Endoscopic and Microbiological Findings of *Helicobacter pylori* Infection among Dyspeptic Patients in Suez Canal University Hospital

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**ABSTRACT**

**Background:** *Helicobacter pylori* (*H.pylori*) infection is a chronic bacterial infection affecting the gastric mucosa leading to wide spectrum of gastrointestinal disorders ranging from chronic gastritis and peptic ulcer disease to gastric carcinoma. **Objectives:** This study was performed to describe endoscopic features and microbiological findings of *H.pylori* related dyspepsia among dyspeptic patients attending Gastrointestinal Tract Endoscopy Unit in Suez Canal University Hospital. **Methodology:** This single-center, cross-sectional descriptive study recruited all patients, aged over 18 years of both sex with dyspeptic symptoms who agreed for endoscopic evaluation. Gastric biopsy samples were obtained; histological examination and culture were performed for every patient with Rapid Urease Test (RUT) positive sample. **Results:** Out of 95 adult patients with dyspeptic symptoms underwent upper endoscopy after giving consent, 96.8% were diagnosed to have *H.pylori* infection using histological examination while only 7.4% of them were positive for *H. pylori* by culture. **Conclusion:** There is a high prevalence of *H.pylori* associated dyspepsia. Culture has a little yield in diagnosing *H.pylori* infection compared to histological examination.

**INTRODUCTION**

*Helicobacter pylori* (*H.pylori*) is a gram-negative micro aerophilic bacterium that specifically infects the stomach leading to chronic colonization of the gastric mucosa.

There is a high prevalence of *H. pylori* infection throughout the world; as more than 50% of the global population were found to be infected. Overall, the infection is more prevalent in developing (50.8%) compared to developed (34.7%) countries. Africa had the highest prevalence of *H. pylori* infection (70.1%), and based on regional prevalence estimates, there were approximately 4.4 billion individuals with *H pylori* infection worldwide in 2015. Geographical location, age and socio-economic status have significant impact on the prevalence of *H.pylori* infection.

*H. pylori* is causally linked to a wide spectrum of gastrointestinal disorders ranging from chronic gastritis and peptic ulcer disease to gastric adenocarcinoma and gastric mucosa-associated lymphoid tissue (MALT) lymphoma. Peptic ulcers develop in 1–10% of those infected, while gastric adenocarcinoma and gastric MALT lymphoma present in 0.1–3% and <0.01% of infected individuals, respectively.

There are several methods for diagnosing *H.pylori* infection. Invasive techniques involve Upper Gastrointestinal (UGI) Endoscopy to diagnose *H.pylori* related gastric pathology and the other tests based on tissue biopsies taken using the endoscopy as histopathological examination, rapid urease test (RUT) and molecular methods. Non-invasive techniques include blood antibody test, stool antigen test and urea breath test.

*H. pylori* infection is typically treated with combinations of 2–3 antibiotics along with a proton pump inhibitor (PPI), taken concomitantly or sequentially, for periods ranging from 3 to 14 days. The initial course used for eradication therapy referred to as “first-line” therapy usually offers the greatest likelihood of treatment success; so it should be carefully selected for proper management. Unfortunately, the success rate of first-line triple therapy has fallen in many countries, with eradication rates of just 55–57% reported from countries in Western Europe. A number of factors contribute to treatment failure, including high bacterial load, low gastric pH, impaired mucosal immunity, poor patient compliance and antibiotic resistance associated with global antibiotic abuse.

In the setting of this dynamic and serious *H. pylori* infection with high prevalence, wide range of clinical features, different empiric antimicrobials used for eradicating it and rising reports of antibiotic resistance, we needed to understand our current situation regarding *H. pylori* prevalence, clinical, endoscopic, histopathological and laboratory features in order to
improve its management outcomes and minimize its hazardous complications.

METHODOLOGY

Study design:
This cross sectional descriptive study included 95 adult patients with dyspeptic symptoms who were submitted to UGI endoscopy at Gastrointestinal Endoscopy Unit in Suez Canal University Hospital. All patients with gall bladder or pancreatic diseases presenting with dyspepsia, those who were on H.pylori eradication therapy till 4 weeks or on anti-secretory drugs till 2 weeks before endoscopy were excluded.

