Seroprevalence of Anti-*Helicobacter pylori* and Anti-CagA IgG Antibodies in Iranian Dyspeptic Patients

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Abstract

Background: *Helicobacter pylori*, a worldwide infection, is associated with several infectious diseases including gastric ulcer, peptic ulcer, and gastric cancer resulting from the cytotoxin-associated gene A (CagA). The purpose of this study was to evaluate the seroprevalence of anti-*H. pylori* and anti-CagA IgG antibodies in Iranian dyspeptic patients.

Methods: In this prospective epidemiological survey, a total of 659 patients were evaluated for the presence of general anti-*H. pylori* IgG, and then for anti-CagA IgG by two commercial ELISA kits.

Results: The prevalence of general anti-*H. pylori* IgG was 58.1% (383 of 659 patients) which increased progressively with age ($P<0.05$) and was not significantly influenced by the sex ($P=0.08$). The prevalence of anti-CagA IgG antibody in seropositive and seronegative patients for general *H. pylori* IgG was 52.9% (37 of 70) and 61.9% (13 of 21), respectively.

Conclusion: This is the first report on the high prevalence of anti-CagA IgG in both seropositive and seronegative patients for general IgG, indicating the importance of this antibody in diagnosis of *H. pylori* positive patients after seroconversion of the general IgG.

Background

Helicobacter pylori is a fastidious and microaerophilic gram-negative bacterium infecting the epithelial lining of the stomach that was initially isolated from a human gastric biopsy in 1983.[1] Cytotoxin-associated gene A (CagA) is one of the most studied virulence factors of *H. pylori*. The positive strains for CagA have been more closely associated with gastric disease compared to CagA-negative strains. The CagA toxin is encoded by the *cagA* gene as part of the pathogenicity island.[2] This gene, which is associated with type I strains, is responsible for severe forms of gastrointestinal diseases and is present in about 50%-70% of *H. pylori* strains.[3] The presence of CagA-positive strains in the human stomach might be associated with gastritis, peptic ulcer, duodenal ulcer, and recently the development of gastric carcinoma.[4,5]

Helicobacter pylori has worldwide distribution, but its prevalence varies among different ethnicities and countries.[6] Low socioeconomic status, low level of education, crowded living places in childhood, consumption of alcohol and poor oral hygiene, gender and occupation are among the risk factors for *H. pylori* infections.[7] Several epidemiological studies have shown that a continuous decrease of *H. pylori* prevalence is associated with an improved standard of living,[8,9] but many epidemiological aspects of this infection still remain unknown.[10] This infection is highly prevalent in developing countries, being higher in less developed countries,[11-13] and common in 57%-91% of the Iranian population.[10,14] In one study conducted in 2013 in Iran including southeast Iran, the *H. pylori* seroprevalence rate was 77.6% (for patients aged 1 to 90 years).[10] Despite its high prevalence in Iran, a representative cross-sectional study on this infection and its CagA status has not been available in this area.

The purpose of the current study was to investigate the *H. pylori* prevalence and its virulence factor (*CagA*-toxin) seroprevalence in dyspeptic patients. Two serological kits were used to detect the anti-*H. pylori* and anti-CagA IgG antibodies.

Materials and Methods

Samples

For this prospective cross-sectional study, a total of 659 serum samples were collected from Iranian dyspeptic patients in 2016. Individuals' demographics, including sex, age, and medical historical data were collected. They were aged 17 to 72 years, (mean age ± SD = 40.42 ± 11.32 years), stratified into 10-20, 21-30, 31-40, 41-50, 51-60, and >61 years age groups (Table 1). A total of 91 serum samples were randomly selected from the investigated population to check the anti-CagA IgG status.

Immunoassay Test

The commercial enzyme-linked immunosorbent assay (ELISA) kits for *H. pylori* IgG (Monobind, USA) and CagA IgG (Euroimmun, Germany) were used to evaluate the presence of anti-*H. pylori* and anti-CagA IgG antibodies, as described by the manufacturers. The plates were read at 450 nm by an Elisa reader (Tecan, Switzerland), and the seropositive status was determined.

Statistical Analysis

Data entry was performed and statistical significance was determined using the nonparametric Pearson chi-square, Mann-Whitney and Kruskal-Wallis tests in SPSS software, version 21.0 (IBM corporation). The Pearson's chi-square test was used to compare the categorical data and to find the significance in sex and age groups. Logistic regression tests were run to check the relationship between *H. pylori* prevalence and variables. The *P* value less than 0.05 was considered statistically significant.

