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# Agreement between Serology and Histology for detection of Helicobacter pylori infection

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# Histopathological Diagnosis of *Helicobacter pylori*: Influencing Factors

Sir,

I read the article by Iqbal *et al*. published in JCPSP 2013, Vol. 23 (11): 784-786 with great interest.[1] The authors aimed to make a comparison between serology and histology for detection of *Helicobacter (H.) pylori* infection. Among the 50 study subjects, 30 (60%) subjects were found positive for *H. pylori* infection with serological testing. Twenty-five (50%) subjects were identified positive for *H. Pylori* infection with histopathological diagnosis. Among 30 seropositive subjects, 5 subjects found no evidence of *H. pylori* infection with histological evaluation. As a result, the authors reported a substantial agreement between serology and histopathology to detect the *H. pylori* infection (Cohen's Kappa coefficient, 0.72). I appreciate the efforts of the authors but some points need to be clarified before making a judgement about the results of the study.

In patients with atrophic gastritis, the diagnosis of active *H. pylori* infection is difficult. During the progression course of atrophy, the density of *H. pylori* in the stomach mucosa decreases, and during the late stages of atrophy the infection may completely disappear.[2] The density of *H. pylori* colonization may significantly influence test results. Additionally, the endoscopic diagnosis of *H. pylori* infection in patients with bleeding or perforated duodenal ulcers is limited by a decreased sensitivity in standard invasive tests, rapid urease test and histology.[3]

The prepyloric antrum has been the preferred site of biopsy. The sensitivity of distal antral biopsy was 96 - 97% and the sensitivity of two biopsies from virtually anywhere in the stomach was 100%.[4] The staining technique used for the identification of *H. pylori* is as important as the site and number of biopsies. For example sole reliance on haematoxylin and eosin when the density of *H. pylori* is low, is unwise and giemsa staining may improve the diagnostic accuracy in these circumstances.[3]

Considering the data presented above I would like to ask the authors of the present series as to how many biopsies were obtained and what was the gastric site of diagnosis? What were the endoscopic diagnosis in these patients? Which stains were used for the histopathological diagnosis of *H. pylori*? Was there any clinical parameter that could influence the results of the histopathological evaluation, e.g. previous *H. pylori* treatment or recent use of proton pump inhibitor?

I think the answers to these questions would improve the power of this study.

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# Agreement Between Serology and Histology for Detection of *Helicobacter pylori* Infection

Sir,

We read the recent report “A substantial agreement found between serology and histopathology results to detect the *Helicobacter pylori* infection” by Iqbal *et al*. with reservation. Fifty subjects were included by non-probability purposive sampling from laboratory data who had serological testing of *H. pylori* IgG antibody, prior to histological evaluation of endoscopic gastric or/and duodenal biopsies. Thirty (60%) subjects were found positive for *H. pylori* infection with serological testing. However, 25 (50%) subjects were identified positive for *H. pylori* with histopathological diagnosis. Among 30 seropositive subjects, 5 subjects found no evidence of *H. pylori* infection with histological evaluation. Authors concluded that “serology assesses the presence of *H. pylori* in the stomach even when the bacteria are irregularly distributed on the gastric mucosa and may be missed on taking biopsy”.

The choice of diagnostic test for *H. pylori* depends upon cost, availability, clinical situation, population prevalence of infection, pretest probability of infection, factors that influence certain test results such as proton pump inhibitors and antibiotics. Methods available for detecting *H. pylori* infection include serology, rapid urease test, histology, 13/14 C-urea breath test (UBT) and polymerase chain reaction. The results of rapid urease test, histology and UBT are all affected by previous intake of antibiotics, acid reducing drugs e.g., proton pump inhibitor and histamine-2-receptor blockers. It was not informed whether the biopsy samples were collected from patients who were on any of these medicines previously.[1-3]

