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Endoscopic and histopathological findings in adult dyspeptic patients, and their association with *Helicobacter pylori* infection in Dhaka, Bangladesh

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ABSTRACT

Objectives: Conventional upper-intestinal endoscopy is usually performed to diagnose *Helicobacter pylori* (*H. pylori*) associated diseases, using gastric mucosa from the biopsy. The objective of our study was to identify the prevalence of *H. pylori* and its relation with endoscopic findings and histopathological features in dyspeptic adult patients.

Methods: Gastroduodenal biopsy specimens were collected from 143 adult dyspeptic outpatients who attended the Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Dhaka Medical College Hospital (DMCH), for endoscopy. *H. pylori* was identified by rapid urease test (RUT), *ureC* gene PCR, and histological staining (Giemsa).

Results: The study population was divided into *H. pylori*-positive cases (47; 32.9%) and *H. pylori*-negative cases (96; 67.1%), based on the case definitions used in the study. The highest rate of *H. pylori* infection was found in the 41–50 years age group (25.5%). Endoscopically, 101 (97.1%) dyspeptic patients had gastritis, with the majority of *H. pylori* infections found among histopathologically diagnosed duodenal ulcer patients. Endoscopic findings were significantly correlated with histological findings ($p < 0.001$).

Conclusion: Significant correlations between endoscopic and histopathological findings were observed. Early detection and prompt treatment of *H. pylori* infection are essential for the prevention of serious complications.

Introduction

Dyspepsia is a term used for acute, chronic, or recurrent pain or discomfort centered in the upper abdomen. It may be associated with upper abdominal fullness, early satiety, bloating, burning, belching, nausea, retching, and vomiting (Conroy and Siddiqi, 2007). In the western world, the prevalence of dyspepsia has been reported as ranging from 25% to 50% (Niknam et al., 2014), while in Asia 8–30% of people suffer from dyspepsia (Ghoshal et al., 2011). Dyspeptic individuals are over two times more likely to be *Helicobacter pylori* (*H. pylori*)-positive than asymptomatic individuals (Aminde et al., 2019). As many as 80% of developing country residents carry *H. pylori* in their gastric mucosa,

but only around 10–20% of infected individuals become symptomatic (Klusters et al., 2006). The most common symptom of *H. pylori* infection is dyspepsia, which is considered one of the most common causes of patient referrals to gastroenterology centers (Mapel et al., 2013). The prevalence of *H. pylori* infection in adult dyspeptic patients in India has been reported as 32.9% (Srinivas et al., 2016). A Bangladeshi study reported a prevalence of 47.8% *H. pylori*-positive cases among dyspeptic adult patients (Saha et al., 2018).

H. pylori has been linked to gastritis, duodenal ulcer, gastric carcinoma, and mucosa-associated lymphoid malignancies (Mishra et al., 2008). It is classified as a class 1 carcinogen by the World Health Or-

PCR, Polymerase Chain Reaction.

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ganization (WHO) and the International Agency for Research on Cancer (Smith et al., 2014). Treatment for *H. pylori* infection is recommended in all symptomatic individuals in order to prevent the development of gastric adenocarcinoma and for the successful treatment of *H. pylori*-induced mucosa-associated lymphoid tissue (MALT) lymphoma (Fock et al., 2009).

Several invasive and noninvasive techniques are currently used for detecting *H. pylori* infection, including rapid urease test (RUT), urea breath test, culture, PCR, serological tests, and histopathological methods (Krogh et al., 2005). Each test has its benefits and limitations in different clinical situations. None of these diagnostic tools is considered to be the gold standard, due to poor sensitivity or specificity. Conventional endoscopy, however, is a powerful diagnostic tool for diseases of the upper gastrointestinal tract, as it is necessary to view the condition of the mucosal lining of the stomach and duodenum (Nguyen et al., 2010). Moreover, gastric biopsy samples obtained during endoscopy are the best specimens for the isolation of *H. pylori* (Mégraud and Lehours, 2007). The choice of diagnostic test depends on the prevalence of *H. pylori*, the incidence of age-related gastric cancer in the area, the accessibility, advantages, and disadvantages of each method, and the different clinical circumstances for each patient (Selgrad and Malfertheiner, 2017).

