Prevalence and Association of *Helicobacter Pylori* Infection in Bowel Disease at Dr. Cipto Mangunkusumo General National Hospital 2010–2021

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ABSTRACT

Background: *Recent studies showed contrasting associations between Helicobacter pylori infection and organic bowel disorders, where positive associations were reported in colorectal carcinoma (CRC) and colorectal polyp. In contrast, a protective association was observed in patients with inflammatory bowel diseases (IBD). We aim to determine the association between H. pylori infection and CRC, colorectal polyps, and IBD in Indonesian tertiary Hospitals.*

Method: *We retrospectively collected electronic medical record data from patients referred to Dr. Cipto Mangunkusumo General National Hospital from 2010 to 2021 who underwent endoscopies and H. pylori tests. We performed a chi-square analysis with a significant p-value of < 0.05.*

Results: *Three hundred and fourteen patients were enrolled. Overall, the prevalence of H. pylori infection in organic bowel disease was 61.7% (n = 194), with 9.9% (n = 31) of them having CRC, 20.3% having colorectal polyps (n = 64), and 31.5% (n = 99) having IBD. A significant association between H. pylori infection and IBD was observed (RR = 0.36; 95% CI: 0.18–0.70; p = 0.000). However, no significant association was found between H. pylori infection and CRC (RR = 0.60; 95% CI: 0.22–1.66; p = 0.31) and colon polyps (RR = 0.59; 95% CI: 0.30–1.15; p = 0.10).*

Conclusion: *This study showed H. pylori infection lowers the risk of IBD (RR = 0.36; 95% CI: 0.18–0.70; p = 0.000). However, insignificant association was observed between H. pylori infection, CRC, and colorectal polyps.*

Keywords: *Helicobacter pylori, inflammatory bowel disease, colorectal cancer, colorectal polyps*

ABSTRAK

Latar belakang: *Beberapa studi telah menunjukkan adanya korelasi positif antara Helicobacter pylori dengan kanker kolon, polip kolon, dan inflammatory bowel disease (IBD). Penelitian ini dilakukan untuk mengetahui adanya hubungan antara infeksi Helicobacter pylori dengan kanker kolon, polip kolon, dan IBD pada rumah sakit rujukan pusat di Indonesia.*

Metode: *Penelitian retrospektif dilakukan di RSUPN Dr. Cipto Mangunkusumo pada rentang tahun 2010-2021 dengan data rekam medis elektronik pasien yang melakukan pemeriksaan H. pylori dan terdiagnosis satu dari tiga kelainan usus (kanker kolon, polip kolon, IBD). Dilakukan analisis univariat dan bivariat chi square untuk menentukan hubungan dengan signifikansi p < 0.05.*

Hasil: *Total 314 data pasien yang memenuhi kriteria inklusi. Secara keseluruhan, prevalensi H. pylori positif*

pada kelainan organik usus yaitu 6.4% (n = 20) dengan 1.27% (n = 4) kanker kolon, 2.54% (n = 8) polip kolon, dan 2.54% (n = 8) IBD. Terdapat hubungan bermakna antara H. pylori dan IBD (RR = 0.36; 95% CI: 0.18–0.70; p = 0.000). Namun tidak ditemukan hubungan bermakna antara H. pylori dan kanker kolon (RR = 0.60; 95% CI: 0.22–1.66; p = 0.31), dan polip kolon (RR = 0.59; 95% CI: 0.30–1.15; p = 0.10).

Simpulan: *Studi ini menunjukkan bahwa infeksi H. pylori menurunkan resiko kejadian IBD (RR = 0.36; 95% CI: 0.18–0.70; p = 0.000) Namun tidak ditemukan adanya hubungan bermakna antara infeksi H. pylori dengan CRC dan polip kolon.*

Kata kunci: *Helicobacter pylori, inflammatory bowel disease, kanker kolon, polip kolon*

INTRODUCTION

The relationship between *Helicobacter pylori* infection and organic bowel disease is still up for debate. Several studies have shown a link between *H. pylori* infection and the incidence of inflammatory bowel disease (IBD) that consists of ulcerative colitis and Crohn's disease, as well as colon polyps and colon cancer. However, the association of *H. pylori* infection with organic bowel disease still needs further study.

