The Prevalence of *Helicobacter pylori* Infection in Bleeding and Non-Bleeding Gastric Ulcers: A Cross-Sectional Case-Control Study

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**Abstract**

**Introduction:** *Helicobacter pylori* is a known and important cause of peptic ulcer disease, and can result in many different complications, both gastrointestinal and systemic. The gastric complications include upper gastrointestinal bleeding.

The costs associated with testing and treatment of complications of *H. pylori* infection is also high, both in private and public setting. Studies in Iran showed high prevalence of *H. pylori* infection, with figures as high as 89.2% in the adult population. In South Africa, patients with bleeding gastric ulcers receive empirical eradication therapy, an expensive practice in a resource limited country like South Africa. It is for this reason that we conducted a case-control study to determine the difference in prevalence of *H. pylori* infection in bleeding and non-bleeding gastric ulcers.

**Aim:** To determine the difference in prevalence of *H. pylori* infection in bleeding and non-bleeding gastric ulcers.

**Methods:** In this prospective cross-sectional case-control study, a total of 173 patients who underwent upper endoscopy at Steve Biko Academic Hospital were recruited. All patients with gastric ulcer on upper endoscopy had antral mucosal biopsy taken and CLO test done on this specimen, in addition to the CLO test, the 42 with a history of upper gastrointestinal bleeding had additional biopsies send for histology for detection of *H. pylori*. The CLO tests were evaluated 24 h later and results documented as either positive or negative.

**Results:** From the 173 patients enrolled, 131 patients were found to have no history of upper gastrointestinal bleeding, while 42 patients were found to be bleeding on upper endoscopy or had a recent history of bleeding. Of the total of 173, 134(77.5%) tested negative for *H. pylori* infection on CLO test and 39(22.5%) tested positive. Of the bleeding group, 7(16.7%) were CLO test positive and 35(83.3%) were negative. In the non-bleeding group of patients, 99(75.6%) were CLO test negative and 32(24.4%) tested positive. There was a 100% correlation between CLO test and histology and 7(16.7%) tested positive.

**Conclusion:** The prevalence of *H. pylori* infection in this South African population with bleeding gastric ulcer was found to be lower than in patients with gastric ulcers that were not bleeding. This was, however, not statistically significant (p value 0.404). To our knowledge there is no South African data for comparison with our study group.

The sensitivity of CLO test was as high as histology. This finding suggests that CLO test can be used reliably in bleeding peptic ulcer.

**Keywords:** Gastric ulcer; Bleeding; *Helicobacter*; Prevalence

**Prevalence of *H. pylori* in bleeding peptic ulcer disease**

Studies to address the role of *H. pylori* in bleeding peptic ulcer are few with conflicting results. In a study conducted in Iran, it was found that *H. pylori* infection has a protective role in bleeding peptic ulcer after controlling for confounders (crude odds ratio 0.24, 95% CI 0.21-0.79). The study went on to conclude that, "H. pylori infection was found less frequently in bleeding compared to non-bleeding peptic ulcer disease" [4].

A case-control study in elderly patients concluded that in this population, risk of upper gastrointestinal bleeding increases with NSAID use, "While *H. pylori* infection was associated with a low risk for gastric bleeding" [5]. To support the previous studies on the decreased prevalence of *H. pylori* in bleeding peptic ulcer, a study by Sesh et al. showed that the rate of *H. pylori* infection was lower in...
Sensitivity of histology for *H. pylori*

Histology is considered as a gold standard test in the detection of *H. pylori* infection. Factors that have an influence on the results of histology include the site where the biopsy is taken, and the number and size of the biopsies. In addition to this factor the method of staining and the level of experience of the examining pathologist also play a role in the results [15].

The sensitivity of the histology is reduced by the same factors which reduce the sensitivity of the rapid urease test, this includes the use of proton pump inhibitors, bismuth based compounds and antibiotics. The reduction in sensitivity is as a result of reduction in the prevalence and density of *H. pylori* throughout the stomach [12,16]. A study done showed that the sensitivity of histology can be increased by about 10% if biopsy of the corpus is done in addition to the antral biopsy [17].

Aim

To determine the difference in prevalence of *H. pylori* infection in bleeding and non-bleeding gastric ulcers.

Subjects and Methods

Setting

This cross sectional case-control study with prospective data collection was conducted on all patients referred to Steve Biko Academic Hospital gastroenterology department found to have gastric ulcer on diagnostic and or therapeutic upper endoscopy.

Patient selection

All patients who came to the gastroenterology department for upper endoscopy found to have gastric ulcer were included in the study provided an informed consent was signed or verbal consent given. Those excluded in the study were patients with no proven gastric ulcer during upper endoscopy.

