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Jacobs Journal of Experimental Cardiology and Research

Research article

Helicobacter pylori Infection is a Significant Risk Factor for Hyperhomocysteinemia in Patients with Coronary Artery Disease

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Received: 12-17-2015

Accepted: 02-16-2016

Published: 04-29-2016

Abstract

Background
The association between *Helicobacter pylori* infection and concentration of homocysteine is complicated in the pathogenesis of coronary artery disease.

Aims
We aimed to determine whether seropositivity to *Helicobacter pylori* infection is an independent risk factor for hyperhomocysteinemia patients with cardiovascular disease.

Methods
The *H. pylori* IgG, IgA and homocystein levels in 96 patients with cardiovascular disease and 64 participants free of cardiovascular disease as control subjects were determined by ELISA assay.

Results
The results of present study showed that seropositivity to *H. pylori* IgG and IgA levels of CAD patients was significantly higher than controls and CAD patients with negative anti *H. pylori* IgG and IgA. A significant correlation was found between seropositivity to *H. pylori* IgG and homocysteine levels of CAD patients in comparison with controls and CAD patients with seronegativity to *H. pylori* IgG and IgA (r=0.233, P= 0.019).

Conclusion
The involvement of *H. pylori* infection in atherosclerosis process is based on the chronic inflammation which might facilitate the CAD-related pathologies. Moreover, effect of the presence of *H. pylori* infection on homocysteine levels elevation in CAD patients (as a risk factor independent of other traditional factors) was remarkable.

Keywords: Cardiovascular disease; *Helicobacter pylori*; Homocysteine

Abbreviations:
CAD: Coronary Artery Disease;
DM: Diabetes mellitus;
HCY: Homocysteine;

HDL: High-Density Lipoprotein;
H. pylori: *Helicobacter pylori*;
HTN: Hypertension

Background

Cardiovascular disease is the most common cause of mortality and morbidity in the United States and many other nations [1]. Coronary atherosclerosis process is multi-factorial. Traditional and classic cardiovascular risk factors such as diabetes mellitus (DM), hypertension (HTN), smoking and obesity have introduced as major causes, but significant proportions of patients with coronary artery disease (CAD) do not have these traditional risks. Other factors which may affect this chronic process were evaluated [1-3]. For example infection-related chronic inflammation from *Helicobacter pylori* (*H. pylori*) is one of the CAD risk factor, because the CAD risk factors plasma fibrinogen, C-reactive protein, and blood leukocyte count have been elevated in seropositive subjects [2]. *H. pylori* infection is the most common infection worldwide especially in developing countries [3]. According to many research reports, 70-90% of apparently healthy people of developing countries are estimated to be infected with *H. pylori* [3-5]. *H. pylori* is a Gram-negative bacterium with perfect adaptation to the acidic environment of the stomach and high affinity to gastric epithelial cells. Recently, possible association between *H. pylori* infection and extragastric disorders has been also suggested [6-8]. An indirect association between the prevalence of *H. pylori* and the occurrence of CAD is demonstrated by many research studies [3-5]. A significant association of *H. pylori* infection with CAD (OR 3.18, 95%CI 1.08-9.40) was showed by a multivariate logistic regression analysis [3]. According to majority of findings the involvement of *H. pylori* in this process is based on the chronic inflammation which might facilitate the CAD-related pathologies [3, 5]. Several mechanisms have been proposed for how *H. pylori* might accelerate macrovascular complications and increase CAD risk [3, 4, 9]. It has been demonstrated that *H. pylori* is an important and amazing cause of elevated levels of homocysteine (HCY) and is prevalent in the Caucasian population, ranging from 30 to 40% incidence. On the other hand, HCY is recognized as an independent risk factor for cardiovascular diseases. HCY has been demonstrated to be toxic to the endothelial cells and lipoproteins due to generation of oxygen radicals. High level of HCY appears to be one of the factors responsible for the increased risk of vascular damage and clinical coronary heart disease events [10]. The result of a study on 116 patients with CAD who were matched with 116 controls via age and sex although showed a minor association between *H. pylori* infection and CAD, but a stronger correlation between higher levels of triglycerides (fats) and lower levels of high density high-density lipoprotein (HDL) -cholesterol was found in the H. pylori-infected patients [11-14]. Based on the above findings, these results could be consistent with the hypothesis that *H. pylori* infection might modify the serum lipid concentrations in a way that could increase the risk of CAD [10]. Hence knowing the inflammation as a cardiovascular risk factor in the one hand and *H. pylori* and hyper-homocysteinemia involvement in CAD incidence on the other hand made us to evaluate the *H. pylori* infection effect on HCY levels and atherosclerosis processes. On this matter we have examined whether *H. pylori* seropositivity is associated with hyperhomocysteinemia and cardiovascular disease occurrence.

