The Relationship Between Hyperplastic Gastric Polyps And Helicobacter Pylori

ABSTRACT

Objective: Helicobacter pylori (H. pylori) is a gram-negative bacterium. It is urease positive, mobile, microaerophilic, and spiral-shaped, and it settles in the stomach and the proximal duodenum. It is associated with chronic gastritis, stomach ulcers, duodenal ulcers, stomach cancer, and MALT lymphoma. It can also cause premalignant lesions, such as metaplasia and gastric atrophy. Although several studies are investigating the correlation between H. pylori and hyperplastic polyps (HPs) of the stomach, uncertainty in this regard continues.

Methods: Data from 5378 patients who underwent esophagogastroduodenoscopy at the Department of Gastroenterology, Gülhane Training and Research Hospital, University Of Health Sciences between October 2016 and March 2019 were retrospectively analyzed, and patients with gastric polyps were evaluated for polyp pathologies and normal mucosa biopsies.

Results: Sixty-one stomach polyps were detected in 49 patients after the retrospective analysis of the data between October 2016 and March 2019. Of the polyps found, 36 were hyperplastic (73%). There was no statistically significant difference between HPs and the presence of H. pylori, age, gender, anatomical location of polyps in the stomach, size, number, presence of metaplasia, or atrophy. The mean age was statistically lower in H. pylori-positive cases.

Conclusions: No correlation was observed between HPs and the presence of H. pylori. There is a need for more extensive, multi-centered, and prospective studies evaluating the relationship between HPs and H. pylori.

Keywords: Helicobacter Pylori, Hyperplastic, Stomach, Polyp

Hiperplastik Mide Polipleri İle Helikobakter Pilori Arasındaki İlişki

ÖZET

Amaç: Helikobakter pilori (H. pilori), gram-negatif bakteridir. Üreaz pozitif, hareketli, mikroaerofilik, spiral şekilli olup mide ve proksimal duodenuma yerleşmektedir. Kronik gastrit, mide ülseri, duodenum ülseri, mide kanseri ve MALT Lenfoma gibi hastalıklarla ilişkilidir. Ayrıca metaplasi, gastrik atrofi gibi premalign lezyonlara neden olabilir. H. pilori ile midenin hiperplastik polipleri (HP) arasındaki ilişkiyi araştırılmış olmasının rağmen bu konudaki belirsizlik sürmektedir.

Gerek ve Yöntem: Sağlık Bilimleri Üniversitesi Gülhane Eğitim ve Araştırma Hastanesi Gastroenteroloji Kliniği Endoskopi Ünitesinde Ekim 2016 - Mart 2019 tarihleri arasında özofagogastroduodenoskopi yapılan 5378 hastanın verilerini retrospektif olarak analiz edildi ve mide polipi saptanılan olguların polip patolojilerini ve normal mukoza biyopsileri değerlendirildi.

Bulgular: Ekim 2016 - Mart 2019 arasında verilerin retrospektif taramasında 49 hastada 61 adet mide polipi saptandı. Poliplerin 36’ı (%73) hiperplastik polipti. HP ile H. pilori varlığı, yaş, cinsiyet, polibin midedeki anatominik lokalizasyonu, boyutu, sayısı, metaplasi ve atrofi varlığı açısından istatistiksel olarak anlamı fark gözlemedi. H. pilori pozitif olgularda ortalama yaş ise istatistiksel olarak anlamı şekilde daha düşük bulundu.

Sonuç: Sonuç olarak; hiperplastik polipler ile H. pilori varlığı arasında korelasyon gözlememidi. HP ile H. pilori arasındaki ilişkiyi değerlendiriren daha büyük sayıda, çok merkezli, propektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Helikobakter Pilori, Hiperplastik, Mide, Polip
INTRODUCTION
Marshall and Warren discovered the Helicobacter pylori (H. pylori) bacterium in 1983 (1). It is a gram-negative and urease positive, microaerophilic, spiral-shaped, and motile bacterium localized in the stomach and proximal duodenum (1–3).

The prevalence and incidence of H. pylori vary depending on age and the socioeconomic levels of countries. In developing countries, the frequency varies according to age, with 5% of patients between the ages of 0–5, 25% in their 30s, and around 50% aged 60 and over. The prevalence, which varies between 60–85% in developing countries, has declined to 10–30% in developed countries (4). The frequency of H. pylori is around 80% in Turkey (5).

