Research Article

Impact of Helicobacter pylori Infection on Gastric Variceal Bleeding among Patients with Liver Cirrhosis

Mohamed A. Elsebaey,1 Mohamed A. Tawfik,1 Samah A. Elshweikh,1 Manal Saad Negm,1 Mohammed H. Elnaggar,1 Ghada Mahmoud Alghazaly,1 and Sherief Abd-Elsalam2

1Internal Medicine Department, Tanta University, Egypt
2Tropical Medicine Department, Tanta University, Egypt

Correspondence should be addressed to Sherief Abd-Elsalam; Sherif_tropical@yahoo.com

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Background and Aims. Currently, it is well known that Helicobacter pylori- (H. pylori-) related peptic ulcer is one of the main causes of nonvariceal bleeding in cirrhotic patients. However, there is a lack of data to identify the exact effect of H. pylori infection on variceal bleeding. This study was conducted to identify the impact of H. pylori infection on gastric variceal bleeding in cirrhotic patients.

Patients and Methods. 76 cirrhotic patients with gastric varices were included in this prospective study and divided into 2 groups: nonbleeding gastric varices (32 patients) and bleeding gastric varices (44 patients). The fasting serum gastrin level was measured. Mucosal biopsies from the gastric body and antrum were examined to determine the patterns of gastritis and the presence of H. pylori.

Results. The frequency of H. pylori infection in the studied patients was 59.2%. There were significant differences between both groups regarding liver decompensation (P = 0.001), red color sign over gastric varices (P = 0.0011), prevalence of H. pylori infection (P = 0.0049), histological patterns of gastritis (P = 0.0069), and serum gastrin level (P = 0.0200). By multivariate analysis, Child C cirrhosis, red color sign over gastric varices, and H. pylori-induced follicular gastritis were independent risk factors for bleeding from gastric varices.

Conclusion. H. pylori-induced follicular gastritis is considered as an additional risk factor for bleeding from gastric varices.

1. Introduction

Gastric variceal bleeding is a serious complication of portal hypertension in cirrhotic patients and is associated with significant morbidity and mortality [1]. Although the incidence and bleeding risk of gastric varices are lower than that of esophageal varices, whenever bleeding occurs, it is usually more severe, requires more blood transfusions, and is associated with higher rebleeding and mortality rates [2–4]. Therefore, the prognosis of patients with gastric variceal bleeding is still far from satisfactory [5].

Most of the cirrhotic patients are immunocompromised; therefore, they are more susceptible to infections, and it seems that there is association between infections and the cirrhosis-related complications such as variceal bleeding [6, 7]. Currently, it is well known that Helicobacter pylori- (H. pylori-) related peptic ulcer is one of the main causes of nonvariceal bleeding in cirrhotic patients [8–10]. However, there is a lack of population-based data to identify the exact effect of H. pylori infection on gastric variceal bleeding in cirrhotic patients.

There are limited studies that discussed the relation between H. pylori infection and variceal bleeding [11]. To address this issue, we conducted this study to assess the effect of H. pylori infection on bleeding from gastric varices in cirrhotic patients.

2. Patients and Methods

Between January 2017 and May 2018, we performed this prospective study at the gastroenterology and hepatology
unit of Internal Medicine Department, Tanta University Hospital, Egypt.

In this study, 298 patients were assessed for enrollment in the study. However, 222 patients were excluded: 10 patients had previous medication for Helicobacter pylori; 31 patients received antibiotics in the last month, 62 patients received proton pump inhibitors in the last 2 weeks, and 119 patients were also excluded due to the presence of isolated esophageal varices. So finally, 76 patients with gastric varices were enrolled in the study.

A total of 76 cirrhotic patients with gastric varices were enrolled in this study. All cirrhotic patients who attended for screening of varices and the endoscope revealed nonbleeding gastric varices and those who presented with upper gastrointestinal bleeding (UGIB) and the endoscope revealed gastric varix as a source of bleeding were recruited in this study. Patients who had previously undergone H. pylori treatment or had received proton pump inhibitor (PPI) or antibiotics within the previous 2 or 4 weeks were excluded from the study.

The patients were divided into 2 groups: group I (nonbleeding gastric varices) included 32 patients who attended for variceal screening in which the endoscope revealed nonbleeding gastric varices and group II (bleeding gastric varices) included 44 patients presented with UGIB in whose gastric varix was the source of bleeding.

The study protocol was done in accordance with the ethical guidelines of the 1975 Helsinki Declaration. A written informed consent was obtained from all patients for participation in the current study. Detailed history taking, thorough clinical examination, and routine laboratory investigations were done for all patients. The severity of liver cirrhosis was assessed using Child-Pugh classification [12].