Patient assessment was done using close ended questionnaire including sociodemographic data, smoking status, usage of Non-steroidal anti inflammatory drugs (NSAIDs), antibiotics or Proton Pump Inhibitors (PPIs) and history of presenting symptoms.

The study was approved by the Ethics Committee of Suez Canal University Faculty of Medicine. Written, informed consent was obtained from each patient included in this study.

Gastric biopsy specimens:
Upper GI endoscopy was done for all participants with 2 tissue biopsies taken from both antrum and corpus for each patient. One part of the specimen was used for Rapid urease test (RUT) and another section was added into brucella broth (Merck Germany) and was transferred to the Microbiology Laboratory in Faculty of Medicine, Suez Canal University within 3 hours.

Histopathological examination and culture of H. pylori
After hematoxylin and eosin staining, all biopsies were examined histopathologically by blinded gastrointestinal pathologists. Histological findings were reported based on Sydney classification of chronic gastritis.

In the microbiology lab, the gastric biopsies were crushed and the resulting extracts were cultured on brucella agar (Merck, Germany) who were supplemented with 7% defibrinated sheep blood, 7% fetal calf serum (FCS) and antibiotic supplements (10 mg/l vancomycin, 5 mg/l amphotericin B, 5 mg/l trimethprim and 20 U/ml polymyxin B). The plates were incubated at 37 °C for 5-7 days under micro-aerophilic conditions (10% CO₂, 5% O₂, and 85% N₂, Merck Camp Gas Pak). Bacterial isolates were identified according to colony morphology, Gram stain and biochemical reactions.

Statistical analysis
Statistical analyses were performed using the statistical software package IBM SPSS for Windows, version 20.0 (Armonk, NY: IBM Corp). Data were prepared as tables and graphs, F-test (ANOVA) was used to compare quantitative data (expressed as mean ± standard deviation). Chi-square test was used to compare qualitative data (expressed as number and percentage). Significant P value will be considered at a level of ≤ 0.05.

RESULTS
This study included 95 patients, 58 females (61.1%) and 37 males (38.9%), with mean±SD of age was 42.79 ± 16.94 years. The main clinical presentation and the main indication for referral to endoscopy unit among the studied patients was the persistent abdominal pain (63.2%), followed by nausea and vomiting, heart burn and other dyspeptic symptoms (Table 1). Dyspepsia with unexplained Iron Deficiency Anemia (IDA) was detected in 2.1% of our study patients as a cause for seeking an UGI endoscopy. Regarding use of NSAIDs, 46 patients were users of NSAIDs (48.4%), while 49 patients were non users (51.6%). Among the enrolled patients, 23 patients were smokers (24.2%), while 72 of them were non-smokers (75.8%).

Table 1: Frequency of clinical presentations among studied patients (n=95)

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>No. of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>60</td>
<td>63.2</td>
</tr>
<tr>
<td>Nausea &amp; vomiting</td>
<td>24</td>
<td>25.3</td>
</tr>
<tr>
<td>Hematemesis &amp; melena</td>
<td>22</td>
<td>23.2</td>
</tr>
<tr>
<td>Heart burn</td>
<td>20</td>
<td>21.1</td>
</tr>
<tr>
<td>Weight loss</td>
<td>7</td>
<td>7.4</td>
</tr>
<tr>
<td>Changed bowel habits</td>
<td>4</td>
<td>4.2</td>
</tr>
<tr>
<td>Bloating</td>
<td>3</td>
<td>3.2</td>
</tr>
<tr>
<td>Anorexia</td>
<td>2</td>
<td>2.1</td>
</tr>
<tr>
<td>Others (iron deficiency anemia)</td>
<td>2</td>
<td>2.1</td>
</tr>
</tbody>
</table>

