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Comparison of the Diagnostic Accuracy of Serological and Histology Tests for Helicobacter Pylori in Patients with Dyspepsia and Metabolic Syndrome

Hamid Vahedi [1], Maryam Yarmohammadi [2], Mohammad Bagher Sohrabi [3]*, Pouneh Zolfaghari [4], Elahe Yahyaei [5], Maryam Rezaali [6], Fatemeh Khodaei[5,3]

[1] Dept. of Gastroenterology, School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran.
[2] Dept. of Pathology, School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran.
[3] School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran.
[4] Vice-chancellery of Health, Shahroud University of Medical Sciences, Shahroud, Iran.
[5] Vice-chancellery of Treatment, Shahroud University of Medical Sciences, Shahroud, Iran.
[6] Imam Hossain Hospitals, Shahroud University of Medical Sciences, Shahroud, Iran.

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Abstract

Background: *Helicobacter pylori (H. pylori) infection is a major cause of chronic gastritis, especially in metabolic syndrome patients. The use of a accessible and easy diagnostic method, can speed up the treatment of this infection This study compared two methods of histology and serology for diagnosis of H. pylori in metabolic syndrome patients.*
Methods*: This study was done on 175 metabolic syndrome patients with dyspepsia referred to Shahroud Imam Hossain hospital in 2014. From each patient, standard biopsy and serology tests were taken with endoscopy. This data will be analyzed with sensitivity, specificity, positive and negative predictive value.*
Results*: Of the 175 patients studied, 90 (51.4%) were male and 85 (48.6%) were female. The mean patient age was 46.9±18.6 years. From 175 patients, 114(65.1%) and 149 (85.3%) patients tested positive by serology and histology, respectively. For the serological test, sensitivity, specificity, positive predictive value and negative predictive value were 66.4%, 42.3%, 86.8%, and 18.1%. It was also found that with IgG values higher than 1.3, there was a sensitivity of 90.7%, and specificity of 72.8%, which was considered a positive test. The cut-off point performance test means that maximum at this point with 78.3% the area under the curve (AUC), there is the highest sensitivity and specificity.*
Conclusions*: Due to the relative sensitivity and specificity of serological tests in comparison with other diagnostic methods as well as the simplicity, speed, and low cost, it is recommended that this test be used for screening metabolic syndrome patients.*

Keywords: Helicobacter pylori, Metabolic syndrome, Serology, Histology.
***Corresponding to:** MB Sohrabi, **Email:** mb.sohrabi@yahoo.com
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Introduction

Helicobacter pylori (H. pylori), a gram negative, spiral, microaerophilic, is primarily located in the human gastric mucosa.[1] This bacterium is the main cause of chronic gastritis and peptic ulcers, and it is considered the major risk factor for adenocarcinoma and gastric lymphoma.[1-2] In 1994, it was classified as carcinogenic by the World Health Organization (Class I confirmed human carcinogen).[1] Dyspepsia is a common finding in these patients and may be due to gastric inflation. About 30–50 percent of human populations are infected by this stomach bacterium in countries with higher levels of socioeconomic status, but in developing countries this percentage rises to 80 percent.[2] In developing countries, such as Iran, 70% are infected at the age 10, and the infection rate increases with age. H. pylori infection is diagnosed on the basis of clinical and laboratory findings, microbiological methods, and histopathological examinations.[3] Invasive methods of diagnosis can be divided into two categories: direct and indirect. Invasive procedures, such as endoscopy, are prepared by culture of biopsy specimens, staining of samples, and identification of urease activity.[4] Although endoscopic examination is invasive, expensive, and time consuming, it is of critical importance in determining clinical prognosis on the basis of the localization of a lesion is. Histological diagnosis is frequently used to determine tissue inflammation and severity of precancerous alterations.[5] These tests determine the presence or absence of anti-H.pylori antibodies in the serum of samples. Most patients with H.pylori infection have a significant amount of antibodies in their serum. Class and subclasses of antibodies to H. pylori are different. The IgA and IgG type antibodies are seen in chronic infections, and IgM be found in acute infections.[6-7] Metabolic syndrome (MS) is a global epidemic and appears in common genetic and environmental media, and it is characterized by cardio metabolic risk factors, such as abdominal obesity, atherogenic dyslipidemia, glucose intolerance, and elevated blood pressure.[8] MS is a heterogeneous disease that develops because of insulin resistance (IR), and in 2011, the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) specified the major components of MS as abdominal obesity, IR, elevated body pressure, and dyslipidemia.[8] Given the prevalence of metabolic syndrome and disorders of the multiple Internal organs and tracts, including the immune system, serological diagnosis testing of H. pylori infection may be impaired.[9] Considering the high prevalence of MS among individuals and high prevalence of H. pylori infection, this study was done with the aim of comparing the diagnostic accuracy of serological and histology tests for H. pylori in patients with dyspepsia and metabolic syndrome.

