

# Helicobacter pylori serology and the diagnosis of H. pylori infection in children

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## Abstract

**Serological screening accuracy rate may be dependent on clinical and pathological determinants. The aim of this study was to evaluate the accuracy of Hp serology test (Roche Biomedical Lab., Labcorp), in the diagnosis of Hp infection in 121 children who were seen in the Pediatric Gastroenterology Clinic at the Marshall University Joan C. Edwards School of Medicine in Huntington. Positive serology detected children with Hp-associated gastritis with a sensitivity of 51.6%. Positive serology significantly correlated with the degree of gastric inflammation and density of Hp organisms in the gastric mucosa (ANOVA  $p < 0.001$ ). The Labcorp Hp-ELISA test had a poor accuracy rate for the detection of Hp-gastritis in children. Gastric biopsies should always be performed to establish the diagnosis of Hp infection in children.**

## Introduction

*Helicobacter pylori* (HP) has been recognized as the major etiological factor resulting in peptic ulcer disease in adults and children (1,2). A commonly available enzyme-linked immunosorbent assay (ELISA) is a common non-invasive method used to detect *Hp* infection (3,4).

Serological testing for *Hp* has the potential of being a cost-effective method, particularly by sparing the endoscopic procedure (5-10). Since the immune response to *Hp* organisms is dependent on various mucosal and systemic factors, i.e. antigenic load and host immune competence, it is critical to investigate the correlation between serology test result, gastric inflammation and/or the density of *Hp* organisms (antigenic load) in the gastric mucosa.

The goal of our study was to evaluate the accuracy rate of the commercially available *Hp* serology test (Roche Biomedical Lab., Labcorp), for the diagnosis of *Hp* infection in 121 children who were seen at the Pediatric Gastroenterology Clinic at the Marshall University Joan C. Edwards School of Medicine in Huntington between April 1994 and December 1996.

## Materials and methods

We reviewed all upper endoscopies performed in symptomatic children who were seen at the Pediatric Gastroenterology Clinic at the Marshall University Joan C. Edwards School of Medicine from April 1994 and December 1996. *Hp* serology was routinely determined in every new patient with clinical symptoms suggestive of *Hp* infection. None of the children had antibiotic treatment for at least one month prior to endoscopy.

Charts were reviewed for age, gender, serum *Hp* anti-IgG antibody (*Hp*Ab) results, and histology. *Hp* serum antibody level was determined by an outside reference laboratory -

Roche Biomedical Laboratory, Inc. (Labcorp) prior to the endoscopic procedure. This serological test measures IgG antibody, utilizing the Cobras-Core anti-*Hp* EIA method. In adults, the test showed an adequate sensitivity and specificity rate (> 90%) compared to histology (11).

## Endoscopy procedure

Parental consent was obtained for each endoscopic procedure. Regardless of the mucosal appearance, in each procedure, at least two antral biopsies were obtained for routine pathological examination.

Inflammation (gastritis) was assessed by H & E staining and was graded according to Sydney criteria (12). *Hp* organism density was assessed by Giemsa staining in all antral biopsies and was graded on a 0-3 scale previously described by El-Zimaity et al (13) that rated colonization as either absent (0), scant (+1), moderate (+2) or heavy (+3). Positive *Hp* infection was defined as the presence of *Hp* bacteria in the tissue. *Hp*-associated gastritis disease was considered whenever *Hp* organisms and histological gastritis were found on the same biopsy.

The pathologist was blinded to the serology results at the time of biopsy evaluation.

## Statistics

Regression analysis was used to assess the correlation between positive serology and the histological factors of gastritis, *Hp* organisms and *Hp*-associated gastritis. ANOVA test was used to assess the correlation between positive serology and the degree of gastric inflammation and *Hp* density. StatWorks™ software was used for all analysis (Data Metrics, Inc. 1985, Philadelphia, Pa.)

## Results

A total of 121 patients were included in the study with a mean age of  $11.8 \pm 4$  years (range -2-18 yrs.) and male/female ratio of 0.98:1.0. The major presenting clinical symptoms of these children were abdominal pain (82.6%) and vomiting (37.2%).

Positive *Hp* serum antibody was found in 21/121 (17%) patients. Gastritis was found in 49 (40%) patients with the following histological grading: grade +1 in 34 patients, grade +2 in 14 patients, and grade +3 in one patient. *Hp* organisms were detected in 32 (26%) patients and with the following grading: grade +1 in 19 children, grade +2 in eight children and grade +3 in five children. In one patient, *Hp* organisms were found with normal histology. None of our patients had gastric ulcer and one patient had a duodenal ulcer.

*Hp* serology detected *Hp*-gastritis with a sensitivity, specificity, positive and negative predictive values of 51.6%, 94.4%, 76.2% and 85%, respectively. Since immune response is enhanced by the inflammatory process, we further evaluated the correlation between positive serology and several factors including age; the presence of *Hp* organisms on histology; gastritis; and *Hp*-associated gastritis. Multiple regression analysis showed a significant correlation with age ( $p = 0.049$ ), but not with *Hp* organisms ( $p = 0.731$ ), gastritis ( $p = 0.972$ ), or *Hp* associated gastritis ( $p = 0.672$ ).