Those found to have gastric ulcer were then grouped into bleeders and non-bleeders. Bleeding gastric ulcer was defined as follows:

1. History of melena stools or hematemesis
2. Bleeding identified on endoscopy

Measurements

All patients with gastric ulcer had an antral biopsy taken for CLO test. The biopsy sample was immediately inserted into the CLO test gel during endoscopy. This was then stored at room temperature and read 24 h later. The HP fast CLO test was used. The results of the CLO test was recorded as either positive or negative 24 h later. The group of patients who were classified as bleeders had additional biopsies taken from the antrum sends for histology in addition to CLO testing. The histology was done by the NHLS at Steve Biko Academic hospital. With the results documented as either *H. pylori* present or absent. A data capture sheet with different parameters used to capture all the patients information and results, parameters included information about the use of antibiotics or proton pump inhibitors (Figure 1).

Approval

The study protocol was approved by the Faculty of Health Sciences Research Ethics Committee of the University of Pretoria.
Statistical Analysis

Logistic regression adjusting for confounders was used to test differences in *H. pylori* outcome between bleeding and non-bleeding gastric ulcer patients. From a total number of patients who visited the gastroenterology clinic for upper endoscopy, 173 were found to have gastric ulcers and therefore suitable for this study, 131 patients were found to have no history of upper gastrointestinal bleeding, while 42 patients had history or were found to be bleeding on upper endoscopy. The average age of the study population was 56.8 ± 15.3 years. The mean age in the non-bleeding group was 55.8 ± 15.5 years and in the bleeding group was 59.9 ± 14.3 years. The two groups of study population (bleeders and non-bleeders), were further compared in terms of gender, use of proton pump inhibitor and antibiotics use. The total study population consisted of 92 (53.2%) females and 81 (46.8%) male. The bleeding group of patients was made up of 22 (52.4%) female and 20 (47.6%) male patients. While the non-bleeding group consisted of 70 (53.4%) females and 60 (46.6%) males. A number of patients in both groups were found to be on either proton pump inhibitor, antibiotics or both. Of the total study population 62 (35.8%) were on proton pump inhibitors. The non-bleeding group of patients on proton pump inhibitors were 41 (31.3%). In the bleeding group of patients 21 (50%) were on proton pump inhibitors. The last parameter assessed between the group of bleeding and non-bleeding patients was the use of antibiotics. Of the 173 study population, 30 (17.3%) were found to be on antibiotics, of these, 3 (7.1%) were bleeders and 27 (20.6%) were non-bleeders. The study population had a total of 173 participants, with 39 (22.5%) testing positive for *H. pylori* on CLO test. This consisted of 7/42 (16.7%) of bleeders and 32/131 (24.4%) non-bleeders. From the population of 42 bleeding patients, 21 (50%) were on proton pump inhibitors. There was a 100% correlation between CLO test and histology, 35 (83.3%) in the bleeding group had both CLO test and histology tests negative and 7 (16.7%) positive. The bleeding group of patients on proton pump inhibitor testing positive for both tests were 4 (19.0%), and 17 (81.0%) were negative. Lastly, in the bleeding group of patients, those not on proton pump inhibitors who had both CLO test and histology positive were 3 (14.3%) and 18 (85.7) had the test negative.

Results

From the 173 patients enrolled, 131 patients were found to have no history of upper gastrointestinal bleeding, while 42 patients were found to be bleeding on upper endoscopy or had a recent history of bleeding. Of the total of 173, 134 (77.5%) tested negative for *H. pylori* infection on CLO test and 39 (22.5%) tested positive. Of the bleeding group 7 (16.7%) were CLO test positive and 35 (83.3%) were negative. In the non-bleeding group of patients, 99 (75.6%) were CLO test negative and 32 (24.4%) tested positive. There was a 100% correlation between CLO test and histology, 35 (83.3%) in the bleeding group had both CLO test and histology tests negative and 7 (16.7%) positive. The bleeding group of patients on proton pump inhibitor testing positive for both tests were 4 (19.0%), and 17 (81.0%) were negative. Lastly, in the bleeding group of patients, those not on proton pump inhibitors who had both CLO test and histology positive were 3 (14.3%) and 18 (85.7) had the test negative.

Discussion

There is clear data in the literature about the role of *H. pylori* in peptic ulcer disease. According to international literature the prevalence of *H. pylori* is higher in developing countries or areas with low socio-economic status. Its role in contributing to bleeding in peptic ulcer disease is not clear. There is conflicting data in the literature, with some showing decreased association between *H. pylori* and bleeding peptic ulcer, while other literature report *H. pylori* as an independent risk factor of bleeding peptic ulcer disease.

