Clinical, Endoscopic and Histopathological Study of Helicobacter pylori Related Gastritis in Adults Tertiary Care Teaching Hospital

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Abstract

Introduction: Helicobacter pylori are major etiological factor in the development of peptic ulcer disease.

Aim and Objective: To find out the association of H. pylori with gastric lesions in endoscopic biopsy specimen in semi-urban regions, and to study the specificity and sensitivity of rapid urease test (RUT), to evaluate the usefulness of Giemsa stain in addition to histopathological examination for identification of H. pylori.

Materials and Methods: A prospective study of 50 adult patients presenting with upper abdominal pain, dyspepsia, vomiting, and hematemesis is undertaken to evaluate the relationship of this symptom complex to inflammatory gastroduodenal lesions with special reference to H. pylori infection. The clinical, endoscopic findings, RUT and histopathological evaluation of gastric antral specimen with special stains to demonstrate the organism are presented and analyzed.

Key words: Gastritis, Helicobacter pylori, Rapid urease test, Upper gastrointestinal endoscopy

INTRODUCTION

The understanding of etiopathogenesis of peptic ulcer, expressed as gastritis, gastric ulcer, duodenitis, and duodenal ulcer has been revolutionized during last decade with the discovery in 1983, of a new pathogen categorized as Helicobacter pylori by Marshall and Warren.¹² Several reports have subsequently supported the association of H. pylori as a major etiological factor in the development of peptic ulcer disease³ and recent reports also suggest its association with gastric carcinoma and lymphoma.⁴ Bacterium has been classified as Class I definite gastric carcinogen to human.¹⁹ A prospective study of adult presenting with upper abdominal pain, dyspepsia, vomiting, and hematemesis is undertaken to evaluate the relationship of this symptom complex to inflammatory gastroduodenal lesions with special reference to H. pylori infection. The clinical, endoscopic findings, rapid urease test (RUT) and histopathological evaluation of gastric antral specimen with special stains to demonstrate the organism are presented and analyzed.

In addition to more common inflammatory cell infiltration it is only recently the histopathologic effect of H. pylori on gastric epithelium at light microscopic level has been stressed and this has been studied systematically, describing striking changes in surface epithelium and attributing them as specific for H. pylori colonization and correlating them with type of cytotoxin, production and risk of peptic ulcer.⁵ H. pylori infection can be diagnosed by invasive⁶ (requiring endoscopy) and non-invasive technique.⁶

In this study, the various methods of identification of H. pylori and histopathological features associated H. pylori in gastric mucosa in patients, presenting with dyspepsia are discussed in detail.

MATERIALS AND METHODS

In this study, endoscopic biopsies were taken from 50 patients, who attended gastroenterology department
with complaints of nausea, vomiting, dyspepsia, flatulence, and fullness were screened with detailed clinical history regarding socioeconomic status, housing conditions, water supply, etc. After thorough clinical evaluation, patients suspected to have gastric lesions were subjected to the endoscopic biopsy procedure.

Methodology

Endoscopy

Upper gastrointestinal endoscopy was performed with flexible fiber optic endoscope manufactured by Pentax model number 29P.

• Informed consent was obtained from patients. Relevant history and clinical details were recorded
• After overnight fasting, endoscopy was done on the following morning, endoscopic changes were noted in esophagus, stomach, and duodenum was recorded
• Three gastric biopsy specimens were taken from antrum and corpus, and one was immediately used for RUT (Annexure 1), and the other was immediately fixed in 10% buffered neutral formalin for histopathological evaluation.

Histopathologic Study of Biopsy Specimens

The biopsy specimens that were fixed in 10% buffered neutral formalin were processed in automatic tissue processor for paraffin embedding, and then 3-5 μ sections were cut. The sections were stained with hematoxylin and eosin (H and E) (Annexure II) for evaluation of histopathological features and special stains such as Giemsa and Alcian blue/periodic acid–Schiff stain (Annexure III) used to detect Helicobacter pylori organisms.

Gastritis was defined and classified according to established histological criteria with revised updated Sydney system.

