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Helicobacter pylori prevalence in colorectal polyps: Increased risk of neoplastic transformation

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Abstract

Aim: The aim of this study was to investigate the prevalence of *Helicobacter pylori* (HP) in colorectal polyps and whether this infection differs according to neoplastic and dysplastic polyp types.

Materials and Methods: A total of 593 patients (mean age 59.5±12.0), 279 females and 314 males, who underwent colonoscopy and endoscopy at Erzurum Training and Research Hospital were included in the study. The patients were grouped into two groups with endoscopic findings. These groups are patients with colorectal polyps (n=330) and those with normal colonoscopy results (n=263). The presence of *H. Pylori* infection was diagnosed with endoscopic biopsy. Hematological parameters were analyzed.

Results: *H. Pylori* positivity was detected at a rate of 59.1% in patients with colorectal polyps, while this rate was found to be 21.3% in the normal colonoscopy group ($p<0.001$). In patients with *H. Pylori*-positive colorectal polyps, 92.3% of the polyps were neoplastic polyps, and 7.7% were non-neoplastic polyps. The frequency of dysplasia was 66.2% in the *H. Pylori* positive group and 24.4% in the *H. Pylori* negative group. *H. Pylori* positivity increases the risk of neoplastic polyps by 3.2 times (OR=3.2, CI=1.6-6.4, $p<0.001$) and dysplasia by six times (OR=6.0, CI=3.6-9.8, $p<0.001$).

Conclusion: Our study demonstrated that *H. Pylori* infection is strongly associated with colorectal polyps, especially neoplastic and dysplastic polyps. The findings suggest that *H. Pylori* infection might be a possible risk factor for the colorectal cancer development and that *H. Pylori* eradication can be considered in cancer prevention strategies.

Introduction

Helicobacter pylori (HP) infection is one of the most prevalent bacterial infections around the world and is particularly associated with upper gastrointestinal (GI) diseases. HP, which infects more than 50% of the global population [1], is most often acquired in childhood [2]. This bacterium, which can cause serious pathologies such as chronic gastritis, peptic ulcers, and gastric cancer, is also increasingly drawing attention to its effects on the lower gastrointestinal system. Colorectal polyps, which frequently occur in the colon or rectum, might be an essential precursor to precancerous lesions and colorectal cancer. Colorectal cancer is a significant contributor to morbidity and mortality globally, and since it presents a substantial economic burden on the population due to surgery, chemotherapy, and terminal care costs, prevention and early diagnosis of this disease are of great importance with regard to public health.

In recent studies, it has been reported that HP infection is not limited to the stomach but could also contribute to the development of colorectal polyps. Many studies have indicated that HP infection may cause chronic inflammation and metaplasia in the GI mucosa. It is thought that these inflammatory processes, also seen in the colon mucosa, may contribute to the formation of precancerous lesions, especially adenomatous polyps. For example, in a meta-analysis conducted by Rokkas et al. [3], it was found that the risk of developing colorectal polyps and cancer increased in HP-positive individuals. Similarly, another study by Wang et al. [4] emphasized that HP infection has been linked to an increased frequency of colorectal polyps, which might potentially raise the risk of colorectal cancer. These findings indicate that HP may potentially pose a risk for the development of colorectal cancer. However, the pathophysiological mechanisms underlying the association between HP infection and colorectal polyp are still unclear. In this context, studies examining the relationship between HP infection and the development of

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colorectal polyps in more detail are needed. The current literature suggests that HP may be a contributing factor in the development of colorectal polyps through mechanisms such as chronic inflammation, epithelial cell proliferation, and DNA damage. However, the generalizability of these findings and their importance in clinical practice are still a matter of debate. There is still a lack of complete understanding whether HP contributes to the formation of colon polyps, triggers inflammatory responses, or directly stimulates polyp development through its effects on the mucosa.

