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Association between Helicobacter. *pylori* and Coronary Artery Disease

Research Article

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Abstract: The high prevalence of both Helicobacter.*pylori* infection and coronary atherosclerosis in our country prompted us to assess the probable association between both conditions. This cross-sectional study recruited 153 patients scheduled to undergo coronary artery angiography. Patients were divided into two groups on the basis of coronary angiography results. Sixty-nine patients had coronary atherosclerosis and the 84 remaining patients were normal. Characteristics and pre-angiographic serum levels of triglyceride, low-density lipoprotein cholesterol, high-density lipoprotein, and Helicobacter.*pylori* IgG antibody were assessed in the patients and compared between the groups. Helicobacter.*pylori* infection occurred in 88 (57.51%) patients: 40 (58%) in the atherosclerotic group and 48 (57.1%) in the control group with no significant differences (P=0.918). Our multivariable analysis revealed that Helicobacter.pylori infection was not an independent predictive factor for coronary artery disease (P =0.915). Also, the prevalence of atherosclerosis risk factors with respect to the seropositive and seronegative Helicobacter.*pylori* infection was assessed in the case group, which showed no significant difference. Furthermore, the prevalence of seropositive Helicobacter.*pylori* infection in terms of the number of diseased coronary vessels was evaluated, this demonstrated no significant association between the number of the diseased vessels and Helicobacter.*pylori* infection. This study demonstrated that Helicobacter.*pylori* infection was not an independent predictive factor of atherosclerosis.

Keywords: *Coronary artery disease • Helicobacter.pylori • Immunoglobulin G antibody*

1. Introduction

Atherosclerosis is a principal cause of death all over the world [1,2]. Several studies have thus far sought to identify the predictors of atherosclerosis, with more recent publications focusing on the inflammatory effects of infectious agents such as Chlamyda.*pneumoniae* and Helicobacter.*pylori* (*H.pylori*) on atherosclerosis. Despite all those efforts, however, controversy still abounds about the role of H.*pylori* as a determinant factor of atherosclerosis and ischemic disease [3-9].

H.*pylori* is a gram-negative micro-aerophilic spiral bacterium that survives and colonizes in the human gastric mucosa layer. It leads to range of diseases comprising gastritis and gastric ulcers, cancers, and lymphomas [10-12]. Infection with H.*pylori* occurs worldwide with a prevalence spectrum from 20-50% in industrial countries to 80% in developing countries [10,13]. As a developing country, Iran is burdened

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Table 1. Univariate analysis of demographic characteristics and H.*pylori* infection seropositivity between two groups*.

Patient characteristics	Case-group	Control-group n (%)	P-value
Patient number (n=153)	69	84	
Age (Y) mean ± SD	60.5±1.05	57.57±1.10	0.061
Gender			
Female n (%)	16(23.2%)	39(46.4%)	0.003
Male n (%)	53(76.8%)	45(53.6%)	
Cigarette smoking habit n (%)	30(43.5%)	23(27.7%)	0.042
Diabetes mellitus n (%)	14(20.3%)	16(19%)	0.847
Hypercholesterolemia n (%)	23(33.8%)	18(21.4%)	0.087
Hypertension n (%)	29(42%)	35(41.7%)	0.964
Family history of atherosclerotic disease n (%)	28(40.6%)	29(34.5%)	0.441
BMI mean ± SD	27.7±0.46	28±0.50	0.702
TG mean ± SD	197.74±13.90	208.27±10.27	0.535
HDL mean ± SD	43.46±1.54	47.61±1.14	0.029
LDL mean ± SD	104.60±4.97	82.66±4.12	0.005
Seropositive H.pylori n (%)	40(58%)	48(57.1%)	0.918

Standard deviation, SD; Body mass index, BMI; triglyceride, TG; low density lipoprotein cholesterol, LDL; high density lipoprotein, HDL; H.pylori, Helicobacter. pylori

with a high prevalence of H.*pylori* infection and atherosclerosis. A lot of research is made to find the exact predictors of young age atherosclerosis in our society and H.*pylori* infection is one of noticeable suggestion. We, therefore, conducted the present study to evaluate the possible correlation between H.*pylori* infection and atherosclerosis in our population.

2. Material and Methods

This cross-sectional study, conducted from April 2006 to April 2007, recruited 153 adult patients scheduled for coronary angiography. The study was approved by our hospital ethics committee, and informed consent was obtained from all the patients.

Patients with a history of valvular disease, atherosclerotic cardiomyopathy, and antibiotic therapy against H.*pylori* infections were excluded from the study.

The patients were divided into two groups with and without coronary artery disease (CAD) according to the diagnosis of CAD based on coronary angiography.

