Peptic ulcer bleeding: is *Helicobacter pylori* a risk factor in an endemic area?

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**Background/Objective:** A high prevalence of *Helicobacter pylori* infection has been reported in Iran. Although the importance of *H. pylori* in the induction of peptic ulcer disease is clearly defined, only few studies have addressed its role in bleeding from peptic ulcers. We evaluated the role of *H. pylori* in peptic ulcer bleeding. **Methods:** Patients with acute peptic ulcer bleeding (PUB) and those with peptic ulcer disease without bleeding ('controls') were enrolled. Upper GI endoscopy and rapid urease test were performed in both groups. Histological study for detection of *H. pylori* was performed in patients with active bleeding, if RUT was negative. Other variables evaluated included sex, age, smoking, previous history of bleeding, non-steroidal anti-inflammatory drugs use, ulcer size, ulcer location, and duration of acid-peptic disease. Multivariate logistic regression analysis was performed to identify independent risk factors. **Results:** 161 patients with PUB and 287 control patients were enrolled. *H. pylori* infection was seen more frequently in patients with duodenal ulcer than gastric ulcer (88.9% vs. 60.5%, p<0.001). Univariate analysis showed that patients with PUB were more often male, older in age, used NSAID, had history of PUB in the past, had ulcer located in the stomach and not in the duodenum, and more often had large ulcer (>1 cm). Logistic regression analysis showed that *H. pylori* infection was protective in PUB after controlling for confounders (OR 0.41, 95% CI 0.21-0.79), when ulcer location was not entered in the model. A second model including ulcer location (to test for a residual effect) showed that *H. pylori* infection was not a significant risk factor in PUB (OR 0.61, 95% CI 0.30-1.24). **Conclusions:** *H. pylori* may not be an independent factor in bleeding from peptic ulcers. The lower frequency of this infection in these patients can be described by the higher frequency of bleeding from gastric ulcers, which are less *H. pylori* related compared with duodenal ulcer. [Indian J Gastroenterol 2005;24:59-61]

Peptic ulcer bleeding (PUB) is the most common complication of peptic ulcer disease, which results in high patient morbidity and medical care costs. In a study from a large health maintenance organization, the annual incidence of hospitalization for acute PUB was 102 per 100,000; the incidence was twice as common in males as in females, and increased with age. Between 20% and 30% of patients with ulcer disease bleed. The major risk factors for bleeding are *Helicobacter pylori* infection, NSAID use, and stress. Eradication of *H. pylori* reduces rebleeding rates. Studies in Iran show a high prevalence of *H. pylori* infection (more than 85% in the adult population). We studied the role of *H. pylori* in PUB, controlling for other risk factors.

**Methods**

Consecutive patients with acute upper gastrointestinal bleeding due to gastric or duodenal ulcers, who presented with hematemesis, melena or both, and control patients with peptic ulcer disease without bleeding, seen in two referral hospitals, were prospectively enrolled over a two-year period (February 2000 to January 2002). Exclusion criteria were: presence of systemic disorders such as chronic liver disease and portal hypertension, cardiac disease or renal failure; gastric surgery; previous intake of antibiotics or proton-pump inhibitors (within 30 days).

Gender, age, current smoking, NSAID use including aspirin (any dose within last week), duration of acid-peptic disease (years), and history of previous PUB were asked for.

All patients in the case group were hospitalized and upper GI endoscopy was performed within 24 hours of admission after hemodynamic stability. Endoscopy was performed by two expert gastroenterologists who used the same definitions and diagnostic criteria. An ulcer was defined as a circumscribed mucosal break at least 0.5 cm in diameter and with a perceptible depth. Ulcer location and size were noted. We used open-mouth biopsy forceps to estimate ulcer size, which was categorized as more than or less than 1 cm diameter.

Antral biopsies near the incisura angularis were taken for rapid urease test to detect *H. pylori* infection. If blood, fresh or old, was present at the biopsy sites, it was washed. In patients with active bleeding or in the presence of fresh blood in the stomach, histological assessment by hematoxylin and eosin staining (H&E) was performed for detection of *H. pylori* infection, if
The study was approved by the institutional review board of the Digestive Disease Research Center of Tehran University of Medical Sciences.