Our study aims to investigate the prevalence of HP in colorectal polyps and also to determine whether the presence of HP varies according to the neoplastic and dysplastic features of the polyps themselves, thus providing a more comprehensive understanding of the potential effects of HP on the pathogenesis of colorectal cancer. Therefore, our study will establish the basis for studies that will investigate the possible clinical and societal benefits of the potential relationship between HP infection eradication and colorectal cancer prevention strategies.

Materials and Methods

A total of 593 patients (mean age 59.5±12.0), 279 female and 314 male, who underwent simultaneous endoscopic biopsy and colonoscopy due to their current complaints and were found to have colorectal polyps (n=330) and those who have normal colonoscopy findings (n=263), were included in this study. Exclusion criteria were inflammatory bowel disease, familial polyposis syndromes, history of colon polyps and colorectal cancer in first-degree relatives, use of antibiotics and proton pump inhibitors in the last month to avoid false-negative results, and patients who did not accept colonoscopic and endoscopic biopsy were excluded from the study.

The Erzurum Training and Research Hospital's Ethics Committee approved the study protocol with issued decision number 2024/09-179 on September 11, 2024. The Declaration of Helsinki's ethical criteria were followed when conducting the research.

Statistically analysis

Statistical analyses were performed with IBM Statistical Package for Social Sciences software, version 22 (IBM Corp., Armonk, NY). According to G-Power Analysis, the sample size for our research with a power of 95%, a type 1 error of 0.04, and an effect size of 0.3 was planned to be at least 257 people in both groups. Kolmogorov-Smirnov test was used to determine whether the variables were normally distributed or not. For non-normally distributed data, we used the Mann-Whitney U test (for two groups). For normally distributed data, we employed the Student's t-test to compare means between two groups, under the assumption that the data follows a normal distribution. Comparisons between categorical variables were performed with the Chi-square test, assuming the expected frequencies in each category are sufficiently large for valid application of this test. The nonnormally distributed data were represented by medians and quartiles. The normally distributed data were expressed as the mean ± standard deviation. Additionally, the Odds Ratio (OR) and 95% confidence interval (CI) were calculated to assess the strength of associations. Statistically significant p-value was considered as $p<0.05$.

Results

In Table 1, no difference was found in terms of age between patients with and without colorectal polyps (p=0.456). The groups were also compared in terms of hematological parameters. Hemoglobin (12.2±2.3) was lower in the colorectal polyp group, and no difference was found in iron and ferritin parameters (p=0.307, p=0.087, respectively).

Table 2 showed a significant difference between the groups regarding gender distribution (p<0.001). Male gender was detected more frequently in the colorectal polyp group (59.7%), and female gender was detected more frequently in the other group (55.5%). HP positivity was detected significantly more frequently in the colorectal polyp group (59.1%) than in the other group (21.3%) (p<0.001). In addition, the frequency of GI symptoms was indicated between the groups with and without colorectal polyps. In the colorectal polyp group, the frequencies of symptoms were found to be, from most to least: constipation (60%), abdominal pain (43.3%), nausea (26.7%), diarrhea (16.7%), weight loss (10%), vomiting (6.7%) and hematochezia (3%). The frequency of symptoms in the group without colorectal polyp was as follows: abdominal pain (58.2%), constipation (51%), nausea (37.3%), weight loss (30%), diarrhea (27.4%), vomiting (20.5%) and hematochezia (4.2%).

In Table 3, patients with colorectal polyps were grouped into two HP positive and negative groups. In the HP positive group, the frequency of neoplastic polyps (92.3%) was detected more frequently than in the HP negative group (78.5%) (p=<0.001). In the non-neoplastic polyp group, HP negativity was detected more frequently (%21.5) (p=0.001). In addition, the frequency of dysplasia detected in the pathology in the HP-positive group (66.2%) was detected more frequently than in the HP-negative group (24.4%) (p< 0.001).

Additionally in Table 3, we analyzed the relationship between HP and the risk of colorectal and neoplastic polyps. The frequencies of HP were 5.33 times higher in the Colorectal polyp group (OR=5.33, CI=3.6-7.7, p<0.001), 3.2 times higher in the Neoplastic Polyp group (OR=3.2,

Table 1. Demographic and laboratory parameters in colorectal polyp and non-colorectal polyp groups.

