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Original Article

Association of Gastric Pre-cancerous Lesions with *Helicobacter pylori*

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Abstract

Objective: Although the incidence of gastric cancer has decreased, it is still an important health problem worldwide. In this study, we aimed to investigate the relationship between *Helicobacter pylori* and histopathological findings of dyspepsia patients with gastric premalignant lesions, evaluated according to the Sydney classification system.

Methods: In our study, patients who applied to Atatürk University Internal Medicine and Gastroenterology outpatient clinics between 2016 and 2021, were over 18 years old, described as dyspepsia, and underwent endoscopic biopsy were evaluated retrospectively.

Results: In our study, which included a total of 500 patients, 283 (57%) of the patients were females. The mean age of the patients was 54.25 ± 15.482. The majority of patients diagnosed with *H. pylori* gastritis were women, aged < 55 years, and living in the city center. In the pathology reports examined, there were 36 patients with dense *H. pylori* cell density, 133 patients with moderate *H. pylori* cells, 231 patients with mild *H. pylori* cells, and 100 patients without *H. pylori* cells. According to endoscopic biopsy results, *H. pylori* positivity was 80%. In the pathology reports examined, a statistically significant relationship was found.

Conclusion: The role of *H. pylori* in the progression of premalignant chronic gastritis cases to gastric cancer continues to be intensively investigated today.

Keywords: Helicobacter pylori, premalign gastric lesions

INTRODUCTION

The incidence of gastric cancer has shown a decrease, but it continues to be an important health concern all over the world. Worldwide, it ranks second among cancer-related death causes. Given the factors blamed the most in the etiology of gastric cancers, pre-cancerous gastric lesions are a leading factor. In the process of progression into cancer in tissues, *Helicobacter pylori* (*H. pylori*) infection is often considered to initiate a series of transformations such as chronic gastritis, atrophy, intestinal metaplasia, dysplasia, and carcinoma.[1-4] This study has been planned as there is not a sufficient number of studies in our country analyzing and evaluating the premalignant conditions based on parameters of Sydney classification.[5]

METHODS

This study included 500 patients, aged over 18 years, who presented to Internal Diseases and Gastroenterology polyclinics of Atatürk University Hospital from 2017 to 2021, who underwent endoscopic biopsy for any reason whatsoever, and whose pathological biopsy results were evaluated, and shown to be pre-cancerous as per Sydney Classification. Demographics and pathological findings of the patients under examination have been analyzed. According to the Sydney system, they were evaluated in 4 different scoring subgroups consisting of *H. pylori*, chronic gastritis, atrophy, and intestinal metaplasia on a scale of 4 (0-1-2-3) (Table 1).

For data collection, an automated system of the Hospital of Atatürk University Medical School was used. Data were analyzed by using Statistical Package for the Social Sciences version 20.0 (IBM SPSS Corp., Armonk, NY, USA) program. General characteristics and demographics of the groups were determined by frequency analysis (descriptive analysis: frequency analysis relating to a single variable). In pairwise comparisons, the independent sample *t*-test was used for comparing the mean values of 2 independent groups and one-way unidirectional analysis of variance was used for comparing mean values of 2 or more variables under a particular factor. In multiple comparisons, post hoc Duncan analysis was used. Chi-square test was used in determining the relationship between the categorical variables. The conformity of variables to normal distribution was analyzed by a histogram graph. Throughout the study, $P \leq .05$ was accepted and considered statistically significant.

Table 1. Parameters and 4-Scale Values According to the Sydney System

1. *H. pylori*
None → 0
Mild (1-3 bacteria) → 1
Moderate (bacteria layer) → 2
Severe (bacteria clusters) →3
2. Chronic inflammation
Normal → 0
Mild →1
Moderate → 2
Severe →3
3. Atrophy
None → 0
Mild → 1
Moderate → 2
Severe → 3
4. Intestinal metaplasia
None → 0
Mild → 1
Moderate → 2
Severe → 3

This study was planned on the principles of the Helsinki Declaration, patients' rights regulations, and codes of conduct. The study commenced following the ethics committee approval with a decision no. 63, dated April 15, 2021, in the third session of the Medical Research Ethics Committee of Atatürk University Medical Faculty

RESULTS

Of 500 patients included in the study, 217 (43%) were male patients, whereas 283 (57%) were female patients. The mean age of all patients was calculated as 54.25 ± 15.48. Patients were divided into 2 groups; 1 comprising patients < 55 years and the other comprising those ≥ 55 years. Of patients included in the study, 141 were ≥55 years, whereas 359 thereof were <55 years. Age of patients <55 years was on average 46.97 ± 11.24, while the patients ≥55 years had a mean age of 72.77 ± 7.07. The mean age of male patients was 54.49 ± 15.12 and that of female patients was 53.94 ± 15.96.

