Does *Helicobacter pylori* Infection Contribute to the Pathogenesis of Portal Hypertensive Gastropathy? A Cross-Sectional Observational Study at a Tertiary Care Center

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**Abstract**

**Background:** Portal hypertensive gastropathy (PHG) is a routine endoscopic finding in patients with portal hypertension. Several pathophysiological mechanisms have been postulated for the same. Infection with *Helicobacter pylori* is one among them. However, association between them is controversial. The objectives were to detect the presence of *H. pylori* infection in cirrhosis with PHG and also to correlate the severity of PHG with colonization of *H. pylori*.

**Methods:** A total of 100 patients diagnosed with PHG were enrolled in the study. Presence of *H. pylori* was assessed by rapid urease test and histopathological examination. Results were analyzed using frequency tables with cross tabulation, Chi-square test and one sample proportion test.

**Results:** It was observed that 64\% of the patients were positive for *H. pylori*. Relationship of *H. pylori* with PHG was assessed by one sample proportion test and a statistically significant relationship between them was found. Out of the 64 patients with PHG and *H. pylori* infection, 44 (68.7\%) had severe PHG, while only 14 (44\%) out of 36 *H. pylori* negative patients had severe PHG, reflecting a significant relation between the presence of *H. pylori* infection and severity of PHG.

**Conclusion:** An increased prevalence of *H. pylori* infection was established in patients with PHG. Moreover, a direct correlation was found between the presence of *H. pylori* infection and severity of PHG. Thus, eradication therapy for *H. pylori* may be beneficial in patients with PHG.

**Keywords:** Portal hypertensive gastropathy; *Helicobacter pylori*; Cirrhosis; Endoscopy; Variceal bleed

**Introduction**

Cirrhosis with portal hypertension poses a major health problem globally with its high incidence and prevalence in resource limited settings. It is associated with alterations in the gastrointestinal mucosa, with increased risk for development of peptic ulcer disease. Portal hypertensive gastropathy (PHG) is one of the clinically important gastric mucosal lesions as it may cause acute or chronic gastrointestinal blood loss leading to anemia. It can cause bleeding from gastrointestinal tract even after successful variceal obliteration in patients with portal hypertension [1]. Several pathophysiological mechanisms have been postulated for the acquisition of PHG. They include increased serum gastrin leading to increased acid secretion, alteration in the mucosal blood flow, decreased secretion of prostaglandin in the gastric mucosa and the presence of *Helicobacter pylori* infection [2].

Infection by *H. pylori* is highly prevalent, especially in the low socioeconomic strata of developing countries [3], and is responsible for lesions like gastroduodenal erosions and ulcers. In patients with liver cirrhosis and portal hypertension, their prevalence and its associations with PHG are controversial [4-6]. Knowledge of the prevalence of infection by *H. pylori* in patients with cirrhosis of liver and the study of its association with PHG could be useful to derive the pathogenesis and the evaluation of a possible additive effect of *H. pylori* on the same. If *H. pylori* infection has a contributive role in the pathogenesis of PHG, then eradication of *H. pylori* should be beneficial in the management of variceal bleeding secondary to PHG.

**Materials and Methods**

The study was conducted in the Department of Medicine, Victoria and Bowring and Lady Curzon Hospitals, affiliated to Bangalore Medical College and Research Institute (BMCRI), from October 2015 to November 2017. A total of 100 patients who were diagnosed with Liver cirrhosis with portal hypertension and PHG were included in our study. All patients were aged 18 years or older.

Patients with primary or secondary hepatic malignancy and with prior history of gastric surgery were excluded. We also excluded patients with prior therapy for eradication of *H. pylori*...
pylori and patients diagnosed with gastric ulcer or duodenal ulcer on endoscopy.

Prior approval for the study protocol was obtained from institutional ethical committee. After explaining the need for relevant investigations, and their role in the further management, patients were included in the study. Informed written consent was obtained from patient or a responsible attendant before including the patient in the study.

Demographic data, history, clinical examination and investigation details like complete hemogram were recorded in the study proforma. All patients were subjected to endoscopy and two biopsy specimens were taken from two different sites of the antral mucosa. One specimen was sent for histopathological examination for H. pylori and the other for rapid urease test, which was done immediately after taking the specimen.

Statistical methods

The collected data were analyzed using IBM SPSS 23. Variables were transformed with suitable data transformation. Frequency tables and cross tabulation, Chi-square test and one sample proportion were used to interpret the data.

Chi-square test was used to test the independence of two categorical variables. The null hypothesis for the Chi-square test was that the variables are independent. One sample t-test was used to test the hypothesis that the variables have specified proportion.

Results

In our study, we evaluated a total of 100 patients with PHG.

Table 2. Distribution of Endoscopic Findings

<table>
<thead>
<tr>
<th>Endoscopy</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Severe</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Esophageal varices</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Grade I</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td>Grade II</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Grade III</td>
<td>26</td>
<td>26</td>
</tr>
</tbody>
</table>

Age distribution of the study population was between 22 and 78 years with 39% of the patients in the age group less than 35 years. The study had 82% males and 18% females. Majority were found to be in the group with hemoglobin between 8 and 11 g/dL (50%). Of the patients, 73% had platelet count less than 100,000 cells/mm³ and 39% had platelet count in the range of 50,000 - 100,000 cells/mm³.

Of the study group, 75% had hyperbilirubinemia with 58.9% of them having a bilirubin value more than 3 mg/dL. Severity of liver disease was assessed by Child-Pugh class and it was found that 6% of patients were in CPC-A, 38% in CPC-B and 56% in CPC-C (Table 1).