H. pylori have been found to cause various diseases, such as chronic gastritis, peptic ulcers, peptic ulcer-related complications (gastrointestinal bleeding, perforation, gastric outlet obstruction), gastric cancer, and MALT lymphoma (6–10). It also causes precancerous cellular changes, such as metaplasia and atrophy in the gastric mucosa (11, 12). H. pylori's relationship and coexistence with hyperplastic polyp (HP) formation, which is the most common gastric polyp and considered one of the premalignant lesions of the stomach despite its low probability, is not fully known.

We believe this study will help answer whether the polyps can regress with eradication treatment in the presence of the HP and H. pylori relationship or whether there will be recurrence after a polypectomy.

MATERIAL AND METHODS
Study Design: This is a retrospective study evaluating data collected from patients who underwent esophagogastroduodenoscopy. The data were kept in the electronic database of the endoscopy unit and hospital information system at the University of Health Sciences Gülhane Training and Research Hospital Gastroenterology Clinic from October 2016–March 2019. An Olympus video gastroscope (Olympus GIF-Q150, Olympus Corporation; Tokyo, Japan) was used for all procedures.

The pathology of the polyp and the presence of H. pylori, metaplasia, and atrophy in the biopsies obtained from normal mucosa were recorded in the data form. Also, the patients' ages and genders and the anatomical locations, sizes, and number of polyps were recorded. After the esophagogastroduodenoscopy procedure reports issued between October 2016 and March 2019 were reviewed, the data was recorded in the follow-up form, and the relationships between them were evaluated.

This study was approved by the local ethics committee (Ethics Committee Decision Number: 2019/19/122).

Statistical Analysis: Statistical Package for Social Sciences version 22 was used to evaluate the data obtained from the study. Continuous variables (quantitative variables) obtained by measurement were presented as a mean and standard deviation, and median and interquartile width, where necessary. Categorical variables (qualitative variables) were presented as frequency and percentage values. The Chi-square test and Fisher's exact test were used for statistical evaluation of the categorical variables. The quantitative variables used in the study were analyzed in terms of their conformity to a normal distribution using the Kolmogorov–Smirnov or Shapiro–Wilk test. In the statistical evaluation of intergroup differences in terms of the variable/variables of interest, one-way analysis of variance, and Tukey multiple comparison tests were used for normally distributed variables.

In contrast, the Kruskal–Wallis variance analysis and Bonferroni-corrected Mann–Whitney U tests were used for non-normally distributed variables. Correlations between normally distributed continuous variables were analyzed using the Pearson correlation analysis, while non-normally distributed variables were analyzed using the Spearman correlation analysis. The level of significance was set at p < 0.05 in all statistical analyses.

RESULTS
In the retrospective analysis, 61 gastric polyps were detected in 49 patients. Among these polyps, HPs were the most frequent, with 36 cases (73%). H. pylori's positivity rate is 30.6% in all patients. In cases with a polyp size ≥8 mm, H. pylori's positivity was significantly higher (p = 0.034). H. pylori's positivity was not correlated with age, gender, location, size, number of polyps, or the presence of metaplasia and atrophy (Tables 1 and 2). In the HP subgroup, H. pylori's positivity rate is 30.6%. H. pylori's positivity was not correlated with gender, location, size, or number of polyps in the stomach, nor the presence of metaplasia and atrophy. However, the mean age was statistically significantly lower in cases positive for H. pylori (p = 0.032) (Tables 3 and 4).
Table 1. Correlation between gastric polyp and H. pylori (gender, location, size, number, pathology, the presence of atrophy and metaplasia) (n:49)

