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Research Article

# Assessing the Correlation between Helicobacter Pylori Infection and Increased Incidence of Colorectal Cancer, Gastric Atrophy, and Intestinal Metaplasia

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**Abstract**

**Aim:** Our retrospective study was designed to explore the potential link between *Helicobacter pylori* (*H. pylori*) infection and the occurrence of colorectal cancer (CRC), gastric atrophy, and intestinal metaplasia.

**Material and Methods:** We assembled two groups of 150 patients each, categorized based on their endoscopic biopsy results for *H. pylori* - one group testing positive (study group), the other negative (control group). All subjects underwent upper and lower gastrointestinal endoscopies, and we assessed their endoscopic gastric biopsy results as well as any indications of colorectal malignancies.

**Results:** Our investigation established a noteworthy association between the presence of *H. pylori* infection and the incidences of CRC, gastric atrophy, and intestinal metaplasia ($p<0.05$). Our data suggests that individuals testing positive for *H. pylori* faced a 64% greater likelihood of developing CRC compared to those who tested negative. Among patients diagnosed with gastric atrophy, a remarkable 73.9% tested positive for *H. pylori*. Similarly, 78.9% of patients with intestinal metaplasia were also *H. pylori* positive.

**Conclusion:** Our results underscore a meaningful correlation between *H. pylori* infection and a heightened incidence of CRC, gastric atrophy, and intestinal metaplasia. Further, prospective studies will be instrumental in deciphering the underlying causative mechanisms and assessing the feasibility of *H. pylori* eradication as a preventive measure against these conditions.

**Keywords:** Helicobacter pylori, colorectal cancer, gastric atrophy, intestinal metaplasia, endoscopic biopsy

## INTRODUCTION

*Helicobacter pylori* (*H. pylori*), a type of Gram-negative bacteria primarily found in the stomach, has been associated with several gastrointestinal diseases, such as peptic ulcer disease, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma (1,2). More recent studies have expanded our understanding of *H. pylori* infection, demonstrating its associations with extra-gastric disorders such as cardiovascular, metabolic, and neurological diseases (3-5). However, the link between *H. pylori* infection and colorectal neoplasia remains a subject of dispute, with varying conclusions drawn from different studies (6). Moreover, it's been determined that *H. pylori* can induce precancerous changes like atrophy and intestinal metaplasia in the stomach (7), conditions that have been linked with an escalated risk for CRC (8). Yet, the exact relationship between *H. pylori*-induced atrophic gastritis and intestinal metaplasia and CRC risk is still in need of thorough clarification. Hence, our study aims to evaluate the association between *H. pylori* infection and the increased incidence of CRC, gastric atrophy, and intestinal metaplasia. In light of the possible connection, we believe it's crucial to delve further into the multifaceted roles *H. pylori* might play in the pathogenesis of gastrointestinal disorders, as the implications of such research could transform diagnostic strategies and therapeutic interventions for these prevalent conditions. By retrospectively examining a patient cohort presenting with dyspeptic symptoms, we aim to contribute to the current understanding of the role *H. pylori* plays in the development of gastrointestinal malignancies.

**CITATION**

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## MATERIAL AND METHOD

This retrospective study was given ethical approval by our hospital's local committee, as confirmed by the dated decision (17.07.2023, no. 134). Given the retrospective nature of this study, obtaining informed consent from patients was not deemed necessary. In compliance with the 2013 revision of the Declaration of Helsinki, our study encompassed a total of 300 participants. These patients had sought medical consultation at our clinic between January 2010 and December 2022, presenting with various symptoms, including gastrointestinal bleeding, weight loss, and irregular bowel habits such as constipation and diarrhoea. All included patients had undergone upper and lower gastrointestinal endoscopy within this period. Following the endoscopic biopsy results, patients were divided into two distinct groups: those with *H. pylori* infection (n: 150) and those without (n: 150).

To be included in the study, patients had to have:

- Undergone an endoscopic examination of the upper and lower gastrointestinal tract at our institution due to dyspeptic symptoms,
- *H. pylori* infection status (either positive or negative) confirmed through histopathological evaluation,
- Available and current medical records along with follow-up data.

On the other hand, we excluded:

- Any patients with a history of CRC, other malignancies, or inflammatory bowel disease before the endoscopic biopsy,
- Patients lacking necessary medical records or follow-up data,
- Patients who had been previously treated for *H. pylori* infection.

A comparative analysis was undertaken between the two groups on demographic data, tobacco and alcohol use history, NSAID consumption, family history of CRC, body mass indices, gastrointestinal complaints, and findings from the endoscopic gastric biopsy. We also evaluated the endoscopic biopsy results that led to the diagnosis of CRC, focusing on the differences in the number and location of CRC between the two groups.