Results

Table 1 shows the number of tested subjects according to the sex and age groups and their anti-*H. pylori* IgG seroprevalence. A total of 383 patients (58.1%) were positive for this antibody. Males had a seroprevalence of 54.5% compared to 60.3% recorded for females (*P* = 0.08). General *H. pylori* IgG prevalence increased progressively

Table 1. The Seroprevalence of *Helicobacter pylori* IgG Antibody in Iranian Dyspeptic Patients

Parameters	n=659 (% of total)	Seropositive (%)	95% CI
Sex			
Male	253 (38.4)	138 (54.5)	48.4-60.7
Female	406 (61.6)	245 (60.3)	55.6-65.1
Age (y)			
10-20	22 (3.3)	9 (40.9)	20.4-61.5
21-30	91 (13.8)	48 (52.7)	42.5-63.0
31-40	254 (38.5)	150 (59.1)	53.0-65.1
41-50	162 (24.6)	91 (56.2)	48.5-63.8
51-60	73 (11.1)	48 (65.8)	54.9-76.6
> 61	57 (8.7)	37 (64.9)	52.5-77.3
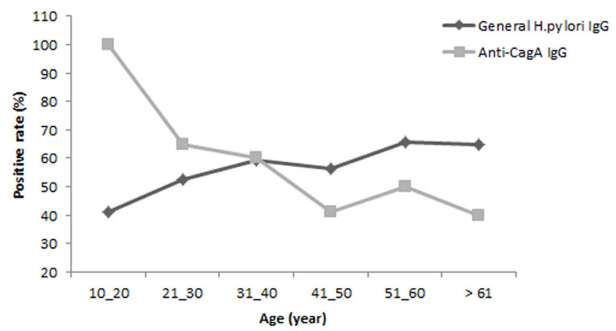
Figure 1. The Rate of General *Helicobacter pylori* IgG and Anti-CagA IgG in Different Age Groups

with age (Figure 1), and this was higher in the patients aged 51-70 years when compared to the patients with other ages (*P* < 0.05).

The seroprevalence of anti-CagA IgG for female and male patients were 51.1% (23 of 45) and 58.7% (27 of 46), respectively. The results also showed a seropositivity rate of 52.9% (37 of 70) and 61.9% (13 of 21) among seropositive and seronegative patients for anti-*H. pylori* IgG, respectively.

Discussion

The overall *H. pylori* seroprevalence was found to be 58.1% among Iranian dyspeptic patients. This is lower than earlier rate in Iran, which were reported as seropositivity rates of 77.6% in southeast Iran,[10] 67.1% in southern Iran,[14] and 86.8% in endoscopy unit of a hospital in Tehran[15] among dyspeptic patients. The detected *H. pylori* seroprevalence in this study was also lower than the reports from Afghanistan,[16] and Pakistan,[17] but higher than those from other Asian countries,[18,19] European countries (like England, France, Italy, Scandinavia, and Belgium), and the United States.[7,20] These seroepidemiological studies were conducted in specific subgroups of the population.

Helicobacter pylori IgG prevalence in Iranian dyspeptic population may be related to socioeconomic and living conditions as risk factors. This may be explained by the association between *H. pylori,* and low socioeconomic status, low level of education, crowdedness, poor oral hygiene, environmental sanitation, and eating spicy foods.[7,21] There are reports on significant risk of *H. pylori* infections for men, but others disproved this dependency.[22] This was approved in the current study (*P* = 0.08), the same as a previous report.[10] Higher prevalence rate of *H. pylori* in the elderly has been reported.[23] Results of the current study showed a strong correlation between seropositivity rates and age increase (*P* < 0.05). Specific environmental factors linked to the higher age groups compared to aging are the major causes of this tendency.[23] The present study also showed high prevalence of *H. pylori* seropositivity rates in younger age groups (52.7% at ≤30 years old and 40.9% at ≤20 years old) in Iran.

The results showed anti-CagA seropositivity rates of 52.9% and 61.9% in seropositive and seronegative patients for anti-*H. pylori* antibody, respectively ($P = 0.05$). The CagA antibodies can be perseved in serum for a long period of time, implying the importance of these in diagnosis of *H. pylori* infections.[24] These antibodies are important in diagnosing *H. pylori* infected patients who have sole positivity for anti-CagA antibodies, after seroconversion of general anti-*H. pylori* IgG. Simultaneous use of the serology test with an antigen-based stool test was recommended to detect the active *H. pylori* infections.

Conclusion

To the best of our knowledge, this is the first report on the high anti-CagA antibody in both seropositive and seronegative patients for general IgG, indicating the importance of this antibody in diagnosis of *H. pylori* infected patients after seroconversion of general anti-*H. pylori* IgG. The high prevalence of anti-*H. pylori* antibody, which was observed in dyspeptic population in this study, should also be considered in evaluating upper gastrointestinal diseases in Iran.

Limitations

We acknowledge that this study has some limitations. The temporality ascertainment of the present study and the number of patients investigated for anti-CagA antibody are the main limitations of this investigation, limiting its accuracy to show the true prevalence in country. More studies are needed on epidemiological and environmental factors.

Authors' Contributions

Study concept and design: MA and AM; Experiments implementation and acquisition of data: SA and MA; Analysis and interpretation of data: MA and AM; Drafting of the manuscript: MA; Administrative, technical, and material support: SA, AM and MRH; Study supervision: AM, MRH and MA.

Conflict of Interest Disclosures

The authors declare that they have no conflict of interests.

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