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Helicobacter pylori surveillance study in the Eastern Anatolia Region; single center

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Abstract

Aim: The prevalence of *Helicobacter pylori (H. pylori)* varies among populations as well as among the world's populations. In this study, we aimed to investigate the frequency and effects of *H. pylori* in our patients living in the Eastern Anatolia Region.

Materials and Methods: This retrospective study was conducted with 2.062 patients living in the Eastern Anatolia Region between 2021 and 2022 and applying to the endoscopy unit for gastroscopy. The demographic characteristics, gastroscopy findings, and histopathological characteristics of the materials taken during the endoscopy of our patients who applied to us for various indications were recorded in the hospital database.

Results: The average age of the patients included in our study was 45.9±16.4 years. 1.100 of these patients were women and 962 were men. 308 of the patients had gastric mucosal atrophy, 224 had intestinal metaplasia, and 1.151 were *H. pylori* positive. Of the *H. pylori*-positive patients, 214 had bulbar ulcers and 48 had stomach ulcers. Intestinal metaplasia and gastric mucosal atrophy were statistically significantly associated with the age of the patients.

Conclusion: *H. pylori* infection causes many changes in the stomach, both endoscopically and histopathologically. However, the main reason for this change is host genetics and the virulence of *H. pylori*.

Introduction

Helicobacter pylori (H. pylori) has a high prevalence worldwide. Its prevalence varies between societies. With the discovery of *H. pylori* infection in the distal gastric mucosa, histopathological changes in the gastric mucosa began to be investigated [1, 2]. *H. pylori* has been histopathologically shown in many studies to cause inflammation, atrophy, and the accumulation of lymphocyte cells, which are chronic inflammatory cells, in the gastric mucosa [3]. The development of chronic inflammation with exposure to *H. pylori* infection and the progression of inflammation to gastric cancer have been supported by many studies [4,5]. With *H. pylori* infection, epithelial atrophy and intestinal metaplasia develop in the gastric mucosa under the influence of host and bacterial virulence. This structural and glandular change in the gastric mucosa due to the effect of *H. pylori* may cause stomach cancer over time [6]. Studies have shown that this exposure from childhood increases the development of precancerous lesions in the stomach by 4 to 9 times [7-10]. The International Agency for Research on Cancer (IARC) committee declared *H. pylori* as a class I carcinogenic bacteria [11]. On the other hand, *H. pylori* infection has a predisposing effect on the development of gastric ulcers, which are the most common cause of upper gastrointestinal (GI) bleeding. Secondary gastric diseases, such as gastric mucosa-associated lymphoma, are caused by *H. pylori* [12–14]. Studies have shown that 10-20% of individuals infected with *H. pylori* develop stomach ulcers, and 1-3% develops stomach cancer [15]. Studies have also shown that the risk of stomach cancer in *H. pylori*-infected patients increases 3-6 times compared to uninfected patients [16, 17]. In this study, we aimed to histopathologically evaluate the relationship between the presence of gastric ulcers, polyps, lesions, and *H. pylori* in patients who underwent gastroscopy for various indications. We indirectly evaluated the relationship of these mucosal changes to precancerous lesions and *H. pylori* and the indirect regional effect of host and *H. pylori* virulence.

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Materials and Methods

Research ethics

Approval for this study was received from the Malatya Turgut Özal University Non-Interventional Clinical Research Ethics Committee on April 18, 2022, and decision number 2022\85. It was prepared taking into account the Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects.

Patient and study design

This retrospective study was conducted with 2062 patients living in the Eastern Anatolia Region between 2021 and 2022 and applying to the endoscopy unit for gastroscopy for various reasons. The anamnesis, demographic characteristics, endoscopic findings, and histopathological characteristics of the patients who underwent gastroscopy for various indications in our endoscopy unit were obtained from the hospital database and recorded. While patients who underwent gastroscopy and stomach biopsies were included in the study, patients who did not have a gastric biopsy and patients with stomach cancer were excluded from the study.