Endoscopy showed mild PHG in 40% of the study group and severe PHG in 60%. Esophageal varices were present in 92% of the patients with 40% of the patients having grade II esophageal varices (Table 2).

Of the patients studied, 9% had liver span less than 10 cm and 35% had hepatomegaly with liver span more than 15 cm. Of the study group, 95% showed altered echotexture suggestive of liver disease. Portal vein caliber was less than 9 mm in 22% of patients studied and 10% had portal vein caliber of more than 13 mm. Of the study group, 87% had portal vein velocity less than 15 cm/s, which is suggestive of portal hypertension (Table 3).

A one sample proportion test with null hypothesis that proportion of patients with H. pylori was 0.5 was tested against the alternate hypothesis that the proportion was greater than 0.5. The null hypothesis was rejected at 5% level of significance (Z-value = 90.028, P < 0.001) implying that more than 50% of the respondents had shown H. pylori positively, indicating a relationship (Table 4).

The Chi-square test indicates that there is a statistically significant relationship between H. pylori status and the grading of PHG at 5% level of significance (Chi-square = 5.67, df= -1, P = 0.017). For patients with H. pylori, it is highly probable
Helicobacter pylori Infection in PHG

Discussion

PHG is a frequent cause of gastrointestinal bleeding in patients with portal hypertension. Endoscopically, gastric mucosa is classically described as a mosaic-like pattern that resembles snake skin, with or without red spots [7]. Histopathologic features include vascular ectasia of the mucosal and submucosal veins and capillaries [8].

The present study was done to assess the prevalence of H. pylori in patients with PHG. If positive in either rapid urease test or histopathological examination or both the tests were considered as positive for H. pylori and negative, if both the tests were negative. Clinical examination was done in all patients and looked for features of liver cell failure, features of portal hypertension and signs of hepatic encephalopathy. Routine blood investigations, coagulation profile, HBsAg and Anti-HCV were done for all patients and recorded in the study proforma. Severity of liver disease was assessed by Child-Pugh classification in all patients. PHG is graded as mild and severe by McCormack [8] classification based on 'Snake-skin' pattern or Cherry red spots with or without diffuse hemorrhage on endoscopy.

In the present study, we could not find any significant relation between Child-Pugh class, the presence or grade of esophageal varices and the severity of PHG (P = 0.931 and 0.068, respectively). Our findings correlate with Pan et al [9] who found that the development of PHG is less influenced either by the severity of cirrhosis (Child-Pugh class) and or by the presence or non-presence of gastric varices. Furthermore, Abbas et al [10] could not find any correlation of Child-Pugh with the severity of PHG.

In our study, the overall prevalence of H. pylori in patients with PHG was 64%, a figure comparable to that of Pan et al [9] who found a prevalence of 62.1%, and also with Safwat et al [11], who found a 60 % prevalence of H. pylori in patients with PHG in their study. Yet, a lower seroprevalence (35.7%) was reported by Sathar et al [12]. This discrepancy could be attributed to the different tools of H. pylori diagnosis as they depend on IgG serology.

Upon investigating the relationship between H. pylori and PHG in cirrhotic patients, we found a statistically significant relation between the two using one sample proportion test. This result suggests that portal hypertensive patients infected with H. pylori are more likely to develop PHG. Our results were in consistent with study conducted by Sathar et al [12], which showed a significant association between H. pylori and PHG in cirrhotic patients. Similarly Safwat et al [11] found a higher prevalence of the infection with H. pylori among patients with PHG rather than those without PHG.

In our current study, out of the 64 patients with PHG and H. pylori infection, 44 (68.7%) had severe PHG, while only 14 (44%) out of 36 H. pylori negative patients had severe PHG (P = 0.017), reflecting a significant relation between the presence of H. pylori infection and severity of PHG. Our results were similar to Sathar et al [12], who noticed a significant relation between H. pylori and severity of PHG (P < 0.001), while other studies showed no correlation with PHG severity [13].

Our study showed an increased prevalence of H. pylori in patients with PHG and a statistically significant linear relationship between presence of H. pylori and severity of PHG. Our findings suggest that gastric mucosa in cirrhosis might provide a conducive environment for the colonization of H. pylori, and eradication therapy for H. pylori may have a role in the management of PHG.

Limitations

Our study was done in an H. pylori endemic area and we have not addressed the prevalence of H. pylori in the general population. Similarly other causes of PHG were not completely ruled out. The results of our study would have shed more light if improvement of PHG was assessed following H. pylori eradication therapy which warrants the need of further follow-up studies.

Table 5. Correlation Between H. pylori Status and Grading of PHG

<table>
<thead>
<tr>
<th>H. pylori status</th>
<th>PHG</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild</td>
<td>Severe</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>20 (31.25%)</td>
<td>44 (68.75%)</td>
<td>64</td>
</tr>
<tr>
<td>Negative</td>
<td>20 (55.55%)</td>
<td>16 (44.44%)</td>
<td>36</td>
</tr>
<tr>
<td>Total</td>
<td>40 (40%)</td>
<td>60 (60%)</td>
<td>100</td>
</tr>
</tbody>
</table>
Conclusion

In our study, we have found a statistically significant prevalence of \textit{H. pylori} infection in patients with PHG. It was shown that a direct correlation exists between the presence of \textit{H. pylori} infection and severity of PHG. It implies that eradication therapy for \textit{H. pylori} may be beneficial in patients with PHG.

However, there was no consistent correlation noted between \textit{H. pylori} and PHG in a few previous studies [13] which warrants further research to show whether routine eradication of \textit{H. pylori} is needed in the management of PHG.

Conflict of Interest

None of the authors have any conflict of interest.

References