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Prevalence and Endoscopic Findings of *Helicobacter pylori* Infection among Dyspeptic Patients in Kenya

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Abstract

Background: *Helicobacter pylori* is the most common cause of chronic human infections worldwide with the highest reported prevalence in Africa. It is associated with numerous upper gastrointestinal diseases such as gastritis, peptic ulcers, and gastric cancer. Endoscopic findings in the stomach usually associated with *Helicobacter pylori* infections include gastritis and gastro-esophageal reflux disease (GERD), however, these findings are suggestive but not diagnostic of *Helicobacter pylori* infection. **Methods:** This was a prospective study conducted between January 2018 and February 2019 at the Aga Khan University Hospital where dyspeptic patients scheduled for gastroduodenoscopy were enrolled. These patients were evaluated for *Helicobacter pylori* infection by rapid urease test, culture and histopathology. Diagnostic findings and patient history collected from medical files were documented and data analyzed. **Results:** A total of 487 dyspeptic patients undergoing esophagogastroduodenoscopy (EGD) were enrolled in the study and 199 dyspeptic patients were positive for *Helicobacter pylori* infection. The prevalence was 54.6% in males and 45.4% in females ($p = 0.1546$. The most common clinical indication and endoscopic findings were heart burn (25.2%) and gastritis (53.7%). Histopathology revealed that 86.1% of the dyspeptic patients had chronic active gastritis ($p < 0.005$) and 52.8% of them had *H. pylori* infection. **Conclusions:** Classical endoscopic findings such as GERD are not always indicative of *H. pylori* infection as its association with *H. pylori* infec-

tion was not statistically significant in this study.

Keywords

Helicobacter pylori, Dyspepsia, Esophagogastroduodenoscopy (EGD), Histopathological Examination

1. Introduction

Dyspeptic patients usually present with a predominant epigastric pain lasting at least 1 month and may be associated with any other upper gastro intestinal symptom such as epigastric fullness, nausea, vomiting, or heartburn [1]. Dyspeptic individuals are over two times more likely to be *Helicobacter pylori* positive, than asymptomatic persons [2]. Infecting more than 50% of the population, *Helicobacter pylori* is the most prevalent human pathogen that causes chronic infection [3]. It has a determinant pathogenic role in the development of gastric adenocarcinoma and gastric mucosa-associated lymphoid tissue (MALT) lymphoma and is categorized as a class I carcinogen by the International Agency for Research on Cancer (IARC), a division of the World Health Organization (WHO) [4]. Patients with *Helicobacter pylori* infection may clinically present with dyspepsia, heartburn, abdominal pain, diarrhea, or halitosis. Accurate diagnosis of *Helicobacter pylori* infection is a crucial part of the effective management strategy to minimize the *Helicobacter pylori*-related gastro-pathologies, and gastric cancer [5]. Although several invasive and non-invasive diagnostic tests are available for the detection of *Helicobacter pylori* and each test has its usefulness and limitations in different clinical situations. The diagnostic preferences are based on the prevalence of *Helicobacter pylori* infection, availability of test, turn-around time and age-related gastric cancer incidence in each area. Conventional EGD is however a powerful diagnostic tool for upper gastrointestinal tract diseases as it's necessary to view the condition of the mucosal lining of the stomach and duodenum [6]. Biopsy specimens are obtained from the gastric antrum and corpus and to perform a histopathology examination on the obtained specimens. Histopathology is the most common diagnostic tool in the direct detection of *Helicobacter pylori* infection and is also the first method used for the detection of *Helicobacter pylori* [7]. Additional biopsies for rapid urease test and culture can be taken during endoscopy if treatment is to be offered upon confirmation of infection [7]. Neither of these diagnostic tools is considered to be the gold standard due to poor sensitivity or specificity. The choice of diagnostic test depends on the prevalence, age-related gastric cancer incidence in each area, accessibility, advantages and disadvantages of each method as well as different clinical circumstances of each patient [8] Aim of the study was to investigate association of *Helicobacter pylori* infection with endoscopic findings amongst dyspeptic patients at Aga Khan University Hospital.

2. Method

2.1. Study Design and Setting

This was a prospective study conducted from February 2018 to November 2019 at Aga Khan University Hospital, Kenya. The Aga Khan University Hospital is a comprehensive care and teaching hospital with inpatient and outpatient services, located in Nairobi County, the capital city of Kenya.

2.2. Sampling and Study Participants

The sample size for this study was calculated using the Chadha sampling formula for sample size estimation considering, a sampling error of 0.05, confidence level 95%, absolute precision required on either side of the prevalence proportion (0.05) and prior prevalence estimate of 67.5% based on a previous study conducted in the hospital [9] a sample of 487 was estimated. A total of 487 dyspeptic patients referred for EGD at the Endoscopy unit of Aga Khan University Hospital, Nairobi were then enrolled in this study. Eligibility criteria included patients showing dyspeptic symptoms undergoing EGD with no risk of bleeding complications. Duration of symptoms was not taken into account, as this was absent in some records of patients that fulfilled eligibility criteria for the study during the study period.

