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Impact of *Helicobacter pylori* Infection on Serum Lipid Profile and Atherosclerosis of Carotid Artery

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Abstract

Background: *Helicobacter pylori* (*H. pylori*) infection has been suggested to be associated with atherosclerosis. The issue is still controversial. It is well known that abnormal lipid profile is related to atherosclerosis and measurement of carotid intima-media thickness. Aim of the study: to investigate carotid intima-media thickness and lipid parameters in *H. pylori*-positive and -negative subjects. Materials & Methods: This study was conducted in Kurdistan Teaching center of Gastroenterology and Hepatology (KCGH) in Sulaimani city during the period of December 2012 to March 2014. One hundred dyspeptic patients with *H. pylori* infection and 74 apparently healthy asymptomatic volunteers with *H. pylori*-negative tests were enrolled in this study. Both groups were comparable in age distribution and gender. *H. pylori* infection (IgG & IgA) were assessed by ELISA tests, Triglyceride, total cholesterol, low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) concentrations were measured by routine enzymatic methods using commercial kits. Carotid intima-media thickness was assessed by high-resolution ultrasound. Results: The mean and maximum values of internal and common carotid intima-media thickness in *H. pylori*-positive subjects were significantly thicker than in *H. pylori*-negative subjects ($p < 0.05$). HDL-C level was lower in patients (*H. pylori* seropositive) than in controls (seronegative subjects), total cholesterol, LDL-C and triglyceride level were found to be higher in patients than in controls ($p < 0.01$). Conclusions: Carotid intima-media thickness as well as all lipid values apart from HDL-C was increased in *H. pylori*-positive subjects. These data indicated that *H.*

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***pylori* infection may had a role in atherosclerotic process.**

Keywords

Dyspepsia, *H. pylori*, Lipid Profile, Atherosclerosis

1. Introduction

Atherosclerosis is a multifactorial disease whose age of onset and progression are strongly influenced by inborn and acquired risk factors [1]. Many studies showed that 80% - 90% of patients who developed clinically significant coronary artery disease (CAD) had at least one of four classical risk factors: hypercholesterolemia, hypertension, diabetes mellitus or smoking [2].

Carotid artery intima-media thickness (CIMT) is now widely used as an early marker for atherosclerotic disease [3]. The intima-media thickness of the common carotid artery (CCA) is thought to be associated with risk factors for stroke.

Atherosclerosis is an inflammatory disease and an association may exist between its development and infection with certain microorganisms [4]. Several studies have suggested that *H. pylori* infection can be involved in the pathogenesis of cardiovascular disease [5] [6]. Some studies have shown a positive correlation between *H. pylori* infection and the risk of cardiovascular disease [7] [8], whereas others have not confirmed such findings [9].

So the aim of this study was to investigate carotid intima-media thickness and lipid parameters in *H. pylori*-positive and -negative subjects.

2. Materials and Methods

This study was conducted in Kurdistan Teaching center of Gastroenterology and Hepatology (KCGH) in Sulaimani city during the period of December 2012 to March 2014. One hundred dyspeptic patients with *H. pylori* infection positive and 74 apparently healthy asymptomatic volunteers with *H. pylori* negative tests were enrolled in this study. Both groups were comparable in age distribution and gender.

2.1. Exclusion Criteria

1—Pregnant women.

2—Patients previously treated for *H. pylori* infection.

3—Who had received antibiotics; proton pump inhibitors or bismuth compounds in the preceding 4 weeks.

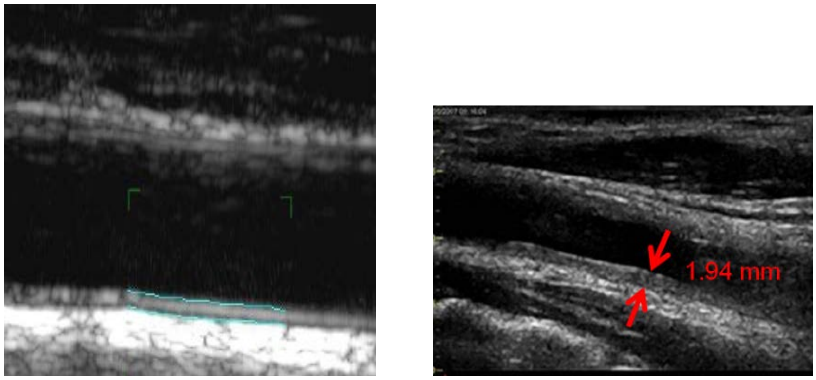
This study was approved by the Ethics Committee for Analysis of Research Projects of Faculty of Medicine, University of Sulaimani and Directory of Health in Sulaimani. Written informed consent was obtained from the patients prior to study participation.