2.1. Upper GI Endoscopy and Gastric Biopsy. Endoscopy was done in all patients, and the endoscopic findings of gastric varices such as variceal location, size, and the presence of red color sign were evaluated [13, 14].

Regarding therapy of gastrointestinal bleeding in these patients, patients with variceal bleeding were resuscitated; blood transfusion was given if a hemoglobin level was less than 8 g/dL. Somatostatin (Sandostatin, Novartis) 100 μg IV as an initial bolus followed by IV infusion of 25 μg/h was administered. Upper endoscopy was done once the patient’s vital signs permitted, and haemostatic procedure was achieved using N-butyl-2-cyanoacrylate (ampoule 0.5 mL) (GluStitch® Twist, GluStitch Inc., Delta, BC, Canada) diluted with 0.8 mL of Lipiodol®, Cyanoacrylate was injected using Olympus video endoscopy and a 23-gauge disposable injection needle (Wilson-Cook Medical Inc., USA), immediately followed by injection of 1-2 mL distilled water then the needle was withdrawn [2].

Regarding prophylaxis of gastrointestinal bleeding in these patients, a nonselective β-blocker (e.g., propranolol) and repeated endoscopic sessions using cyanoacrylate every 4 weeks are performed until endoscopic obliteration is achieved [5].

In patients with nonbleeding gastric varices (group I), endoscopic biopsies from the gastric corpus and antrum were obtained by biopsy forceps at admission. In patients with bleeding gastric varices (group II), biopsies were obtained during the endoscopic follow-up. The biopsy collected from each patient was kept in 10% formalin to be processed later using haematoxylin/eosin and gimsa stains to determine the patterns of gastritis and the presence of H. pylori, respectively.

2.2. Fasting Serum Gastrin Level (Normal Level: 13-115 pg/mL). After an overnight fast, the serum gastrin level was measured by enzyme-linked immunosorbent assay (ELISA) kits provided from Biohit Deutschland GmbH, Germany.

2.3. Statistical Analysis. Statistical analysis of data was done using the Statistical Program for Social Science (SPSS) version 20.0. Quantitative data were analyzed using unpaired t-test and expressed as mean and standard deviation (SD). Qualitative data were analyzed using the chi-square test and were expressed as frequency and percent. Multivariate analysis was done to identify predictive factors of bleeding gastric varices. In all tests, P value was significant if <0.05. (The full detailed form is SPSS 20, IBM, Armonk, NY, United States of America.)

3. Results

Regarding demographic data of the studied patients, there were no significant differences between both groups with regard to age, sex, and etiology of cirrhosis (P = 0.0940, 0.6387, and 0.6587), respectively, while there was significant difference regarding Child-Pugh class (P = 0.001) as shown in Table 1.

Concerning the endoscopic findings of gastric varices, there were no significant differences between both groups regarding type and size of gastric varices (P = 0.9427 and 0.6766, respectively), while there was significant difference regarding the red color sign over gastric varices (P = 0.0011) as shown in Table 1.

The prevalence of H. pylori infection among the studied patients was 59.2%. H. pylori infection was significantly more frequent among patients with bleeding gastric varices compared to those without bleeding (P = 0.0049). Histopathological patterns of chronic gastritis and the fasting serum gastrin level in both groups were shown in Table 2.

In our study, 12 patients (15.79%) had clean base-peptic ulcers. In the nonbleeding group, 4 patients had peptic ulcers: 2 ulcers at the gastric antrum and other 2 ulcers at the duodenal bulb. However, in the bleeding group, 8 patients had peptic ulcers: 3 ulcers at the gastric antrum and other 5 ulcers at the duodenal bulb.

Histopathological patterns of chronic gastritis and fasting serum gastrin levels among H. pylori positive patients were shown in Table 3. In group I (nonbleeding gastric varices), 7 (21.88%) patients had follicular gastritis, while in group II (bleeding gastric varices), 26 (59.09%) patients had follicular gastritis (Figure 1). On the other hand, in group I (nonbleeding gastric varices), 5 (15.63%) patients had atrophic gastritis; in group II (bleeding gastric varices), 2 (4.55%) patients had atrophic gastritis (Figure 2).
By multivariate analysis, Child C cirrhosis, red color sign over gastric varices, and H. pylori-induced follicular gastritis were independent risk factors for bleeding from gastric varices in the studied patients as shown in Table 4.

### 4. Discussion

The possible causative role of H. pylori infection in gastric variceal hemorrhage is less investigated. Indeed, the known risk factors for gastric variceal bleeding such as hepatic functional reserve, gastric variceal location, variceal size, overlying mucosal red color sign, and intravariceal pressure do not easily explain why variceal bleeding and early rebleeding occur unpredictably in patients with cirrhosis [15–18].