### Statistical Analysis

The Shapiro-Wilk test was employed to determine if the variables conformed to a normal distribution. Variables under the normal distribution were presented as mean ± standard deviation, whereas those not under normal distribution were expressed as median values (ranging from minimum to maximum). Categorical variables were given as n (%).

In line with the results of the normality test, comparisons between groups were done using a T-test for those following a normal distribution, and a Mann-Whitney U test for those not conforming to the normal distribution. The differences among categorical variables were ascertained using either a Continuity Correction Chi-Square test or a Pearson's Chi-Square test.

To evaluate the likelihood of colon cancer occurrence in *H. pylori* positive patients, we used logistic regression analysis. IBM SPSS Statistics 25.0 (SPSS Inc, Chicago, USA) was our tool of choice for all statistical analyses. The accepted threshold for statistical significance in the data analysis was established at $p<0.05$.

## RESULTS

The study encompassed 300 participants, evenly divided into 150 *H. pylori* positive and 150 *H. pylori* negative patients. These patients comprised of 134 females (44.7%) and 166 males (55.3%), aged between 37 and 76 years with a mean age of 57.15±7.814 years. Looking at their lifestyle factors, we found that of 94 smokers, 54 (57.4%) tested positive for *H. pylori*, and 40 (42.6%) were negative. Among the 46 alcohol consumers, 28 (60.9%) were *H. pylori* positive, and 18 (39.1%) were negative. For the 128 patients using NSAIDs, *H. pylori* was found positive in 63 (49.2%) and negative in 65 (50.8%). Additionally, out of 33 patients with a familial cancer history, 19 (57.6%) were *H. pylori* positive and 14 (42.4%) were negative. However, statistical analysis revealed no significant correlation between these patient characteristics and their *H. pylori* infection status ($p>0.05$).

In the investigation, we found that of the 138 patients presenting with abdominal pain, 76 (55.1%) tested positive for *H. pylori* while 62 (44.9%) were negative. Among the 79 patients who experienced rectal bleeding, 40 (50.6%) were *H. pylori* positive, and 39 (49.4%) were negative. For patients with diarrhoea, numbering 112, 55 (49.1%) tested positive for *H. pylori*, and 57 (50.9%) were negative. Furthermore, out of the 216 patients who presented with other symptoms, 102 (47.2%) were *H. pylori* positive and 114 (52.6%) were negative. Upon statistical analysis, it was determined that there was no significant correlation between the presence of *H. pylori* and the specific symptoms in either group ($p>0.05$).

The demographic and clinical attributes of the patients across the two groups are encapsulated in Table 1.

Table 2 shows the comparison of endoscopic gastric biopsy results between the two groups.

Out of the 150 patients who tested positive for *H. pylori*, colorectal tumours were found in 14 cases (9.3%), while amongst the 150 patients who were *H. pylori* negative, only 5 cases (3.3%) showed the presence of colorectal tumours. It was thus concluded that a statistically significant association exists between *H. pylori* infection status and the occurrence of CRC ($p<0.05$) (Refer to Table 3).

Our analysis established a significant impact of *H. pylori* positivity on the prevalence of CRC ($p<0.05$). The likelihood

of CRC in patients with *H. pylori* infection is shown to be 64% greater when compared to those without the infection. The odds ratio reflecting the status of CRC in patients who tested positive for *H. pylori* is detailed in Table 3.

Out of 19 patients diagnosed with CRC, 14 tested positive for *H. pylori*, while five were negative for the bacteria. Among the patients positive for *H. pylori*, one patient (7.1%) had a tumour in the caecum, two (14.2%) in the hepatic flexure, three (21.4%) in the splenic flexure, two (14.2%) in the descending colon, and three each (21.4%) in the sigmoid colon and rectum. On the other hand, in the *H. pylori* negative group, the tumour was found in the splenic flexure in one patient (20%), the descending colon in one patient (20%), and the sigmoid colon in three patients (60%).

The majority of tumours identified in both cohorts were classified as adenocarcinomas, accounting for 92.9% in the *H. pylori* positive group and 80% in the *H. pylori* negative group. Meanwhile, mucinous adenocarcinoma was observed in a single patient from each group. The average size of the tumours was slightly larger in the *H. pylori* positive group at 4.5 cm compared to 4.2 cm in the *H. pylori* negative group. When the tumour stages were assessed based on the TNM classification, a total of 15 patients were found to be at stage I and four were at stage II.