Methods

Sampling and coronary angiography

This cross-sectional study was performed in Rasole Akram Hospital of Tehran from Jun 2014 to October 2014. 96 consecutive CAD patients (68 men and 28 women; mean age 52. 95± 1.25 and 51.32±1.61 years old respectively) and 64 controls were enrolled into the study and candidate for coronary angiography and informed consent were selected. Before catheterization, all subjects completed a semi structured questionnaire regarding their past medical and drug history. The diagnosis was based on the decision of an experienced clinician. Coronary angiography was carried out by left-heart catheterization and arteriography using Judkins method, and then a cardiologist separately reviewed the angiography films. According to angiography reports, the clinical and laboratory evaluated patients with ≥50% coronary stenosis were considered as CAD positive group and participants with <50% coronary stenosis considered as CAD negative group or controls. Accordingly, patients with hepatic dysfunction, autoimmune disease, thyroid dysfunction and/or adrenal dysfunction as well as patients who consumed any kinds of glucocorticoids were excluded from study. This study was approved by the Ethical Committee of Iran University of Medical Sciences.

Biochemical Measurements

Fasting blood sample of catheterization participants were taken to measure lipid profiles, immunoglobulins G and A (anti *H. pylori* IgG and IgA) and homocysteine levels. ELISA kit (Diagnostic kit, PISHTAZ TEB Company, Teheran, Iran) was used to measure the homocysteine levels. anti *H. pylori* antibody status was determined by measuring IgG and IgA antibody by ELISA assay (Diagnostic kit, PISHTAZ TEB Company). spectrophotometric assay was used for lipid profiles assay.

Statistical data analysis

Statistical analyses were carried out using SPSS software (version 16.0, Chicago, IL, USA). Unpaired student t-tests and ANOVA test were used for comparing continuous variable. Chi-square test was used for discrete variables. To compare the association of *H. pylori* infection with homocysteine and thereby CAD, logistic regression tests were used by adjusting sex and age plus history of diabetes, dyslipidemia, and/or Hypertension.

Results

Demographic characteristics of four study groups were presented in tables 1 and 2.

No significant differences were found in terms of demographic characteristics between CAD patients and controls with anti H.P IgG positive and negative and between CAD patients and controls with anti H.P IgA positive and negative. As it shown in Table 1,

Table1. Demographic characteristics of CAD patients and controls with positive and negative anti-*H. pylori* IgG

			Control-Negative anti-H.P IgG)	Control-positive anti-H.P IgG)	CAD-Negative anti-H.P IgG	CAD - Positive anti-H.P IgG	P value
			N=21	N=43	N=17	N=79	
Gender		Male	13	19	9	59	0.008
		Female	8	24	8	20	
Smoking		Yes	6	7	6	24	0.309
		No	15	36	11	55	
Diabetes History		Yes	1	4	4	9	0.306
		No	20	39	13	70	
Medication	Aspirin	Yes	14	34	15	69	0.129
		No	7	9	2	10	
	Statin	Yes	8	18	13	59	<0.001
		No	13	25	4	20	
	Lozartan	Yes	5	7	5	21	0.577
		No	16	36	12	58	
Anti H.P IgG(U/ml)			8.05 ± 0.40	67.21 ± 4.00	9.34 ± 2.11	72.49 ± 3.64	<0.001
Anti H.P IgA (U/ml)			15.48 ±	38.90 ±	12.20 ±	46.72 ±	<0.001