| Variables         | H. pylori positive (n:13) | H. pylori negative (n:36) | P value |
|-------------------|---------------------------|---------------------------|---------|
|                   | N (%)                     | n (%)                     |         |
| Gender            |                           |                           |         |
| Female            | 8 (21.1)                  | 30 (78.9)                 | 0.106   |
| Male              | 5 (45.5)                  | 6 (54.5)                  |         |
| Corpus            | 7 (35.0)                  | 13 (65.0)                 |         |
| Location          |                           |                           |         |
| Cardia            | -                         | 2 (100.0)                 |         |
| Fundus            | 1 (25.0)                  | 3 (75.0)                  |         |
| Antrum            | 5 (21.7)                  | 18 (78.3)                 |         |
| Size              |                           |                           | 0.034   |
| >8 mm             | 7 (46.7)                  | 8 (53.3)                  |         |
| 1-8 mm            | 6 (17.6)                  | 28 (82.4)                 |         |
| Number            |                           |                           |         |
| Multiple          | 4 (36.4)                  | 7 (63.6)                  | 0.402   |
| Single            | 9 (23.7)                  | 29 (76.3)                 |         |
| Pathology         |                           |                           | 0.288   |
| Hyperplastic      | 11 (30.6)                 | 25 (69.4)                 |         |
| Other             | 2 (15.4)                  | 11 (84.6)                 |         |
| Atrophy           |                           |                           |         |
| Yes               | 3 (27.3)                  | 8 (72.7)                  | 0.950   |
| No                | 10 (26.3)                 | 28 (73.7)                 |         |
| Metaplasia        |                           |                           | 0.729   |
| Yes               | 4 (23.5)                  | 13 (76.5)                 |         |
| No                | 9 (28.1)                  | 23 (71.9)                 |         |

Table 2. Correlation between gastric polyp and H. pylori (age and size) (n: 49)

| Variables | H. pylori positive (n:13) | H. pylori negative (n:36) | P value |
|-----------|---------------------------|---------------------------|---------|
|           | Mean                      | SD                        | Mean    | SD     |         |
| Age (years) | 57.2                     | 7.2                       | 61.1    | 13.9   | 0.344   |
| Size (mm)  | 11.1                      | 7.3                       | 6.3     | 3.6    | 0.009   |

SD, standard deviation

Table 3. Correlation between hyperplastic gastric polyp and H. pylori (gender, location, size, number, the presence of atrophy and metaplasia) (n:36)

| Variables         | H. pylori positive (n:11) | H. pylori negative (n:25) | P value |
|-------------------|---------------------------|---------------------------|---------|
|                   | N (%)                     | n (%)                     |         |
| Gender            |                           |                           |         |
| Female            | 7 (25.9)                  | 20 (74.1)                 | 0.409   |
| Male              | 4 (44.4)                  | 5 (55.6)                  |         |
| Location          |                           |                           |         |
| Corpus            | 6 (50.0)                  | 6 (50.0)                  |         |
| Antrum            | 5 (22.7)                  | 17 (77.3)                 |         |
| Cardia            | -                         | 1 (100.0)                 |         |
| Fundus            | -                         | 1 (100.0)                 |         |
| Size              |                           |                           |         |
| >8 mm             | 6 (50.0)                  | 6 (50.0)                  | 0.124   |
| 1-8 mm            | 5 (20.8)                  | 19 (79.2)                 |         |
| Number            |                           |                           |         |
| Multiple          | 3 (60.0)                  | 2 (40.0)                  | 0.154   |
| Single            | 8 (25.8)                  | 23 (74.2)                 |         |
| Atrophy           |                           |                           |         |
| Yes               | 3 (37.5)                  | 5 (62.5)                  | 0.678   |
| No                | 8 (28.6)                  | 20 (71.4)                 |         |
| Metaplasia        |                           |                           |         |
| Yes               | 4 (40.0)                  | 6 (60.0)                  | 0.454   |
| No                | 7 (26.9)                  | 19 (73.1)                 |         |
In conclusion, no correlation was found between the HPs and the positivity of H. pylori, according to this result, it can be concluded that H. pylori play a role in the growth of polyps. Gao et al. found that H. pylori's positivity rate is 31.7% in the patients with gastric polyps (16). In the recent studies, H. pylori's positivity rates in the HPs are similar with the present study. Yu et al. and Hu et al. found that H. pylori's positivity rates are 22.7% and 36.4%, respectively (17,18). Also, the study of Nam et al. showed that H. pylori's eradication caused regression in HPs (19).

