

Helicobacter Pylori Infection Among Patients with Upper Gastrointestinal Symptoms: Prevalence and Relation to Endoscopy Diagnosis and Histopathology

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ABSTRACT

Aim: To determine the prevalence of *H. pylori* based on endoscopic biopsy and to investigate the association between *H. pylori* and endoscopy diagnosis and histopathological diagnosis. **Materials and Methods:** Over a period of two years, 228 endoscopic biopsies were included. Endoscopy diagnosis, histopathological diagnosis, and colonization with *H. pylori* were recorded and compared using appropriate statistical tests. **Results:** The overall prevalence of *H. pylori* was 68%; 69.6% in males and 66.7% in females. Duodenal and gastric ulcers were seen more in males (63.2% and 60%) compared with females (32.1% and 40%) ($P < 0.001$). The total rate of colonization of *H. pylori* in duodenal ulcer and gastric ulcer (85.7% and 84%, respectively) was significantly higher than those in gastritis, duodenitis, and gastric cancer (61.8%, 69.2%, and 60%, respectively) ($P = 0.046$). Histologically, chronic active gastritis and chronic follicular gastritis was significantly higher in duodenal ulcer and gastric ulcer (57.1%, 44% and 21%, 40%) in comparison to chronic persistent gastritis (21.4%, 16%) with P value < 0.001 . Similarly, chronic active gastritis and chronic follicular gastritis had higher prevalence of *H. pylori* infection in comparison to chronic persistent gastritis (85.3%, 83.3% vs. 41.4%) with P value < 0.001 . **Conclusion:** This study reveals that the overall prevalence of *H. pylori* infection is high in our setting with no significant difference in gender. Peptic ulcers were common in males. Those with peptic ulcers had higher rates of *H. pylori* colonization. Chronic active gastritis and chronic follicular gastritis were common histological findings in ulcerative diseases with significantly higher *H. pylori* positivity.

Keywords: Duodenal ulcer, gastritis, gastric ulcer, *Helicobacter pylori*, peptic ulcer disease, upper gastrointestinal endoscopy

Key Messages: This study revealed that the overall prevalence of *H. pylori* infection is very high with higher rates in ulcerative diseases and those with chronic active gastritis and chronic follicular gastritis. The high prevalence of the *H. pylori* reflects that it is a major public health burden; therefore, proper strategies of control and eradication should be implemented.

Introduction

Helicobacter pylori (*H. pylori*) is of major concern today because of its causal relationship with gastro duodenal disease. One half of the world's population has *H. pylori* infection, with an estimated prevalence of more than 90% in developing countries.^[1-5] In our country, the reported prevalence of *H. pylori* ranged from 30% to 67%.^[6-10] It is proven that *H. pylori* is the principal cause of chronic gastritis, peptic ulcer disease as well as gastric cancer.^[11-15]

This study aimed to determine the prevalence of *H. pylori* based on histology and to assess its relationship with endoscopy diagnosis and histological diagnosis.

Materials and Methods

This cross-sectional study was conducted at this hospital over a period of two years from April 2011-March 2013. Data analysis was done from all consecutive individuals referred from outpatient as well as inpatient department who had undergone gastric biopsy during upper GI endoscopy for various dyspeptic symptoms like pain abdomen, nausea, vomiting, belching, throat pain, upper gastrointestinal bleeding, weight loss etc. Those with

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chronic liver disease with esophageal varices, chronic kidney disease, and age <14 years were excluded from the study.

The endoscopic diagnosis was categorized into gastritis, duodenitis, duodenal ulcer, gastric ulcer, and neoplasm. Gastritis has been classified in several ways, which differ from institution to another, from one department to another depending upon the examiner. Therefore, all kinds of gastritis were combined into one. If two or more diagnosis were present in a patient, the severest form of disease was recorded.

The biopsy specimens were usually taken from the antrum and other location if required and sent for histological examination. The biopsy specimens were fixed overnight in 10% buffered formalin, processed, embedded in paraffin, and cut and stained with Hematoxylin and Eosin (HandE) and Giemsa stain. There are no other modalities available for diagnosis of *H. pylori* in our institution. Histological reporting was done for diagnosis of gastric mucosa inflammation, atrophy, intestinal metaplasia, neoplasia, and *H. pylori* colonization. Histologically, gastritis was classified into chronic active gastritis (CAG), chronic follicular gastritis (CFG), and chronic persistent gastritis (CPG) according to the Sydney system.^[16]

Informed consent was taken from the patient/patient party. Identity of the patients was not disclosed. The study was approved by the hospital ethical review committee.