This study was conducted to assess the relationship between upper GIT endoscopic findings associated with several gastroduodenal diseases and the presence of *H. pylori* infection among dyspeptic patients in Dhaka, Bangladesh.

Materials and Methods

This study included 143 adult Bangladeshi outpatients who underwent upper gastrointestinal endoscopic examination for various dyspeptic symptoms, including abdominal pain, nausea, vomiting, belching, lower chest pain, upper gastrointestinal bleeding, and weight loss, in the Department of Gastroenterology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, and Dhaka Medical College Hospital, Dhaka. This cross-sectional observational study was conducted over a period of 12 months, beginning in March 2018, in the Department of Microbiology and Immunology, Bangabandhu Sheikh Mujib Medical University (BSMMU).

Patients with severe medical illness and a history of intake of proton pump inhibitors, non-steroidal anti-inflammatory drugs (NSAID), colloidal bismuth compounds, or antibiotics for eradication of *H. pylori* over 4 weeks prior to enrolment were excluded from the study (Tongtawee et al., 2016). Once written informed consent had been collected from each patient, gastric tissues were collected from lesions and sites surrounding the gastric antrum and body. Biopsy samples were obtained using a standard forward-viewing video fiberoptic endoscope (Olympus EVIS EXERA III, CV-190, USA) with the patients in a left-lateral position, under topical lignocaine (2%) anesthesia. To avoid contamination, the endoscope was carefully cleaned and disinfected before and after each procedure. The first biopsy specimen was inoculated immediately into a screw-capped bottle containing rapid urease test (RUT) media; a positive result was indicated by a change in color from yellow to pink within 24 hours after incubation at 37°C. The next specimen was fixed in 10% buffered formalin and transported to the Department of Pathology, BSMMU for histological examination. Another biopsy specimen was collected in PBS for PCR, and stored at –20°C until DNA extraction was performed.

Histological examination

Tissue sections were prepared and stained with hematoxylin and eosin (H&E) for the diagnosis of gastroduodenal diseases and modified Giemsa stain for *H. pylori* detection. Based on histological examination findings, the study subjects were diagnosed as either chronic gastritis,

Table 1
Distribution of study population according to case definition (n = 143)

Study population	Number of cases	Percentage (%)
<i>H. pylori</i> -positive cases	47	32.9
<i>H. pylori</i> -negative cases	96	67.1

chronic gastric ulcer, duodenal ulcer, intestinal metaplasia, or gastric carcinoma.

ureC gene PCR

DNA was extracted from gastric tissues using QIAamp DNA mini kits (Qiagen, Hilden, Germany), according to the manufacturer's instructions. The *ureC* primer sequences used were: *ureC*-F 5'-AAGCTTTAGGGGTGTTAGGGGTTT-3', and *ureC*-R 5'-AAGCTTACTTTCTAACACTAACGC-3'. Amplification was performed according to Lu et al. (1999). The *ureC* gene PCR amplification products were 294 base pairs, and were electrophoresed in 2% agarose gel at 110 V for 42 minutes.

The study populations were categorized into two groups based on the case definitions used for this study. Patients were considered as *H. pylori*-positive when positive results were obtained in at least two of the three testing methods (rapid urease test, histology for *H. pylori*, and PCR for the *ureC* gene)

Data analysis

Descriptive and frequency analyses of the data from the study were expressed as counts, percentages, and means or medians, as appropriate, to provide an overall picture. The data were analyzed using the Statistical Package for Social Sciences (SPSS) version 23 (IBM, Armonk, New York). A chi-square/exact test was used where applicable. *P*-values < 0.05 were considered as denoting statistical significance.

Results

In total, 143 gastric biopsy specimens were collected from outpatients with dyspeptic symptoms who underwent endoscopy in the Department of Gastroenterology, BSMMU and Dhaka Medical College Hospital. RUT, histopathological examination, and PCR amplification of *ureC* gene for detection of *H. pylori* were performed.