Demographic characteristics, comprised of age, sex, body mass index (BMI), history of diabetes mellitus, hypertension, hypercholesterolemia, family history of atherosclerotic disease, and cigarette smoking habit, were assessed in the patients and compared between the groups. Additionally, the serum levels of triglyceride (TG), low-density lipoprotein cholesterol (LDL), high-density lipoprotein (HDL) were routinely measured before angiography for all patients.

2.1. Coronary artery disease

The diagnosis of CAD was based on coronary angiography results. CAD was diagnosed if ≥50% stenosis was detected in at least one coronary artery. All the coronary angiographies were performed by the same cardiologist in our center.

2.2. Helicobacter. pylori- specific immunoglobulin G antibody (H.*pylori* IgG antibody):

Two milliliters of blood were taken from all the patients and kept in - 80 °C.

H.*pylori* IgG antibody titers were measured by the enzyme-linked immunosorbent assay (ELISA) method using the commercial kit of Euroimmune (Germany).

According to the manufacturer's instruction, patients with IgG antibody titers higher than 22 Ru/ml were considered seropositive for H.*pylori* infection.

2.3. Statistical analysis

The univariate analysis of the continuous variables was carried out by Student's *t*-test, and the categorical variables were compared via the chi-square test and Fisher's exact test, as appropriate. The variables were included into a multivariate logistic regression model, and the association of the independent predictors with CAD in the final model was expressed as odds ratio

Table 2. Distribution of H.*pylori* infection seropositivity in the groups in terms of sex.

	Case-group n (%)	Control-group n (%)	P-value
Female:	16	39	0.769
Seropositive H.*pylori*	10 (62.5%)	22(56.4%)	
Seronegative H.*pylori*	6(37.5%)	17(43.6%)	
Male:	53	45	1
Seropositive H.*pylori*	30(56.6%)	26(57.8%)	
Seronegative H.*pylori*	23(43.4%)	19(42.2%)	

** Data are presented as n (%).H.pylori, Helicobacter. pylori*

Table 3. Distribution of H.*pylori* infection seropositivity in the groups in terms of cigarette smoking habit.

	Case-group n (%)	Control-group n (%)	P-value
Cigarette smoking habit:	30	23	0.837
Seropositive H.*pylori*	18(60%)	15(65.2%)	
Seronegative H.*pylori*	12(40%)	8(34.8%)	
No-Cigarette smoking habit:	39	60	0.779
Seropositive H.*pylori*	22(56.4%)	32(53.3%)	
Seronegative H.*pylori*	17(43.6%)	28(46.7%)	

** Data are presented as n (%).H.pylori, Helicobacter. pylori*

Table 4. Predictive factors of CAD between groups.

Patient characteristics	P-value	Odds Ratio	95% Confidence Interval
Age (Y)	0.005	1.063	1.018-1.109
Gender	0.001	4.876	1.944-12.231
HDL	0.050	0.965	0.932-1.000
LDL	0.002	1.016	1.006-1.026

High-density lipoprotein, HDL; low -density lipoprotein cholesterol, LDL; Triglyceride, TG

(OR) with 95% confidence intervals (CIs).

SPSS version 16.0 (SPSS Inc., Chicago, I.L.) statistical software was used for the statistical analyses. All the P-values were 2-tailed, with the statistical significance defined as P-value≤0.05.

3. Results

A total of 153 patients, who underwent coronary angiography, were enrolled into the study. The patients consisted of 55 (35.9%) women and 98 (34.1%) men at a mean age of 58.8±9.64 years. CAD was diagnosed in 69 patients (case group), and the remaining 84 patients had normal coronary vessels (control group). The mean age, BMI, diabetes mellitus, hypertension, hypercholesterolemia, family history of atherosclerotic disease, and TG serum level were not significantly different between the two groups. But there was a statistically significant difference between the groups in regards to sex distribution, cigarette smoking habit, HDL, and LDL serum levels. Assessment of H.*pylori* IgG antibody titers revealed that H.*pylori* infection totally occurred in 88 (57.51%) patients: 40 (58%) in the atherosclerotic group and 48 (57.1%) in the control group. There was no significant difference between two groups (P-value=0.918) (Table 1). Also, the prevalence of seropositive H.*pylori* infection were evaluated in patients according to the sex and smoking habit which did not show any significant difference between the groups (Tables 2 and 3). The multivariable analysis demonstrated that age, female gender, LDL, and HDL are only the predictive factors of CAD and H.pylori infection was not an independent predictive factor for CAD (P-value=0.915) (Table 4).

Additionally, the prevalence of CAD risk factors in the case group was compared between seropositive and seronegative subgroups, which were not indicative of any significant difference between the groups (Table 5). The prevalence of seropositive H.*pylori* infection with respect to the number of diseased coronary vessels was also evaluated, which showed no significant association between the number of diseased vessels and H.*pylori* infection (Table 6).

Table 5. Prevalence of CAD risk factors according to seropositive and seronegative H.*pylori* infection in the case group *.