	3.18	3.68	1.15	3.24	
LDL-C (mg/dl)	105.16 ± 6.84	93.97 ± 3.87	99.27 ± 5.41	98.37 ± 3.08	0.507
HDL-C(mg/dl)	39.53 ± 2.60	38.06 ± 2.06	35.07 ± 1.64	36.96 ± 0.93	0.550
Cholesterol (mg/dl)	189.26 ± 11.28	167.58 ± 6.37	168.80 ± 7.85	169.12 ± 4.27	0.199
TG (mg/dl)	152.89 ± 22.46	142.25 ± 16.29	174.07 ± 23.64	126.53 ± 7.19	0.154
FBS(mg/dl)	102.40± 4.96	103.21± 6.84	106.26± 6.60	104. 08± 2.53	0.983
Age(years)	57.76 ± 2.36	55.49 ± 1.65	56.35 ± 2.47	59.79 ± 1.23	0.187
SBP(mmHg)	126.55 ± 2.61	131.79 ± 2.98	132.40 ± 1.82	131.04 ± 15.70	0.652
DBP(mmHg)	78.35 ± 2.19	80.02 ± 1.91	81.27 ± 2.48	83.15 ± 1.56	0.366
BMI (Kg/m^2)	27.42± 0.74	27.58± 0.46	27.58± 0.96	26.41 ± 0.27	0.224

Anti H.P, anti-helicobacter pylori; BMI, body mass index; FBS, fast blood sugar; HDL, high-density lipoprotein; LDL-C, low-density lipoprotein; SBP, systolic blood pressure; TG, triglyceride; DBP=diastolic blood pressure. Values are means±sd

the anti *H. pylori* IgG (72.49 ± 3.64U/ml) and IgA (46.72 ± 3.24 U/ml) levels of CAD patient with positive anti *H. pylori* IgG were significantly more than those were found in CAD patients with negative anti *H. pylori* IgG (9.34 ± 2.11 and 12.20 ± 1.15 U/ml) . 8.05 ± 0.40 and 15.48 ± 3.18 U/ml were achieved for anti *H. pylori* IgG and anti *H. pylori* IgA of controls with negative anti H.P. IgG, respectively , which are lower significantly than those found for CAD patient with positive and negative anti *H. pylori* IgG. The Anti *H. pylori* IgG (67.21 ± 4.00 U/ml) and anti *H. pylori* IgA (38.90 ± 3.68 U/ml) levels of the control group with positive anti *H. pylori* IgG were lower than CAD patient with positive anti *H. pylori* IgG but significantly higher than negative anti *H. pylori* IgG CAD patients. According to Table 2, 64.96 ± 2.97 and 43.63 ± 3.07 U/ml of

Table 2. Demographic characteristics of CAD patients and controls with positive and negative *H. pylori* anti IgA

			Control-Negative anti-H.P IgA N-14	Control-Positive anti-H.P IgA N=50	CAD-Negative anti-H.P IgA N=8	CAD-Positive anti-H.P IgA N=88	P value
Gender		Male	7	25	6	62	0.067
		Female	7	25	2	26	
Smoking		Yes	4	9	3	27	0.372
		No	10	41	5	61	
Diabetes History		Yes	1	4	2	11	0.490
		No	13	46	6	77	
Medication	Aspirin	Yes	9	39	6	78	0.089
		No	5	11	2	10	
	Statin	Yes	5	21	6	66	<0.001
		No	9	29	2	22	
	Lozartan	Yes	4	8	2	24	0.458
		No	10	42	6	64	
Anti H.P IgG(U/ml)			15.62 ± 5.31	56.81 ± 4.72	21.16 ± 11.20	64.96 ± 2.97	<0.001
Anti H.P IgA(U/ml)			6.81 ± 0.63	38.06 ± 3.24	7.40 ± 0.48	43.63 ± 3.07	<0.001
LDL-C(mg/dl)			100.25 ± 7.79	97.24 ± 3.98	107.25 ± 9.10	97.67 ± 92.02	0.768
HDL-C(mg/dl)			39.42 ± 2.40	38.33 ± 1.96	39.75 ± 3.25	36.36 ± 0.85	0.501
Cholesterol(mg/dl)			178.77 ± 9.79	173.93 ± 7.02	176.88 ± 11.61	168.33 ± 4.00	0.728