The study populations were categorized into two groups according to the case definitions used in this study: *H. pylori*-positive patients (n = 47) and *H. pylori*-negative patients (n = 96) (Table 1).

Of the 47 *H. pylori*-positive cases, 91.5% were found to be positive by rapid urease test, followed by *ureC* gene PCR (89.3%), and histological staining (74.4%).

Of all 143 patients, 71 (49.7%) were female and 72 (50.3%) were male, giving an almost equal male:female ratio of 1.00:1.01). Of the 47 (32.9%) patients infected with *H. pylori*, 22 (46.8%) were male and 25 (53.2%) were female; thus, infection did not differ significantly between males and females (*p* = 0.553). Age and sex data for the patient cohort are shown in Table 2.

The most common endoscopic finding was erosive gastritis (53; 37.1%), followed by gastritis (48; 33.6%), gastric ulcer (20; 14.0%), duodenal ulcer (11; 7.7%), and gastric carcinoma (five, 3.5%).

The prevalences of *H. pylori* in relation to different endoscopy diagnoses are shown in Table 3. The overall prevalence of *H. pylori* infection in gastritis was 15 (31.9%), in erosive gastritis 14 (29.8%), in gastric ulcer eight (17.0%), in duodenal ulcer seven (14.9%), in gastric carcinoma one (2.1%), and in normal gastric mucosa two (4.3%). Endoscopic findings such as gastritis, gastric ulcer, and duodenal ulcer were not significantly associated with *H. pylori*.

The rates of *H. pylori* infection for different gastroduodenal diseases detected by histopathology are shown in Table 4. Histologically, the

Table 2
Age and sex distribution of study population

Characteristics	All patients (n = 143)	<i>H. pylori</i> (+) (n = 47)	<i>H. pylori</i> (-) (n = 96)	p-value
Age, mean years (%)	42.33 ± 14.30	44.03 ± 16.20	41.48 ± 13.31	0.260
Age group				
≤ 20	7 (4.22)	2 (4.3)	5 (5.2)	0.960
21–30	23 (16.08)	7 (14.9)	16 (16.7)	
31–40	25 (17.48)	9 (19.1)	16 (16.7)	
41–50	39 (27.27)	12 (25.5)	27 (28.1)	
51–60	25 (17.48)	10 (21.3)	15 (15.6)	
> 60	24 (16.78)	7 (14.9)	17 (17.7)	
Sex				
Male	72 (50.35)	22 (46.80)	50 (52.08)	0.553
Female	71 (49.65)	25 (53.20)	46 (47.92)	

Table 3
Prevalence of *H. pylori* in relation to endoscopic findings

Endoscopic finding	<i>H. pylori</i> (+) (n = 47)	<i>H. pylori</i> (-) (n = 96)	All patients (n = 143)	p-value
Gastritis, n (%)	15 (31.9%)	33 (34.4%)	48 (33.6%)	0.251
Erosive gastritis, n (%)	14 (29.8%)	39 (40.6%)	53 (37.1%)	
Gastric ulcer, n (%)	8 (17.0%)	12 (12.5%)	20 (14.0%)	
Duodenal ulcer, n (%)	7 (14.9%)	4 (4.2%)	11 (7.7%)	
Gastric carcinoma, n (%)	1 (2.1)	4 (4.2)	5 (3.5%)	
Normal, n (%)	2 (4.3)	4 (4.2)	6 (4.2%)	

Table 4
H. pylori infection status and gastroduodenal disease diagnosed by histopathological examination among the study population (n = 143)

Histopathological finding	<i>H. pylori</i> -positive cases, n (%)	<i>H. pylori</i> -negative cases, n (%)	All patients, n = 143 (%)	p-value
Chronic gastritis	31 (30.7)	70 (69.3)	101 (70.63)	0.390
Chronic gastric ulcer	7 (36.8)	12 (63.2)	19 (13.28)	0.882
Duodenal ulcer	5 (55.5)	4 (44.5)	9 (6.30)	0.134
Intestinal metaplasia	2 (50.0)	2 (50.0)	4 (2.80)	0.459
Gastric carcinoma	1 (33.3)	2 (66.7)	3 (2.09)	0.986
Normal dyspeptic	1 (14.3)	6 (85.7)	7 (4.90)	0.283