The density of Helicobacter pylori, chronic inflammation, neutrophil polymorphic activity, glandular atrophy, and intestinal metaplasia was recorded in all cases of gastritis and graded as mild, moderate and marked scale according to the guidelines provided by the updated, revised Sydney system, using the visual analog scale. The most prevalent appearance on each slide was matched with the graded panel that resembles it most closely. Lesion being active was signified by the presence of neutrophils within glandular and surface epithelial layer. Glandular atrophy was identified, when gastric glands were correspondingly decreased in amount and widely separated. An increase in lymphocytes and plasma cells in lamina propria categorizes the gastritis as chronic. Infiltration involving up to 1/3 of gastric pits and surface are designated as mild between 1/2 and 2/3 as moderate as and more than this as severe gastritis.

Apart from graded variables described in the updated, revised Sydney system, special attention has been thrown on non-graded variables such as surface epithelial changes, mucin depletion, erosions, lymphoid follicles, cells drop out, foveolar hyperplasia, pseudopyloric metaplasia, and endocrine hyperplasia.

OBSERVATIONS AND RESULTS

This study covered 50 patients clinically suspected to have gastritis and undergone upper gastrointestinal endoscopy. In the 50 cases, 35 were males with age ranging from 20 to 70 years (mean age 45 years) 15 were females with age ranging from 20 to 60 years (mean age 40 years).

When the patients were divided into six groups according to their age (<20, 21-30, 31-40, 41-50, 51-60, and 61-70), there was a significant increase in the Helicobacter pylori positivity in the age group of 41-50 years (53.8%) followed by 31-40 years (50.0%) (Figure 1 and Table 1).

Abdominal pain with dyspepsia more than 3 months is the most common clinical presentation followed by abdominal discomfort with vomiting and nausea. Abdominal discomfort with anemia was noticed in some cases.

![Figure 1: Age/Percentage Distribution](image)

Table 1: Age/percentage distribution

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>Total number of cases</th>
<th>Helicobacter pylori positive cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below 20</td>
<td>4</td>
<td>1</td>
<td>25.0</td>
</tr>
<tr>
<td>21-30</td>
<td>6</td>
<td>2</td>
<td>33.3</td>
</tr>
<tr>
<td>31-40</td>
<td>20</td>
<td>10</td>
<td>50.0</td>
</tr>
<tr>
<td>41-50</td>
<td>13</td>
<td>7</td>
<td>53.8</td>
</tr>
<tr>
<td>51-60</td>
<td>5</td>
<td>1</td>
<td>20.0</td>
</tr>
<tr>
<td>61-70</td>
<td>2</td>
<td>1</td>
<td>50.0</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>22</td>
<td>44.0</td>
</tr>
</tbody>
</table>

H. pylori: Helicobacter pylori
The clinical presentations of the patients are summarized in Figure 2 and Table 2.

### Endoscopic Examination

Upper gastrointestinal endoscopy revealed 12 cases showed gastric ulcer ranging from 0.5 to 2 cm with erosion and edema; 12 cases antral gastritis with duodenal ulcer; 5 cases showed nodularity of gastric mucosa; 6 cases with patchy erythematous gastric mucosa; 5 cases were with duodenal erosion and edema with ulceration ranging from 0.25 cm × 1 cm to 1.5 cm × 3 cm and 10 patients did not show any endoscopically detected lesion.

Endoscopic findings in all the 50 cases (Table 3).

Endoscopic findings and corresponding histopathologic diagnosis of 50 endoscopic biopsies are listed in Table 4.

In 10 cases, where endoscopy was normal, there was histological evidence of chronic active gastritis in one case and mild gastritis in one case and eight cases shows normal gastric mucosa. These shows an apparent lack of correlation between endoscopic and histopathological diagnosis of gastritis in dyspeptic patients.

### RUT

RUT for detection of *H. pylori* from endoscopic specimen.

The biopsy specimen was subjected to urease testing in 50 cases, of which there were 24 positive cases. Among the 24 urease positive cases, 22 cases were detected histopathologically for *H. pylori*.

In the 26 urease negative gastritis biopsy, Giemsa staining also did not detect *H. pylori*.

RUT is a simple, cheap test, performed at endoscopy room itself using Heli-check test device. It contains urea solution with an indicator that detects alkalinity resulting from formation of ammonia in most infected patients (70%) and gives a positive result within 2 h. In cases of a positive result, it shows a change in color from yellow/orange to pink/red. Whereas, in cases of a negative result, the color remains as yellow color itself. Urease test detects up to 0.3 unit of urease present in the sample.

### Limitations of This Test

1. The test is pH sensitive, and therefore, any contamination in the reaction wells will change the reaction
2. Biopsy specimen collected in preservatives with acidic or basic pH such as formalin should not be used for Heli-Check RUT test device.

