ALIMENTARY TRACT AND PANCREAS

Colonization by *Helicobacter pylori* and its relationship to histological changes in the gastric mucosa in portal hypertension

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Abstract In order to investigate the relationship between *Helicobacter pylori* infection of the gastric mucosa and mucosal changes in portal hypertension, gastric fundic and antral biopsies were obtained from 66 patients with portal hypertension and 49 controls with non-ulcer dyspepsia (NUD). Gastric mucosa from portal hypertensive patients exhibited typical vascular dilatation and congestion, while mild dilatation of lamina propria blood vessels was not uncommon in NUD patients with histological evidence of gastritis. Colonization of the gastric mucosa by *H. pylori* infection was significantly less in portal hypertensive (51.5%) compared to controls (75.5%; *P* < 0.01). The difference was more apparent in patients with marked vascular dilatation (18.8% colonization) compared to patients with minimal vascular dilatation (66.7%). *H. pylori* infection was significantly associated with active superficial gastritis (*P* < 0.001), and with atrophic gastritis (*P* < 0.001), in both study groups. *H. pylori*-negative superficial gastritis was significantly more common in portal hypertension (23/66 patients) than in controls (7/49; *P* < 0.05). *H. pylori* infection was not more common in patients who had undergone repeated sclerotherapy. The results suggest that the gastric mucosa of portal hypertension does not provide a hospitable environment for *H. pylori* colonization, particularly when mucosal congestion is marked. *H. pylori* infection does not add significantly to the gastropathy of portal hypertension.

Key words: gastritis, *Helicobacter pylori*, portal gastropathy.

INTRODUCTION

*Helicobacter pylori*, a spiral micro-aerophilic organism, colonizes the gastric mucosa and may be causally related to gastritis and peptic ulcer disease. The prevalence of *H. pylori* in apparently healthy individuals shows marked geographic variation, with a high prevalence in developing countries, including southern India. Factors contributing to gastric mucosal colonization are not very clear, but the spiral shape of the organism, its ability to produce urease, and its micro-aerophilism offer it survival advantages in the gastric mucosa.

Abnormalities of the microcirculation of the gastric mucosa have been described in portal hypertension, and are reflected in a hypoxia of the gastric mucosa. These changes may be accentuated after sclerotherapy or oesophageal transection. Apart from typical ‘congestive gastropathy’, gastric and duodenal erosions and ulcers are common in patients with portal hypertension. Reports on the prevalence of *H. pylori* in cirrhosis with portal hypertension have been conflicting. We predicted that mucosal hypoxia in portal hypertension may favour extensive colonization of the gastric mucosa by *H. pylori*, in turn leading to gastroduodenal erosive disease. The present study was carried out to assess the prevalence of *H. pylori* in the gastric mucosa of patients with portal hypertension and to assess the relationship of *H. pylori* to gastritis and vascular changes in these patients.