Numerous epidemiological studies link *H. pylori* infection to colon polyps or colon cancer. *H. pylori* is a class 1 carcinogen because it makes a lesion that increases the risk of developing stomach cancer.[1] According to research by Sonnenberg et al, the prevalence of *H. pylori* infection in the general population increased at the same time as various gastrointestinal disorders, including erosive esophagitis, Barrett's esophagus, and esophageal cancer.[2] Colon cancer and colon polyps were linked to *H. pylori* infection in a different meta-analysis by Rokkas et al.[3]

As one of the developing countries, Indonesia has a fairly high prevalence of *H. pylori* infection. The relationship between *H. pylori* infection and the occurrence of organic bowel disease has not been much discussed. This study aims to determine the prevalence and relationship of *H. pylori* infection in patients with organic abnormalities of the intestine (inflammatory bowel disease, colon polyps, and colon cancer) in Indonesia with a sample of patients undergoing esophagoduodenoscopy and colonoscopy at Dr. Cipto Mangunkusumo General National Hospital, Jakarta, Indonesia, from 2010 to 2021.

METHOD

Research Design and Population

The study was conducted at Dr. Cipto Mangunkusumo General National Hospital in Indonesia using total sampling. The inclusion criteria are patients who are ≥ 18 years of age, undergo an *H. pylori* examination, and undergo an endoscopic examination. The inclusion diagnosis is that the patient has at least one of three intestinal abnormalities (colon cancer, colon polyps, or IBD), diagnosed as H. pylori positive infection for the first time while on Dr. Cipto Mangunkusumo General National Hospital, and has a complete medical record.

The study was conducted with the approval of the Universitas Indonesia Ethics Committee with protocol number 20-07-0753 using secondary data in the form of medical records. Electronic medical record data is collected from patients performing EGD and colonoscopy examinations at the Digestive Endoscopy Center, Dr. Cipto Mangunkusumo in 2010–2021, who underwent examination of *H. pylori* through both histopathological tissue biopsy and the urea breath test.

The diagnosis of colon cancer, colon polyps, and inflammatory bowel disease is established through colonoscopy and biopsy. The diagnosis of *H. pylori* is obtained through a urea breath test and tissue histopathological examination with biopsy, with both or either test positive included

Statistical Analysis

Statistical analysis is done using IBM SPSS version 25. The method of analysis used is chi-square for bivariate analysis to determine the significance of $p < 0.05$ and, a confidence interval of 95%.

RESULT

In this study, a total sampling method was carried out with a total of 338 patient records obtained from electronic medical records. The group with *H. pylori*-negative consisted of 274 patients, with 22 patients excluded due to incomplete medical records. The *H. pylori*-positive group consisted of 64 patients, with two patients excluded due to incomplete medical records.

Out of a total of 314 patients meeting the inclusion

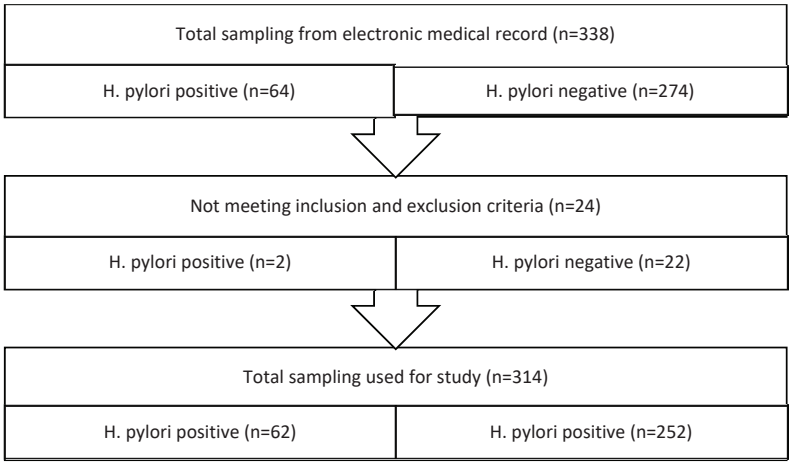

Figure 1. Flowchart of data collection

criteria, there were 131 male (41.7%) and 183 (58.2%) female patients. No significant differences were found between gender and the incidence of *H. pylori* infection ($p = 0.157$). There were 62 (19.74%) patients with a positive diagnosis of *H. pylori* infection and 252 (80.25%) patients with *H. pylori* negative. The demographics of patients are shown in Table 1.