### Demonstration of *H. pylori* by Giemsa Stain

Although the *H. pylori* organisms were visible in the H and E stain, demonstration by Giemsa stain is considered as the gold standard for *H. pylori* detection. It facilitates the identification of *H. pylori* by darkening the organism.

Using Giemsa stain, the spiral-shaped bacteria of *H. pylori* is attached to brush borders of gastric foveolar cells and inside the gastric pits. The distribution was mostly patchy and single. Lying close to surface epithelium and more densely distributed within the lumen of gastric pits. The organisms are absent in the areas of intestinal metaplasia.

In this study, *H. pylori* were demonstrated using Giemsa stain in 22 out of 50 biopsies.

### Association between Gastritis and Presence of *H. pylori*

Most of the biopsy specimen, which was positive for *H. pylori* showed histological evidence of gastritis.
A total of 24 cases showed chronic active antral gastritis and activity implying the presence of a high number of neutrophilic polymorphs in the lamina propria and within the epithelium.

Relationship between H. pylori Density and Severity of Gastritis
There was no correlation between the degree of inflammation, noted in the histopathologic study and density of H. pylori organisms.

Histopathology of Gastric Antral Biopsies
Table 5 shows details of histopathological findings of all the 50 gastric biopsies. Out of the 50 cases, only 22 cases show gastritis with H. pylori positive.

The presence or absence of H. pylori with varying degree of chronic inflammation, neutrophilic polymorphic activity, glandular atrophy, intestinal metaplasia, and gastric surface epithelial changes was recorded in 50 cases.

DISCUSSION

Chronic gastritis is defined as the presence of chronic mucosal inflammatory changes eventually leading to mucosal atrophy and epithelial metaplasia. By far the most important etiological association is chronic infection by the bacillus H. pylori. The organism is a worldwide pathogen that has the highest infection rates in developing countries.

Sex Distribution
Age and sex related possibility of H. pylori was studied. In this study, out of 35 male cases, 16 cases (45%) are positive for H. pylori and out of 15 female cases (40%) are positive for H. pylori. The male to female ratio is 2:1 which is in contrast to the study literature and study conducted by Khan.

Age Distribution
The higher prevalence of H. pylori is in the age group of 41-50 years, which had the highest percentage (53.8%) and followed by the age group 31-40 years (50.0%) (Figure 1). This is in consonance with Abdul Rahman E Fakhro who states that prevalence of H. pylori increased with advanced age. Anderson states that the prevalence of H. pylori in adults approximates 100% in many developing tropical countries.

The prevalence of H. pylori in this study is 44%. It does not coincide with the study of Fakhro et al., in their study the prevalence rates are 79.4%.

This high percentage may be due to low socioeconomic according to James et al.

In this study, 45 cases out of 50 show dyspepsia, abdominal pain, and iron deficiency anemia. These are the most common symptoms encounter in other studies also.

Perusal of literature shows epigastric pain, which is the most common symptom (92%) followed by vomiting (51%) and hematemesis (17%) in H. pylori associated chronic gastritis.

As per a study conducted by Desai et al. who revealed that geographic and social patterns play a role in the transmission of H. pylori. According to Anderson, East Asian countries

<table>
<thead>
<tr>
<th>Table 4: Comparison of endoscopic and histopathological findings</th>
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<tbody>
<tr>
<td><strong>Endoscopic feature</strong></td>
</tr>
<tr>
<td>Gastric ulcer with erosion – 12</td>
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<tr>
<td>Antral gastritis with duodenal ulcer – 12</td>
</tr>
<tr>
<td>Nodularity of gastric mucosa – 5</td>
</tr>
<tr>
<td>Patchy erythematous changes - 6</td>
</tr>
<tr>
<td>Gastric ulcer duodenitis – 5</td>
</tr>
<tr>
<td>Unremarkable mucosa – 10</td>
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<tr>
<th>Table 5: Details histopathological findings</th>
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<tbody>
<tr>
<td><strong>Histopathology</strong></td>
</tr>
<tr>
<td>Normal gastric mucosa</td>
</tr>
<tr>
<td>H. pylori associated CAAG</td>
</tr>
<tr>
<td>H. pylori associated chronic non active gastritis (mild)</td>
</tr>
<tr>
<td>Chronic gastritis with atrophy</td>
</tr>
<tr>
<td>Chronic gastritis with intestinal metaplasia</td>
</tr>
<tr>
<td>H. pylori negative chronic non active gastritis</td>
</tr>
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</table>

CAAG: Chronic active antral gastritis, H. pylori: Helicobacter pylori
where widespread sanitation has been introduced, the prevalence of *H. pylori* has shown downward trend.