On the basis of a serology, one can not be able to decide whether to treat or not. A positive result with serology does not tell whether the patient has current infection or had a past infection that is now cured.[4,5] Serology is inferior to active testing in sensitivity and especially specificity. The false-positive results include both actual false positives for active infection and true positive for antibody, not infected. The drawbacks are treatment of people who are not actively infected, waste of resources, inconveniences to patients, contribution to antibiotic resistance. This method is reliable only for population surveys and not for individual patients. Serum IgG against *H. pylori* suggests gastric mucosal immunological response against *H. pylori* infection. It certainly does not assess the presence of *H. pylori* irregularly distributed on the gastric mucosa something that is done by the UBT in the gastric mucosa. The current practice of using positive *H. pylori* serology for commencing treatment needs to be discouraged in primary care practice.

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**Authors' Reply (to both letters):**

We thank the readers for their comments and the opportunity to clarify a number of points from our work. We looked at the agreement between serology and histology of *H. pylori* infection. In our small series of cases, we are saying that serological testing for IgG provides an inexpensive, non-invasive and convenient method to detect *H. pylori* infection having substantial agreement with histology in our setting. It is important to understand that ideally non-invasive testing should be limited to *H. pylori* tests that detect active infection only which include stool antigen test and urea breath test. Serologic antibody tests do not distinguish between currently active infection with a past exposure and an infection that has been cured.

Endoscopic biopsy remains a gold standard diagnostic test for active *Helicobacter pylori* (*H. pylori*) infection; however, it is an invasive and costly technique. By precisely guiding diagnosis and treatment; histology potentially reduced the number of patients inappropriately treated but the cost-effectiveness analysis supports the continued practice of initial non-invasive approaches to guide antibiotic use.

World over, there is a shift in diagnosis from testing with IgG to *H. pylori* antigen testing of human stool by enzyme immunoassay or immune chromatography and urea breath test, which measures radio-labeled carbon dioxide by a mass spectrometer or scintillation counter. Both the tests are currently not available in our setup and have their limitations. Serological testing can be regarded as representing a primary approach for evaluation of *H. pylori* status in patients with uncomplicated dyspeptic disease, who do not immediately require endoscopic studies or previously not treated for peptic ulcer disease, especially in a setup like ours where the seroprevalence of *H. pylori* is about 58-60%. *H. pylori* serological tests detect antibodies to *H. pylori* with a sensitivity and specificity of approximately 90%. In populations with high disease prevalence, the positive predictive value of the test rises dramatically, thus facilitating diagnosis and subsequent treatment if invasive testing is not required or opted.

Moreover, the management of *H. pylori* infection requires a multi-disciplinary approach and it is strongly recommended that there should be close local collaboration and interaction between primary care

physicians, specialist gastroenterologists, microbiologists and possibly public health doctors. Non-invasive tests are options of choice in primary care setting. Adding testing for *H. pylori* infection to history-taking has been recommended in patients at high risk of having peptic ulcer disease. It would avoid endoscopies in some patients and lead to more accurate treatment of peptic ulcer disease in most patients. Furthermore, a proportion of dyspeptic patients presenting in primary care for the first time are patients with peptic ulcer disease who are *H. pylori* positive and could get benefit from diagnosis and consequent treatment of the infection.

Infection with *H. pylori* can be patchy, and, as a result, multiple biopsy specimens may be necessary for diagnosis with endoscopy. However, this is at the discretion of gastroenterologist performing the endoscopy. In our series of cases atleast two biopsies were taken from gastric antrum. In contrast, serology demonstrates the systemic humoral response and thus presence or absence of disease, irrespective of pattern of distribution of *H. pylori*, in the gastric mucosa.

Our article is based on retrospective analysis of data and unfortunately we do not have a robust explanation for the missing clinical information. Due to the absence of a national health system the complete clinical information by physicians like the previous treatment and use of proton pump inhibitors is hardly provided. We propose performing a prospective clinical trial that we hope will be able to provide a more robust answer to some of the questions that have been raised.

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