METHODS

Sixty-six unscreened patients with portal hypertension (PH) undergoing diagnostic endoscopy or sclerotherapy were prospectively evaluated. The majority of them (42) had cirrhosis of the liver, with non-cirrhotic portal fibrosis (10) and extrahepatic portal venous obstruction (14) being less common. All patients underwent complete evaluation including biochemical tests of liver function, ultrasonography, and liver biopsy wherever possible. Cirrhosis was diagnosed on the basis of clinical and laboratory data supported by liver biopsy. Where biopsy was not possible due to coagulopathy, ascites or patient refusal, the diagnosis was made on clinical and laboratory grounds supported by ultrasonographic and nuclear scan criteria. Of the cirrhotics, 10 (23.8%) were alcoholics, 16 (38.1%)...
were post-hepatic cirrhosis, one (2.4%) had Wilson’s disease and the other 15 (35.7%) had cryptogenic cirrhosis. Non-cirrhotic portal fibrosis was diagnosed on the basis of clinical and laboratory data, ultrasound examination of the portal venous system and/or splenopancreatography, and an essentially normal liver biopsy. Extrapancreatic portal venous obstruction was diagnosed on the basis of demonstration of the extrapancreatic block at ultrasonography and/or splenopancreatography. Forty-nine subjects with non-ulcer dyspepsia (NUD) undergoing diagnostic endoscopy served as the controls. Non-ulcer dyspepsia was diagnosed in patients with dyspepsia who had a normal endoscopy and did not have evidence of gallstone disease. These patients were used as controls since a concurrent study in the same department has shown that the prevalence of *H. pylori* in patients with NUD is the same as in a group of asymptomatic adult southern Indian volunteers.5 None of the subjects had received treatment with bismuth, omeprazole or antibiotics within the past month. Patients with portal hypertension (PH) and controls (NUD) were well-matched for age and sex (NUD range 17–60, median 34.4; PH 10–69, median 36.6 years), and were of comparable ethnicity and socio-economic status. All the subjects underwent upper gastrointestinal endoscopy with biopsies of the gastric mucosa. A ‘mosaic’ pattern of the gastric mucosa was seen in only nine of the 66 patients with PH, and in none of the controls. Patchy or diffuse erythema of the mucosa was seen in 31 patients with PH, and in 12 controls. A minimum of two biopsies each were taken from the antrum (2 cm proximal to the pylorus) and body, at least one being from the anterior and another from the posterior gastric wall. Biopsies were fixed in Bouin’s solution, processed routinely and evaluated independently by two histopathologists (M.M. and S.V.) who were not aware of the individual diagnosis. Haematoxylin-eosin (H&E)-stained sections were examined histologically for dilatation and increase in the numbers of vascular channels11–14 and gastritis.15 The diameter of the vascular channels was measured using a micrometer eyepiece, and the average of the measurements by the two observers independently was graded on a scale of 1 to 4 as follows:

0 = 2–10 microns
1 + = 10–20 microns
2 + = 20–30 microns
3 + = 30–40 microns
4 + = > 40 microns

The location of these changes in the superficial (foveolar) or deep (glandular) lamina propria was noted. Gastritis was recorded according to Whitehead’s classification19 as superficial or atrophic gastritis (mild, moderate, severe) and the activity of gastritis was noted. The presence of *Helicobacter pylori* was noted and confirmed in additional sections stained by a modified Giemsa technique.20 *H. pylori* numbers were semi-quantitatively assessed on a scale of 0 to 4, as follows:

0 = no bacteria visible
1 + = very occasional curved bacteria
2 + = few curved bacteria in most fields
3 + = many bacteria seen in most fields
4 + = numerous bacteria in almost every field

The scores given by one pathologist agreed with her fellow pathologist in >90% of specimens. Where these was discordance, it was resolved by mutual agreement between the two pathologists. Statistical analysis of the data was performed using the Chi-squared test.

**RESULTS**

*Helicobacter pylori* was detected in the gastric mucosa of 37 of the 49 (75.5%) patients with non-ulcer dyspepsia. Only 34 of the 66 (51.5%) patients with portal hypertension showed colonization of the gastric mucosa by *H. pylori*. This difference was statistically significant (*P* < 0.01). No significant differences were noted between different types of portal hypertension with regard to *H. pylori* colonization of the gastric mucosa (cirrhosis 57.1%, non-cirrhotics 41.6%). *H. pylori* colonization was equally common in untreated portal hypertension, after sclerotherapy, and after surgical therapy (Table 1).

Vascular changes noted in patients with portal hypertension consisted of oedema of the subepithelial lamina propria pushing down the glandular components, and a variable degree of increase in the number and size of the capillaries and veins in the lamina propria. There was good reproducibility of grading of the vascular dilatation between the two histopathologists, with a coefficient of variation <2%. As shown in Table 2, minor dilatation of the vessels (grade 1–2+) was common in both NUD and in PH, but dilatation greater than this was seen only in patients with PH. Furthermore, in NUD, vascular dilatation was invariably found only in the presence of gastritis (in 18/41, 22.6% of patients with gastritis, compared to 0/8 patients without gastritis). Vascular dilatation was equally common in untreated portal hypertension and after sclerotherpay, but was less frequent in patients who had undergone surgical treatment (Table 1; *P* = 0.02).

