There was no disparity between the groups in terms of Hp colonization in the antrum ( $p=0.09$ ,  $p>0.05$ ; Mann-Whitney U test).

When the correlation between esophagitis development and gastric Hp localization was investigated, it was found that HP colonization in the corpus was weakly negatively correlated with esophagitis development ( $r_s=-0.12$ ,  $p=0.01$ ,  $p<0.05$ , Spearman's correlation analysis). Whereas, it was found that Hp colonization in the antrum was not correlated with esophagitis development ( $r_s=-0.54$ ;  $p=0.19$ ,  $p>0.05$ , Spearman's correlation analysis) (Figures 2).

When the groups were compared according to corpus and antrum gastritis scores, the mean corpus gastritis score of the study group was  $1.94$  ( $SD\pm 1.24$ ); in the control group, the mean was  $2.39$  ( $SD\pm 1.23$ ). Corpus gastritis score was significantly lower in the study group ( $p=0.01$ ,  $p<0.05$ ;

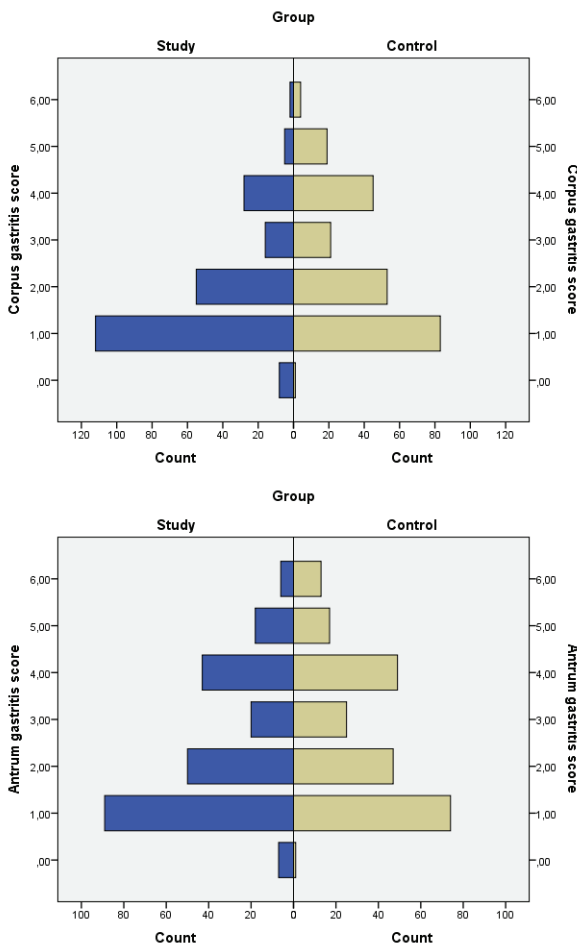
Mann-Whitney U test). Antrum gastritis scores were  $2.33$  ( $SD\pm 1.47$ ) and  $2.63$  ( $SD\pm 1.61$ ), respectively. There was no significant difference between the groups in terms of antral gastritis scores ( $p=0.17$ ,  $p>0.05$ ; Mann-Whitney U test). It was found that corpus gastritis score was negatively correlated with esophagitis development ( $r_s=-0.19$ ;  $p=0.00$ ,  $p<0.05$ , Spearman's correlation analysis). Whereas, antrum gastritis score was not correlated with esophagitis development ( $r_s=-0.86$ ;  $p=0.63$ ,  $p>0.05$ , Spearman's correlation analysis) (Figures 3).

## DISCUSSION

Hp infection and GERD are common diseases worldwide. The nature of the relationship between Hp and RE has not been fully understood. In 1997, Labenz first reported the protective role of Hp infection for GERD (7). Afterwards, some authors highlighted the interaction between these diseases involving gastric acid secretion. The acidity of reflux content is an important factor in the pathophysiology of RE and for this reason efficacious treatments are set on suppression of gastric acid secretion (3). Hp infection may contribute to GERD through the agency of diverse mechanisms. It may have both preventive and offensive roles in the incidence and severity of GERD (5-10). Hp infection has been shown to be one of the most important reasons contributing to inflammation and atrophy of the gastric corpus and as a result it has been shown to cause gastric hyposecretion (11).