UGI endoscopy:
It was found that 4.2% from the studied populations had normal endoscopic findings. For those who had endoscopic abnormalities, distribution of gastritis was mainly antral gastritis occurring in 30.5% of patients followed by pan gastritis in 28.4% of patients. Associated mucosal nodularity was present in 7.4%. Diffuse erosive gastroduodenitis was found in 18.9% of patients, while Gastro Esophageal Reflux Disease (GERD) was present in 34.7%, mainly of Type B. Ulcers were found in 5.3% of patients. Gastric carcinoma was found only in 3.2% of the enrolled patients. Gastric polyps and barrette esophagus were found in only 1.1% of the patients (Table 2).
The patients were tested negative to have H.pylori by histological examination. Diagnostic tools include invasive techniques using UGI endoscopy and tests based on tissue biopsies taken by endoscopy as well as non-invasive techniques including blood antibody test and stool antigen test. The aim of this work is to optimize the plan of management of H.pylori infection and minimize its hazardous complications through understanding its current clinical presentations, endoscopic features and microbiological findings.

Only one patient was found to have positive culture result for H.pylori with normal endoscopic findings. This patient was tested positive for H.pylori by histopathological examination with mild density and associated atrophic changes.

**Gastric Carcinoma Patients:**

Only 3 patients of the total study population were found to have gastric masses by endoscopy and diagnosed to have gastric cancer (GC) by histopathological examination. 2 of those patients were females and 1 was male. One of GC patients aged less than 40 years and 2 of them aged from 40 to 60 years.

All of those patients were tested negative to have H.pylori infection by culture. H.pylori infection hadn’t been tested in those patients using histopathological examination.

**Relation between age, gender and endoscopic findings:**

Comparing between different age groups according to endoscopic findings, there was a significant statistical difference in the frequency of GERD and PUD among age groups (p<0.05). GERD was found to be more prevalent among patients aged ≥40 years with the mean ±SD of age of 36.06 ± 13.82. PUD was found to be more prevalent among patients aged more than 40 years with the mean ±SD of age of 63.60 ± 19.77.

Comparing between males and females regarding endoscopic findings and clinical presentations, no significant statistical differences between them were found (p>0.05)

**DISCUSSION**

*Helicobacter pylori* is a common bacterial infection linked to a wide spectrum of gastrointestinal disorders ranging from gastritis and peptic ulcer disease to gastric cancer. There is a high prevalence of H. pylori infection throughout the world; as more than 50% of the global population were found to be infected, being more prevalent in developing countries. There are several methods for diagnosing *H.pylori* infection with variant sensitivity and specificity. Diagnostic tools include invasive techniques using UGI endoscopy and tests based on tissue biopsies taken by the endoscopy as well as histological examination, RUT and molecular methods and other non-invasive techniques including blood antibody test and stool antigen test. The aim of this work is to optimize the plan of management of *H.pylori* infection and minimize its hazardous complications through understanding its current clinical presentations, endoscopic features and microbiological findings.

Our study included patients with RUT positive gastric biopsies. 96.8% of those patients were diagnosed positive by histopathological examination. 61.1% of our study populations were females. Persistent abdominal pain was the commonest clinical presentation and indication for referral to the endoscopy unit (63.2%)
followed by vomiting and other dyspeptic symptoms. Dyspepsia with unexplained IDA was detected in 2.1% of our study patients as a cause for seeking an UGI endoscopy. All of IDA patients were positive for \textit{H. pylori} infection by histological examination.

In our work, 60.9% of patients diagnosed positive by histopathological examination were females. This may be due to increased number of female patients over males in our study sample (61.1% and 38.9% respectively). These results are consistent with those studies done in Egypt\textsuperscript{14}, Kuwait\textsuperscript{15}, and Nigeria\textsuperscript{16}. Zamani \textit{et al}\textsuperscript{8} also reported increased prevalence of \textit{H. pylori} infection in developing countries among females. Although, these results are against those of other studies done in Egypt\textsuperscript{17}, China\textsuperscript{18} and India\textsuperscript{19} which reported increased prevalence of \textit{H. pylori} infection among males. Other studies done in Egypt\textsuperscript{20} and Iran\textsuperscript{21} reported no gender differences among \textit{H. pylori} infected patients.