2.3. Study Procedures and Data Collection

The study protocol was approved by the Institutional Ethics Committee of the Aga Khan University Hospital (Ref: 2017/REC-97 (vl)) and the Kenyatta University Ethical Review Committee PKU/509/1602-PKU/447/E39. Data was collected from patient medical records containing the patient identification, age, sex, clinical presentation, presumptive diagnosis, laboratory investigations and results.

2.4. EGD

During the EGD of the dyspeptic patients, gastric biopsies were collected from suspected are of each anatomical site, the antrum and the corpus by a gastroenterologist. During each EGD session, endoscopic findings were reported and recorded.

2.5. Rapid Urease Test

Rapid urease test (RUT) was conducted from an additional antrum biopsy placed on Pronto Dry Urease® Test according to the manufacturer's instructions. Rapid Urease Test positive samples, pink to red were placed in transport media for processing in the microbiology laboratory.

2.6. Histopathology

Biopsy specimens from the greater curvature of the mid-antrum, the lesser curvature of the angulus, and the greater curvature of the mid-corpus, were collected and fixed in 10% buffered formalin for 24 hours and then embedded in

paraffin. *Helicobacter pylori* bacilli cells were identified by Giemsa staining while host tissues were analyzed under Haematoxylin and Eosin staining by a pathologist.

2.7. Culture

Helicobacter pylori was isolated from grinded gastric biopsy samples in 1.5 ml of BHI broth supplemented with 10% fetal bovine serum and inoculated on Brucella agar (Brucella agar (BD Difco, USA) supplemented with 7% sheep blood. The plates were incubated up to 7 days at 37˚C in anaerobic jars containing Campy-gen kit (BD) sachets creating microaerophilic conditions.

Helicobacter pylori isolates were identified on the basis of colony morphology, Gram staining results, and positive reactions for oxidase, catalase, and urease.

2.8. Study Variables

The following data were collected: socio-demographic characteristics including gender, age, previous *Helicobacter pylori* infection, endoscopic findings, histopathology findings, rapid urease test and culture results, clinical presentation: epigastric pains, acid reflux, bloating, dysphagia, nausea/vomiting and belching.

2.9. Data Management and Statistical Analysis

The data generated were coded, entered, validated and analyzed using R. We tested for association in categorical variables using the chi-squared test, reporting corresponding p-values. In case of small numbers in a given group (< 5), the Fischer's exact test was used, and the corresponding p-value reported. Continuous data were analyzed using *t*-test and categorical data were analyzed using Chi-square test.

3. Results

In the duration of the study, a total of 487 dyspeptic patients were enrolled with mean age of 39.23 years a range between 0.5 and 86 years, and mode of 35 years. Among the patients, 266 were male and 221 were female, with 80.3% residing in urban areas. All patients underwent EGD and routine biopsy for detection of presence or absence of *H. pylori* based on histopathological test. There were no significant differences in sex and age distribution based on the source of enrollment.

Based on histopathology results, 199 (40.86%) of dyspeptic patients were infected by *H. pylori*; 98 (49.3%) were female and 101 (50.7%) were male and this was not statistically significant (0.1546). The characteristics of the study population are shown on Table 1.

The infection by *H. pylori* did not differ significantly between males and females (p = 0.1546). The highest prevalence *H. pylori* infection was obtained in the age group of 31 - 40 (25.1%) and lowest amongst patients below 10 years. We observed patients with previous *H. pylori* infection was statistically significant

Table 1. Characteristics of the study population.

	Frequency (%)	*H. pylori* positive	Odds ratio (95% CI)	p-value
Sex				
Males	266 (54.6)	101 (50.7)	0.7683 (0.5344 to 1.1045)	0.1546
Females	221 (45.4)	98 (49.3)	Ref.	
Age group				
<10	39 (8.0)	16 (8.0)	Ref.	
11 - 20	71 (14.5)	21 (10.6)	0.6038 (0.2668 to 1.3662)	0.2259
21 - 30	101 (20.7)	30 (15.1)	0.6074 (0.2819 to 1.3088)	0.2030
31 - 40	89 (18.2)	50 (25.1)	1.4668 (0.6930 to 3.1050)	0.3167
41 - 50	65 (13.3)	42 (21.1)	2.6250 (1.1609 to 5.9354)	0.0204
51 - 60	69 (14.2)	22 (11.1)	0.6729 (0.2980 to 1.5194)	0.3404
≥60 years	53 (10.8)	18 (9.0)	0.7393 (0.3145 to 1.7376)	0.4884
Residence				
Urban	391 (80.3)	163 (81.9)	Ref.	
Rural	68 (14)	24 (12.1)	0.7630 (0.4462 to 1.3046)	0.3229
Immigrant	28 (5.7)	12 (6.0)	1.0491 (0.4833 to 2.2772)	0.9036
Previous *H. pylori* infection				
No	461 (94.7)	181 (91.0)	Ref.	
Yes	26 (5.3)	18 (9.0)	3.4807 (1.4824 to 8.1726)	0.0042

compared with patients who had no previous *H. pylori* infection in the study ($p < 0.0042$).