Descriptive and frequency analysis of the data from the study was expressed as counts, percentage, and means or medians as appropriate to provide the overall picture. The data were analyzed using Statistical Package of Social Sciences (SPSS) version 14 for windows. Chi-square test with exact test was used where applicable. *P* values of < 0.05 were considered to denote statistical significance.

Results

During the study period of two years, 980 diagnostic upper gastrointestinal endoscopies were performed for a range of indications, of which 332 biopsies were taken. Among 332 patients, 104 patients were excluded for various reasons, leaving 228 for the study. The age of the patients ranged from 16-87 (mean of 44.7 ± 15.8). Among all the patients, 126 (55.3%) were females and 102 (44.7%) were males.

The overall prevalence of *H. pylori* infection was 68% (n = 155/228). The distribution of colonization in <20 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, and > 70 years age groups was 90.9%, 63.3%, 69.1%, 56.8%, 72.7%, 74.3%, and 56.3%, respectively. The prevalence of *H. pylori* was highest in the <20 age group (90.9%) and lowest among ≥70 age group (56.3%); however, the difference was not statistically significant [Table 1]. Similarly, the overall prevalence among male and female counterpart was similar (69.6% and 66.7%, respectively). However, rate of *H. pylori* infection was significantly

higher among males in comparison to females in >70 age group (*P* = 0.049).

Endoscopy finding was divided into gastritis, duodenitis, duodenal ulcer, gastric ulcer, and gastric cancer, which was diagnosed in 144 (63.2%), 26 (11.4%), 28 (12.3%), 25 (11%), and 5 (2.2%) patients, respectively. It was noted that duodenal ulcer and gastric ulcer were seen significantly more common among males than females (n = 19 (67.9%) vs. n = 9 (32.1%) and n = 15 (60%) vs. n = 10 (40%), respectively, *P* < 0.001); in contrast, gastritis was more common among females n = 93 (64.6%) vs. n = 51 (35.4%) among male counterparts.

The colonization rate of *H. pylori* in relation to different endoscopy diagnosis is illustrated in Table 2. The overall prevalence of *H. pylori* infection in gastritis was 89 (61.8%), in duodenitis 18 (69.2%), in duodenal ulcer 24 (85.7%), in gastric ulcer 21 (84%), and in gastric Ca 3 (60%). Those with ulcerative lesion had significantly higher prevalence of *H. pylori* (*P* = 0.046); however, there was no significant difference in the prevalence of *H. pylori* between gastritis, duodenitis, and gastric carcinoma.

Rates of histological features and *H. Pylori* infection in relation to endoscopy diagnosis are shown in Table 3. The histological features were divided into CAG, CPG, and CFG, which were detected in 95 (41.7%), 87 (38.2%), and 42 (18.4%) of cases respectively. CAG was the frequent finding in those who had duodenal ulcer (n = 16; 57.1%), all of which (100%) were colonized with *H. pylori* followed by gastric ulcer (n = 11; 44%). CFG was most common in gastric ulcer (n = 10; 40%), whereas

Table 1: Prevalence of *H. pylori* among different age and gender groups

Age groups (years)	Male, no. (%)	Female, no. (%)	Overall, no. (%)
<20	4/5 (80)	6/6 (100)	10/11(90.9)
20-29	9/16 (56.3)	10/14(71.4)	19/30 (63.3)
30-39	13/22 (59.1)	25/33 (75.8)	38/55 (69.1)
40-49	11/16 (68.8)	10/21 (47.6)	21/37 (56.8)
50-59	17/20 (85)	15/24 (62.5)	32/44 (72.7)
60-69	10/14 (71.4)	16/21 (76.2)	26/35 (74.3)
≥70	7/9 (77.8)	2/7 (28.6)	9/16 (56.3)
Total	71/102 (69.6)	84/126 (66.7)	155/228 (68)