Table 1. Distribution of cases

Characteristic of the subject	*H. pylori-positive*	*H. pylori-negative*
Gender		
Male	31 (50.0)	100 (39.7)
Female	31 (50.0)	152 (60.3)
Colon cancer		
Present	4 (6.5)	27 (10.7)
Absent	58 (93.5)	225 (89.3)
Colon polyps		
Present	8 (12.9)	56 (22.2)
Absent	54 (87.1)	196 (77.8)
Inflammatory bowel disease		
Present	8 (12.9)	91 (36.1)
Absent	54 (87.1)	161 (63.9)

Chi-square bivariate result p<0.001, therefore we have a significant association, with H. pylori infection thought to lessen the risk of IBD (RR = 0.36; 95% CI: 0.18–0.70; $p < 0.001$) in Table 2. For the gender (RR = 1.40; 95% CI: 0.90–2.18; $p = 0.14$), colon cancer (RR = 0.60; 95% CI: 0.22–1.66; $p = 0.31$) and colon polyps (RR = 0.59; 95% CI: 0.30–1.15; $p = 0.10$) no significance was found.

Table 2. Analysis of chi-square

Variable	*p-value*	Odds Ratio	Relative Risk	CI 95%
Gender	0.14	1.52	1.40	0.90–2.18
Colon cancer	0.31	0.58	0.60	0.22–1.66
Colon polyps	0.10	0.52	0.59	0.30–1.15
Inflammatory bowel disease*	0.000*	0.26	0.36	0.18–0.70

*p value < 0.05

DISCUSSIONS

H. pylori is thought to be one of the most common human pathogens. A systematic review and analysis showed that it is estimated approximately 4.4 billion individuals with H.pylori infection worldwide in 2015.[4] A study conducted by Maulahela et al in Indonesia with a sample taken from 4 big cities between 2014 and 2017 with a total result of 193 positive patients.[5] Another study by Syam et al in 2016 showed that the prevalence of *H. pylori* infection in Indonesia is 22.1%, relatively lower than in other countries in Asia. This could be affected by Indonesian geneticpolimorphism.[6]

The mechanisms by which *H. pylori* can cause organic bowel disease are not yet fully understood. However, some theories suggest that there is a possible theory of migration that underlies this. Another theory is that *H. pylori*, as a carcinoid precursor, can cause prolonged inflammation in the intestinal mucosa, which over a certain period can lead to the emergence of neoplasm.[7] In this study, a significant association between *H. pylori* infection and intestinal organic abnormalities was found only in IBD. This could happen because this study only included patients who were newly diagnosed with *H. pylori* infection, thus the progress of the disease into becoming a carcinogen was thought to be over the span time of the study. Therefore the low number of patients with *H. pylori* infection included in this study does not have numbers of colorectal cancer and colon polyps as expected.

H. pylori Infection with Colon Polyps and Colorectal Cancer

According to numbers from the World Cancer Research Fund, colorectal cancer is estimated to account for 1.9 million new cases by 2020, or 10.7% of the total number of new cases of cancer worldwide,

making it the third most prevalent cancer worldwide.[9] With the addition of new cases totaling 12.5% and 12.2% of all new malignancies, there will be 1.1 million more cases of colon cancer by 2020, making it the fifth-most prevalent cancer in the world after breast, lung, prostate, and non-melanoma cancers.[10] Most colon cancers originate from adenomatous polyps.

An adenomatous polyp is a pre-malignant lesion that will mostly develop into cancer.[11] Colon cancer risk is increased by *H. pylori*, the breakdown of the cell cycle and inflammation are two of the mechanisms that have given rise to theories. The presence of CagA is linked to an increase in gastric cancer and performs a pathogenic role in *H. pylori*.[8] The serum release of gastrin, which acts as a growth hormone on colon mucous cells, is a result of *H. pylori* infection. *H. pylori* infection can result in hypergastrinemia, which disrupts healthy gut flora and is thought to be carcinogenic. Endocrine research has shown that hypergastrinemia has an association between rectal cell proliferation and stimulation of colon cancer cell growth, as well as colon adenoma growth.