Table 5
Relationship between endoscopic findings and histopathological findings among the study population (n = 143)

Endoscopic findings	Histopathological findings						Total
	Gastritis, n (%)	Chronic gastric ulcer, n (%)	Duodenal ulcer, n (%)	Intestinal metaplasia, n (%)	Gastric carcinoma, n (%)	Normal, n (%)	
Gastritis	98 (97.1)	0 (0)	0 (0)	0 (0)	0 (0)	3 (2.9)	101 (70.6)
Gastric ulcer	0 (0)	19 (95.0)	0 (0)	1 (5.0)	0 (0)	0 (0)	20 (13.9)
Duodenal ulcer	1 (9.1)	0 (0)	9 (81.8)	1 (9.1)	0 (0)	0 (0)	11 (7.6)
Gastric carcinoma	0 (0)	0 (0)	0 (0)	2 (40.0)	3 (60.0)	0 (0)	5 (3.5)
Normal	2 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	4 (66.7)	6 (4.2)
Total	101 (70.6)	19 (13.3)	9 (6.3)	4 (2.8)	3 (2.1)	7 (4.9)	143 (100)

highest rate of *H. pylori* infection was found among patients with duodenal ulcer (55.5%), followed by intestinal metaplasia (50%), gastric ulcer (39.8 %), gastric adenocarcinoma (33.3%), chronic gastritis (30.7%), and normal gastric mucosa (14.3%).

The relationships between histopathology findings and endoscopic findings are shown in Table 5. Of the 101 endoscopically reported gastritis patients, 98 (97.1%) had gastritis and three (2.9%) had normal gastric mucosa. Of the 20 cases of gastric ulcer reported on endoscopy, 19 (95.0%) had chronic gastric ulcer and one (5.0%) had intestinal metaplasia. Of the 11 endoscopically reported duodenal ulcer patients, nine (81.8%) also had duodenal ulcer according to histopathological examination, one (9.1%) had gastritis and one (9.1%) had intestinal metaplasia. Of the five endoscopically reported gastric carcinoma patients, three (60.0%) showed gastric adenocarcinoma histologically and two (40.0%)

exhibited intestinal metaplasia. Endoscopic findings were significantly correlated with histological findings ($p < 0.001$).

Discussion

In total, 143 gastric biopsies were collected from dyspeptic patients who underwent endoscopy examination in the Department of Gastroenterology, BSMMU and Dhaka Medical College Hospital, Dhaka. For this study, *H. pylori* was detected by both phenotypic methods, such as rapid urease test and histological staining for *H. pylori*, and genotypic methods, such as *ureC* gene PCR. According to the definition of *H. pylori*-positive cases used in this study, only 47 (32.9%) were classified as *H. pylori*-positive and 96 (67.1%) as *H. pylori*-negative. This finding was in agreement with the findings of Niknam et al. (2014), who reported 31%

H. pylori positivity among the adult dyspeptic population in Iran, and Aftab et al. (2018), who reported a 47% prevalence of *H. pylori* infection in adult dyspeptic patients in Bangladesh. In our study, only one gastric tissue biopsy was used in each test for determining *H. pylori*, although the organism is unevenly distributed throughout the gastric mucosa; this could have been a contributing factor to the comparatively lower prevalence of *H. pylori* detected. Moreover, the possible noncompliance of some participants with regard to not using proton pump inhibitors during the 4 weeks prior to endoscopic examination might have produced false-negative results with the rapid urease test and histopathology. Recently, several studies from Asian and Middle-Eastern countries have reported declining trends in *H. pylori* infection with improvements in hygiene conditions (Chen et al., 2007); Alazmi et al., 2010; Yim et al., 2007).