Considering the correlation of H. pylori with parameters such as age, gender, location, size, the number of polyps in the stomach, and the presence of metaplasia and atrophy in the HPs, the positivity of H. pylori was not correlated with the location, size, and the number of HPs or the presence of metaplasia and atrophy. The mean age was found lower only in cases positive for H. pylori, statistically. Rather than associating this result with HPs, the opinion of the researcher is that H. pylori are related to age distribution. In the literature, the findings on this subject are contradictory. The study by Horward and Pai (20) found no correlation between H. pylori and the location, number, size of HPs, and the presence of intestinal metaplasia; however, studies are reporting a correlation between HPs and H. pylori (21-23).

Our study has some limitations. This is a retrospective study with a small sample size. Furthermore, there is no long-term follow-up of the polyps. There is a need for more extensive, multi-centered, and prospective studies evaluating the correlation between HPs and the positivity of H. pylori, as well as the long-term response of polyps to the eradication therapy.

In conclusion, no correlation was found between the HPs and the positivity of H. pylori.

**Table 4.** Correlation between hyperplastic gastric polyp and H. pylori (age and size) (n: 36)

| Variables | H. pylori positive (n:11) | H. pylori negative (n:25) | P value |
|-----------|---------------------------|---------------------------|---------|
| Age (years) | Mean | SD | Mean | SD | 0.032 |
| 58.6 | 6.9 | 63.9 | 12.9 |
| Size (mm) | Mean | SD | Mean | SD | 0.061 |
| 11.4 | 7.9 | 7.0 | 3.9 |

SD, standard deviation

**DISCUSSION**

In the HP subgroup, the positivity of H. pylori was not correlated with gender, location, size, or the number of polyps in the stomach, nor the presence of metaplasia and atrophy; however, the positivity of H. pylori was significantly higher in cases with a polyp size >8 mm.

The incidence of polyps, one of the stomach's premalignant lesions, ranges from 0.6 to 6% (13, 14). Fundic gland polyps are more common in areas where the prevalence of H. pylori is low. In contrast, HPs are more prevalent in areas where the infection of H. pylori is more common (14, 15). However, the role of H. pylori in the formation of HPs is not fully known.

This study detected 49 cases of gastric polyps. Considering the correlation of H. pylori with parameters such as age, gender, location, size, number, pathology of the polyp, and the presence of metaplasia and atrophy, no difference was found in terms of age and gender. No difference was found in the non-polypoid gastric mucosa in terms of precancerous lesions, such as metaplasia and atrophy, in which H. pylori demonstrated a role in the etiology. A positive correlation was observed between the size of polyps and HPs. The positivity of H. pylori was significantly higher in the cases with polyp sizes greater than 8 mm. Although there is no correlation between the presence of polyp and H. pylori positivity, according to this result, it can be concluded that H. pylori play a role in the growth of polyps. Gao et al. found that H. pylori's positivity rate is 31.7% in the patients with gastric polyps (16). In the recent studies, H. pylori's positivity rates in the HPs are similar with the present study. Yu et al. and Hu et al. found that H. pylori's positivity rates are 22.7% and 36.4%, respectively (17,18). Also, the study of Nam et al. showed that H. pylori's eradication caused regression in HPs (19).

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In conclusion, no correlation was found between the HPs and the positivity of H. pylori.