Changes of superficial gastritis were noted in 28 of 49 (57.1%) patients with NUD, and in 49 of 66 (74.2%) patients with PH. *H. pylori* was detected in 21 out of 28.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Colonization of the gastric mucosa by <em>H. pylori</em> and prevalence of vascular changes in patients with PH</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>H. pylori</em> present</td>
<td>Vascular change*</td>
</tr>
<tr>
<td>Unreated PH (n = 26)</td>
<td>14 (53.8%)</td>
</tr>
<tr>
<td>Post-sclerotherapy (n = 29)</td>
<td>16 (55.1%)</td>
</tr>
<tr>
<td>Post-surgery* (n = 11)</td>
<td>4 (36.3%)</td>
</tr>
<tr>
<td>NUD (n = 49)</td>
<td>37 (75.5%)</td>
</tr>
</tbody>
</table>

*Defined as 1+ or more.

*Three had a splenorenal shunt and eight had gastric devascularization.*
(75%) patients with NUD who had superficial gastritis compared to 24 of 49 (48.9%) patients with PH and superficial gastritis. *H. pylori*-negative superficial gastritis was significantly more common in PH than in NUD ($P < 0.05$; Table 3).

Atrophic gastritis was noted in 13 patients with NUD (26.5%) and in nine patients with PH (13.6%). All patients with atrophic gastritis were positive for *H. pylori* (Table 3). Activity of the gastritis (neutrophil polymorph infiltrate in the lamina propria) was noted in 29 patients with NUD (59.2%) and in 31 patients with PH (46.9%).

Active gastritis was strongly associated with the presence of *H. pylori* histologically ($P < 0.001$). Histological changes of gastritis were absent in eight patients with NUD and in eight with PH.

In patients with PH, vascular changes were noted with equal frequency in the gastric body (59%) and antrum (61.1%). Vascular dilatation was usually detected in both body and antral mucosa histologically (35) but in a small number such dilatation was confined to the antrum (6) or body (4) alone. Colonization by *H. pylori* was more common in the antrum (34/66, 51.5%) than in the body (39/66, 28.7%). All patients with *H. pylori* in the body of the stomach also had the organism in the antrum. In patients with PH, an inverse relationship was noted between *H. pylori* colonization and the degree of vascular dilatation in the mucosa (Table 4).

**DISCUSSION**

The prevalence of *H. pylori* in asymptomatic adults in southern India is very high (88%). In this population, the prevalence of *H. pylori* infection in patients with non-ulcer dyspepsia is not different from that in asymptomatic adults, and the incidence of gastritis is similar in both groups. Serological surveys in Indians have demonstrated that 87% of persons in the second decade of life have been exposed to infection, and that there is no further age-related rise in prevalence as seen in Western countries. High rates of asymptomatic *H. pylori* infection have also been reported from other developing countries.

This study was carried out to test the assumption that the hypoxic gastric mucosa of portal hypertension may facilitate extensive colonization by *H. pylori* in a part of the world where the background prevalence of *H. pylori* infection is very high. An earlier study had shown that, in a Western population, *H. pylori* colonization was seen less frequently in portal hypertensive. However, a study from Japan reported that *H. pylori* colonization was more common in liver cirrhosis.

A study of the natural history of congestive gastropathy reported that colonization by *H. pylori* appeared to be less frequent in endoscopically severe congestive gastropathy than in mild congestive gastropathy or in cirrhosis without endoscopic gastropathy. This study did not include control subjects other than cirrhotics, and the background prevalence of *H. pylori* is therefore not available for comparison. Others have reported a correlation between the degree of histological gastritis and *H. pylori* infection in patients with congestive gastropathy. The present study suggests that colonization of the gastric mucosa by *H. pylori* is significantly less common in patients with portal hypertension than in subjects with non-ulcer dyspepsia, in whom the prevalence of this infection is the same as in the normal population in this geographic region.