With regard to the clinical signs, 25.2% of the patients presented with heartburn as the sole clinical indication. Most of the *H. pylori* infected patients, based on histopathology results, dyspeptic patients had a higher rate of developing heartburn as the sole clinical indication and may imply that it is highly suggestive of *H. pylori* infection in the study (Table 2).

As part of the study, the biopsies were screened for presence of *H. pylori* using rapid urease test and bacterial culture. A total of 169 (84.9%) of histopathology *H. pylori* positive biopsy specimen were rapid urease test positive while only 120 (60.3%) were culture positive. The rapid urease test had a sensitivity of 84.92% while the specificity was 100%. Only biopsies that were rapid urease positive were processed for culture.

The most common endoscopic finding was gastritis 262 (53.7%) followed by nodular gastritis 92 (18.9%), GERD (5.3%), gastric ulcer 18 (3.7%), duodenal ulcer 14 (%) and gastric cancer 7 (1.4%) were detected. The endoscopic findings such as gastritis, gastric ulcer, duodenal ulcer were not significantly associated with *H. pylori*. Thirty-six patients were had no pathological abnormalities reported after EGD. Patients with *H. pylori* infection had significantly higher endoscopic finding of gastritis than patients who were *H. pylori* negative. The histopathological findings of the study patients undergoing EGD are shown in Table 3.

Table 2. Relationship between clinical indications of the study population and *H. pylori* status.

	Frequency (%)	Histopathology *H. pylori* positive	Odds ratio	p-value
Clinical Indication				
Heartburn	122 (25.2)	41 (20.6)	Ref.	
Belching	6 (1.2)	3 (1.5)	1.9756 (0.3818 to 10.2237)	0.4169
Bloating	32 (6.5)	18 (9.0)	2.5401 (1.1493 to 5.6139)	0.212
Constipation	51 (10.4)	36 (18.1)	4.7415 (2.3314 to 9.6430)	<0.0001
Dysphagia	28 (5.7)	17 (8.5)	0.4146 (0.1512 to 1.1373)	0.0873
Epigastric	32 (6.6)	17 (8.5)	0.3041 (0.1162 to 0.7955)	0.0153
Hematemesis	4 (0.8)	2 (1)	0.2683 (0.0339 to 2.1260)	0.2128
Melena	42 (8.7)	16 (8.0)	0.1651 (0.0664 to 0.4108)	0.0001
Nausea	70 (14.4)	24 (12.1)	0.1400 (0.0611 to 0.3206)	<0.0001
Vomiting	72 (14.8)	20 (10.1)	0.1032 (0.0445 to 0.239)	<0.0001
Others	28 (5.7)	5 (2.5)	0.0583 (0.0180 to 0.1887)	<0.0001

Table 3. Relationship between endoscopic findings of the study population and *H. pylori* status.

	Frequency (%)	Histopathology	Rapid urease test	Culture positive
Endoscopic findings				
Gastritis	262 (53.7)	108 (59.29)	103 (72.8)	66 (55)
Nodular gastritis	92 (18.8)	32 (16.1)	29 (17.1)	27 (22.5)
GERD	26 (5.3)	22 (11)	5 (2.9)	3 (2.5)
Gastric ulcer	18 (3.7)	15 (7.5)	11 (6.5)	7 (5.8)
Duodenal ulcer	14 (2.8)	11 (5.5)	7 (4.1)	7 (5.8)
Hiatus hernia	12 (2.5)	0 (0)	0 (0)	0 (0)
Gastro-duodenal ulcer	8 (1.6)	5 (2.5)	5 (2.9)	4 (3.3)
Erythematous gastritis	5 (1.02)	3 (1.5)	3 (1.7)	1 (0.83)
Gastric cancer	7 (1.4)	1 (0.1)	1 (0.6)	1 (0.83)
Other	7 (1.4)	3 (1.5)	3 (1.7)	2 (1.66)
No abnormalities	36 (7.4)	3 (1.5)	3 (1.7)	2 (1.66)

In general, most of the patients had a histopathological finding of chronic active gastritis (86.1%) while only 1.7% of the patients had hiatal hernia as shown in Table 4. Patients who had *H. pylori* had significantly higher chronic active gastritis (91.9%) as compared to *H. pylori* negative subjects (9.1%).