Endoscopic evaluation

Gastroscopy was performed by a single experienced gastroenterologist. According to the results of the gastroscopy report, patients with normal gastric mucosa, gastropathy, erosion of the gastric mucosa, gastric ulcer, and bulbar ulcer were recorded separately according to their characteristics. Patients with polyps were classified according to their location as the esophagus, proximal stomach, and distal stomach. Polyps of patients with stomach polyps were removed en bloc, and while those with benign polyps were included in the study, those with malignant polyps were not included in the study. During the endoscopy of all patients, biopsy samples were taken for histological and diagnostic purposes from the lower and upper ends of the corpus greater curvature, the lower and upper ends of the lesser curvature, the posterior and anterior parts of the antrum, and the incisura angularis. Biopsy samples were fixed in formalin and sent to the pathology laboratory.

Pathological evaluation

H. pylori and mucosal histopathological changes were determined by hematoxylin-eosin staining and Giemsa staining. Identification of *H. pylori* was made by Giemsa staining, while gastric mucosal inflammation, lymphocytic infiltration, glandular atrophy, and intestinal metaplasia were determined by hematoxylin-eosin staining by experienced pathologists.

Statistical analysis

Statistical analyses were used to analyze the findings obtained in the study using NCSS (Number Cruncher Statistical System) 2020 Statistical Software (NCSS LLC, Kaysville, Utah, USA). While evaluating the research data, mean, standard deviation, median, minimum, and maximum values were used as quantitative variables. Descriptive statistical methods such as frequency and percentage were used for qualitative variables. The suitability of the data for normal distribution was evaluated using the Shapiro-Wilks test and Box Plot graphics. Student's t-test was used in the quantitative evaluation of two normally distributed groups; the Kruskal-Wallis test was used to compare variables that did not show a normal distribution in three or more groups, and Dunn's test was used to determine the group causing the difference. Wilcoxon Signed Rank test was used for intra-group evaluation. Chi-Square test and Fisher Freeman Halton test were used to compare qualitative data. The results were evaluated within the 95% confidence interval and the significance level was accepted as $p<0.05$.

Results

The study was conducted with a total of 2.062 patients, 53.3% (n = 1.100) of whom were women and 46.7% (n = 962) of whom were men, who applied to our endoscopy unit for gastroscopy with various indications between 2021 and 2022. The ages of the patients ranged between 14 and 103, and the average age was determined to be 45.9±16.4. A statistically significant difference was found between the patients' complaints according to the presence of a bulbar

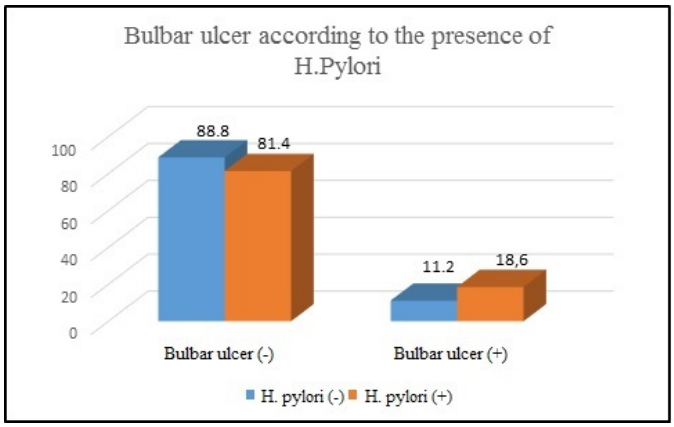

Figure 1. Distribution of the presence of bulbar ulcers by the presence of *H. Pylori*.