As per study the high percentage of *H. pylori* positive individuals having gastric lesions were found to have a history of intake of spicy and non-vegetarian food. *H. pylori* infection highly frequent in dyspeptic patients and it is cardinal risk factor for chronic gastritis.\textsuperscript{16,17}

Endoscopic Features

Fiber optic gastroscopy helps collecting biopsy specimens under direct vision.

In this study, there were 12 cases gastric ulcer with erosion, out of which 8 cases (66\%) were positive for *H. pylori*, and 12 cases of duodenal ulcer in which 9 cases were positive (70\%) and small proportion of cases showing patchy erythematos changes, nodularity of gastric mucosa and of unremarkable mucosa were also found in endoscopy examination.

Normal looking gastric mucosa is most common single endoscopic finding, accounting for 20\% cases. Although the results of endoscopic examination may show normal mucosa,\textsuperscript{7} histopathological examination may show positive for *H. pylori*. In these cases, the risk of re-infection is always there.

The positivity rate for duodenal ulcer is 70\%, and gastric ulcer is 66\% in our study. It is comparable to study by Tytget (1988) who found that 15 patients of duodenal ulcer and 9 out of 11 (81.8\%) patients with gastric ulcers have the organism. And in 2002, Abdul Rahman E Fakhro,\textsuperscript{14} studied antral biopsy specimens from 25 patients with symptoms and diagnosis of duodenal ulcer, among whom the positivity rate is 84\%. In a study by Zhang *et al.*,\textsuperscript{18} the prevalence of *H. pylori* in gastric ulcer is 80.8\%. Duodenal ulcer is usually associated with *H. pylori* infection. Treatment of duodenal ulcer must, therefore include acid reduction and *H. pylori* eradication all the time.

One line of research currently favors *H. pylori* infection as a causal factor in both mucosa-associated lymphoid tissue (MALT) and non-MALT gastric lymphomas.\textsuperscript{19}

When the density of *H. pylori* is low, application of endoscopic brush cytology helps in rapid detection.

Good evidence exists in the literature that *H. pylori* can cause chronic active gastritis. Most compelling and direct evidence are studied by Dr. Marshall *et al.* and subsequently by Moris and Nicholson.

As further evidence of pathogenicity, secretory immunoglobulin A directed against *H. pylori* has been isolated, and phagocytosis of the organism has been shown by intragastric neutrophil. Others have successfully eradicated the organism with antibiotics, with resultant improvement of histologic gastritis.

In this study, it is found that more or less the antral biopsies colonized by *H. pylori*, showed evidence of gastritis. It confirms the previously reported the high prevalence of *H. pylori* infection in association with antral gastritis further supporting the contention that *H. pylori* are the etiologic agent of this lesion in most cases.

*H. pylori* are now accepted cause of gastritis and peptic ulcer disease in adult.\textsuperscript{3}

Table 6 shows a comparative analysis of various studies in children, reporting relationship between *H. pylori* infection and histological evidence of gastritis percentage in adults. This shows 50\% of cases of gastritis show *H. pylori* positivity in contrast to the pediatric cases. Probably environmental factors, socioeconomic status, alcohol, and smoking modified the development of gastritis with typical symptoms in adults.

According to Dixon degree of chronic inflammatory cell infiltration is correlated to the extent and density of *H. pylori* colonization. However, we could not find a significant correlation between these two factors and the differences can be explained\textsuperscript{20} as follows:

1. Difference immunological, as well as histological responses in various age groups, could be due to genetic, social cultural economical, and psychological factors.
2. Some patients may have chronic inflammation (gastritis due to other causes and *H. pylori*, and infection) simultaneously
3. Partially treated a patient may show lower degrees of inflammation.

**CONCLUSION**

*H. pylori* are now widely recognized as the most common cause of primary or unexplained gastritis in adults as well
as children. RUT is a simple, cheap test, performed at endoscopy room itself using Heli-check test device. A “test and treat” strategy is recommended for most patients with undifferentiated dyspepsia. With this approach, patients undergo a noninvasive test for \textit{H. pylori} infection and if positive, are treated with eradication therapy. This strategy reduces the need for antisecretory medications as well as the number of endoscopies.

**REFERENCES**