Materials and Methods

All patients referred to the Shahroud Imam Hossain Hospital Gastroenterology polyclinic with gastrointestinal problems were selected. Exclusion criteria included the

following: patients who received proton pump inhibitors, histamine type 2 (H2) receptor antagonists and H. pylori eradication therapy in the last month, pregnant women, patients who had been diagnosed with malignancy and patients who had undergone gastric surgery. Patients who were between18 -70 years old, patients without psychiatric or systematic disease like diabetes, chronic kidney, and systematic infection were included in this study. A total of 175 patients were enrolled and approved by the Shahroud Imam Hossain Hospital. All eligible patients who provided written, informed consent were recruited for this study. Then, endoscopy division was used following local anesthesia of the pharynx, which was performed with procaine. Using the endoscope, six biopsy specimens were obtained from the large and small curvature, and anterior and posterior walls of the gastric antrum and corpus mucosa of all patients. The specimens were transferred to the pathology laboratory and fixed with 10% formalin. H. pylori were observed in the biopsy specimens by microscopic examination of the slides stained with hematoxylin and eosin. Slides were examined by two experienced pathologists. Also, 5 ml of venous blood was taken from each patient to measure IgG against H. pylori by ELISA (Biotech Trinity of Germany). Serology test results were analyzed according to the manufacturer recommendations. If the antibody titer equal or greater than 1.1 units, the test was positive, between 0.8 and 1 unit was considered borderline (suspicious), and less than 0.7 unit was negative. It should be noted that, for better results, only greater than or equal to 1.1 units antibody was considered positive, and negative results and borderline values were considered negative.

Diagnostic criteria for metabolic syndrome (ATP III) include the following: abdominal obesity (waist circumference) for men >102 cm, and for women >88 cm; triglycerides, ≥150 mg/dL; HDL cholesterol for men <50 mg/dL and for women <40 mg/dL; blood pressure ≥130/85; fasting glucose ≥110 mg/dL.

SPSS version 16 was used to analyze and tabulate the data. In this study, pathological tests were standard procedures, and the sensitivity, specificity, and positive and negative predictive value of serology tests (IgG) were calculated based on pathological tests. Receiver Operating Characteristic Curve (ROC curve) was used to estimate the cut-off point for seropositive tests. In ROC analysis, the accuracy of each test with the area under the curve (AUC) (from 0 to 100%) is expressed. Continuous variables were presented as mean and standard deviation, whereas frequency and percentage were used for the presentation of categorical variables.

Results

Of the 175 patients studied, 90 (51.4%) were male and 85 (48.6%) were female. The mean patient age was 52.9±18.6 years (rang 28–69 years). Body mass index was 25.7±5.6 kg/m2, and the average amount of IgG against H. pylori in patients was 1.3±1.2 international units (range 0–2.5 international units). Histology test results were positive for H. pylori in 149 patients (85.3%), while serologic testing for H. pylori was positive in 114 patients (65.1%). The age group of 51–60 years were the most commonly serologically positive. Serological and histological tests results for separate age groups are shown in Table 1. In this table, to investigate the prevalence of pathology and serology at different ages, the age classification was used. The average duration of digestive problems was 19.3±15.7 months (range 4–35 months). For the serology testing of IgG, 114 patients (65.3%) were positive, 26 patients (14.7%) were borderline (suspicious), and 35 (20%) were negative. Table 2 shows that 149 cases (85.3%) tested positive by histology. Considering the results of histology as the gold standard in comparison with the results of serology, the sensitivity, specificity, positive predictive value and negative predictive value of serological test was 66.4% (95% CI: 61.5%–71.0%), 42.3% (95% CI: 37.6%–46.4%), 86.8% (95% CI: 82.4%–91.5%), and 18.1% (95% CI: 15.5%–21.4%), respectively. The results are shown in Table 2.

Table 1: Relative frequency distribution of H. pylori in patients in different age groups in terms of histology and serological methods

Age Groups (Year)	Histology		Total Histology Number (%)	Serology			Total Serology Number (%)
	Negative Number (%)	Positive Number (%)		Negative Number (%)	Borderline Number (%)	Positive Number (%)	
>40	3 (11.5)	9 (6.1)	12(6.9)	2(5.7)	2(7.7)	8(7.1)	12(6.9)
40-50	7 (20)	41 (27.5)	48(27.4)	11(31.4)	7(26.9)	30(26.3)	48(27.4)
51-60	11(42.3)	65 (43.6)	76(43.4)	12(34.3)	10(38.5)	54(47.4)	76(43.4)
61-70	5(14.3)	34(22.8)	39(22.3)	10(28.6)	7(26.9)	22(19.3)	39(22.3)
Total	26 (14.7)	149 (85.3)	175 (100)	35 (20)	26 (14.9)	114 (65.1)	175 (100)