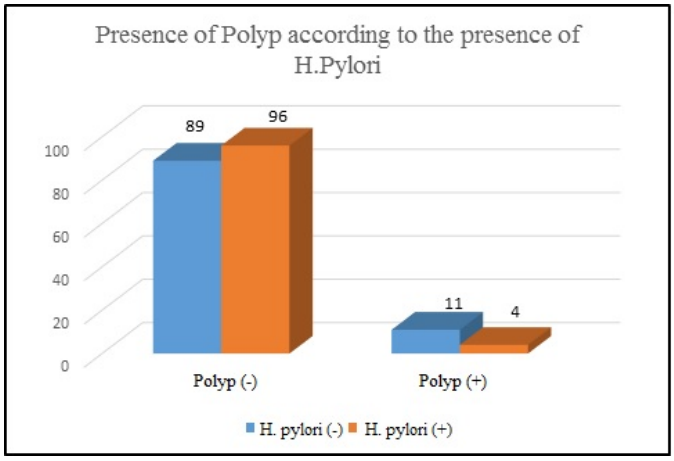

Figure 2. Distribution of polyp presence according to the presence of *H. pylori*.

Table 1. Evaluation of the relationship between *H. pylori* and gastric mucosal changes.

		H. pylori		p
		Negative	Positive	
Atrophy	None	766 (84.1)	988 (85.8)	[c]0.267
	Present	145 (15.9)	163 (14.2)	
Intestinal metaplasia	None	785 (86.2)	1053 (91.5)	[c]0.001**
	Present	126 (13.8)	98 (8.5)	
Bulbar ulcer	None	809 (88.8)	937 (81.4)	[c]0.001**
	Present	102 (11.2)	214 (18.6)	
Gastric ulcer	None	875 (96.0)	1103 (95.8)	[c]0.803
	Present	36 (4.0)	48 (4.2)	
Presence of polyps	None	811 (89.0)	1105 (96.0)	[c]0.001**
	Present	100 (11.0)	46 (4.0)	

[c]Pearson Chi-Square Test **p<0.01.

Table 2. Evaluation of atrophy and intestinal metaplasia by age.

		Age		p
		Mean±SD	Median (Min-Max)	
Atrophy	None	44.88±16.16	43 (14-103)	[d]0.001**
	Present	51.43±16.31	52 (18-90)	
Intestinal metaplasia	None	44.59±16.01	43 (14-103)	[d]0.001**
	Present	56.31±15.29	58 (21-91)	

[d]Student T Test **p<0.01.

ulcer (p=0.001; p<0.01). The presence of a bulbar ulcer was higher in patients with a history of previous ulcers and upper gastrointestinal bleeding. A statistically significant difference was found between the complaints of the patients according to the presence of stomach ulcers (p=0.001; p<0.01). While the incidence of stomach ulcers was higher in patients with a history of Barrett's esophagitis and suspected upper gastrointestinal bleeding, the incidence of stomach ulcers was lower in patients who underwent gastroscopy due to dyspepsia. A statistically significant difference was found between the patients' complaints according to the presence of polyps (p=0.001; p<0.01). While the incidence of polyps was lower in patients who underwent gastroscopy due to dyspepsia, the incidence of gastric polyps was higher in patients who underwent gastroscopy due to malignancy. Gastropathy was present endoscopically in 95.9% of the patients (n = 1.980). Normal upper GI endoscopy appearance was present in 3.8% of the patients (n = 78). There was an endoscopic appearance of eroded mucosa in 14.7% of the patients (n = 304). 15.4% of the patients had an endoscopic bulbar ulcer, and 4.1% (n = 85) had an endoscopic gastric ulcer. Polyps were present in 7.1% of the patients (n = 147). In the histopathological evaluation of gastric biopsies taken from patients for endoscopic diagnosis, atrophy was detected in 14.9% (n = 308), intestinal metaplasia in 10.9% (n = 224), and *H. pylori* in 55.8% (n = 1.151). Of the 1.151 patients who were *H. pylori* positive, 18.6% (n=214) had bulbar ulcers and 4.2% (n=48) had gastric ulcers. The incidence of intestinal metaplasia in *H. pylori*-positive patients was found to be statistically significantly lower (p=0.001; p<0.01). The incidence of bulbar ulcers in *H. pylori*-positive patients was found to be statistically significantly higher (p=0.001; p<0.01) (Figure 1). The incidence of polyps in *H. pylori*-positive patients was found to be statistically significantly lower (p=0.001; p<0.01) (Figure 2) (Table 1). The ages of those with gastric mucosal atrophy were statistically significantly higher (p=0.001; p<0.01). The ages of those with intestinal metaplasia were found to be statistically significantly higher (p=0.001; p<0.01) (Table 2).