The reasons for the observed decrease in *H. pylori* infection in portal hypertension are not clear. It has been postulated that severe atrophy of the gastric glands in

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**Table 2** Degree of vascular ectasia in the gastric mucosa in PH and NUD

<table>
<thead>
<tr>
<th></th>
<th>Superficial</th>
<th>Deep</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 + ++ ++++</td>
<td>0 +</td>
</tr>
<tr>
<td>NUD</td>
<td>19 23 7</td>
<td>31 5</td>
</tr>
<tr>
<td>PH</td>
<td>9 19 22 14</td>
<td>2 21 6 17</td>
</tr>
</tbody>
</table>

**Table 3** Prevalence of *H. pylori* in relation to histological changes observed in the gastric mucosa

<table>
<thead>
<tr>
<th></th>
<th>Superficial gastritis</th>
<th>Atrophic gastritis</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>NUD</td>
<td>Total 28</td>
<td>Mild 10 Moderate 10 Severe 6</td>
<td>+ 20</td>
</tr>
<tr>
<td>H. pylori +</td>
<td>21 10 2 1</td>
<td></td>
<td>28 9</td>
</tr>
<tr>
<td>PH</td>
<td>Total 49</td>
<td>Mild 6 Moderate 3 Severe 0</td>
<td>31 35</td>
</tr>
<tr>
<td>H. pylori +</td>
<td>24 6 3</td>
<td></td>
<td>27 7</td>
</tr>
</tbody>
</table>

**Table 4** Relationship of *H. pylori* numbers in the gastric mucosa to the degree of vascular dilatation in patients with portal hypertension

<table>
<thead>
<tr>
<th>Vascular dilatation</th>
<th>H. pylori</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0 6 2 7 8 9</td>
</tr>
<tr>
<td>+</td>
<td>4 1 6 2 0 4</td>
</tr>
<tr>
<td>2 +</td>
<td>5 2 4 3 1 2</td>
</tr>
<tr>
<td>3 +</td>
<td>4 1 0 0 1 0</td>
</tr>
<tr>
<td>%Positive</td>
<td>68.4 66.7 58.8 38.5 18.2</td>
</tr>
</tbody>
</table>
severe congestive gastropathy may account for a decreased prevalence of H. pylori infection. In our subjects with PH, atrophic gastritis was less frequent than in controls, and severe atrophy was not seen in any of the subjects. Hence, we cannot attribute the observed decrease in H. pylori prevalence to gastric atrophy. H. pylori is micro-aerophilic, this characteristic being an adaptive mechanism for survival in the low oxygen tensions found in the gastric mucosa. It is possible that the gastric mucosal oxygen tension in portal hypertension is too low to allow H. pylori colonization. A relationship with mucosal vascular changes is suggested by the observation of decreased H. pylori colonization in subjects with higher grades of vascular dilatation. It is also possible that other factors such as alterations in gastric mucus or altered expression of bacterial receptors on gastric epithelial cells may be operative in such patients and explain decreased gastric mucosal colonization by H. pylori in PH.

The study reconfirms earlier data that active gastritis is very strongly associated with H. pylori infection, as also atrophic gastritis. In the present study, superficial gastritis was more common in portal hypertension (74.2%, 49/66 patients) than in non-ulcer dyspepsia (57.1%, 28/49), while atrophic gastritis was less common in portal hypertension (13.7%, 9/66) compared to non-ulcer dyspepsa (26.5%, 13/49 patients). The increase in superficial gastritis in portal hypertension in this study was largely H. pylori negative. These findings need to be substantiated in further studies.

The prevalence of H. pylori was similar in untreated PH, and in patients who had undergone repeated sclerotherapy. Repeated endoscopic interventions in the latter group apparently did not lead to increased colonization, a reassuring factor in view of the reported transmission of H. pylori at endoscopy. Furthermore, the incidence of vascular changes in the gastric mucosa was not increased in patients who had undergone repeated sclerotherapy. This contrasts with other reports that endoscopic or histologic evidence of congestive gastropathy may appear or worsen after sclerotherapy. Doppler ultrasound studies have shown that blood flow in oesophageal varices may sometimes be towards the stomach, and in such cases sclerotherapy may be expected to reduce gastric mucosal congestion. This may explain the differences between these studies.

We conclude that colonization of the gastric mucosa by H. pylori is less common in patients with portal hypertension than in control subjects, possibly because of the vascular congestion and resultant hypoxia.

REFERENCES

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