HELCILOBACTER PYLORI INFECTION IN DYSPEPTIC PATIENTS IN INDUSTRIAL BELT IN JHARKHAND
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ABSTRACT

BACKGROUND
The present study is done to study different aspects of Helicobacter pylori such as its prevalence, association with upper gastrointestinal pathology, diagnosis and treatment outcome. Gastric antral biopsy and serology for Helicobacter pylori was done for all dyspeptic patients. Histopathology, Gram stain and biopsy urease test was done from the gastric biopsy specimen. The prevalence of Helicobacter pylori infection was 58.8%. The sensitivity, specificity, positive and negative predictive value for histopathology was 96.9%, 100%, 100% and 95.8%, respectively; for biopsy urease, the values were test 80.4%, 100%, 100% and 78.2%, respectively; for Gram stain, the values were 85.6%, 97.1%, 97.6% and 82.5%, respectively; and for serology, the values were 94.8%, 77.9%, 86% and 91.4%, respectively. Mostly peptic ulcer and duodenitis cases followed by chronic active gastritis were associated with Helicobacter pylori infection. Repeat biopsy revealed eradication of Helicobacter pylori in 90.7% cases. In dyspeptic patients, endoscopic biopsy not only detects Helicobacter pylori infection, but also reveals different gastric pathologies.

KEYWORDS
Helicobacter Pylori, Dyspepsia, Endoscopy, Gastric Biopsy.

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BACKGROUND
Helicobacter pylori (H. pylori) is a gram-negative, microaerophilic, motile and spiral or curved bacterium found in the luminal surfaces of gastric epithelium. It has been implicated as an important agent in the pathogenesis of peptic ulcer and gastritis since its isolation by Warren and Marshal in 1983.1 As prevalence of H. pylori infection is strongly correlated with socioeconomic condition, it is found in 80% in Low- and Middle-Income Countries (LMICs) as compared to 20-50% in industrialised countries. It affect mainly adolescents and middle-aged adults.4 The life-time risk of peptic ulcer in H. pylori infected patients ranges from 3% in USA to 25% in Japan where eradication treatment drastically lowers recurrence rate. 72-98% of patients with gastric MALT lymphoma have H. pylori infection and eradication treatment leads to regression in early cases.

In contrast to developed countries, H. pylori infection is usually acquired during childhood by the age of 5 years in developing countries. Usually, patients with uninvestigated, uncomplicated dyspepsia undergo non-endoscopic (noninvasive) methods for H. pylori infections- and eradication therapy is advised for those with positive results. But, non-endoscopic methods are not appropriate for patients with accompanying alarming symptoms (weight loss, persistent vomiting or gastrointestinal bleeding) or for patients (>45 years) with new-onset dyspepsia. This is true for developed countries, but in LMICs where H. pylori infection is high resulting in peptic ulcer in many, it is better to diagnose it by endoscopic biopsy examination and then treat those cases whose endoscopic biopsy specimen shows evidence of H. pylori infection. Thus, unnecessary side effects of the drugs and cost to patients may be averted in H. pylori negative cases.

Endoscopic biopsy of chronic dyspeptic cases not only reveals ulcer and inflammation related to H. pylori, but also leads to diagnosis of other pathologies such as gastric cancer, gastric lymphoma, diabetic gastropathy, etc. Keeping all these options in mind, endoscopic biopsy of all patients presenting with dyspepsia to the gastrointestinal.

Case Report
Mahatma Gandhi Memorial Hospital (MGM) is a 514 bedded tertiary care hospital catering the people of Jamshedpur and its surrounding areas. This prospective study was carried out from February 2012 to December 2014. After written informed consent, endoscopic biopsy was done in 159 cases presenting with dyspepsia after oral Xylocaine spray as local anaesthesia.

Inclusion Criteria
• Patients with dyspepsia for more than one month.
• Patients between 15 to 75 years of age.

Exclusion Criteria
• Patients with upper gastrointestinal bleeding, gastrointestinal malignancy, documented H. pylori eradication or life-threatening conditions.
Patients taking proton pump inhibitor, H2 receptor antagonist or antibiotics within four weeks preceding the study.