In the current study, the frequency of H. pylori infection was 59.2%. This was consistent with a study of Devrajani et al. [19] who showed that the H. pylori infection rate in cirrhotic patients was 56%. In various studies, the overall prevalence of H. pylori infection in cirrhotic patients ranged from 35.1% to 70.6%. This discrepancy is perhaps related to the different investigational tools used for the diagnosis of H. pylori infection [20–23].

The present study clearly demonstrated that the prevalence of H. pylori infection was significantly higher in patients with gastric variceal bleeding than those without bleeding (72.73% and 40.62%, respectively) \((P = 0.0049)\). This means that H. pylori infection might be implicated as a risk factor for bleeding from gastric varices. In contrary to our results, Sakamoto et al. [11] reported higher rates of H. pylori infection in patients without variceal bleeding in comparison to those with bleeding (55.4% and 31.6%, respectively).
theory is that local alkalization of ammonia produced by *H. pylori* urease in the vicinity of G cells stimulates gastrin release. Another possible mechanism is that *H. pylori* infection reduces the number of antral D cells and somatostatin concentration, resulting in a lack of physiologic inhibition of somatostatin on G cells and hence increased gastrin secretion [27, 28].

Our results revealed that the rate of follicular gastritis was significantly higher in *H. pylori* positive patients with bleeding gastric varices than those without bleeding (71.88% and 38.46%, respectively) (\(P = 0.0199\)). This explains why the gastrin level was significantly higher in *H. pylori* positive patients with bleeding gastric varices compared to those without bleeding (78.34 ± 35.2 and 51.15 ± 46.92 pg/mL, respectively) (\(P = 0.0380\)). On the other hand, Sakamoto et al. [11] documented, in their study, that *H. pylori* infection was commonly associated with atrophic gastritis and concomitant hypochlorhydria.

On the basis of our findings, we supposed that *H. pylori*-induced follicular gastritis might increase the risk of gastric variceal bleeding through the deleterious effect of gastric hyperacidity associated with hypergastrinemia. From a viewpoint of acid-related concerns, hyperacidity in cirrhotic patients can be a relatively aggressive factor for mucosa-overlying varices causing erosions, ulcerations, and eventually variceal rupture which could be ameliorated by long-term receiving PPI [29].

Several studies reported that the majority of esophageal variceal bleeding that occurred at the distal esophagus near the esophagogastric junction was associated with a decreased esophageal acid clearance. Moreover, the incidence of this bleeding could be reduced by long-term administration of PPI [29–31]. The results of these reports regarding the deleterious effect of hyperacidity on varices, in part, support our results.

To our knowledge, this is the first study to document *H. pylori* infection as a risk factor for bleeding from gastric varices especially if *H. pylori* was associated with follicular gastritis. This could be attributed to hyperacidity associated with follicular gastritis.

In addition, *H. pylori* infection might worsen the liver functions and portal hypertension through overproduction of proinflammatory cytokines such as tumor necrosis factor-\(\alpha\), interleukins, nitric oxide, and endothelin-1 [32–38]. This in turn has a harmful effect on the gastric varices especially in patients with advanced liver cirrhosis.

### Table 3: Histopathological patterns of chronic gastritis and the fasting serum gastrin level among *H. pylori* positive patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Nonbleeding gastric varices ((N = 13))</th>
<th>Bleeding gastric varices ((N = 32))</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N)</td>
<td>%</td>
<td>(N)</td>
</tr>
<tr>
<td>H. pylori-induced chronic gastritis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follicular</td>
<td>5</td>
<td>38.46%</td>
<td>23</td>
</tr>
<tr>
<td>Atrophic</td>
<td>5</td>
<td>38.46%</td>
<td>2</td>
</tr>
<tr>
<td>Others (superficial or erosive)</td>
<td>3</td>
<td>23.08%</td>
<td>7</td>
</tr>
<tr>
<td>Fasting serum gastrin level</td>
<td>Mean ± SD</td>
<td>51.15 ± 46.92</td>
<td>78.34 ± 35.2</td>
</tr>
</tbody>
</table>

![Figure 1: Histopathological pattern of follicular gastritis.](image1)

![Figure 2: Histopathological pattern of atrophic gastritis.](image2)

*Figure 1: Histopathological pattern of follicular gastritis.*

*Figure 2: Histopathological pattern of atrophic gastritis.*
5. Conclusion

The prevalence of *H. pylori* infection in cirrhotic patients was 59.2%. In addition to decompensated cirrhosis and red color sign over gastric varices, *H. pylori*-induced follicular gastritis is considered as a risk factor for bleeding gastric varices.

Data Availability

The authors’ institution does not allow public data access.

Conflicts of Interest

The authors declare that they do not have any conflict of interest.

Authors’ Contributions

All authors contributed equally to this work. All the authors participated sufficiently in the work and approved the final version of the manuscript.

References


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