Based on the pathology reports studied, the number of patients with a severe *H. pylori* cell concentration was 36, the number of those with a moderate one was 133, the number of those with a mild one was 231, and the number of those free of *H. pylori* cells was 100. According to endoscopic biopsy results, the rate of *H. pylori* positivity was 80%.

MAIN POINTS

- *Helicobacter pylori* infection is often considered to initiate a series of transformations such as chronic gastritis, atrophy, intestinal metaplasia, dysplasia, and carcinoma.
- According to endoscopic biopsy results, the rate of *H. pylori* positivity was 80%.
- The relationship between the degree of atrophy, chronic inflammation, intestinal metaplasia, and the concentration of *H. pylori* cells was statistically significant.
- Today, the role played by *H. pylori* in the progression of premalignant chronic gastritis cases to gastric cancer continues to be widely investigated.

Mean age of patients without *H. pylori* cells were 57.67± 16.52. The mean age of those with a mild concentration of *H. pylori* cells was 54.8 ± 15.05, and mean age of those with a moderate one was 51.6 ± 15.536, and the mean age of those with a severe one was 51.03 ± 13.19. There was no statistically significant relationship between the concentration of *H. pylori* cells and mean age (P=.064).

The relationship between the degree of atrophy and the concentration of *H. pylori* cells is shown in Table 2. The relationship between the degree of atrophy and the concentration of *H. pylori* cells was statistically significant (P=.002).

The relationship between the degree/level of intestinal metaplasia and the concentration of *H. pylori* cells is shown in Table 3. The relationship between the degree of intestinal metaplasia and the concentration of *H. pylori* cells was statistically significant (P=.000).

The relationship between the degree of chronic inflammation and the concentration of *H. pylori* cells is shown in Table 4. The relationship between the degree of chronic inflammation and the concentration of *H. pylori* cells was statistically significant (P=.000).

DISCUSSION

The discovery of *H. pylori* completely changed the long-held and accepted opinions of the etiology of all forms of gastritis, and the infection caused by this organism has started to appear as one of the most important causes underlying gastritis.[6] Of the pathology reports we analyzed, a significant part of gastritis cases had been diagnosed with *H. pylori* gastritis. Our findings were in line with those reported in the literature.

The association of *H.pylori* infection with the demographic characteristics of patients has been investigated in many studies. With advancing age, a significant increase has been found in the prevalence of *H. pylori.* Similar results have been outlined in another study conducted in Japan.[6,7] In a study performed in Northern Europe, it has been found that *H. pylori* prevalence peaked in individuals aged over 50.[8] When we take a look at the distribution of the patients included in our study among the age groups, unlike the studies in the literature, the majority of the patients diagnosed with *H. pylori* gastritis were individuals under the age of 55. Underlying this differentiation of our results from those presented in the literature may be differences in geographic conditions, differences in dietary habits, or differences in accessing healthcare facilities. The distribution of *H. pylori* based on sex has been analyzed in many studies. Likewise, in a meta-analysis conducted by De Martel et al[9], *H. pylori* prevalence was higher in men than in women. Results from another study carried out in Saudi Arabia were similar, as well.[10] However, another study conducted by Khoder et al[11] showed a higher *H. Pylori* prevalence in women than in men. In our study, too, female patients were making up the majority of the patients diagnosed with *H. pylori* gastritis. Cultural differences and socioeconomic differences may be effective in these differences in results.