Patients taking NSAID or corticosteroid.

Pregnancy.

Dyspepsia was defined based on Rome in criteria as having one more of the following conditions- postprandial fullness (termed as postprandial distress syndrome), early satiation (inability to finish a normalised meal or postprandial fullness) and epigastric pain or burning (termed epigastric pain syndrome).

The following investigations were carried out on each selected patient-

A total number of four endoscopic biopsies were taken from the antral area one of which was used for biopsy urease test, one for imprint cytology for Gram stain and the remaining two for histopathology. Two more biopsies were taken from the body of stomach or any other pathology visible by endoscopy such as an ulcer, area of hyperaemia or growth. These samples were also used for histopathological examination.

Biopsy Urease Test (BUT) - antral biopsy specimens were inserted in 1 mL of urea broth with phenol red as a pH indicator and incubated at 35°C. Urease present in H. pylori converts urea to ammonia increasing the pH of the broth, which changes the color from bright yellow to pink.

Imprint cytology- a biopsy specimen was Gram stained for imprint cytology. Histopathology- Formalin fixed specimens were processed for histopathological examination using Haematoxylin and Eosin (H and E) and Giemsa stain used especially of H. pylori detection. Sections were separately examined by two pathologists. A consensus was reached through joint review when there was a discrepancy.

Seroimmunocromatographic Test (ICT) for detection of H. pylori antibodies was performed for each case using the commercially available test kit from 'SD Bio Standard Diagnostics Pvt. Ltd.' (Lot No. NO10007) according to manufacturer's instruction. When both control and test line was visible, the test was regarded as positive.

Triple therapy containing pantoprazole, clarithromycin and amoxicillin combination was given twice daily to each patient with H. pylori infection for 14 days. Pantoprazole was continued for one month after completion of the triple therapy course. Repeat endoscopy was performed in these patients after three months to evaluate the outcome of treatment.

Clearance from Ethical Committee of IGH was obtained to conduct the study.

Dichotomised data were used to calculate sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and accuracy. The values are given with 95% confidence interval. Each method was tested against combination of histopathology and BUT as gold standard. Open Epi, version 3.03a was used to obtain the p value, which was considered significant when <0.05.

RESULTS

Total numbers of 159 patients were enrolled in the present study over a period of three years from February 2012 to December 2014. The age range of the patients of our study group was 15 to 75 years. Out of them, 118 were males and 47 females. Overall prevalence of H. pylori infection among these patients was 58.8% (97/165). Males were more affected (66%, n=78/118) than females (40.4%, n=19/47), which was statistically significant (p=0.001). It was observed that the most affected age group was between 15 to 30 years (72%). Among the 11 diabetics, 4 were positive for H. pylori (36.3%), whereas only one case out of 8 alcoholics (12.5%) was showing such positivity (Table 1).

Histopathological evaluation of the tissue sections showed a highest association with H. pylori (480.5%) infection in the chronic active gastritis category followed by 76.5% in peptic ulcer (Table 2). H. pylori were easily detected by Giemsa stain on the biopsy sections (Image 1). One of the two gastric adenocarcinomas was associated with H. pylori infection.8-10 Sensitivity, specificity, PPV, NPV and diagnostic accuracy of Gram stain and serology were compared with gold standard (Table 3). Out of 97 positive cases, only 54 presented for repeat endoscopy and this could only be evaluated for treatment outcome.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number of Cases</th>
<th>HP Positive</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-30</td>
<td>18</td>
<td>13</td>
<td>72.33</td>
</tr>
<tr>
<td>31-45</td>
<td>42</td>
<td>24</td>
<td>57.13</td>
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<tr>
<td>46-60</td>
<td>51</td>
<td>36</td>
<td>70.58</td>
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<td>61-70</td>
<td>38</td>
<td>24</td>
<td>63.15</td>
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<tr>
<td>Gender</td>
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</tr>
<tr>
<td>Male</td>
<td>113</td>
<td>78</td>
<td>69.0</td>
</tr>
<tr>
<td>Female</td>
<td>46</td>
<td>19</td>
<td>31.0</td>
</tr>
<tr>
<td>Diabetics</td>
<td>11</td>
<td>04</td>
<td>36.3</td>
</tr>
<tr>
<td>Alcoholics</td>
<td>08</td>
<td>01</td>
<td>12.5</td>
</tr>
</tbody>
</table>