More than half of patients (51.1%), diagnosed positive by histopathological examination aged >40 years, with the mean± SD age of 42.79 ±16.94 years. This may be due to increased number of patients over the age of 40 in our study sample (51.6% of our study populations aged >40 years). Amer and his colleagues\textsuperscript{5} detected similar results of \textit{H. pylori} infection prevalence, with an age group ranging from 16 to 69 years and mean age of 40.5 years. Although, other studies showed different results of increased incidence of \textit{H. pylori} infection with age\textsuperscript{18,22}, and a different peak age group of infected patients between 13 and 47 years\textsuperscript{14,15}.

The prevalence of \textit{H. pylori} associated dyspepsia in our study was more common in rural areas (62.1%) than urban areas (37.9%). These results were explained by Mohammad \textit{et al}.,\textsuperscript{22} in a study conducted among Egyptian school children that detected increased prevalence of \textit{H. pylori} infection with low socioeconomic status, most probably due to bad hygienic procedures. Other studies reported no significant socio demographic or environmental impact on \textit{H. pylori} infection\textsuperscript{25}.

Persistent abdominal pain was found to be the major clinical presentation and the main cause of referral to endoscopy unit among the studied patients (63.2%), followed by vomiting (25.3%) and other dyspeptic symptoms. These findings are consistent to those of other studies conducted in Egypt\textsuperscript{5,14,24} and India\textsuperscript{19}, showing that recurrent abdominal pain is the commonest clinical presentation of \textit{H. pylori} infection followed by persistent vomiting, weight loss and UGI bleeding. Dyspepsia with unexplained IDA was detected 2.1% of our study patients as a cause for seeking an UGI endoscopy. All of IDA patients were positive for \textit{H. pylori} infection by histological examination.

There was no significant difference in the use of NSAIDs was found among patients tested positive for \textit{H. pylori} by histological examination (50% for both users and non-users). Sander\textsuperscript{25} reported similar prevalence of \textit{H. pylori} infection in patients with and without short and long term NSAIDs use. Furthermore, similar results were found in Matsukawa \textit{et al}.,\textsuperscript{26} study conducted in Japan that reported \textit{H. pylori} infection to be a proved risk factor for developing gastritis, but no evidence had been found that it increases gastric ulcer formation in NSAIDs users with dyspepsia.

Smoking wasn't found to be more prevalent among \textit{H. pylori} positive patients (76.1% of \textit{H. pylori} positive patients by histological examination were non smokers) and these results don't match with those of Ghosh \textit{et al}.,\textsuperscript{27} study that showed a strong relationship between cigarette smoking and \textit{H. pylori} infection. Werdmuller \textit{et al}.,\textsuperscript{28} reported a strong relationship between cigarette smoking and \textit{H. pylori} infection.

Frequency of endoscopic findings of our patients was ranging from normal endoscopic findings, gastritis, PUD to cancer. Distribution of gastritis was detected to be mainly antral (30.5%) than pan gastritis (28.4%) and these results don't match with those of Wadea and Elhawary\textsuperscript{14} study that detected more distribution of pan gastritis of about 76.2%. GERD was detected in about 34.7% of our studied patients mainly of type B. Wadea and Elhawary\textsuperscript{14} detected different prevalence of GERD in about 49.5% mainly of type A. Our study showed a prevalence of PUD of about 5.3% of total population. This percentage is close to that found by Chandrashekar S. and Madhura\textsuperscript{16} reaching about 10%. Other studies showed higher prevalence rates of PUD reaching about 15% in Hong Kong\textsuperscript{29} and 17% in Iran\textsuperscript{30}.

Using histological examination, our study found that about 96.8% of the studied patients were infected with \textit{H. pylori}, mostly of mild degree (51.6%). Also, 93.7% of patients found to have chronic gastritis with associated atrophy of about 16.8%. These results are in agreement with those of Wadea and Elhawary\textsuperscript{14} study that concluded that mild \textit{H. pylori} infection was detected in 98% of the patients, while degree of associated atrophy was only 2%. Other Nigerian study reported different results of moderate \textit{H. pylori} infection being the most common with a prevalence rate of ≈43.2%\textsuperscript{16}.