Positive serology was significantly correlated with increased inflammatory index and increased *Hp* density in the gastric mucosa (ANOVA test,  $p < 0.001$ , coefficient of correlation 0.51-0.53 (Table 1).)

## Discussion

Histologic confirmation of *Hp* organisms in the gastric mucosa is considered the "gold standard" for the diagnosis of *Hp* infection in children (1). In the managed care environment, cost-containment and cost-effectiveness have become major players in the diagnostic process.

Since *Hp* infection has been determined to be the major

**Table 1. *Hp* Serology, Histological Grading and *H. Pylori* Density of the 121 Children Evaluated with *Hp* infection.**

<u>Parameter</u>	<u>Hp-Serology+</u>	<u>Hp-Serology-</u>	<u>p Value*</u>
<b>Gastritis:</b>			
Normal (G-0)	04 (6%)	68	
Mild (G-1)	06 (18%)	28	
Moderate (G-2)	10 (71%)	04	
Severe (G-3)	01 (100%)	00	0.000
			$r = 0.53^{**}$
<b>Hp-density:</b>			
+0	05(6%)	84	
+1	09(47%)	10	
+2	03(38%)	05	
+3	04(80%)	01	0.000
<b>Total</b>	<b>21</b>	<b>100</b>	$r = 0.51^{**}$
*ANOVA analysis			
**Coefficient of Correlation			

etiological factor for peptic ulcer disease, prior serological screening for *Hp* infection has emerged as a possible method to reduce the cost of testing adults (6-10), and children (14). Concurring with a previous recommendation (15), we showed that the accuracy of the commercially available *Hp*-serology is inadequate for children and cannot be used as a screening tool for "test to treat" protocol.

In our study, positive serology detected *Hp*-associated gastritis with a sensitivity and positive predictive value of 51.6% and 76.2%, respectively. Utilizing the same serological test-kit in children, similar accuracy rate was reported by Rocha de Oliveira et al (16). In addition, concurring with our finding, direct correlation was found between test sensitivity and increasing age.

On the other hand, in comparing our study with other serological tests, we reported a lower accuracy rate (3,17-19). It is now accepted that a significant variability in accuracy rate among tests will be found once using different population (20). Thus, it is now recommended that

*Hp* test-kit should be initially validated locally before utilizing it for clinical purposes.

Histological evidence of *Hp*-associated gastritis was reported in 31 patients, but positive serology was found in only 16 patients (52%). The development of serum antibody is closely related to the host's immune mechanism (21), and the gastric antigen load (*Hp* density) (22). We further examined the correlation between serology results and the degree of gastric inflammation and/or density of *Hp* organisms colonizing the gastric mucosa. Data showed that positive serology was directly related to the grading of antral inflammation and/or *Hp* density in the gastric mucosa (ANOVA  $p < 0.000$ ; coefficient of correlation: 0.51-0.53) (Table 1).

This data supports the correlation between antibody development and the host immune response.

## Conclusion

In summary, the low sensitivity and low positive predictive value of the *Hp* serology test (Labcorp) to detect *Hp*-associated gastritis in children is unacceptably low. We postulate that

the mild gastric inflammation and the lower bacterial inoculation, commonly seen in children, are crucial factors in this finding.

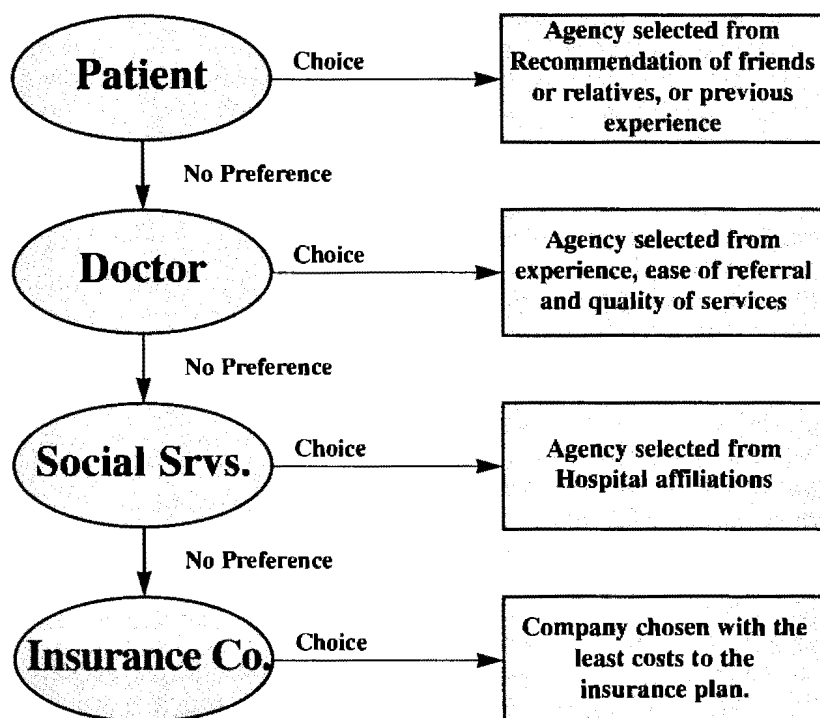
Our results lead us to conclude that serology should not be used to diagnose *Hp* infection in children, and that endoscopy remains the "gold standard" for diagnosing this disease in children.

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