Statistical analysis

Continuous variables are presented as mean (standard deviation). The independent samples t test was used to compare the mean of quantitative variables in two groups. The chi-square test was used to compare qualitative variables in the two groups. Univariate analysis was performed to identify possible risk factors of PUB and also identify intermediate variables for the final model.10

We used logistic regression analysis to identify confounding variables for the effect of \( H. pylori \) on PUB. All variables (except ulcer location, which was an intermediate variable), which had a 10% or more change in the \( \beta \) of \( H. pylori \) in the logistic model, were selected for the final model. \( H. pylori \), age, NSAID use, and ulcer size were introduced in the final logistic regression model. The model was retested including ulcer location to test for a residual effect of \( H. pylori \) in PUB. We used SPSS release 11.5.0 (SPSS Inc, Chicago, IL, USA) for all statistical tests.

Results

The study subject comprised 161 patients with PUB (117 men; mean age 48.3 [18.2] years) and 287 control patients with peptic ulcer but no bleeding (166 men; mean age 39.1 [13.6] years). Overall, 399 (89.1%) patients had duodenal ulcer, 39 (8.7%) gastric ulcer, and 10 (2.2%) had both. The Table shows the frequency of possible risk factors in the case and control groups.

\( H. pylori \) infection was seen more frequently in patients with duodenal ulcer than with gastric ulcer (88.9% vs. 60.5%, p<0.001). On univariate analysis, there was statistically significant relationship between PUB and sex, age, NSAID use, history of previous PUB, \( H. pylori \) status, ulcer size, and ulcer location. No correlation was found between smoking or duration of acid-peptic disease and PUB.

On logistic regression, sex, history of previous bleeding, smoking, and duration of acid-peptic disease were not identified as confounders. Age, NSAID use, ulcer size, and \( H. pylori \) status were entered in logistic regression models (n=414). \( H. pylori \) infection was found to have a protective role in PUB after controlling for confounders (crude odds ratio 0.24, 95% CI 0.13-0.41; adjusted odds ratio 0.41, 95% CI 0.21-0.79). The second model included age, NSAID use, ulcer size, \( H. pylori \) status, and ulcer location. Cases with both gastric and duodenal ulcers were not included (n=10). \( H. pylori \) infection was not found to have a significant role in PUB after controlling for confounders in this model (odds ratio 0.61, 95% CI 0.30-1.24).

Discussion

This study showed that \( H. pylori \) infection was found less frequently in PUB compared to non-bleeding peptic ulcer disease. This difference in two groups persisted after adjusting for confounders. Three explanations can be provided for this finding: (a) a measurement error of \( H. pylori \) infection in patients with PUB, (b) a role of ulcer type as an intermediate factor, and (c) an independent effect of \( H. pylori \) in PUB.

The rapid urease test gives a high number of false negative results when used to diagnose \( H. pylori \) infection in patients with PUB.11 Some authors have reported a low sensitivity of histological methods in patients with PUB.12,13 However Gisbert et al14 showed that the sensitivity and specificity of H&E staining performed on two specimens from the antral area in patients with bleeding duodenal ulcer are similar to those of the \( 13\text{C}- \) urea breath test, at 90% and 92%, respectively. Other studies have also demonstrated a high sensitivity of histology in patients with PUB.11,15 Blood in the antrum might reduce the sensitivity of the rapid urease test but has no effect on culture, histology, urea breath test, and serology.16,17

The controversial results with regard to accuracy of histology in patients with PUB may be explained, at least in part, by the number and site of gastric biopsies, as it has been demonstrated that the distribution of \( H. pylori \) in the stomach can be patchy, and biopsy-based
methods may not be reliable if only one sample is taken or if only biopsies from antrum are obtained.\textsuperscript{18,19} We performed H&E staining for only one antral specimen in actively bleeding patients (in addition to the rapid urease test), which bears a risk of underestimating the frequency of \textit{H. pylori} infection; however, the measurement error associated with this method could not be large enough to explain the difference in the two groups.

The univariate analysis showed that \textit{H. pylori} infection was more frequent in duodenal compared to gastric ulcer, and bleeding was seen more frequently in gastric ulcer. This observation explains that ulcer location is an intermediate variable in the induction of PUB.

The second multivariate logistic regression analysis did not show a significant effect for \textit{H. pylori} in PUB. This finding does not support the protective role of the organism.

In conclusion, this study suggests that \textit{H. pylori} may not be an independent factor in bleeding from peptic ulcers. The lower frequency of this infection in these patients can be attributed to the higher frequency of bleeding from gastric ulcers, which are less \textit{H. pylori} related compared with duodenal ulcer.

References


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Acknowledgements: This study was supported by a grant from Tehran University of Medical Sciences. We also thank Dr S Naseri Moghaddam, Dr Zohreh Movahedi and Dr Shadi Kolahdoozan for their collaboration during this study

Received October 7, 2004. Received in final revised form February 10, 2005. Accepted March 4, 2005