P = 0.049

Table 2: Prevalence of *H. pylori* in relation to endoscopy diagnosis

Endoscopy	Male, no. (%)	Female, no. (%)	Overall, no. (%)
Gastritis	32/51 (62.7)	57/93 (61.3)	89/144 (61.8)
Duodenitis	11/17 (64.7)	7/9 (77.7)	18/26 (69.25)
Duodenal ulcer	16/19 (84.2)	8/9 (88.8)	24/28 (85.7)
Gastric ulcer	12/15 (80)	9/10 (90)	21/25 (84)
Carcinoma		3/5 (60)	3/5 (60)
Total	71/102 (69.6)	84/126 (66.7)	155/228 (68)

P = 0.046

Table 3: *H. pylori* infection and histological features in relation to endoscopy diagnosis

Endoscopy diagnosis	CFG, no. (%)			CPG, no. (%)			CAG, no. (%)		
	Total	HP+	HP-	Total	HP+	HP-	Total	HP+	HP-
Gastritis	24/144 (16.7)	20/24 (83.3)	4/24 (16.7)	62/144 (43)	23/62 (37.1)	39/62 (62.9)	58/144 (40.3)	46/58 (79.3)	12/58 (20.7)
Duodenitis	2/26 (7.7)	2/2 (100)	0	14/26 (53.8)	6/14 (42.9)	8/14 (57.1)	10/26 (38.5)	10/10 (100)	0
Duodenal ulcer	6/28 (21.4)	5/6 (83.3)	1/6 (16.7)	6/28 (21.4)	3/6 (50)	3/6 (50)	16/28 (57.1)	16/16 (100)	0
Gastric ulcer	10/25 (40)	8/10 (80)	2/10 (20)	4/25 (16)	4/4 (100)	0	11/25 (44)	9/11 (81.8)	2/11 (18.2)
Total	42/228 (18.4)	35/42 (83.3)	7/42 (16.7)	87/228 (38.2)	36/87 (41.4)	51/87 (58.6)	95/228 (41.7)	81/95 (85.3)	14/95 (14.7)

CPG was common in non-ulcerative disease (duodenitis – $n = 14$; 53.8%; gastritis – $n = 62$; 43%). CAG and CFG were more common in ulcerative diseases, whereas CPG was more common in gastritis and duodenitis ($P < 0.001$). Those who had histological features of CAG had highest prevalence of *H. pylori* ($n = 81$; 85.3%), followed by CFG ($n = 35$; 83.3%) and CPG ($n = 35$; 41.4%) with P value < 0.001 .

Intestinal metaplasia was identified in 5% (11/228) of the sample, amongst which 6 (55%) had *H. pylori* positivity. The mean age of the patient with intestinal metaplasia was 55.7 ± 11.9 (range = 32-71), of which 5 were females and 6 were males. All the diagnosed 5 gastric cancer cases were females, of which 3 (60%) were *H. pylori*-positive.

Discussion

Since *H. pylori* was first discovered by Warren and Marshall in 1983, it has radically changed our understanding and clinical management of gastroduodenal disease, and much has been researched about its clinical aspects and its epidemiology.^[17] Its incidence and prevalence differs in relation to different factors like geography, ethnicity, age, and socio-economic factors — high in developing countries and lower in the developed world.^[2,3] Overall, researchers found a consistent pattern in most developing nations, where 70 to 90% of adults harbored the bacteria; most individuals acquired the infection as children, before age ten.^[4,5] Nepalese data show that the prevalence of *H. pylori* infection varies widely from 30-67%.^[6-10] The overall prevalence of *H. pylori* infection in our study was 68% (155/228) among symptomatic patients referred for endoscopies in our local setting. This is at the highest end of the range earlier reported in our country. The high prevalence was possibly because the study was done amongst only symptomatic patients.

The prevalence of active *H. pylori* infection was highest in the youngest group of < 20 years (90.9%), which probably reflects the acquisition of the infection during childhood. In terms of age, our data did not coincide with most published studies conducted previously, in which prevalence is seen to rise until it peaks in middle-aged individuals, around 50-60 years. No significant difference was found in the prevalence of infection by gender, except in ≥ 70 year group. Some studies has shown male predominance in infection,^[18-20] whereas others have not found any gender difference as in our study.^[10,21]