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### Table 1: Patient Details

<table>
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<tr>
<th></th>
<th>Bleeders</th>
<th>Non-Bleeders</th>
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<tr>
<td><strong>GENDER</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>81 (46.8%)</td>
<td>61 (46.6%)</td>
</tr>
<tr>
<td>F</td>
<td>92 (53.2%)</td>
<td>70 (53.4%)</td>
</tr>
<tr>
<td><strong>RACE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>82 (47.4%)</td>
<td>69 (52.7%)</td>
</tr>
<tr>
<td>W</td>
<td>91 (52.6%)</td>
<td>62 (47.3%)</td>
</tr>
<tr>
<td><strong>PPI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
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<td>41 (31.3%)</td>
</tr>
<tr>
<td>NO</td>
<td>111 (64.2%)</td>
<td>90 (68.7%)</td>
</tr>
<tr>
<td><strong>ANTIBIO</strong></td>
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<td></td>
</tr>
<tr>
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<td>27 (20.6%)</td>
</tr>
<tr>
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<td>104 (79.4%)</td>
</tr>
<tr>
<td><strong>CLO TEST</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>39 (22.5%)</td>
<td>32 (24.4%)</td>
</tr>
<tr>
<td>NO</td>
<td>134 (77.5%)</td>
<td>99 (75.6%)</td>
</tr>
<tr>
<td><strong>POS</strong></td>
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<td></td>
</tr>
<tr>
<td>YES</td>
<td>7 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>35 (83.3%)</td>
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</table>

The purpose of this study was to determine the difference in prevalence of *H. pylori* infection in patients with bleeding and non-bleeding gastric ulcer disease and to secondly determine the accuracy of CLO test in bleeders. To our knowledge this is the first report from South Africa on the prevalence of *H. pylori* in bleeding gastric ulcer. A study done in Iran showed prevalence of *H. pylori* infection, to be as high as 89.2% in the adult population [2]. We found the prevalence of 22.5% in this study population (average age of 56.8 ± 15.3), this prevalence of infection found in this study was lower than that published in international literature. Whether this is the true reflection of the prevalence of the infection is unclear, as few of our patients were already on antibiotics and proton pump inhibitors, both of which decrease the infection load resulting in false negative results on rapid urease test. Midolo P and Marshall BJ showed in their study that the sensitivity of this test can be reduced by as much as 25% [11]. In this study group, 35.8% of the population was on proton pump inhibitors while 17.3% were on antibiotics.

When comparing the prevalence of *H. pylori* infection between bleeding and non-bleeding patients, we found that the prevalence of *H. pylori* was lower in the bleeding patients, 16.7% as compared to 24% in non-bleeding group. This was, however not statistically significant. This finding in our study was in agreement with most of the international literature, which showed decreased association between *H. pylori* and bleeding peptic ulcer disease. In comparing our data with international literature, we are mindful of the fact that there might be demographic differences in our subjects as compared to those in international literature. Our population had a distribution of both

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**Figure 2-5.**
black and white participants, with black population making up 47.4% and the remaining 52.6% made up of white patients. We found no South African data to compare our findings to published studies found that through different mechanisms, the sensitivity of the rapid urease test is reduced in bleeding peptic ulcer disease.

In our bleeding study population we also aimed to test the accuracy of the CLO test and improve the pick-up rate by doing histology. We found that there was a 100% correlation between results of CLO test and that of histology. 35(83.3%) patients in the bleeding group were negative on both CLO test and histology and 7(16.7%) were positive. Our study did not show any difference in the sensitivity of the two tests in our bleeding population.

Histology in our study was done by the national health laboratory services, pathologist were blinded to results of CLO test. More than one pathologist did the histology in this population of bleeding patients. National health laboratory services are also a training facility for pathologist. As El-Zimaity HM reported, the sensitivity of histology can also be affected by the experience of the examining pathologist [15].

**Conclusion**

The prevalence of *H. pylori* infection in this South African population was lower in bleeding than in non-bleeding gastric ulcers groups. This was, however not statistically significant as the p value was 0.404. The finding in this study was consistent with most of the
international literature, which showed decreased association between H. pylori infection and bleeding peptic ulcer disease.

The sensitivity of CLO test was found to be as high as histology in bleeding gastric ulcer population in this South African group. We found that there was a 100% correlation between CLO test and histology in this population. This finding are inconsistent with the findings in international literature but suggest that CLO test can be used with confidence in bleeding gastric ulcers, a larger study is needed to confirm this findings, a problem in a resource limited setting like ours.

References