A form designed to collect demographic data: name, age, gender, chief compliant of patients and duration of illness. Ten ml venous blood aspirated after overnight fasting then centrifuged at 5000 r/min for 5 min. Sera were tested for *H. pylori* IgG & IgA antibodies at Sulaimani Central lab., using ELISA tests (Nova Lisa, Nova-Tec, Germany), according to the standard operating procedures. That has a sensitivity of 97% and a specificity of 98.8%. Triglyceride, total cholesterol, low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) concentrations were measured by routine enzymatic methods using commercial kits (Elab Science, Germany).

Subjects were evaluated for both internal carotid (IC) and common carotid (CC) arteries and plaque occurrence by using high resolution grey-scale Doppler ultrasonography: Philips, En visor, Version C.1.3, 2007. In a semi-dark room, the subject lay supine with slightly hyper extended neck and rotated away from the imaging transducer. Both carotid arteries were scanned. CIMT was defined as the distance between the leading edge of the lumen intimal interface and the leading edge of the media adventitia interface of the far wall (3) **Figure 1**.

2.2. Statistical Analysis

All data were analyzed using Excel and SPSS (Version 20 software) computer program. Statistical analysis



(a) (b)

Figure 1. (a) Carotid intima-media thickness measurement in control group; (b) Carotid intima-media thickness measurement in patients.

included descriptive statistics like: a frequency, distribution tables, and correlation coefficient analysis. To assess the correlation between different variables, bivariate correlation coefficient analysis was performed. In this analysis, the statistical significant association was determined. All p values were based on 2-sided tests and $p < 0.05$ was considered statistically significant.

3. Results

Both groups of H. pylori seropositive and seronegative groups were comparable in mean age and gender, **Table 1**.

Both H. Pylori IgG and IgA levels were statistically higher in the patients group compared to the control group ($p < 0.01$) as shown in **Table 2**.

Significant differences were found between patients and controls in the levels of all lipid profile, ($p < 0.01$) as revealed by **Table 3**.

The intima-media thickness of both CCA and ICA was significantly higher in patients than in controls as shown in **Table 4**.

There was significant correlation between *H. Pylori* IgG concentration and total cholesterol, LDL-C level and inverse correlation with HDL-C level decreased; No significant correlation between *H. Pylori* IgG concentration and TG level; Also highly significant correlation between *H. Pylori* IgG level and carotid thickness ($p < 0.01$), **Table 5**.

4. Discussion

Some studies have demonstrated a relationship between *H. pylori* infection and extra digestive_tract disease [5] [6]. In this respect, cardiovascular disease is one of the most important diseases suggested to be related to infection which may be due to effect of infection on lipid metabolism [10]-[12].

Pellicano *et al*. reported significantly higher prevalence of *H. pylori* infection in patients with CAD than in controls (77% vs. 59%) [13]. Although these studies have suggested a relationship between *H. pylori* infection and coronary heart disease; some of the underlying mechanisms still need to be discovered. It has been reported that chronic *H. pylori* infection results in decreased HDL-C levels and these lipid alterations could, partially contribute to the initiation and development of coronary atherosclerosis [14] [15]. Infection and inflammation are associated with a decrease in HDL-C levels.

Major risk factors of atherosclerosis may explain only 50% of its etiology. Therefore, looking for new risk factors of atherosclerosis is necessary. HDL-C is a well known parameter inversely related to the risk for cardiovascular disease (CVD). It plays a key role in the reverse cholesterol transport, protects LDL against oxidation and reduces lipoprotein associated peroxides [16].

In the present study, HDL-C level was significantly lower in patients (*H. pylori* seropositive) than in controls (seronegative subjects), total cholesterol, LDL-C and triglyceride level were found to be significantly higher in patients than in controls ($P < 0.01$). Concerning the changes in serum lipids in seropositive subjects, the results of our study were similar to other studies [14] [17]-[21]. Buzás reported that the increase of cholesterol and

Table 1. Characteristics of patients and controls.