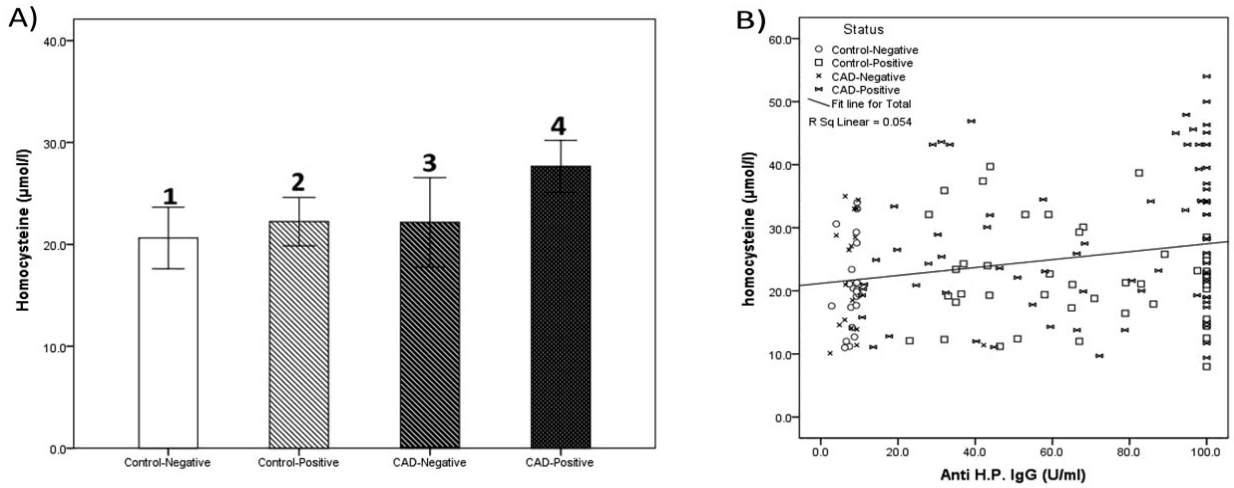
TG(mg/dl)	165.85 ± 28.64	±	139.76 ± 14.73	±	192.50 ± 35.53	±	128.71 ± 6.68	±	0.099
FBS(mg/dl)	99.07 ± 6.27	±	104.08± 6.05		112.62 ± 8.99	±	103.72 ± 2.53	±	0.817
Age(years)	57.79 ± 3.10	±	55.80 ± 1.50	±	59.12 ± 2.99	±	59.18 ± 1.19	±	0.370
SBP(mmHg)	128.36 ± 3.06	±	130.60 ± 2.71	±	134.43 ± 4.46	±	131.00 ± 1.78	±	0.882
DBP (mmHg)	78.64 ± 2.71	±	79.73 ± 1.74	±	81.29 ± 3.10	±	82.96 ± 1.46	±	0.418
BMI(kg/m^2)	27.99 ± 0.79	±	27.53 ± 0.44	±	26.65 ± 1.51	±	26.61 ± 0.37	±	0.306

Anti H.P, anti-helicobacter pylori; BMI, body mass index; FBS, fast blood sugar; HDL, high-density lipoprotein; LDL-C, low-density lipoprotein; SBP= systolic blood pressure; TG, triglyceride; DBP=diastolic blood pressure. Values are means±sd

anti *H. pylori* IgG and Anti *H. pylori* IgA respectively of CAD patient with positive *H. pylori* IgA were significantly higher than those found for CAD patients with negative anti *H. pylori* IgA (21.16 ± 11.20 and 7.40 ± 0.48 U/ml), controls with negative anti *H. pylori* IgA (15.62 ± 5.31 and 6.61± 0.63U/ml) and the control subjects with positive anti *H. pylori* IgA (56.81 ± 4.72 and 38.06 ± 324 U/ml) respectively. As it shown in Figure 1 (A), the serum homocysteine concentration of CAD patients with positive anti *H. pylori* IgG (27.70 ± 1.28 µmol/L) was significantly (P= 0.05) higher than CAD patients with negative anti *H. pylori* IgG (22.16 ± 2.19 µmol/L). The difference between HCY levels of CAD patients with positive anti *H. pylori* IgG (27.70± 1.28µmol/L(and the control group with positive anti H.P. IgG (22.38 ± 1.19 µmol /L) was also significant (P=0.02). The homocysteine levels of CAD patients with positive anti *H. pylori* IgG (27.70 ± 1.28 µmol/L) was significantly (P=0.02) higher than control subjects with negative anti H.P IgG positive (20.62 ± 1.51 µmol /L). The serum homocysteine concentration of the control subjects with negative anti H.P IgG positive (22.38 ± 1.19 µmol /L) and control group with negative anti H.P IgG (20.62± 1.51 µmol /L) was not different significantly (P= 0.936). A significant correlation with r= 0.233 , P=0.0.19 was identified between anti *H. pylori* IgG and homocysteine levels of CAD patients with positive anti *H. pylori* IgG (Figure 1 B), while the correlation between anti *H. pylori* IgG and homocysteine levels of CAD patients with negative anti *H. pylori* IgG was not significant (r= 0.005, P=0.493). The correlation between anti *H. pylori* IgG and homocysteine levels of control group with positive and negative anti H.P IgG was not significant (r= -0.071, P=0.325 and r= -0.071, P=0.325, respectively). It is worth to note that correlation between anti *H. pylori* IgG and homocysteine levels of all subjects was significant (r= 0.233, P=0.002).

