Original Article

Association between *Helicobacter pylori* Infection and Atherosclerotic Coronary Artery Disease

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ABSTRACT

Background and Objectives: **Cardiovascular disease is the most common cause of death in developed countries. In addition to traditional risk factors for cardiovascular disease, nowadays, accumulating evidence indicates that a variety of infections contribute to pathogenesis of atherosclerosis, (We investigated whether *Helicobacter pylori* infection is related to Prpevalence of coronary heart disease) there is controversy concerning the impact of *H.pylori* infections in atherosclerosis.**

Materials and Methods: **This case-control study was carried out on 130 subjects who underwent coronary angiography in the School of Medicine, Tehran University of Medical Sciences, Iran, from Oct 2006 to Oct 2007. According to angiography findings, the patients were grouped into cases (n=70) with Coronary Artery Disease (CAD), and normal control group (n=60). Then, using ELISA method, specific anti *H.pylori* IgGs were measured in all subjects. The connection between CAD and *H.pylori* infection was studied.**

Results: **Among the 130 patients, anti-*H.pylori* IgGs were detected in 80% of cases and 65% of control subjects (P=0.05). The investigation shows that CAD correlated significantly with hypertension, diabetes, and smoking (P<0.05) although there was no associations between these traditional risk factors, and *H.pylori* infection.**

Conclusion: **These findings raise the possibility that exposure to *H.pylori* may lead to an increased risk of coronary artery disease independent of other risk factors.**

Key words: *Helicobacter pylori*, Coronary artery disease, Sero-epidemiology, Iran

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Introduction

Today, cardiovascular diseases (CAD) are the main causes of death in developed countries and atherosclerosis is considered as the pathology of these diseases (1). The reasons of the risk of coronary atherosclerosis are not the same in all patients, and different causes may result in the occurrence and the progression of atherosclerosis in different patients. In humans, no single factor can account for all the causes of CAD, and in high percentage of patients have none of traditional risk factors such as hypertension, smoking, obesity, hypercholesterolemia or genetic predisposition (1). Due to this fact, medical researchers are beginning to find other risk factors to express causes of coronary atherosclerosis incidence.

Clinical and experimental studies indicate that inflammatory diseases have a role in atherosclerosis (2). Many epidemiological investigations have shown significant relationship between coronary ischemia and various infectious agents such as bacterial and viral (3-5). *Helicobacter pylori* is one of various spiral, gram negative and microaerophilic bacteria which produces colonies in human and primates' stomach and results in infectious and inflammatory diseases (6).

In this research, we attempted to study the link between *H.pylori* infection and coronary atherosclerosis and also correlation between this infectious factor with other risk factors such as diabetes, hypertension and smoking.

Materials and Methods

This case-control study was performed from Oct 2006 to Oct 2007 in Imam Khomeini Hospital, Tehran University of Medical Sciences, Iran and sampled by a simple randomized method. Patients with unstable angina, stable angina, myocardial infarction and patients with chest pain suspicious for CAD that referred to cardiac department of this hospital were studied.

The patients with a history of any inflammatory disease (endocarditis, infectious respiratory disease and arthritis), hepatitis B and C, HIV positive antibody and also presence of high titer IgA antibody to *Helicobacter* were excluded from the scope of the investigation.

The positive angiography was defined as ≥50% diameter stenosis of at least one coronary vessel.

All patients underwent coronary angiography at Imam Khomeini Hospital. Case patients (n=70) had any angiographic evidence of atherosclerotic coronary artery disease, whereas control patients (n=60) had no angiographic evidence of atherosclerotic CAD. Then, Serum samples were collected for *H.pylori* antibody (IgA & IgG) testing quantified by ELISA method in all patients (*H pylori* IgA :DRG Instruments Gmbh Kit, Germany: samples with a concentration lower than 5 arbU/ml were considered negative and higher than 5 arbU/ml as positive. Sensitivity 0f kit was >98%, Specificity >98%. *H pylori* IgG: RADIM S.P.A Kit. Italia, Samples with IgG values less than 15 UR/ml were noncreative, higher than 30 UR/ml were reactive ,between 15-30 UR/ml were weakly reactive).

Our participants filled out a short health questionnaire, including questions on past and concomitant health problems, history of hypertension, current medication, socio-demographic data, smoking, age, sex and alcohol consumption record.

Statistical analysis was carried out by using the SPSS (version 11) for Windows statistical software system. Probability values of ≤0.05 were considered statically significant.

The present study was approved by the Ethic Committee of Cardiovascular Center of Tehran University of Medical Science.