	Patients with colorectal polyps (n=330)	Patients with normal colonoscopy (n=263)	p
Age (mean±SD)	59.8±12.2	59.0±11.8	0.456*
Hemoglobine	12.2±2.3	13.8±2.8	**0.035***
Iron (u/dL)	61(9-112)	52(2-198)	0.307**
Ferritin (ng/mL)	40(1-1501)	30(6-841)	0.087**

*Student-T test was applied **Mann-Whitney U test was employed to compare the variables. P<0.005 is considered significant.

Table 2. Gender distribution and *H. Pylori* frequency and symptoms in groups with and without colorectal polyps.

	Patients with colorectal polyps (n=330)	Patients with normal colonoscopy (n=263)	Total (n=593)	p
Gender (n)				
Female	133(40.3)	146(55.5)	279(47)	**<0.001***
Male	197(59.7)	117(44.5)	314(53)	
HP positivity n(%)	195(59.1)	56(21.3)	251(42.3)	**<0.001***
GIS Symptoms (%)				
Abdominal pain	43.3	58.2	56.7	
Nausea	26.7	37.3	36.2	
Vomiting	6.7	20.5	19.1	
Weighting Loss	10	30	28.7	
Diarrhea	16.7	27.4	26.3	
Constipation	60	51	51.9	
Hematochezia	3.3	4.2	4.1	

*The variables were compared with the Pearson's Chi-square test. Data are presented as number (%). P<0.005 was considered significant. HP: *Helicobacter Pylori*; GIS: Gastrointestinal System.

Table 3. Relationship between HP presence and polyp types in the colorectal polyp group.

	HP positivity (n=195)	HP negativity (n=135)	OR	CI	p
Colorectal polyps n(%)	195(59.1)	135(40.9)	5.33	3.6-7.7	**<0.001**
Neoplastic Polyps n(%)	180(92.3)	106(78.5)	3.2	1.6-6.4	**<0.001**
Tubular Adenoma	115(63.8)	75 (70.7)			
Tubulovillose	51(28.3)	26(24.5)			
Villose adenoma	10(5.5)	4(3.7)			
Serrate polyp	4 (2.4)	1(0.9)			
Nonneoplastic Polyps n(%) (Hiperplastik, Hamartamatöz, Enflammatuar)	15 (7.7)	29 (21.5)	---	---	**0.001**
Displasia n(%)	129(66.2)	33(24.4)	6.0	(3.6-9.8)	**<0.001**

Chi-square test with Odds Ratio (OR) and CI: Confidence interval (CI).

CI=1.6-6.4, p<0.001), and 6.0 times higher in the Dysplasia group (OR=6.0, CI=3.6-9.8, p<0.001).

Discussion

In this study, a notable increase in HP infection was observed in patients with colorectal polyps, suggesting that it might be a contributing risk factor for the development of colorectal polyps. It reveals a strong association between HP positivity and the types of polyps with malignant potential. These findings are consistent with previous studies supporting the impact of HP on the pathogenesis of colorectal cancer [5,6]. It is thought that HP infection may trigger inflammatory processes in the gastrointestinal tract, leading to such findings. Clinical observations support an inseparable link between long-standing chronic inflammation and the development of common cancers of the GI tract, endocrine organs, and soft tissues [7]. Chronic inflammation is involved in every stage of carcinogenesis from initiation to progression. Under continuous inflammatory exposure, excessive reactive oxygen species production can cause genomic instability, leading to cancer initiation. Inflammation is a crucial regulator of cancer progression through multiple mechanisms, including acceleration of cell cycle and proliferation, evasion of apoptotic cell death, and stimulation of tumor neovascularization [8,9]. One of the underlying mechanisms may be that HP infection can trigger neoplastic changes by causing cellular changes such as inflammation, epithelial cell proliferation, and DNA damage in the colonic mucosa. Studies have also reported that the destruction of the gastric acid barrier is associated with colorectal cancer [10]. Hypergastrinemia, seen as a result of gastric barrier damage, can create a pro-inflammatory environment and lead to a microenvironment that favors tumor development through macrophage activation and chemotaxis. HP infection itself is an essential factor that can increase basal and stimulated gastrin levels [11]. Many studies have shown that gastrin levels are high in patients with colorectal cancer [12,13].