Table 1. Relationship of H Pylori (HP) Infection with Different Groups of Patients

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>Number of Cases</th>
<th>HP Positive</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unremarkable</td>
<td>38</td>
<td>09</td>
<td>23.68</td>
</tr>
<tr>
<td>GERD</td>
<td>17</td>
<td>12</td>
<td>70.58</td>
</tr>
<tr>
<td>Chr. Sup. Gastr.</td>
<td>25</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>Chr. Act. Gastr.</td>
<td>41</td>
<td>33</td>
<td>80.48</td>
</tr>
<tr>
<td>Atr. gstr</td>
<td>19</td>
<td>10</td>
<td>52.63</td>
</tr>
<tr>
<td>Duodenitis</td>
<td>06</td>
<td>04</td>
<td>66.66</td>
</tr>
<tr>
<td>Peptic ulcer</td>
<td>17</td>
<td>13</td>
<td>76.47</td>
</tr>
<tr>
<td>Gastric carcinoma</td>
<td>02</td>
<td>01</td>
<td>50</td>
</tr>
</tbody>
</table>

Table 2. Association of H. Pylori with Different Types of Histopathology Diagnosis
The most important change observed in the long term. H. pylori as a cause of gastric carcinoma is a well-accepted entity and is presently classified by the WHO as type 1 carcinogen. The decrease in the prevalence of H. pylori and atrophic gastritis is related to the decrease in the incidence of gastric cancer in the western countries.

Dyspeptic patients with normal histology are often found to have H. pylori positivity (23.6%). Invasive endoscopy and biopsy in search of H. pylori infection incidentally helps in histological characterisation of the upper gastrointestinal tract and may detect other gastric pathologies, which have to be treated as early as possible.

In our study, we found two gastric adenocarcinomas confirmed on histology, one being associated with H. pylori. Chronic gastritis, and by implication, adenocarcinoma could be prevented by the early histological characterisation through endoscopic biopsy and detection of H. pylori. Though epidemiological studies show that H. pylori may actually protect or minimise the acid reflux diseases, most clinicians favour its eradication because of its potentiality to increase the risk of developing gastric carcinoma and MALT lymphoma.

Identification of H. pylori infection is critical in the management of patients suffering from gastroduodenal ulcer diseases, dyspepsia and for prevention of a large number of cases, which might lead to gastric carcinomas. As there is no gold standard test for the detection of the presence of H. pylori in the gastroduodenal tract, we applied four different methods for its detection in our study. If any of the two tests (BUT and histopathology) is positive, we considered this as confirmatory. BUT allows rapid detection of H. pylori with a prevalence rate of 58.8%. Different studies are known to be infected by this organism which is the principal cause of peptic ulcer disease and main risk factor for the development of gastric carcinoma. However, a major proportion of the infected population remains asymptomatic. Human beings are the only known reservoir of infection and the route of transmission is still not clear. The major risk factors for the development of H. pylori infection include poor sanitation, lack of safe and portable drinking water supply in many areas, poor personal hygiene and last, but not the least, poor living condition because of low socioeconomic status.10-11

Out of 159 patients in our study, 97 showed positivity for H. pylori with a prevalence rate of 58.8%. Different studies from India show prevalence rate around 80% whereas in Bangladesh it ranges from 50% to >90%, in Japan 70%, in Africa 70-90%, in Germany 48.8%, in Switzerland 26.6% and in North America 7.1 to 30%. From the above observation, it is clear that H. pylori is more prevalent in LMICs than the developed countries. Even Tam and our study was done in an industrial belt, which is relatively developed compared to the rural areas, our high prevalence maybe due to lack of personal hygiene and health education. Public health interventions are therefore pertinent for this group of people in such a comparatively developed area.