In patients with polyps detected during endoscopy, they originated from the distal stomach in 82% (n = 123), from the proximal stomach in 10.7% (n = 16), and from the esophagus in 7.3% (n = 11). All of these polyps were benign in nature. A statistically significant difference was found between the ages of the patients according to the location of the polyps (p=0.023; p<0.05). As a result of pairwise comparisons made to determine the source of the difference, the ages of patients with polyps in the proximal stomach were statistically significantly higher than those with polyps in the distal stomach (p=0.020; p<0.05). A statistically significant difference was found between the frequency of intestinal metaplasia in patients according to the location of the polyps (p=0.010; p<0.05). The incidence of intestinal metaplasia in patients with polyps in the proximal stomach was higher than in those with polyps in the distal stomach and in those with polyps in the esophagus. The incidence of *H. pylori* and atrophy in the patients did not show a statistically significant difference according to the polyp location (p>0.05) (Table 3). In patients with polyps in the distal part of the stomach, the incidence of intestinal metaplasia was found to be statistically significantly lower compared to *H. pylori* positivity (p=0.001; p<0.01).In patients with polyps detected during endoscopy, they originated from the distal stomach in 82% (n = 123), from the proximal stomach in 10.7% (n = 16), and from the esophagus in 7.3% (n = 11). All of these polyps were benign in nature. A statistically significant difference was found between the ages of the patients according to the location of the polyps (p=0.023; p<0.05). As a result of pairwise comparisons made to determine the source of the difference, the ages of patients with polyps in the proximal stomach were statistically significantly higher than those with polyps in the distal stomach (p=0.020; p<0.05). A statistically significant difference was found between the frequency of intestinal metaplasia in patients according to the location of the polyps (p=0.010; p<0.05). The incidence of intestinal metaplasia in patients with polyps in the proximal stomach was higher than in those with polyps in the distal stomach and in those with polyps in the esophagus. The incidence of *H. pylori* and atrophy in the patients did not show a statistically significant difference according to the polyp location (p>0.05) (Table 3). In patients with polyps in the distal part of the stomach, the incidence of intestinal metaplasia was found to be statistically significantly lower compared to *H. pylori* positivity (p=0.001; p<0.01). In patients with polyps in the proximal esophagus and stom-

Table 3. Evaluations according to polyp localization.

		Polyp			p
		Esophagus	Proximal stomach	Distal stomach	
Age	Mean±SD	57.9±18.1	69.4±11.6	59.3±14.6	[a]0.023*
	Median (Min-Max)	60 (22-89)	73 (45-89)	61 (20-90)	
H. pylori	None	8 (72.7)	12 (80.0)	83 (67.5)	[b]0.693
	Present	3 (27.3)	3 (20.0)	40 (32.5)	
Atrophy	None	7 (63.6)	11 (73.3)	94 (76.4)	[b]0.576
	Present	4 (36.4)	4 (26.7)	29 (23.6)	
Intestinal metaplasia	None	8 (72.7)	5 (33.3)	90 (73.2)	[b]0.010*
	Present	3 (27.3)	10 (66.7)	33 (26.8)	

[a]Kruskal Wallis Test; [b]Fisher Freeman Halton Test *p<0.05.

Table 4. Evaluation of atrophy and intestinal metaplasia in polyps according to the presence of *H. pylori*.

