Noninvasive diagnosis of Helicobacter pylori among patients with dyspepsia.

Suresh Thapa 1, Jiwan Thapa 2, Binod Karki 2, Dibas Khadka 2, Anuja Bhandari Thapa 3

1 Department of Internal Medicine, Pokhara Academy of Health Sciences, Western Regional Hospital, Nepal.
2 Department of Medicine, Gastroenterology Unit, National Academy of Medical Sciences, Bir Hospital.
3 Department of Pathology, National Academy of Medical Sciences, Bir Hospital.

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ABSTRACT
Introduction: Helicobacter pylori (H. pylori) infection is a common disease with disparity in geography, age, race and socioeconomic status. Present study aims to assess the accuracy of noninvasive diagnostic tests.

Methods: This is a hospital based cross sectional, observational study of 100 dyspeptic patients during November 2017 – June 2018. Profile of dyspeptic patients were recorded in a proforma and accuracy of serology and stool antigen test for H. pylori was compared with histology detection in gastric biopsies.

Results: Mean age of patients was 39.5±13.7 years with almost equal gender distribution. Prevalence of H. pylori was 56% with dyspeptic symptoms in gastric biopsies. Significant association of the infection was seen in patients with a longer duration of dyspepsia, pangastritis on endoscopy and chronic gastritis on histologic examination. Stool antigen test had good sensitivity (71%) and specificity (82%) for H. pylori detection compared with standard histological diagnosis.

Conclusions: Overall prevalence of H. pylori was 56% and was more common in patients of age > 44 years with dyspepsia. Stool antigen has a good diagnostic accuracy and can be used in resource limited settings. However, we recommend a community based study in larger population.

Key words: Dyspepsia; Gastritis; Helicobacter pylori; Noninvasive tests.

Correspondence: Suresh Thapa, Department of Internal Medicine, Pokhara Academy of Health Sciences, Western Regional Hospital, Nepal. Email:suresh817@icloud.com.
INTRODUCTION

Helicobacter pylori (H. pylori) is the most common infectious disease worldwide, affecting nearly half of the world population. The prevalence of infection varies by geographic area, age, race, ethnicity and socioeconomic status with rates as high as 80% in developing countries.[1] Most infections are transmitted by oral-oral route during childhood.[2] The infection rates between men and women are similar.[3] H. pylori causes functional dyspepsia and gastroduodenal diseases like peptic ulcer, gastritis, mucosa associated lymphoid tissue (MALT) lymphoma and gastric carcinoma. Eradication of this infection results in improvement in most gastroduodenal symptoms like abdominal discomfort, heartburn, nausea and postprandial fullness.[4] Prevalence of infection ranges from 16-70%, as detected by isolated tests in Nepal.[3,5] H. pylori infection can be diagnosed by invasive tests (histological examination, culture and rapid urease test) and by non-invasive techniques (serology, urea breath test and stool antigen) with varying sensitivity and specificity.[1] Choice of these tests depend on availability, cost, invasiveness, nature and ease of performance in developing country like ours. Endoscopic biopsy examination and staining remains the gold standard test as of now but its application is limited in many centers of Nepal due to the unavailability of resources. [6] Noninvasive and cheaper tests may address this problem with similar diagnostic accuracy. The aim of our study was to compare few relatively cheaper noninvasive tests (the stool antigen and serology) with histological diagnosis of H. pylori among dyspeptic patients at our center.

METHODS

This was a cross sectional, observational study performed at gastroenterology unit of Western Regional Hospital, Pokhara, Nepal from December 2017 to June 2018. All dyspeptic patients of age >18 years, not on proton pump inhibitors, antacids, antibiotics, non-steroidal anti-inflammatory agents for past two weeks were taken for the study. Patients refusing to consent, age <18 years, history of treatment for H. pylori and those currently on above drugs were excluded from the study. Dyspepsia was defined as upper abdominal or retrosternal discomfort with bloating and early satiety. Informed consent was taken from the patients before enrollment. Ethical clearance was taken from the Institutional Review Committee.

Demographic characters and dyspeptic symptoms were recorded in a structured proforma before subjecting the patients for upper gastrointestinal endoscopy UGIE). Tissue samples were taken from the stomach by punch biopsy as per the Sydney protocol, and stored in two ml of 10% formalin before histological examination for H. pylori by Giemsa stain. Three ml of blood was collected from all the participants and the serum was separated. Serological test was done with a commercial test kit by Nantong Egnes Biotechnology Co. Ltd., China. Significant antibody level against H. pylori was denoted by two visible pink rose color bands in the test region within 20 minutes.
Stool antigen test was carried out with chromatographic lateral flow immunoassay commercial kit from the same company. Approximately 5 ml of stool sample was collected in a container and analyzed as per standards provided by the kit company. The positive result was indicated by a pink-colored band on the test along with control region. The positive and negative results of H. pylori were categorized according to the age, gender and various demographic characters. Data was computed in Microsoft Excel for Windows 10 and statistical analysis was done by SPSS 17 and chi-square test where applicable. The sensitivity, specificity and accuracy of serology and stool antigen test were compared with histological diagnosis. The p-value less than 0.05 was considered to be statistically significant.