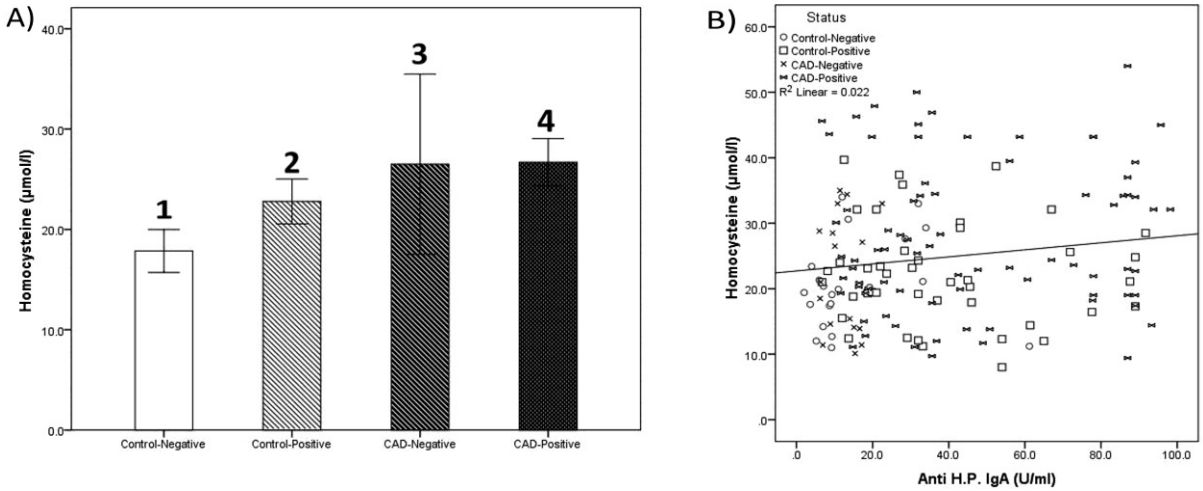
As it shown in Tables 2 and Figure 2 (A), there was not a significant (P=1) difference between the homocysteine levels of CAD patients with positive anti *H. pylori* IgA (24.70 ± 0.80 µmol/L(as comparison with CAD patients with negative anti *H. pylori* IgA (26.50± 4.49 µmol/L). Serum homocysteine concentration of CAD patients with positive anti *H. pylori* IgA (24.70 ± 0.80 µmol/L µmol/L) was not significantly (P= 0.1) higher than control subjects with positive anti *H. pylori* IgA (22.79± 1.12 µmol /L) but was higher than controls with negative anti H.P. IgA positive (17.85± 1.07 µmol /L) significantly (P=0.01). The difference between homocysteine levels of the control subjects with positive anti H.P IgA (22.79 ± 1.12 µmol /L) and controls with negative anti *H. pylori* IgA (17.85± 1.07 µmol /L) was not different significantly (P=0.34). Serum homocysteine

Figure 1. (A): Homocysteine levels of CAD patients with positive and negative anti *H. pylori* IgG and controls with positive and negative anti *H. pylori* IgG (B): The correlation between homocysteine levels and anti *H. pylori* IgG levels of CAD patients with positive and negative anti *H. pylori* IgG and of controls with positive and negative anti *H. pylori* IgG groups were identified



A)
4 P=0.020 (in comparison with 1)
4 P=0.020 (in comparison with 2)
4, P=0.0 5 (in comparison with 3)
3, P=1.000 (in comparison with 2)
2, P=0.936 (in comparison with 1)
3, P=0. 935 (in comparison with 1)
B)
Correlation in all subjects, r= 0.233, P=0.002.
○) Correlation in controls with negative anti *H. Pylori* IgG, r= 0.324, P= 0.076.
□) Correlation in controls with positive anti *H. Pylori* IgG, r= -0.071, P=0.325
⧫) Correlation in CAD patients with negative anti *H. Pylori* IgG, r= 0.005, P=0.493
⧫⧫) Correlation in CAD patients with positive anti *H. Pylori* IgG, r= 0.233, P=0.0.19

Figure 2. (A): Homocysteine levels of CAD patients with positive and negative anti *H. pylori* IgA and controls with positive and negative anti *H. pylori* IgA. (B): The correlation between homocysteine and anti *H. Pylori* IgA levels of CAD patients with positive and negative anti *H. pylori* and of controls with positive and negative anti *H. pylori* IgA groups.