Results

The mean age of patients in cases was 62±7.7, and in controls, 61±7.4 years. Comparison of these values by an independent sample test showed no statistical difference (P=0.61).

The sex ratio in cases was 62% men and 38% women, and in controls, 51% men and 49% women. Comparison of these ratios by Chi-square test showed no statistical difference (P>0.05; odds ratio=1.6; 95% CI=0.79 to 3.22).

In cases, 80% of patients were seropositive for *H.pylori* (IgG titer), while in controls, 65% of patients showed positive IgG antibody titer for *H.pylori*. Comparison of these ratios by Chi-square test showed statistical difference (P=0.05; odds ratio=2.2; 95% CI=1.01 to 4.86).

Results of assessing risk factors showed a significant relationship between CAD and traditional risk factors (Table 1).

Table 1: Main clinical features and seropositivity for *H.pylori* of patients and controls

Clinical data	Cases n (%)	Controls n (%)	*P* Value
Age mean (year)	62±7.7	61±7.4	0.61
Male	43 (62)	31 (51)	0.126
Female	27 (38)	29 (49)	
Hypertension	40 (58)	14 (23)	<0.001
Diabetes	31 (45)	14 (23)	0.007
Smoking	55 (79)	10 (17)	<0.001
Seropositive *H.pylori*	56 (80)	38 (65)	0.05

The mean age of seropositive patients was 61±7.3 yr and in seronegative patients was 61.02±8.1 yr. A comparison of these averages showed no statistical difference, (Table 2).

In the seropositive patients, the sex distribution was as follows: 55.3% men and 44.7% women. In contrast with seropositive patients, in seronegative ones, the sex distribution was 61.1% men and 38.9% women which in chi-square comparison did not show any statistical difference (P>0.05; odds ratio=0.788; 95% CI=0.36 to 1.725), (Table 2).

There was no significant association between *H.pylori* and traditional risk factors, (Table 2).

Table 2: Main clinical features of patients with and without *H.pylori* infection

Clinical data	Seronegative *H.pylori* n (%)	Seropositive *H.pylori* n (%)	*P* Value
Age mean (year)	61.02±8.1	61.7±7.3	0.64
Man	22 (61.1)	52 (55.3)	0.35
Woman	14 (38.9)	42 (44.7)	
Hypertension	16 (44.5)	38 (40.5)	0.41
Diabetes	9 (25.0)	36 (38.5)	0.11
Smoking	14 (39.0)	43 (46.0)	0.3

Discussion

Atherosclerotic lesions (atheromata) are asymmetric thickenings of the intimal layer of the artery (7-9). This idea which infections play an important role in atherosclerosis and its clinical manifestations has been taken into consideration (8,9). *H.pylori* is one of the most common human infections which its transmission mode is not yet clear (9-11). Several studies report a relation between this infection and the majority of upper gastrointestinal diseases (10, 12). A met analysis of 18 epidemiological studies show that only small absolute differences in body mass index, hypertension, or hematological risk factors were found between subjects who were seropositive and those who were seronegative for *H.pylori* (11).

Our study shows the significant association between known risk factors of coronary disease such as diabetes, hypertension and smoking with CAD (Table 1). Besides, in patients, there was no significant relation between *H.pylori* infection and diabetes, hypertension and smoking (Table 2).

The Logistic regression analysis showed an independent relationship between *H.pylori* and CAD (P=0.05), although this relationship was not as significant as association between classic risk factors and CAD. So, *H.pylori* infection may be introduced as a risk factor of CAD incidence, independent of known risk factors (13-17).

Gunn *et al*. in a case-control research, determined serological status for cagA and *H.pylori* in 342 cases with acute myocardial infarction and 214 control subjects free of clinical CAD. Accordingly, the association of chronic *H.pylori* infection with risk of

myocardial infarction appeared to be limited to cagA bearing strains (12). In addition, in a case-control Study, Ridker *et al.* discovered a minimal evidence link between *H.pylori* exposure and risk for future myocardial infarction (13). Jin SW *et al.* found a modest influence on CAD and progressive atheroma caused by *H.pylori* infection (14).

Conclusion

The link between *H.pylori* infection and coronary atherosclerosis requires further studies. *H.pylori* infection is a potentially curable disease and for this reason, the identification of this condition as a coronary risk factor may have important implications for the prevention for ischemic heart disease.

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This work has been carried out at Tehran University in the Imam Khomeini Hospital complex. The authors declare that they have no conflict of interests.

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