Gastric cancer was found by histopathological examination in about 3.2% of our studied patients. Near results were found in Wadea and Elhawary\textsuperscript{34} study with a frequency of 1%. A different prevalence of GC was reported, being responsible for about 17.4% of dyspeptic symptoms in the age group ≥ 50 years\textsuperscript{30}. A surprising finding in our study is that 33.3% of GC patients aged less than 40 years which doesn't match with Ogutu \textit{et al}. study results. Regarding \textit{H. pylori} infection status in GC patients, all GC patients were diagnosed as RUT positive, unfortunately they were culture negative.
Positive culture for \textit{H. pylori} was detected only in 7.4\% in our population. Although, histological examination diagnosed about 96.8\% of \textit{H. pylori} positive cases. This confirms the concept that bacteriological culture is not recommended as the first line of investigations for diagnosing \textit{H. pylori} infection as it is a too demanding and complicated technique with a very low yield\textsuperscript{31}.

Normal endoscopic findings were detected in 4.2\% of our studied patients. Only one patient with normal endoscopic findings was diagnosed to have \textit{H. pylori} infection by culture. Chandrashekhar S. and Madhura\textsuperscript{19} study showed that about 30\% of dyspeptic patients had normal endoscopic findings, 33.3\% of them were diagnosed to have \textit{H. pylori} infection by RUT and histopathological examination. No significant statistical difference between males and females was found related to endoscopic findings (p>0.05). These results were in agreement with those of Wadea and Elhawary\textsuperscript{14} study regarding all endoscopic findings except for pan gastritis and mucosal nodularity which were more prevalent among females than males (p-values 0.01 and 0.004, respectively).

There is a significant statistical difference in the frequency of GERD and PUD detected among different age groups in the current study (p<0.05). PUD was found to be more prevalent among patients aged >40 years with the mean ±SD of age of 63.60 ± 19.77. Similar findings were detected in Hong Kong 29 as PUD being more prevalent in older age groups with mean ±SD of age of PUD patients (51.2 ±14.9) vs. (7.3 ±16.4) for non-PUD. This significant relation doesn't match with that of Ogutu \textit{et al.}\textsuperscript{30} study conducted in East Africa that reported PUD to be the most prevalent pathological finding in both young (less than 50 years) and older patients (50 years and above).

Limitation:

Although \textit{H. pylori} culture is the gold standard for detection of \textit{H. pylori} infection, culture of \textit{H. pylori} infection was too complicated and had a low yield comparing with histopathological testing. Antibiotic susceptibility is a difficult issue by routine methods due to rapid death of this fastidious organism. Further molecular diagnostic techniques are needed for proper diagnosis of \textit{H. pylori} infection and to study its antibiotic susceptibility pattern in our institution. Larger studies are needed over longer periods to confirm association of demographic, clinical, endoscopic features and microbiological findings of \textit{H. pylori} infection.

**CONCLUSION**

In conclusion, there is a high prevalence of \textit{H. pylori} associated dyspepsia, more in females, in rural areas and decreasing with age. \textit{H. pylori} associated dyspepsia usually presents with recurrent abdominal pain and vomiting (63.2\%, 25.3\% respectively). Gastritis and GERD are found to be the commonest endoscopic findings associated with \textit{H. pylori} infection (60.9\% and 34.8\% respectively). Our study also concluded that there is a low frequency of PUD among \textit{H. pylori} positive patients with dyspepsia. Microbial culture has a little yield in diagnosing \textit{H. pylori} infection. Gastric cancer was detected endoscopically and proved histologically in 3.2\% of RUT positive dyspeptic patients. This emphasizes the importance of endoscopic tool for early detection of GC, regardless of age.

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- Each author listed in the manuscript had seen and approved the submission of this version of the manuscript and takes full responsibility for it.
- This article had not been published anywhere and is not currently under consideration by another journal or a publisher.

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