A)
4 P=0.011(in comparison with 1)
4 P=0.114(in comparison with 2)

4, P=1.000 (in comparison with 3)
3, P=0.197(in comparison with 1)
2, P=0.346 (in comparison with 1)
2, P=0.754(in comparison with 3)
B)
Correlation between all groups, r= 0.197, P=0.006
○) Correlation for controls with negative anti *H. pylori* IgA, r= 0.324, P= 0.076.
□) Correlation for controls with positive anti *H. pylori* IgA, r= -0.081, P=0.335.
♦) Correlation for CAD patients with negative anti *H. pylori* IgA, r= 0.007, P=0.489.
♦♦) Correlation for CAD patients with positive anti *H. pylori* IgA, r= 0.075, P=0.256.

Table 3. Homocysteine and anti *H. pylori* IgG and IgA levels of CAD patients with positive and negative anti-H.P IgG

			(Negative anti-H.P IgG) n=21	(Positive anti-H.P IgG) n=43	(Negative anti-H.P IgG) N=17	(Positive anti-H.P IgG) N=79	value
Gender		Male	13	19	9	59	0.008
		Female	8	24	8	20	
Smoking		Yes	6	7	6	24	0.309
		No	15	36	11	55	
Diabetes History		Yes	1	4	4	9	0.306
		No	20	39	13	70	
Medication	Aspirin	Yes	14	34	15	69	0.129
		No	7	9	2	10	
	Statin	Yes	8	18	13	59	<0.001
		No	13	25	4	20	
	Lozartan	Yes	5	7	5	21	0.577
		No	16	36	12	58	
Hemocysteine(µmol/L)			20.62 ± 1.51	22.38 ± 1.19	22.16 ± 2.19	27.70 ± 1.28	0.003
Anti H.P IgG (U/ml)			8.05 ± 0.40	67.21 ± 4.00	9.34 ± 2.11	72.49 ± 3.64	<0.001
Anti H.P IgA (U/ml)			15.48 ± 3.18	38.90 ± 3.68	12.20 ± 1.15	46.72 ± 3.24	<0.001