In our study, we clearly showed that the prevalence of Hp infection was significantly lower in the study group compared to the age and sex matched control group (Odds ratio 1.56, 95% confidence interval 1.08-2.27;  $p=0.02$ ,  $p<0.05$ , Chi square test). When the literature is reviewed, similarly, many studies have shown that the incidence of HP is lower in GERDs, and that Hp infection may have a protective effect on GERD (9-12). In a systematic review, Raghunath et al. (8) estimated the Hp rate in patients with and without GERD and showed a lower incidence in patients with GERD. These results suggest that the elimination of Hp may increase the incidence of GERD (7). However, there are also studies reporting conflicting results in the literature, and there are some publications reporting that the eradication of Hp has a curative effect on GERD (14-18).

The features of Hp gastritis have already been studied in GERD patients. The negative correlation between the severity of corpus gastritis activity and the severity of GERD was also confirmed by our study in accordance with the study by DeKoster et al. (19). In our study, the intensity of Hp colonization in the corpus and the severity of gastritis were milder in the RE group than in the control group. Hp colonization in the corpus was found to be weakly negatively correlated with esophagitis development ( $r_s=-0.12$ ;  $p=0.01$ ,  $p<0.05$ , Spearman's correlation analysis). In addition, we found that corpus gastritis score was lower than



**Figure 3:** Corpus gastritis and antral gastritis scores in study and control groups. Corpus gastritis score was negatively correlated with esophagitis, whereas antrum gastritis score did not correlate with esophagitis ( $r_s=-0.19$ ;  $p=0.00$ ,  $p<0.05$  and  $r_s=-0.86$ ;  $p=0.63$ ,  $p>0.05$  respectively, Spearman's correlation analysis).

the study group. There was also a negative correlation with esophagitis development ( $r_s=-0.19$ ;  $p=0.00$ ,  $p<0.05$ , Spearman correlation analysis). The higher intensity of corpus gastritis in the control group suggests that Hp infection of the gastric mucosa has two possible mechanisms effective in the development and evolution of GERD: first, the exposure of esophageal mucosa to acid may be reduced and the development of erosion may be prevented by suppressing acid release in patients with reflux and severe gastritis in the corpus mucosa; secondly, continuous release of inflammatory mediator in the proximal stomach may have direct or indirect effects on the esophageal mucosa by increasing the sensitivity to acid (10, 20).

Hp infection in the antrum dominant gastritis type is characterized by hypergastrinemia and lower pH. Patients with antral gastritis have a high risk of peptic ulcer or GERD due to low pH. After the elimination of Hp infection, acid secretion will at least normalize in antral-dominant gastritis. The prospect is that the eradication of Hp in these patients should improve RE or at least not affect RE (5, 21, 22). In our study, it was found that there was no correlation between Hp colonization in the antrum and esophagitis development ( $r_s=-0.54$ ;  $p=0.19$ ,  $p>0.05$ , Spearman's correlation analysis). It was also found that the antrum gastritis score was not correlated with esophagitis development ( $r_s=-0.86$ ;  $p=0.63$ ,  $p>0.05$ , Spearman's correlation analysis). This difference may be due to the fact that the prevalence of Hp infection and the type of gastritis it causes are different in Asian and Western populations. Epidemiological studies show that the prevalence of GERD is more common in Western countries than in Asian countries (20 to 40%, 5 to 17%, respectively). According to the previous studies based on Asian population, it is reported that the prevalence of GERD is lower in patients with Hp infection and the rates of GERD-related complications are also low. The reason for this is that Hp infection is mainly located in the corpus in East Asian patients and causes inflammation here (5, 6). However, in the Far East, European and North American populations, Hp infection generally causes antral-dominant gastritis and related complications (5).

In conclusion, this study showed that the frequency of Hp infection in the corpus and corpus gastritis score was significantly lower in patients with erosive reflux esophagitis than in the control group. Furthermore, it demonstrated that Hp colonization and corpus gastritis score were negatively correlated with esophagitis development. Therefore, Hp infection in the corpus and associated gastric hyposecretion may be important to prevent the progress of RE.

**Ethics Committee Approval:** This study was approved by the Ethical Committee of Mersin City Training and Research Hospital.

**Informed Consent:** Written consent was obtained from the participants.

**Peer Review:** Externally peer-reviewed.

**Author Contributions:** Conception/Design of Study- S.Y., H.P.; Data Acquisition- S.Y., H.P.; Data Analysis/Interpretation- S.Y., H.P.; Drafting Manuscript- S.Y., H.P.; Critical Revision of Manuscript- S.Y., H.P.; Final Approval and Accountability- S.Y., H.P.; Technical or Material Support- S.Y., H.P.; Supervision- S.Y., H.P.

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