Upon infection of an individual with *H. pylori*, cytotoxic agents are released from the gastric mucosa leading to the initiation of an inflammatory response. As the severity of *H. pylori* increases, the chronic inflammation that ensues engenders an increase in lymphocyte and plasma cells homing to lamina propria. This increase is also accompanied by an increased neutrophil activity.[12] Changes in gastric mucosa

Table 2. Relationship Between the Degree of Atrophy and *H. pylori* Concentration

		Degree of Atrophy, n (%)				
		None	Mild	Moderate	Evident	*P*
The concentration of *H. pylori* cells, n (%)	None	65 (65.0)	22 (22.0)	8 (8.0)	5 (5.0)	***.002****
	Mild	195 (84.4)	21 (9.1)	12 (5.2)	3 (1.3)	
	Moderate	114 (85.7)	12 (9.0)	5 (3.8)	2 (1.5)	
	Severe	33 (91.7)	3 (8.3)	0 (0.0)	0 (0.0)	

**P* < .05 is considered significant for statistical analyses.

Table 3. Association Between Intestinal Metaplasia Level and *H. pylori* Concentration

		Degree of Intestinal Metaplasia, n (%)				
		None	Mild	Moderate	Evident	*P*
The concentration of *H. pylori* cells, n (%)	None	51 (51.0)	21 (21.0)	22 (22.0)	6 (6.0)	***0.000****
	Mild	175 (75.8)	26 (11.3)	17 (7.4)	13 (5.6)	
	Moderate	105 (78.9)	13 (9.8)	11 (8.3)	4 (3.0)	
	Severe	27 (75.0)	6 (16.7)	3 (8.3)	0 (0.0)	

**P* < .05 is considered significant for statistical analyses.

Table 4. The Relationship Between the Degree of Chronic Inflammation and the Concentration of *H. pylori* Cells

		Degree of Chronic Inflammation, n (%)				
		Normal	Mild	Moderate	Evident	*P*
The concentration of *H. pylori* cells, n (%)	None	0 (0.0)	35 (35.0)	56 (56.0)	9 (9.0)	***.000****
	Mild	3 (1.3)	64 (27.7)	108 (46.8)	56 (24.2)	
	Moderate	0 (0.0)	8 (6.0)	69 (51.9)	56 (42.1)	
	Severe	0 (0.0)	5 (13.9)	14 (38.9)	17 (47.2)	

**P* < .05 is considered significant for statistical analyses.

occurring as a result of an inflammatory process becoming chronic may progress to cancerous lesions. This process has been defined as Correa's cascade. At the initial steps of the cascade, mostly a chronic mucosal infection caused by environmental factors (*H. pylori* infection, high salt intake, smoking, etc.) takes place, which is followed by parietal cell loss and multifocal glandular atrophy. Atrophy progresses more and more over time, and goblet cells with mucin come about in gastric mucosa and intestinal-type epithelium develops (intestinal metaplasia). In the next step of the cascade, a neoplastic cell phenotype characterized by dysplasia occurs. Finally, invasive carcinomas develop when neoplastic cells go beyond lamina propria. It has been suggested that *H. pylori* is one of the most important factors in etiopathogenesis within Correa's cascade processes.[13] Indeed, many studies have set forth that there is a positive correlation between *H. pylori* concentration with chronic inflammation, intestinal metaplasia, and atrophy. Ohkuma et al investigated the association between *H. pylori* infection and degree of gastritis, atrophy, and intestinal metaplasia and found a direct relationship between *H. pylori* infection and degree of gastritis. They determined that atrophy and intestinal metaplasia increased as a result of *H. pylori* infection.[14] A study in Japan found that there was a statistically significant association between *H. pylori* cell concentration and degree of atrophy and intestinal metaplasia.[15] In another study, Sipponen et al[16] also determined a positive correlation between *H. pylori* and inflammation levels. In yet another study, Grgov et al[17] found a negative correlation between *H. pylori* cell density and frequency of atrophy and intestinal metaplasia. They found a positive correlation between *H. pylori* cell density and degree of inflammation. In our study, there was a statistically significant association between *H. pylori* density and chronic inflammation. Again, similarly, there was a statistically significant association of the degree of intestinal metaplasia and atrophy with the concentration of *H. pylori* cells.

Due to the nature and characteristics of our study, incidence and prevalence values to be applied to the generality of the society cannot be calculated. Furthermore, our study has provided information regarding the relationship between the parameters of the Sydney system and demographics such as age, sex, etc. The fact that it is one of the very few studies performed on this subject in Erzurum and its surrounding area is a strong aspect of our study. As it was a retrospective study and there were limited data available, patients' demographic characteristics, habits, and socioeconomic properties could not be assessed in detail. It was unknown whether the patients included in our study were on treatment or not. Therefore, no pre- and post-treatment evaluation could be made. This has been considered our study's limitation.