Table 2: Comparison of serology and histology in the diagnosis of Helicobacter pylori infection in metabolic syndrome patients

	Positive Histology (%)	Negative Histology (%)	Total
Seropositive	99	15	114
Seronegative	50	11	61
Total	149	26	175

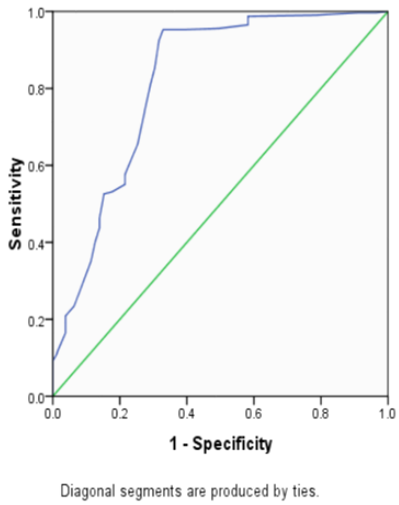

Figure 1: Evaluate the diagnostic value of serologic testing for H. pylori in patients undergoing MS (ROC Curve)

According to figure number one (curve ROC), cut-off point, was 1.3 unit, and area under the ROC curve (AUC) was 78.3 percent (95% CI: 69.4%–87.1%).

In other words, IgG values higher than 1.3, with a sensitivity of 90.7%, and specificity of 72.8%, were considered positive, and less than this level considered a negative test. The cut-off point performance test means that maximum at this point, the AUC with 78.3%, have the highest sensitivity and specificity.

Discussion

In this study, the sensitivity of the serological test based on biopsies from patients with metabolic syndrome was 66.4%, the specificity was 42.3%, the positive predictive value was 86.8%, and the negative predictive value was 18.1%, respectively. In Salimi study, sensitivity, specificity, positive predictive values, and negative predictive values were similar to our study.[8] Although the relationship between MS and H. pylori, which is one of the infectious agents that associated with MS, has not been completely explained, H. pylori infection impairs the balance of proinflammatory cytokines and CRP, angiotensinogen, free fatty acids, and leptin, and thus, reactive oxygen radicals begin to accumulate.[9-12] Subclinical chronic inflammation occurs via impaired cytokine balance and stimulated macrophages. This leads to unresponsiveness to insulin in the peripheral tissue and subsequently to MS.[13-14] In the study of Aslan in more than 150 MS patients, sensitivity and specificity of IgG were 78% and 76%, respectively. In the study of Gunji sensitivity and specificity were 73.7% and 49.6%, respectively, and in the study of Al-Humayed, sensitivity was 77% and specificity was 37.3%, which are similar to our study.[15-17] In the study of Islam and Longo-Mbenza, sensitivity and specificity of IgG were 83% and 75%, respectively.[18-19] In the Kucukazmanin study, the sensitivity and specificity of serologic tests were 67% and 93%, respectively.[20] In this study, the positive predictive value was 91.8%, and the negative predictive value was 26.9%, but the results of similar studies, such as the study of Sung, Hasler in India and Elizalde and Takashima in Japan, a significant difference was observed, probably because of trials, sample size, or population differences in these areas.[21-24] The present study differs from some studies, such as research by Henry in Italy and Ando and Kanbay,[25-27] in that these studies considered the urea breath test, stool antigen tests for H. pylori, and other comparisons. A study conducted by Kyriazanos showed that the combination of serology and histology have higher positive predictive values than either test alone.[28] Although this study only determined the sensitivity and specificity of serologic tests for detection of H. pylori in patients with metabolic syndrome, a two-year-old study by Sam brook and Papa Michael showed that the accuracy of these tests in metabolic syndrome, in comparison to biopsy, are significantly lower than in non-MS patients.[29-30] Unfortunately, despite numerous studies, conclusions cannot be made as few major studies have been conducted with sufficient sample size. Furthermore, there are limited studies in different races, and with non-identical specimens that have been designed and implemented. Therefore, small studies are often difficult due to uncontrolled confounding factors, which often occur due to the sample size.

The limitations of this study were small sample size and high cost of laboratory kits, which was resolved with the financial support of Imam Hussein hospital officials.

Finally, this study showed that the correlation between the results of serological tests of patients with and without MS do not exist, and therefore IgG serology testing is valuable since it is a sensitive and non-invasive diagnosis of H. pylori infection and is easy to implement at low cost. Furthermore, it can be used for epidemiological studies and screening. Also according to the findings of this study (Figure ROC), a cut point of 1.3 can be used for serological diagnosis of H. pylori infection in MS patients.

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Conflict to Interest

The authors declared that they have no conflict of interest.

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