Anti H.P, anti Helicobacter pylori
Values are means± sd

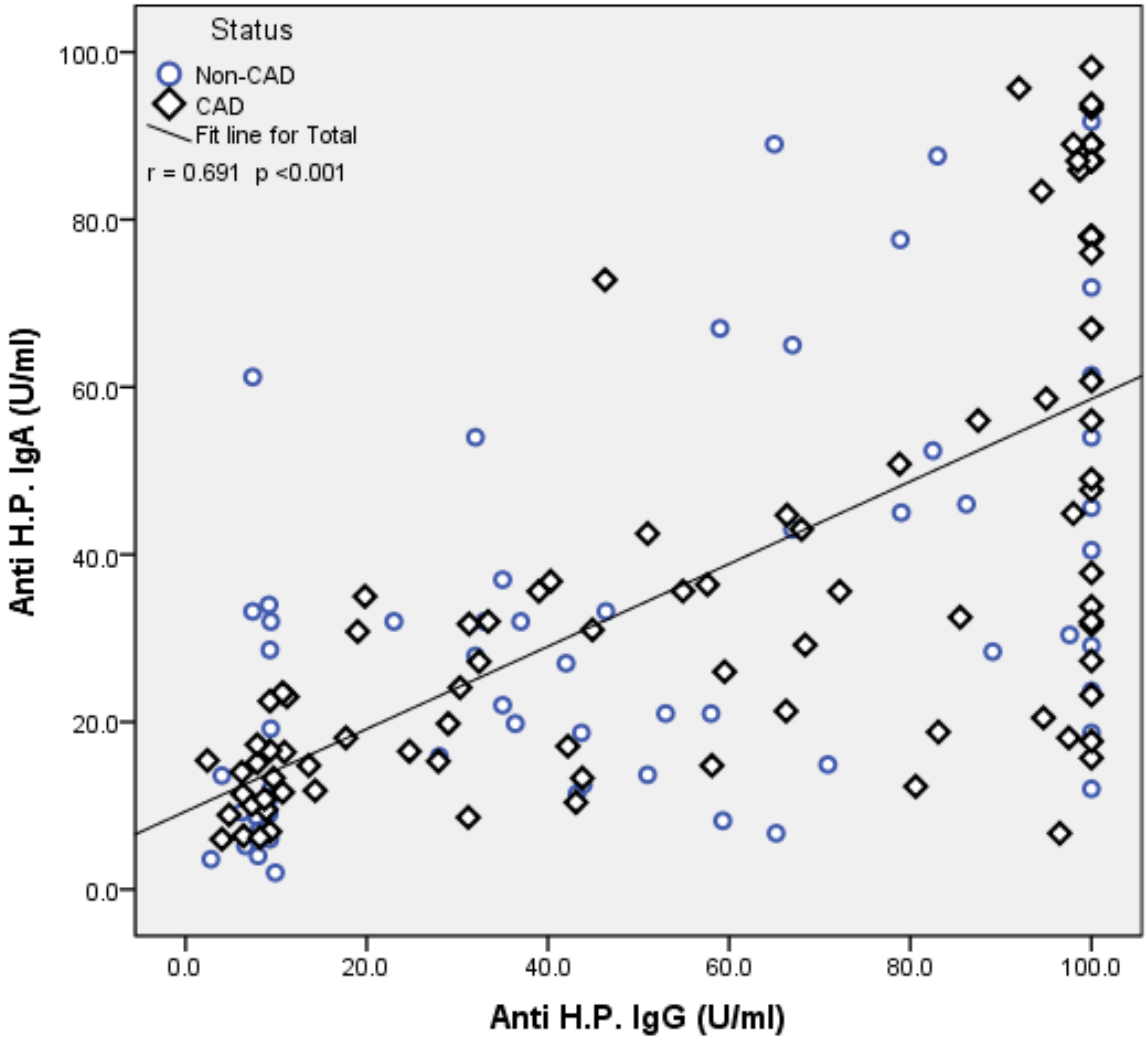
Table 4. Homocysteine and anti *H. pylori* IgG and IgA levels of CAD patients with positive and negative anti *H. pylori* IgA and the control subjects with positive and negative anti-*H. Pylori* IgA

		Controls-Negative anti-H.P IgA N=14	Controls-positive anti-H.P IgA N=50	CADs-Negative anti-H.P IgA N=8	CADs-Positive anti-H.P IgA N=88	P value
Gender	Male	7	25	6	62	0.067
	Female	7	25	2	26	
Smoking	Yes	4	9	3	27	0.372
	No	10	41	5	61	
Diabetes History	Yes	1	4	2	11	0.490
	No	13	46	6	77	
Medication Aspirin	Yes	9	39	6	78	0.089
	No	5	11	2	10	
Statin	Yes	5	21	6	66	<0.001
	No	9	29	2	22	
Lozarta	Yes	4	8	2	24	0.458
n	No	10	42	6	64	
Iemocysteine (µmol/L)		17.85 ± 1.07	22.79 ± 1.12	26.50 ± 4.49	24.70 ± 0.80	0.007
Anti H.P IgG (U/ml)		15.62 ± 5.31	56.81 ± 4.72	21.16 ± 11.20	64.96 ± 2.97	<0.001
Anti H.P IgA(U/ml)		6.81 ± 0.63	38.06 ± 3.24	7.40 ± 0.48	43.63 ± 3.07	<0.001

Values are means±sd

concentration of CAD patients with negative anti *H. pylori* IgA (26.50± 4.49 µmol/L) was not significantly (P= 0.75) higher than control subjects with positive anti *H. pylori* IgA (26.50 ± 4.49 µmol /L). A significant correlation (P<0.001, r=0.691) was found between anti *H. pylori* IgA and anti *H. pylori* IgG of CAD patients in comparison with non CAD patients (Figure 3).

Figure 3. Correlation between anti *H. pylori* IgG and anti *H. pylori* IgA of patients with controls. r= 0.691, p< 0.001.