Many patients still attribute symptoms of dyspepsia to diet, stress, and lifestyle factors; however, it is now proven that *H. pylori* is the principal cause of chronic gastritis and is strongly associated with peptic ulcer disease as well as gastric cancer, including gastric lymphoma (MALT type).^[11] Prevalence of ulcerative disease in our study was 23.3% (53/228) and was significantly higher in males. The colonization rate by *H. pylori* was 85.7% (24/28) and 84% (21/25) in case of duodenal ulcer and gastric ulcer, respectively. A review article reported a colonization rate of *H. pylori* of 93% for patients with duodenal ulcer and 80% for those with gastric ulcer.^[22] Zhang C also found the colonization rate of 80.0% by *H. pylori* in cases of gastric ulcer, which was similar to our study.^[23] Lower *H. pylori* positivity in duodenal ulcers in our study can be due to prior treatment with proton pump inhibitors as those cases were not excluded. Moreover, the biopsy included tissue mostly from the antral mucosa only. It is suggested that four specimens (two antral, two corpus) should be sent for higher occurrence of the *H. pylori* positivity. For yielding positive rates after treatment, corpus biopsy is reported particularly helpful.^[24] Logan *et al.* showed that potent acid suppression with proton pump inhibitors resulted in a proximal shift of *H. pylori* from antrum to corpus in stomach.^[25]

According to the histological features, CAG was the most common finding followed by CPG and CFG (41.7%, 38.2%, and 18.4%, respectively). Rate of colonization with *H. pylori* was significantly higher in CAG and CFG in comparison to CPG (85.3%, 83.3% vs. 41.4%). In CFG, the *H. pylori* positivity should have been 100% as it has been proven that lymphoid aggregates with germinal centers are characteristic of chronic *H. pylori* gastritis.^[22] Again, this discrepancy is perhaps due to prior intake of proton pump inhibitors who were not excluded from the study, and absence of biopsy sample from corpus.

It is stated that the relative risk of developing gastric carcinoma is 3-6 folds greater in association with *H. pylori* infection versus control.^[13,14] The evidence supportive of an etiological association between *H. pylori* infection and gastric cancer was sufficient for a Working Group of the International Agency for Research on Cancer to classify such infection as a definite cause of cancer.^[15] Interestingly, in our study, all the cases of carcinoma stomach ($n = 5$) were detected only in females and *H. pylori* activity was noticed in 3 out of them (60%). Intestinal metaplasia was detected in 5% of the total sample ($n = 11$), 55% of which were colonized with *H. pylori*. However, the numbers were too small to comment on. Intestinal metaplasia and the

pre-malignant lesion could be detected more if a biopsy from incisura angularis was included. Reports have suggested that maximum degrees of atrophic changes and intestinal metaplasia are consistently identified in this region.^[26] The study done by Zhang C showed tight link between *H. pylori* infection and progression of the gastric pre-cancerous lesions, glandular atrophy, and intestinal metaplasia in various gastric lesion.^[19] Further studies need to be done in this regards as it is suggested that the development of gastric cancer spans over decade sequentially starting with the acquisition of *H. pylori* infection and the development of chronic active gastritis.^[27]

There are several limitations with our study. Firstly, our data sheet did not capture data on socio-economic status, education, previous use of drugs like Proton pump inhibitors, NSAID, or anti-platelets. Hence, we were unable to assess the association of these variables with *H. pylori* prevalence. Secondly, the biopsy sample from stomach was taken from antrum and other sites only if indicated. Therefore, topographic classification of gastritis, as described in the Sydney system, was not possible in this study.

Conclusion

Based on this study, the prevalence of *H. pylori* detected by histopathology among adult patients with gastrointestinal symptoms was high (68%). Rate of *H. pylori* infection was higher in youngest age group and lowest among oldest age group with no differences according to gender. Ulcerative lesions were found more common in male, whereas gastritis was common among female patients. The colonization of antrum with *H. pylori* was very high in ulcerative disease in comparison to non-ulcerative diseases. Histological diagnosis of CFG and CAG was seen commonly in ulcerative disease with higher *H. pylori* positivity rate in comparison to CPG.

The high prevalence of the *H. pylori* infection reflects that it is a major public health burden in developing countries like ours and thus an important agenda for public health investigation followed by implementation of proper strategies of control and eradication. Patients presenting for endoscopy for various complaints should routinely have their *H. pylori* status checked, regardless of indication. The disease has low mortality but has considerable individual suffering and consequently loss of manpower and also cumulative high cost for symptomatic therapy. In-depth further studies need to be done to evaluate the local antibiotic resistance pattern and to assess whether *H. pylori* infection is strongly related to pre-cancerous lesions like intestinal metaplasia and gastric cancer in this part of world.

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