The study population ranged from 18 to over 65 years of age, with a mean age of 44.03 ± 16.20 years for *H. pylori*-positive cases. The prevalence of active *H. pylori* infection was highest in the 41–50 years age group (25.5%) and lowest (4.3%) in the < 20 years age group. Helaly et al. (2009) also found the highest percentage of *H. pylori* infection in the 41–50 years age group. The acquisition of *H. pylori* can occur at a young age as part of normal flora; however, in absence of treatment, infection can persist throughout the individual's lifetime and manifest later in life.

Higher prevalences of *H. pylori* have been found to be associated with lower socioeconomic groups, as well as with large families, poor hygiene, low standards of living, and overcrowded conditions (Rastogi et al., 2016). Studies have also suggested that older age groups have been more exposed to other etiological factors, such as NSAIDs, smoking, and stress, which are all potential contributing factors to a higher prevalence of *H. pylori* (Mabeku et al., 2018).

Among the 143 dyspeptic cases in our study, 71 (49.7%) were female and 72 (50.3%) were male, giving an almost equal male:female ratio. The prevalence of *H. pylori* infection was slightly higher in the female population (53.20%) compared with males (46.80%), although this difference was not significant. This finding was similar to that in a study by Singh et al. (2002), which did not find any significant association between *H. pylori* infection and sex distribution. However, another study found males to have a greater prevalence of *H. pylori* infection (Ibrahim et al. (2017)).

Among the 143 cases in our study, the majority of patients were endoscopically reported as having erosive gastritis (37.1%), followed by gastritis (33.6%), gastric ulcer (14.0%), duodenal ulcer (7.7%), and gastric carcinoma (3.5%); these figures were similar to those found in another study conducted in Dhaka (Kismat et al., 2019). In our study, gastritis was the most common endoscopic abnormality among the study population, and also among those who were found to be infected with *H. pylori*. However, there was no statistically significant association between gastritis and *H. pylori* infection.

The most common histopathological finding was chronic gastritis (70.63%), followed by gastric ulcer (13.28%), duodenal ulcer (6.30%), intestinal metaplasia (2.80%), gastric carcinoma (2.09%), with 4.90% found to have normal gastric mucosa.

In this study, 55.5% of the duodenal ulcer patients and 30.7% of the chronic gastritis patients were infected with *H. pylori*. These findings were in agreement with those of Helaly et al. (2009), who found 54.5% of duodenal ulcer patients and 41.1% of gastritis patients to have *H. pylori* in Egypt. In our study, among the 47 *H. pylori*-positive cases, 50% had intestinal metaplasia according to histopathology, which was similar to the finding of Lee et al. (2007).

Among the 101 endoscopically reported gastritis patients, 97.1% had gastritis, and 2.9% had normal mucosa. Of the six endoscopically diagnosed normal cases, 33.3% were diagnosed with gastritis of various grades, and 66.6% had normal mucosa. Out of 20 endoscopically diagnosed gastric ulcer cases, 19 (95.0%) were diagnosed as chronic gastric ulcer and one (5.0%) as intestinal metaplasia in histopathology. 81.8% of the duodenal ulcer cases in endoscopy were diagnosed as duodenal

ulcer in histology. Out of six gastric carcinoma cases in endoscopy, three (60.0%) were diagnosed as adenocarcinoma and two (40.0%) as intestinal metaplasia in histology. Endoscopic findings were significantly correlated with histological findings ($p < 0.001$).

Clinicians should test and treat *H. pylori* infection if resources are available. In resource-poor settings, where the confirmatory test is not available or may not be cost effective, empirical therapy is recommended.

Conclusion

H. pylori infection is one of the major causes of dyspeptic symptoms in the Bangladeshi population. Although its prevalence is declining, it is still a public health burden in a developing country like Bangladesh because it causes considerable individual suffering and, consequently, loss of manpower. Proper evaluation and eradication therapy are needed to overcome this situation. Since significant correlations between endoscopy and histopathology findings have been observed, endoscopic examination can be used as an alternative for gastric disease detection where histopathology is not available. However, normal endoscopic appearance is a poor predictor of histological findings. *H. pylori* infection may be positively associated with duodenal ulcer and intestinal metaplasia in a statistically significant manner.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Ethical Approval Statement

Ethical clearance was granted by the Institutional Review Board (IRB), BSMMU.

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