RESULTS

A total of 100 dyspeptic patients fulfilling the inclusion and exclusion criteria were studied. Mean age was 39.54±13.77 years with male: female ratio of 1.3:1. 56% of patients were diagnosed to be infected with H. pylori by histology. H. pylori infection had significantly higher association with age of above 44 years. Significant association of infection was also seen in officers and farmers, followed by businesspersons. 78% and 48% patients had history of alcohol and smoking respectively, though not statistically significant. H. pylori was found to have significant positive association with duration of dyspeptic symptoms, pangastritis on endoscopy, atrophic and chronic gastritis features in pathologic examination (p value <0.001). The serum antibody test is quick, simple and inexpensive with good sensitivity (75%) but low specificity (36%). The stool antigen test has good sensitivity (71%) and specificity (82%) and can be a reliable noninvasive diagnostic test in our settings.

<table>
<thead>
<tr>
<th>Serology</th>
<th>Histopathology positive</th>
<th>Histopathology negative</th>
<th>P value</th>
<th>Kappa Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>42 (75%)</td>
<td>28 (64%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>14 (25%)</td>
<td>16 (36%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>56 (100%)</td>
<td>44 (100%)</td>
<td>0.21</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Chi-square test
Table 2: Stool antigen test compared with histology

<table>
<thead>
<tr>
<th>Stool antigen test</th>
<th>Histopathology positive</th>
<th>Histopathology negative</th>
<th>P value</th>
<th>Kappa coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>40 (71.43%)</td>
<td>8 (18.18%)</td>
<td>&lt;0.001</td>
<td>0.52</td>
</tr>
<tr>
<td>Negative</td>
<td>16 (28.57%)</td>
<td>36 (81.82%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>56 (100%)</td>
<td>44 (100%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Chi- square test

Table 3: Accuracy of noninvasive tests

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Serum antibody test</th>
<th>Stool antigen test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>75%</td>
<td>71%</td>
</tr>
<tr>
<td>Specificity</td>
<td>36%</td>
<td>82%</td>
</tr>
<tr>
<td>PPV</td>
<td>60%</td>
<td>83%</td>
</tr>
<tr>
<td>NPV</td>
<td>53%</td>
<td>69%</td>
</tr>
</tbody>
</table>

PPV= Positive Predictive Value; NPV= Negative Predictive Value

Figure 1: Age distribution of H. pylori test results
DISCUSSION

H. pylori is a gram-negative, microaerophilic bacterium that inhabits the stomach and duodenum and causes a chronic low-level of inflammation. In developing countries like Nepal, histological diagnosis of H. pylori is difficult in many centers due to unavailability of endoscopy facility and limited pathology service. Special stains for biopsy specimens improve visual detection of the bacteria but chance of interobserver variability is high. To address this problem, a few cheaper, available noninvasive tests can be used for diagnosis of H. pylori infection.

Age group >44 years was significantly associated with H. pylori infection among the dyspeptic patients. This finding is similar to that of a study by Murray LJ et al.[7] A higher prevalence of alcoholism and smoking in this age group probably added the symptoms. Our study showed nonsignificant higher infection of male compared to female against few studies which demonstrated significant association of male (58-61%).[7,8] The reason for observed gender difference was not known, but a better hygienic practice and indoor activities may be the reasons for the lower prevalence among women, which needs further study. Santos IS, et al demonstrated that the low socio-economic conditions (current or past) and ethnicity had significant association with infection.[9] However, our study did not demonstrate such variability.

Our study showed a prevalence of 56% by standard histopathological staining of H. pylori. Nepal belongs to a low socioeconomic region with poor sanitation and limited access to safe drinking water, with an increased chance of feco-oral transmission. In a study done by Shrestha S, et al., prevalence of H. pylori detected by biopsy among the dyspeptic patients in Kathmandu was 50%[9], which is comparable to our study. However, this incidence is much higher than that in Lumbini region study from western Nepal.[10] Another study from Pokhara showed the overall prevalence of H. pylori to be only 29.4%. However, the prevalence was higher in symptomatic patients with gastritis, duodenitis, gastric and/or duodenal ulcers.[11] The prevalence is lower compared to a similar study from low socioeconomic country Ethiopia (81%).[12] H. pylori was positive in 67% of chronic gastritis patients, significantly lower than that described by Shakya RP (90%)[10] and much higher than the other Nepalese study by Shrestha UK (41%)[11] and Shrestha S (44%).[8]

Diagnostic accuracy of stool antigen test in our study showed lower sensitivity and specificity compared with histopathological examination than described by Gisbert JP et al., which showed a mean sensitivity, specificity, positive predictive value and negative predictive value of 91%, 93%, 92% and 87%, respectively.[13] However, this test had a significant diagnostic accuracy (p value <0.001). In a study done by Raj P, et al. in the USA, the serum H. pylori antibody test had a sensitivity of 88.4% and a specificity of 93.4%, which was much higher than in our study.[14] The higher specificity could be due to a lower overall prevalence of this infection in the west as compared to Nepal.
Various noninvasive tests have variable diagnostic value in different geographical regions. The relative ease and less patient discomfort in performing stool assay with significant detection rate can be applied in our setting.

CONCLUSION

Chronic gastritis was significantly associated with infection. Among the noninvasive methods applied, stool antigen assay had significant detection rate compared with histology and thus might be a reliable test in settings where endoscopy service is not available, though further studies in larger populations is needed for definitive recommendation.

CONFLICT OF INTEREST

None

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None

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REFERENCES