Today, the role played by *H. pylori* in the progression of premalignant chronic gastritis cases to gastric cancer continues to be widely investigated. We believe that studies with a larger sample size and also including a control group of healthy volunteers shall provide more valuable results. A sufficient number of studies might furnish more significant and relevant results regarding the epidemiology of pre-cancerous lesions in our country.

Ethics Committee Approval: Ethical committee approval was received from Medical Research Ethics Committee of Ataturk University Medical Faculty (Date: April 15, 2021, Decision No: 3/63).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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REFERENCES

1. Kyrlagkitsis I, Karamanolis DG. Premalignant lesions and conditions for gastric adenocarcinoma: diagnosis, management, and surveillance guidelines. *Hepatogastroenterology*. 2003;50(50):592-600.
2. Nai GA, Parizi ACG, Barbosa RL. Association between Helicobacter pylori concentration and the combining frequency of histopathological findings in gastric biopsies specimens. *Arq Gastroenterol*. 2007;44(3):240-243. [CrossRef]
3. El-Zimaity HM. Gastric atrophy, diagnosing, and staging. *World J Gastroenterol*. 2006;12(36):5757-5762. [CrossRef]
4. Almouradi T, Hiatt T, Attar B. Gastric intestinal metaplasia in an underserved population in the USA: prevalence, epidemiologic and clinical features. *Gastroenterol Res Pract*. 2013;2013:856256. [CrossRef]
5. Dixon MF, Genta RM, Yardley JH, Correa P. Classification and grading of gastritis: the updated Sydney system. *Am J Surg Pathol*. 1996;20(10):1161-1181. [CrossRef]
6. Greenberg RE, Bank S. The prevalence of Helicobacter pylori in non-ulcer dyspepsia: importance of stratification according to age. *Arch Intern Med*. 1990;150(10):2053-2055.
7. Inoue M. Changing epidemiology of Helicobacter pylori in Japan. *Gastric Cancer*. 2017;20(Suppl 1):3-7. [CrossRef]
8. Roberts SE, Morrison-Rees S, Samuel DG, Thorne K, Akbari A, Williams JG. Review article: the prevalence of Helicobacter pylori and the incidence of gastric cancer across Europe. *Aliment Pharmacol Ther*. 2016;43(3):334-345. [CrossRef]
9. De Martel C, Parsonnet J. Helicobacter pylori infection and gender: a meta-analysis of population-based prevalence surveys. *Dig Dis Sci*. 2006;51(12):2292-2301. [CrossRef]
10. Khan AR. An age-and gender-specific analysis of H. pylori infection. *Ann Saudi Med*. 1998;18(1):6-8. [CrossRef]
11. Khoder G, Muhammad JS, Mahmoud I, Soliman SSM, Burucoa C. Prevalence of Helicobacter pylori and its associated factors among healthy asymptomatic residents in the United Arab Emirates. *Pathogens*. 2019;8(2):44. [CrossRef]
12. Clyne M, Labigne A, Drumm B. Helicobacter pylori requires an acidic environment to survive in the presence of urea. *Infect Immun*. 1995;63(5):1669-1673. [CrossRef]
13. Correa P, Piazuelo MB. The gastric precancerous cascade. *J Dig Dis*. 2012;13(1):2-9. [CrossRef]
14. Ohkuma K, Okada M, Murayama H, et al. Association of Helicobacter pylori infection with atrophic gastritis and intestinal metaplasia. *J Gastroenterol Hepatol*. 2000;15(10):1105-1112. [CrossRef]
15. Asaka M, Sugiyama T, Nobuta A, Kato M, Takeda H, Graham DY. Atrophic gastritis and intestinal metaplasia in Japan: results of a large multicenter study. *Helicobacter*. 2001;6(4):294-299. [CrossRef]
16. Sipponen P, Stolte M. Clinical impact of routine biopsies of the gastric antrum and body. *Endoscopy*. 1997;29(7):671-678. [CrossRef]
17. Grgov S, Stefanovic M, Katic V. The relationship between the density of Helicobacter pylori colonization and the degree of gastritis severity. *Arch Gastroenterohepatol*. 2002;21(3/4):66-72.