Table 4. Histopathology examination findings.

	Frequency (%)	*H. pylori* positive	Odds ratio	p-value
Endoscopic findings				
Chronic active gastritis	346 (86.1)	183 (91.9)	Ref.	
Intestinal metaplasia	17 (4.2)	2 (1)	0.1188 (0.0268 to 0.5272)	0.0051
Dysplasia	9 (2.2)	2 (1)	0.2545 (0.052 to 1.2425)	0.0907
Gastric antrum erythema	7 (1.7)	1 (0.5)	0.1485 (0.0177 to 1.2461)	0.0789
Lymphocytic gastritis	16 (3.9)	6 (3.0)	0.3340 (0.1277 to 0.8739)	0.0254
Gastric carcinoma	7 (1.7)	1 (0.5)	0.1272 (0.015 to 1.0453)	0.055

4. Discussion

In our study, the prevalence of *H. pylori* infection was 40.86%, lower than a previous study conducted at the hospital [9]. However, the previous study was 9 years older and current prevalence might have decreased due to excellent diagnostic modality resulting in earlier treatment, empirical therapy or improved sanitation. This may also not reflect the prevalence of *H. pylori* infection in Kenya as different prevalence rates of *H. pylori* infection have been reported in different regions within the same country [10] [11]. Our prevalence was also low compared to reports from other developing countries such as Nigeria (64%) [12], Tanzania (65%) [13], South Africa (77.6%) [14], Bhutan (73.4%) [15], India (83.3%) [16]. The prevalence of this study was relatively higher than other developed countries such as the United Kingdom 27.4% [17], United States of America 35.6%, Sweden 26.2% and New Zealand 24% [14]. The differences between the prevalence of our study and the studies highlighted above may be due to different diagnostic methods, patient selection, sanitation, urbanization and varied economic status.

Our study also confirms male predominance in *H. pylori* infection than the females as they are naturally more active and less hygienic than females, and poor hygiene is a risk factor *H. pylori* infection [18]. Other factors have been suggested as having a possible explanation of this incongruence such as protective and aggressive immune response exerted by females via estrogen during *H. pylori* infection [18]. This may explain the higher prevalence of *H. pylori* infections among the male than females such as gastritis, gastric cancer and peptic ulcers [18].

Recurrent infection was observed in 9% of *H. pylori* infected patients, which is congruent with reports of high recrudescence or reinfection rate of *H. pylori* [19]. It is reported that the recurrence rates from different studies have ranged between 0% - 23.4% [20]. The recurrence of *H. pylori* infections is related to factors such as sanitation, hygiene, population susceptibility and prevalence of *H. pylori* infection [20]. Clinical indications of nausea, vomiting and melena were suggestive of *H. pylori* infection among the dyspeptic patients ($p < 0.001$). The most frequent symptom among dyspeptic patients was heart burn and con-

stipation, and other studies have reported varying clinical indications [2].

In our study, gastritis was found to be 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 statistical significance between gastritis and *H. pylori* infection. These results do not match with reports in literature that this infection is a major cause of gastritis [21]. Our study also demonstrated the association between *H. pylori* infection and gastric ulcer and duodenal ulcer is statistically significant as also reported by Kumar *et al.* [16].

Atrophy, dysplasia and intestinal metaplasia are of great clinical importance as they are considered as part of the multistep process of cancer development as described by Park *et al.* [22]. The prevalence of atrophy and dysplasia was relatively low in our study at 1% and 2.2% respectively. However the prevalence of metaplasia was 4.2%, considerably higher than atrophy and dysplasia and its prevalence in the general population is known to vary globally [22].

H. pylori has been identified as a Group I carcinogen by the International Agency for Research on Cancer as approximately 89% of all gastric cancers can be attributed to *H. pylori* infection [23]. Gastric cancer is one of the leading causes of cancer mortality worldwide and the 9th highest cause of cancer in Kenya: a major cause of morbidity and mortality [24]. The incidence of gastric cancer is highly variable by region and culture, however, is more frequently diagnosed in developed nations [25]. The frequency of gastric cancer in the study was 1.4%, which is considerably lower than as reported in a study conducted in 2018 where the prevalence was 3.67%.

A limitation in this study is that only rapid urease positive gastric biopsies were processed for bacterial culture hence culture positive samples of rapid urease test negative biopsy specimen could have been missed. It should be noted that this study and its findings were in selected symptomatic population. Clinical indications and endoscopic findings commonly associated with *H. pylori* infection are not always indicative of the infection. It is not possible to attribute the universality of dyspeptic clinical indications and EGD findings to *H. pylori* infections as we found in our study.

Conflicts of Interest

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

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