Patient characteristics	Seropositive H.*pylori*	Seronegative H.*pylori*	P-value
Patient number (n=69)	40	29	
Age (Y) mean ± standard deviation	60.75±1.16	60.17±1.96	0.790
Gender n (%)			
female	22(55%)	17(58.62%)	0.899
male	18(45%)	12(41.37%)	
Cigarette smoking habit n (%)	18(45%)	12(41.4%)	0.765
Diabetes mellitus n (%)	9(22.5%)	5(17.2%)	0.592
Hypercholesterolemia n (%)	12(30.8%)	11(37.9%)	0.537
Hypertension n (%)	17(42.5%)	12(41.4%)	0.926
Family history of atherosclerotic disease n (%)	18(45%)	10(34.5%)	0.380
BMI mean ± SD	27.22±0.62	28.39±70	0.220
TG mean ± SD	189.51±17.45	208.79±22.82	0.497
HDL mean ± SD	45.54±2.09	40.66±2.20	0. 119
LDL mean ± SD	104±7.42	105.39±6.22	0.891

Sandard deviation, SD; H.pylori, Helicobacter. pylori; Body mass index, BMI; triglyceride, TG; high-density lipoprotein, HDL, low-density lipoprotein cholesterol, LDL

Table 6. The prevalence of seropositive H.pylori infection as regards the diseased coronary vessels.

	Seropositive H.pylori n (%)	Seronegative H.pylori n (%)	P-value
Number of diseased vessels:			0.856
No diseased vessel	48(54.5%)	36(55.4%)	
One diseased vessel	3(3.4%)	1(1.5%)	
Two diseased vessels	9(10.2%)	5(7.7%)	
Three diseased vessels	28(31.8%)	23(35.4%)	

H.Pylori, Helicobacter. pylori

4. Discussion

The vast array of studies performed thus far has brought about conflicting results and controversies. These inconsistencies may well have been a consequence of different evaluation methods for H.*pylori* infection and atherosclerosis or even different populations recruited into the studies. In the present study, H.*pylori* infection was evaluated by measuring IgG antibody titers via the ELISA in patients in whom atherosclerosis was assessed by coronary angiography. The prevalence of H.*pylori* infection was 57.51% in the study population: 58% in the atherosclerotic group and 57.1% in the control group. The prevalence of H.*pylori* infection in normal and atherosclerotic patients in different areas of our country has been reported to be within a wide range of 16%-72.2% and 39.4%-70%, respectively [9,14,15]. This sizable difference in range may have resulted from the difference in the measuring factors of infection such as IgA and IgG antibodies, which can detect different phases of infection, and the use of different tests such as urease respiratory test and cytotoxin-associated gene-A (Cag A) with their different sensitivity and specificity. Another likely culprit is the different prevalence of H.*pylori* infection in different geographical areas and socioeconomic conditions of a country. Our hospital, a referral center in Iranian capital city of Tehran, admits patients from all parts of the country; the prevalence obtained in the present study could, therefore, be deemed the average prevalence of the H.*pylori* infection for the country.

Our multivariable analysis showed no significant correlation between H.*pylori* infection and atherosclerosis. While these results are similar to some previously published studies [5,8,16-20], it is not concordant with others [9,21-28]. It is worth repeating that this discrepancy seems to have arisen from the previously various methods of evaluating H.*pylori* infection and atherosclerosis. For instance, there are studies in the medical literature [21,23-25] that either did not use coronary angiography for detecting atherosclerosis or only use it for case groups with myocardial infarction. There are studies [22] whose study population was selected from patients admitted into cardiac clinics due to clinical symptoms of heart burn or angina pectoris. It

is likely that some of these symptoms were secondary to gastric diseases and H.*pylori* infection, hence the higher prevalence of infection in these patients. It could, therefore, be argued that these factors exerted inappropriate effects on the results.

Because there are deleterious effects of H.*pylori* infection on coronary atherosclerosis risk factors [29-33], we decided to divide the case group patients in terms of seropositive and seronegative H.*pylori* infection. The result showed no significant difference in the risk factors between the two groups, and it does not agree with some theories [34].

As we evaluated atherosclerosis using coronary angiography and H.*pylori* infection using IgG antibody serum level, the results give the impression of reliability. Nonetheless, Bazazi and colleagues 9 illustrated that atherosclerosis has a correlation with seropositive IgA H.pylori infection and did not detect any correlation with seropositive IgG H.pylori infection.

We did not evaluate highly virulent strains of H.pylori which create Cag A toxin and thus induce severe infection. However, some studies have reported association with atherosclerosis [3,26,28,35], some others have reported the non-significant role of anti-Cag A antibody in ischemic heart disease [5,7,36]. Future studies are required to shed sufficient light upon this particular point.

In light of the previously mentioned results, we would suggest that H.*pylori* infection is not an independent predictive factor of atherosclerosis until further studies have clarified its effect on atherosclerosis.

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