**REFERENCES**

1. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet 1984;1:1311-5.
2. Suerbaum S, Michetti P. Helicobacter pylori infection. N Engl J Med 2002;347:1175-86.
3. Oluwasola AO, Ola SO, Saliu L, Solanke TF. Helicobacter pylori infection in South Nigerians: a serological study of dyspeptic patients and healthy individuals. West Afr J Med 2002;21:138-41.
4. Singh M, Prasad KN, Yachha SK, Saxena A, Krishnani N. Helicobacter pylori infection in children: prevalence, diagnosis and treatment outcome. Trans R Soc Trop Med Hyg 2006;100:227-33.
5. Ozaydin N, Turkyilmaz SA, Cali S. Prevalence and risk factors of Helicobacter pylori infection in Turkey: a nationally-representative, cross-sectional, screening with the 13C-Urea breath test. BMC Public Health 2013;13:1215.
6. Peterson WL. Helicobacter pylori and peptic ulcer disease. N Engl J Med 1991;324:1043-8.
7. Peterson WL. Review article: Helicobacter pylori gastritis and peptic adenocarcinoma. Aliment Pharmacol Ther 2002;16:40-6.
8. Parsonnet J, Friedman GD, Vandersteen DP, Chang Y, Vogelman JH, Orentreich N, et al. Helicobacter pylori infection and the risk of gastric carcinoma. N Engl J Med 1991;325:1127-31.
9. Hansson LE, Engstrand L, Nyren O, Evans DJ Jr, Lindgren A, Bergström R, et al. Helicobacter pylori infection: independent risk indicator of gastric adenocarcinoma. Gastroenterology 1993;105:1098-103.
10. Kimura N, Ariga M, Icatlo FC Jr, Kuroki M, Ohsugi M, Ikemori Y, et al. A euthymic hairless mouse model of Helicobacter pylori colonization and adherence to gastric epithelial cells in vivo. Clin Diagn Lab Immunol 1998;5:578-82.
11. Rugge M, Capelle LG, Cappellessa R, Nitti D, Kuipers EJ. Precancerous lesions in the stomach: from biology to clinical patient management. Best Pract Res Clin Gastroenterol 2013;27:205-23.
12. de Vries AC, van Grieken NC, Looman CW, Casparie MK, de Vries E, Meijer GA et al. Gastric cancer risk in patients with premalignant gastric lesions: a nationwide cohort study in the Netherlands. Gastroenterology 2008;134:945-52.
13. Morais DJ, Yamanaka A, Zeitune JM, Andreollo NA. Gastric polyps: a retrospective analysis of 26,000 digestive endoscopies. Arq Gastroenterol 2007;44:14-7.
14. Carmack SW, Genta RM, Schuler CM, Saboorian MH. The current spectrum of gastric polyps: a 1-year national study of over 120,000 patients. Am J Gastroenterol 2009;104:1524-32.
15. Gencosmanoglu R, Sen-Oran E, Kurtkaya-Yapicier O, Avsar E, Sav A, Tozun N. Gastric polypoid lesions: analysis of 150 endoscopic polypectomy specimens from 91 patients. World J Gastroenterol 2003;9:2236-9.
16. Gao W, Huang Y, Lu S, Li C. The clinicopathological characteristics of gastric polyps and the relationship between fundic gland polyps, Helicobacter pylori infection, and proton pump inhibitors. Ann Palliat Med 2021;10(2):2108-2114. doi: 10.21037/apm-21-39.
17. Yu X, Wang Z, Wang L, Meng X, Zhou C, Xin Y, Sun W, Dong Q. Gastric hyperplastic polyps inversely associated with current Helicobacter pylori infection. Exp Ther Med. 2020 Apr;19(4):3143-3149. doi: 10.3892/etm.2020.8567. Epub 2020 Feb 27.
18. Hu H, Zhang Q, Chen G, Pritchard DM, Zhang S. Risk factors and clinical correlates of neoplastic transformation in gastric hyperplastic polyps in Chinese patients. Sci Rep. 2020 Feb 13;10(1):2582. doi: 10.1038/s41598-020-58900-z. [Epub ahead of print]
19. Nam SY, Lee SW, Jeon SW, Kwon YH, Lee HS. Helicobacter pylori Eradication Regressed Gastric Hyperplastic Polyp: A Randomized Controlled Trial. Dig Dis Sci 2020 doi: 10.1007/s10620-020-06065-0. [Epub ahead of print]
20. Horvath B, Pai RK. Prevalence of Helicobacter pylori in Gastric Hyperplastic Polyps. Int J Surg Pathol 2016;24:704-8.
21. Elhanafi S, Saadi M, Lou W, Mallawaarachchi I, Dwivedi A, Zuckerman M et al. Gastric polyps: Association with Helicobacter pylori status and the pathology of the surrounding mucosa, a cross sectional study. World J Gastrointest Endosc 2015;7:995-1002.
22. Ljubicić N, Banić M, Kujundžić M, Antić Z, Vrkljan M, Kovacević I et al. The effect of eradicating Helicobacter pylori infection on the course of adenomatous and hyperplastic gastric polyps. Eur J Gastroenterol Hepatol 1999;11:727-30.
23. Dirschmid K, Platz-Baudin C, Stolte M. Why is the hyperplastic polyp a marker for the precancerous condition of the gastric mucosa? Virchows Arch 2006;448:80-4.