The most affected population in our study is the group of young adults of 15 to 30 years (72.2%) followed by the 46 to 60 years group (64.2%). Similar prevalence has been observed by another study in India and one in other countries. The proneness of H. pylori infection in these age groups maybe due to the preference in consuming fast food prepared unhygienically in roadside food stalls.

Our finding also showed that the prevalence of H. pylori infection is significantly ($p=0.001$) higher in males 66_10 than females (40.4%), which is in accordance with another report in other countries- 849. This difference might be due to the habit and lifestyle of the male community compared with that of females. Correlating infected biopsy specimens with histopathology, the most important change observed was chronic active gastritis (80.48%) followed by peptic ulcer (76.47%), similar to a report from Taiwan. Other changes were gastroesophageal reflux disease (70.88%) and duodenitis (66.6%). A study from Glasgow by McColl13-14 et al reported otherwise where peptic ulcer with H. pylori positivity was higher (84.28%). Analysing the pathophysiological course of infection, it is obvious that chronic active gastritis will lead to peptic ulcer by destroying the superficial epithelium in the long term. H. pylori as a causation of gastric carcinoma is a well-accepted entity and it is presently classified by the WHO as type I carcinogen. The decrease in the prevalence of a pylori and atrophic gastritis is related to the decrease in the incidence of gastric cancer in the western countries.

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<table>
<thead>
<tr>
<th>Method</th>
<th>Se (95% CI)</th>
<th>Sp (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
<th>Ac (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram stain</td>
<td>0.86 (0.79-0.93)</td>
<td>0.97 (0.95-0.10)</td>
<td>0.98 (0.94-0.10)</td>
<td>0.83 (0.75-0.91)</td>
<td>0.90 (0.84-0.96)</td>
</tr>
<tr>
<td>Serology</td>
<td>0.95 (0.91-0.99)</td>
<td>0.78 (0.70-0.86)</td>
<td>0.86 (0.79-0.93)</td>
<td>0.91 (0.86-0.96)</td>
<td>0.88 (0.86-0.90)</td>
</tr>
</tbody>
</table>

**Table 3. Validation of Gram Stain and Serology by Comparing with Gold Standard (Histopath + BUT)**

**DISCUSSION**

H. pylori, a common pathogen in humans is ubiquitous and does not spare any part of the globe. Approximately, 50% of world population and >80% of the population in LMICs are known to be infected by this organism, which is the principal cause of peptic ulcer disease and main risk factor for the development of gastric carcinoma. However, a major proportion of the infected population remains asymptomatic. Human beings are the only known reservoir of infection and the route of transmission is still not clear. The major risk factors for the development of H. pylori infection includes poor sanitation, lack of safe and portable drinking water supply in many areas, poor personal hygiene and last, but not the least, poor living condition because of low socioeconomic status.10-11

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Imprint cytology for Gram stain could rapidly detect the organism in 55.51% of cases with a high specificity and sensitivity (Table 3). The advantage of this method over histopathology is that a report can be given on the same day and it is cheap, so cost-effective. Performing the (IgG antibody) serological test by an immunochromatographic method could detect 64.84% of cases superior to other methods. Though sensitivity of this method was high, specificity was not marked (Table 3). Its important disadvantage is that it gives a false positive result in old infections. It can be therefore be useful as a screening test.

All positive cases were treated with triple therapy for 14 days (pantoprazole, clarithromycin, and amoxicillin) followed by pantoprazole alone for the following one month. Confirmation of eradication was performed by repeat endoscopy after a gap of three months of treatment and all were tested for H. pylori. All 54 cases became IL pylori negative and 46 were symptom free. Eight were having persisting symptoms, which warranted follow up.

CONCLUSION
The association of H. pylori infection in dyspeptic patients with various gastric pathologies is quite high. Eradication of H. pylori should be done after confirmation of its presence. Empirical treatment should be avoided because of unnecessary cost and possible side effects. Endoscopic diagnosis is not only accurate, but may also reveal unexpected diagnoses.

REFERENCES