**Table 1. Demographic and clinical characteristics of patients**

| | *H. pylori* (+) (n=150) | *H. pylori* (-) (n=150) | T/U/$\chi^2$ | p* |
|---|---|---|---|---|
| **Age (years)*** | 57.09±8.268 | 57.20±7.359 | -0.118 | 0.906 |
| **Gender** | | | 0.337 | 0.561 |
| **Male** | 86 (57.3%) | 70 (46.6%) | | |
| **Female** | 64 (42.7%) | 80 (53.4%) | | |
| **Habits of patients** | | | | |
| **Smoking** | 54 (36%) | 40 (26%) | 2.618 | 0.106 |
| **Alcohol consumption** | 28 (18.6%) | 18 (12%) | 2.080 | 0.149 |
| **NSAID use** | 63 (42%) | 65 (43.3%) | 0.014 | 0.907 |
| **Family history of colorectal cancer** | 19 (12.6%) | 14 (9.3%) | 0.545 | 0.460 |
| **BMI (kg/m²)** | 29 (20:41) | 29 (21:41) | 11393.5 | 0.848 |
| **Symptoms** | | | | |
| **Abdominal pain** | 76 (50.6%) | 62 (41.3%) | 2.268 | 0.132 |
| **Rectal bleeding** | 40 (26.6%) | 39 (26%) | 0.00 | 1.00 |
| **Diarrhoea** | 55 (36.6%) | 57 (38%) | 0.014 | 0.905 |
| **Constipation** | 76 (50.6%) | 69 (46%) | 0.481 | 0.488 |
| **Others** | 102 (68%) | 114 (76%) | 1.620 | 0.203 |

Variables are expressed as mean±standard deviation, median (minimum:maximum), and n(%). T: Student's t-test, U: Mann-Whitney U-test, Continuity Correction $\chi^2$ test; *p<0.05

**Table 2. Endoscopic gastric biopsy results between the two groups**

| Biopsy findings | *H. pylori* (+) (n=150) | *H. pylori* (-) (n=150) | T/U/$\chi^2$ | p* |
|---|---|---|---|---|
| **Atrophy** | 17 (11.3%) | 6 (4%) | 4.709 | **0.030** |
| **Intestinal metaplasia** | 30 (20%) | 8 (5.3%) | 13.288 | **<0.001** |

Variables are expressed as n(%). T: Student's t-test; U: Mann-Whitney U-test; Continuity Correction $\chi^2$ test; *p<0.05

**Table 3. Examination of H. pylori positivity and negativity in patients diagnosed with CRC**

| *H. pylori* | CRC (+) (n=19) | CRC (-) (n=281) | p* |
|---|---|---|---|
| **Positive** | 14 (73.6%) | 136 (48.3%) | **0.033** |
| **Negative** | 5 (26.4%) | 145 (51.7%) | |
| **Total** | 19 (100%) | 281 (100%) | |

n: number of patients; %: percentage of number of patients; Pearson $\chi^2$ test; *p<0.05

## DISCUSSION

This retrospective analysis provides robust evidence associating *H. pylori* infection with an increased prevalence of CRC, gastric atrophy, and intestinal metaplasia. Our results highlight the far-reaching effects of *H. pylori*, extending beyond its established influence on peptic ulcer disease and gastric cancer, thereby underlining its systemic implications on gastrointestinal wellbeing. Our findings, indicating a 64% greater risk of CRC in individuals positive for *H. pylori*, coincide with a burgeoning agreement in contemporary studies suggesting a linkage between such infections and CRC (9-12). In terms of biological mechanics, the exact pathways remain to be clearly identified, but a theory suggests that the chronic inflammation within gastric mucosa caused by *H. pylori* could incite a systemic inflammatory condition, creating a favourable environment for CRC development (13). Another intriguing hypothesis involves the disruption of gut microbiota by *H. pylori*, which could affect the intestinal environment and thus promote CRC progression (14). The notable association established in our research between *H. pylori* infection and precancerous states such as gastric atrophy and intestinal metaplasia underscores previous research linking *H. pylori* with these premalignant gastric conditions (15,16). The mechanisms contributing to these observations possibly involve inflammation triggered by *H. pylori* and the generation of virulence factors, potentially causing damage and transformation in gastric epithelial cells (17-19).

### Study Limitations

Despite the valuable insights gleaned, our study has inherent limitations due to its retrospective design, limited population scope, and inability to establish causation, alongside potential uncontrolled confounding factors, lack of *H. pylori* strain differentiation, and a relatively modest sample size. Future investigations should seek to overcome these constraints for a more comprehensive and robust elucidation of the associations observed in this study.

## CONCLUSION

In conclusion, this study strongly links *H. pylori* infection to an increased risk of CRC, gastric atrophy, and intestinal metaplasia, highlighting its systemic effects on gastrointestinal health. It underlines the importance of early detection and management of *H. pylori*, suggesting it as a key preventive measure against these conditions. Regardless of the constraints inherent to this study, the results provide a foundational basis for more in-depth investigations into the connection between *H. pylori* and CRC. The ultimate goal is to refine preventive and therapeutic approaches for these prevalent conditions.

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***Conflict of Interest:*** *The authors declare that they have no competing interest.*

***Ethical approval:*** *This retrospective study was given ethical approval by Giresun Training and Research Hospital local committee, as confirmed by the dated decision (17.07.2023, no. 134).*

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