Polyp		*H. pylori*		p
		Negative	Positive	
Esophagus				
Atrophy	None	4 (50.0)	3 (100)	[e]0.236
	Present	4 (50.0)	0 (0.0)	
Intestinal metaplasia	None	6 (75.0)	2 (66.7)	[e]1.000
	Present	2 (25.0)	1 (33.3)	
Proximal stomach				
Atrophy	None	8 (66.7)	3 (100)	[e]0.516
	Present	4 (33.3)	0 (0.0)	
Intestinal metaplasia	None	4 (33.3)	1 (33.3)	[e]1.000
	Present	8 (66.7)	2 (66.7)	
Distal stomach				
Atrophy	None	61 (73.5)	33 (82.5)	[c]0.270
	Present	22 (26.5)	7 (17.5)	
Intestinal metaplasia	None	53 (63.9)	37 (92.5)	[c]0.001**
	Present	30 (36.1)	3 (7.5)	

[c]Pearson Chi-Square Test; [e]Fisher's Exact Test **p<0.01.

Table 5. Evaluation of atrophy in polyps and presence of intestinal metaplasia.

Polyp		Atrophy		p
		None	Present	
Esophagus				
Intestinal metaplasia	None	5 (71.4)	3 (75.0)	[e]1.000
	Present	2 (28.6)	1 (25.0)	
Proximal stomach				
Intestinal metaplasia	None	2 (18.2)	3 (75.0)	[e]0.077
	Present	9 (81.8)	1 (25.0)	
Distal stomach				
Intestinal metaplasia	None	77 (81.9)	13 (44.8)	[c]0.001**
	Present	17 (18.1)	16 (55.2)	

[c]Pearson Chi-Square Test; [e]Fisher's Exact Test **p<0.01.

ach, the rates of atrophy and intestinal metaplasia did not show a statistically significant difference according to *H. pylori* positivity status (p>0.05) (Table 4). The incidence of intestinal metaplasia was found to be statistically significantly higher in patients with polyps and atrophy in the distal part of the stomach (p=0.001; p<0.01). In patients with polyps in the proximal esophagus and stomach, no statistically significant difference was detected between the rates of intestinal metaplasia compared to gastric atrophy (p>0.05) (Table 5).

Discussion

More than half of the world's population is infected with *H. pylori*. The prevalence of *H. pylori* infection varies between geographical regions. On the other hand, in many studies, the dominant genotype of *H. pylori* virulence factors also varies greatly between geographical regions. Studies conducted in the last 30 years have emphasized that the undefined interaction between the virulence effect of *H. pylori*, host characteristics, and the effect of environmental factors may cause oncogenic changes in the gastric mucosa [18]. Therefore, it does not mean that every patient infected with *H. pylori* will have precancerous mucosal changes. As a matter of fact, the presence of *H. pylori* could not be directly detected in advanced stomach cancer cases. On the other hand, while the presence of *H. pylori* and serological or histopathological changes were detected in early-stage gastric cancers in various studies, serological and histopathological changes caused by *H. pylori* were not detected in advanced-stage gastric cancers [11,12]. In our study, where the prevalence of *H. pylori* was evaluated in patients who underwent gastroscopy for various indications, we could not detect a positive linear relationship between *H. pylori* and the presence of intestinal metaplasia and gastric mucosal atrophy. The presence of intestinal metaplasia and gastric mucosal atrophy has been shown to be associated with an increased risk of early-stage gastric cancer in many studies. These mucosal changes were related to age rather than *H. pylori* in our study.