A study by Mohamed et al conducted in Sudan in 2020 showed an association between *H. pylori* infection and colon cancer and colon polyps.[12] In the study, 69 patients, consisting of 44 patients diagnosed with adenocarcinoma, 10 patients with colitis, and 15 patients with juvenile polyposis, were immunohistochemically screened to detect *H. pylori*. *H. pylori*-positive was found in 13 adenocarcinoma patients and three juvenile polyposis patients. Additionally, a positive correlation was found between immunohistochemistry and patient condition (p = 0.028).

A meta-analysis of 33 datasets (17 colon cancer studies and 16 colon polyp studies) conducted by Rokkas T et al in 2013 showed a significant association between *H. pylori* and colon cancer (OR = 1.3; 95% CI: 1.07–1.59; p = 0.01) and a significant relationship between *H. pylori* and colon polyps (OR = 1.5; 95% CI: 1.26–1.79; p = 0.000).[4] Brim et al in Africa in 2014 showed that colon polyps were found more frequently in patients with positive *H. pylori* infection (43% vs. 34%; OR = 1.5; 95% CI: 1.2–1.9; p = 0.001).[7]

Another study that showed a significant correlation between *H. pylori* and colon cancer and colon polyps was conducted by Temoorian et al in 2018. In the study, the diagnosis *of H. pylori* was confirmed by taking blood samples to measure IgG and IgA antibodies against *H. pylori* by ELISA. A total of 50 patients with *H. pylori*-positive (33 patients with adenomatous polyps, 17 patients with colon cancer) showed results of p = 0.003 and p = 0.039 compared to control patients (n = 100).[13]

H. pylori Infection with Inflammatory Bowel Disease

A meta-analysis by Mauna and Simadibrata in 2022 showed significant results with an odds ratio of 0.51 (95% CI: 0.46–0.56) that *H. pylori* infection may reduce the risk of ulcerative colitis in patients.[14] A meta-analysis by Rokkas et all showed H. pylori infection protective association against IBD (RR = 0.62, 95% CI: 0.55–0.71).[15] Another analysis conducted in the Asian population by Wu et all also showed the same result of protective association (RR = 0.48, 95% CI: 0.43–0.54).[16]

Several hypotheses explain the mechanisms that could undermine it. One of the theories is that a patient who had been exposed to H.pylori infection before developed a better immune system to prevent another autoimmune disease or allergies. *H. pylori* bacteria can trigger an immune response on the mucous layer, which then interacts with dendritic cells and T lymphocytes. This results in high IL-12 production, stimulating T-helper 1 polarization that will lower cytokines in the body, thereby reducing the inflammatory effects on the intestines. It is thought that the colonization of H.pylori in gastric mucous may have been protective against IBD by this special mechanism.[17]

Another hypothesis that explains the protective role of *H. pylori* in the occurrence of IBD may be due to an alteration in the immune response to Th1/Th17 pro-inflammation caused by *H. pylori*. It improves the regulation of T immune cells, which increases the expression of Foxp3 in the gastric mucosa. *H. pylori* may increase the production of antibacterial peptides that compete with other pathogenic bacteria in the gastrointestinal tract.[14]

The strength of our research is the method to diagnose colon cancer and colon polyps through colonoscopy, and *H. pylori* infection through histopathology examination. The study used immunohistochemistry to diagnose *H. pylori* on a gastric biopsy because it has high sensitivity and specificity, especially in patients who have just started therapy.[7] The limitation of this study is the small number of H.pylori-positive cases, this could happen because there are patients who have already been diagnosed or underwent therapy

before, so they did not meet the inclusion criteria. Another reason though is that not all patients undergoing endoscopy and colonoscopy are examined for the H. pylori test. It is not commonly done compared to other diagnostic modalities in gastric disease.

CONCLUSION

The study found that H. pylori infection is thought to lessen the risk of IBD, with RR showing a protective association. No significant association was found between *H. pylori*-positive infection and the incidence of colon cancer or colon polyps. Research with more samples and wider variables is recommended for further research. The more variables to be associated with can be beneficial for future research to evaluate prognosis and complications regarding H.pylori infection.

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