Discussion

A wide variety of studies have demonstrated that hyperhomocysteinemia and *H. pylori* infection have been contributed in the cardiovascular disease pathogenesis independent of other conventional risk factors [15-17].As it shown in Tables 1 and 2, there was not a significant difference between demographic characterization of patients with CAD and controls. According to Figures 1(A) and 2 (A), a significant difference was found between anti H.P. IgG and IgA levels of patients with CAD (P= 0.020) and controls (P=0.011). Serum homocysteine concentration of patients with CAD was more than controls significantly. A positive correlation was found between homocysteine levels and anti *H. pylori* IgG in patients with CAD as comparison to the control subjects. It has been proposed that *H. pylori* infection might modify the serum homocysteine concentration in a way that could increase the risk of CAD. The results of a case-control study by Sung et al. showed that *H. pylori* infection increases a twofold risk of CAD [15]. However, the possible mechanism of a chronic infection by *H. pylori* leading to atherosclerosis is yet to be identified. One of the proposed mechanisms is that *H. pylori* chronic infection increases the acute inflammation factors such as fibrinogen and sialic acid, which are predictors of CAD [18]. In consistent with these results, a higher concentration of fibrinogen and total leukocyte count were reported for patients with cardiovascular disease and infected by *H. pylori* as comparison to controls [19]. The other hypothesis is that chronic *H. pylori* infection leads to malabsorption of vitamin B-6, vitamin B-12 and folate, methylation defeat and hyperhomocysteinaemia, thereby

inducing arterial damage. It has been shown that nitric oxide secretion from endothelial cells is inhibited by homocysteine, which comforts platelet aggregation and vasoconstriction. The balance between procoagulants and anticoagulants might be changed by homocysteine via selective manners such as inhibition of the thrombomodulin processing and releasing, decreasing the protein C activation and inducing a protease activator of coagulation factor V [15]. Other mechanisms of *H. pylori* infection that could lead to atherosclerosis are destructive influence of *H. pylori* and its products like cytokines and cytotoxins on coronary endothelium, activation of immune mechanisms, which react with the nuclei of monocytes in atherosclerotic vessel wall and cytoplasm of fibroblast-like cell in atherosclerosis plaques [3]. In agreement with our results, the results of a study on 93 patients under diagnostic coronary arteriography with infection H. pylori, showed a significant decrease of vitamin B12 and folate levels, thereby increasing homocysteine levels. They suggested that homocysteine can induce endothelial damage directly, affect platelet function and coagulation factors and increase the oxidation of LDL-C, which have critical role in cardiovascular disease occurrence [18]. In a study patients with *H. pylori* infection exhibited a decreased secretion of ascorbic acid by gastric mucosa and elevated gastric pH, thereby the folate absorption from diet was decreased due to low ascorbic acid in gastric juice and subsequently a significant rise was found in homocysteine levels [20]. However, it is important to consider that confounding variables such as vitamin deficiency, acute-phase response to vascular diseases, medication use, hypertension, advanced age and gender are well known factors influencing homocysteinemia and should be considered. An inverse relationship was demonstrated between homocysteine levels and *H. pylori* infection in patients with functional dyspepsia in a cross-sectional study by Rasool et al [21]. They showed that 46.2% of H. pylori- positive patients have Hyperhomocysteinemia (>15 μ mol/L) when compared to H. pylori- negative group (44%). They also reported that this was a higher proportion in comparison with that was observed in healthy population [21]. The results of studies demonstrated that *H. pylori* does affect directly HCY metabolism in liver [9, 22]. They showed that disrupted metabolism of HCY, which induced by *H. pylori* lead to an increase of HCY levels similar to those found in diabetic patients, emphasizing the probable impairment of insulin function regarding the regulation of HCY level through the homocysteine/methionine metabolism, which could cause higher levels of HCY in CAD patients infected by *H. pylori* and the importance of *H. pylori* infection in determining the elevated HCY levels.

Conclusion

The present study demonstrated an inverse relationship between homocysteine levels and *H. pylori* seropositivity (IgG and IgA) and atherosclerosis occurrence in patients with CAD. Since classic risk factors are not able to explain all cases of CAD, the results of present study suggest that chronic *H. pylori* infection affect the development or maintenance of CAD, since it induces chronic long term infection within gastric epithelium which leads to not only local but systemic inflammation. According to our findings the involvement of *H. pylori* in this process is based on the chronic inflammation which might facilitate the CAD-related pathologies. Moreover, impact of the presence of *H. pylori* was found on homocysteine levels in such patients.

Study Limitations

In this study, small sample size was investigated and these observations should be confirmed in a larger sample of patients with more analysis works. We analyzed only two independent variables, it should be worthwhile to consider other probable variables involving in CAD disease in future studies.

Acknowledgement

This study was supported by a grant from the Iran University of Medical Sciences. The authors would like to thank Rasool Akram Hospital in the west of Tehran for providing the samples.

Disclosure of interest

The authors declare no conflicts of interest.

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