Based on their histological features, Colon polyps are grouped into two main categories: neoplastic and nonneoplastic. Neoplastic polyps consist of adenomatous polyps and serrated polyps. Nonneoplastic polyps can be

hyperplastic, hamartomatous, juvenile, and inflammatory. But sometimes, adenomatous transformation can also develop in hyperplastic polyps [14]. In our study, HP positivity was detected more prevalent in polyps with neoplastic potential than in non-neoplastic polyps. HP was also found to be more frequent in patients with dysplasia detected in the pathological examination. In a study conducted by Basmaci et al. [15] in our country in 2023, HP frequency was found to be more common in adenomatous polyps, which is consistent with our study. Sonnenberg et al. reported [6] that HP gastritis is more common in adenomatous polyps, high-grade dysplasia, and adenocarcinoma. The finding in our research that HP infection causes a 3.2-fold rise in the prevalence of adenomatous polyps and dysplasia by six times that suggest that this bacterium may be a contributing risk factor in developing colorectal cancer. These results indicate that HP is not only associated with conditions such as peptic ulcer and gastric cancer in the gastrointestinal tract but may also increase the risk of colon cancer. Our findings were consistent with other studies investigating the relationship between colorectal carcinogenesis and HP [4,16].

In our study, we also found that the male gender was more prevalent in the colorectal polyp group, confirming the negative effect of the male gender on the development of colorectal polyps and cancer [14]. The etiology of gender differences in colorectal carcinogenesis remains unclear. Possible explanations include different hormonal and lifestyle factors. Postmenopausal hormone replacement therapy is known to have a protective effect against colorectal cancer [17].

In terms of gastrointestinal symptoms, abdominal pain (58.2%), nausea (37.3%), and weight loss (30%) were reported more frequently in the normal colonoscopy group. This may indicate that patients with colorectal polyps may have milder symptoms. However, constipation was found to be a more common symptom in patients with colorectal polyps (60%), suggesting that polyps may have a significant effect on bowel movements. It should also be noted that all these gastrointestinal symptoms may overlap with the HP infection clinic and affect the clinical presentation of polyps.

Our study findings suggest that eradication of HP infection may have a potential role in colorectal cancer prevention strategies. This finding supports other studies examining the effects of HP on the development of colon cancer. However, the observational nature of this study makes it difficult to establish a causal relationship. The limitations of our study are that it is retrospective, and therefore, information on patients' ethnicity, smoking, alcohol consumption, physical activity, dietary habits, and nonsteroidal anti-inflammatory drug use could not be obtained.

Conclusion

In conclusion, this study demonstrates the association of HP infection with colorectal polyps and its possible effects on the neoplastic potential of polyps. According to these findings, HP infection should be a factor to be considered in colorectal cancer prevention strategies. Future studies may contribute to the development of clinical applications in this area by examining the effects of HP on colorectal polyp and cancer development in more detail. In addition, eradication of HP infection may be a target to be considered among colorectal cancer prevention strategies, and future research in this field is expected to be critical to confirm this hypothesis.

Conflict of interest statement

No conflict of interest was declared.

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No financial resources were received at any stage of this study.

Ethical approval

(Erzurum, Turkiye) (Approval Date: 11.09. 2024, Approval Number: 2024/09-179).

Data availability statement

The datasets analyzed in the current study are obtainable from the corresponding author upon request.

Author contributions

Sedat Ciftel designed this study: Conceptualization, Investigation, Formal analysis, Writing – of the original draft, and Supervision.

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