In studies conducted in Japan, gastroscopic findings, gas-

tric atrophy, intestinal metaplasia, and premalignant and malignant lesions of *H. pylori*-positive patients were examined, taking into account their age and gender. It is emphasized in the data obtained from these studies that *H. pylori* positivity varies between and within societies. Additionally, in terms of gender, the prevalence of *H. pylori* was determined to be lower in women than in men. Studies in Japan have found that lifestyle, ethnicity, socioeconomic factors, and age are associated with *H. pylori* prevalence [19-25]. Many studies and meta-analyses have shown that *H. pylori* infection can cause chronic gastritis, gastric glandular atrophy, gastrointestinal metaplasia, and dysplasia, and this cascade can subsequently lead to gastric cancer [26–28]. On the other hand, another meta-analysis showed that the risk of gastric cancer was reduced after the eradication of *H. pylori* [29]. It has been shown to prevent progression to gastritis, atrophy, metaplasia, and dysplastic changes, which precancerous changes are resulting from the elimination of *H. pylori*, thus preventing progression to gastric cancer.

The frequency of gastrointestinal malignancy is high in people living in the Eastern Anatolia Region. In this study, where we evaluated the prevalence of *H. pylori*, we observed that while we did not see obvious changes in the gastric mucosa due to *H. pylori*, mucosal changes were more prominent in elderly patients. We did not see any statistical significance of mucosal changes such as mucosal atrophy and intestinal metaplasia in patients infected with *H. pylori* in the local population compared to those not infected with *H. pylori*. While more than half of the local people evaluated in our study had *H. pylori* infection, premalignant changes such as gastric atrophy, intestinal metaplasia, polyps, and dysplasia were not associated with *H. pylori*. In contrast to our study, the study by Figueiredo et al. [30] evaluated a large population with chronic gastritis and stomach cancer. They showed that *H. pylori* genetic polymorphism plays an important role in gastric premalignant/malignant lesions. Both bacterial and host genotypes have been shown to cause gastric cancer development. In their research, they emphasized that *H. pylori* infection carries the risk of stomach cancer, depending on its disease-causing effect and the genetic structure of the host. They showed that the Vac A s1a/m1 strain of *H. pylori* causes intense neutrophil and lymphocyte infiltration in the gastric mucosa. In another study conducted in Japan, it was shown that there was a precancerous strain of *H. pylori* with a Cag A positive and a Vac A s1a/m1 genotype [31-33]. They argued that *H. pylori* may have a malignant gastric histopathological effect in the presence of this strain, in the presence of environmental effects, and in the influence of social ethnicity. Changes in host response to *H. pylori*; it has been shown that there may be differences in gastric ulcer, superficial gastritis, gastric erosion, erosive gastritis, diffuse gastritis, glandular atrophy, intestinal metaplasia, dysplasia, early-stage gastric cancer, depending on the patient's age, gender, socioeconomic, and sociocultural impact.

In our study, similar to the literature, bulbar ulcer was associated with *H. pylori*-infected patients, but gastric ulcer was not. While the probability of intestinal metaplasia was found to be lower in patients with *H. pylori* infection, we found that the probability of intestinal metaplasia and atrophy increased as age increased. We found that proximal stomach polyps are more common in elderly patients. All gastric polyps were hyperplastic and fundus gland polyps, and there were no precancerous polyps.

The good aspect of our study is that it reflects endoscopic and histopathological data in the stomach in the presence of *H. pylori* in a rural center in the Eastern Anatolia Region in a short period of time. The limiting features of our study are that the *H. pylori* strain has not been genetically investigated, it is dependent on a single operator, and it is a single-center study. Additionally, since we use forceps biopsy, there is a possibility of sampling error in cases of focal atrophy or intestinal metaplasia.

Conclusion

More than half of the people living in the Eastern Anatolia Region were infected with *H. pylori*. While we did not see a significant relationship between *H. pylori* and gastric mucosal changes such as intestinal metaplasia, polyps, and gastric atrophy, we detected a significant relationship between age and gastric mucosal changes. Gastric mucosal changes vary depending on many factors such as host effect, bacterial virulence, age, gender, and environmental factors.

Ethical approval

This retrospective study was approved by the Turgut Özal University Ethics Committee with the decision dated 18.04.2022 and numbered 2022\85.

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