	Patients	Controls	P value
No.	100	75	
Age: (mean + SD)year	34.2 ± 8.5	30.1 ± 9.7	>0.05
Gender: No. (%)			
Male	54 (54)	39 (52)	>0.05
Female	46 (46)	36 (48)	

Table 2. *H. Pylori* titer in study population.

Investigations	Patients	Controls	P value
	Mean ± SD	Mean ± SD	
H. Pylori IgG (Au/ml)	68.4 ± 37.5	5.9 ± 0.99	<0.01
H. Pylori IgA (Ndx)	1.9 ± 1.4	0.60 ± 0.38	<0.01

Table 3. Lipid profile in study population.

Lipid profile (mg/dl)	Patients	Controls	P value
	Mean ± SD	Mean ± SD	
LDL	97.8 ± 26.6	78.2 ± 11.3	<0.01
HDL	40.6 ± 8.7	59.08 ± 9.3	<0.01
T. cholestrol	172.8 ± 30.5	143.7 ± 25.6	<0.01
S. Triglyceride	151.7 ± 60.9	88.7 ± 24.4	<0.01

Table 4. *H. Pylori* titer and Carotid thickness (CIMT) in study population.

Carotid thickness (mm)	Patients	Controls	P value
	Mean ± SD	Mean ± SD	
ICA	0.6 ± 0.16	0.45 ± 0.08	<0.01
CCA	0.6 ± 0.18	0.49 ± 0.07	<0.01

Table 5. Relationship between *H. Pylori* IgG level and lipid profile, Carotid thickness in patients.

Investigations	Correlation coefficient (r)	P value
LDL (mg/dl)	0.230	<0.01
HDL (mg/dl)	−0.258	<0.01
S. Cholesterol (mg/dl)	0.249	<0.05
TG (mg/dl)	0.031	>0.05
ICA (mm)	0.532	<0.01
CCA (mm)	0.456	<0.01

LDL-C and decrease of HDL-C levels of infected people creates an atherogenic lipid profile which could promote atherosclerosis with its complications [12]. While Akbas *et al*., reported that there was no significant differences in serum HDL-C, LDL-C and T. cholesterol level while serum TG levels of *H. pylori* positive subjects were significantly higher than those of *H. pylori* negative subjects [22]. These differences can be explained by different genetic factors, and type of the sample.

Previous studies have indicated that serum triglyceride and HDL-C levels can change during the acute phase of bacterial infection [23] [24]. These alterations promote atherogenesis, which have been attributed to the action of bacterial lipopolysacchride (LPS) [24]. Volanen expressed that the administration of endotoxin (LPS) induces the production of several cytokines, such as tumor necrosis factor (TNF-α) which increases serum trig-

lyceride level in animals. They have also suggested that changes in lipid profile seem to be related to the production of inflammatory cytokines by cells chronically infected with Gram-negative bacteria [24].

There is considerable evidence suggesting that ultrasonic measurements of early atherosclerosis are clinically significant. In prospective studies increased IMT has been related to an increased risk of cardiovascular diseases [25] [26]. There is conflicting data regarding CIMT and *H. pylori* infection. Some researchers have reported no relationship between *H. pylori* and CIMT [27] [28]. However, Akbas *et al.* reported the mean and maximum values of right and overall CIMT were significantly increased in *H. pylori* positive subjects compared with negative subjects [22]. Mete *et al*. reported that the right, the left and the mean CIMT were significantly higher in *H. pylori* positive group versus *H. pylori* negative group and these finding support our results [29].

We found a high correlation between *H. Pylori* IgG level and HDL level, carotid thickness ($p < 0.01$), and a moderate correlation between the level of *H. Pylori* IgG and T. cholesterol, LDL-cholesterol and triglyceride level. Those may be explained by several hypotheses to describe the mechanisms of this relationship with direct or indirect effects. *H. pylori* is a bacterium with effects like endothelial injury, smooth muscle proliferation, and local inflammation on the vascular wall. This bacterium has also indirect effects as proinflammatory, procoagulant, and atherogenic action; these can change risk factors (lipid profile, coagulation, levels of oxidative metabolites), production of cross-reactive antibodies, malabsoprtion of nutrients and vitamins, and metabolic factors such as overproduction of ammonia [30].

Acute and chronic infections causing the inflammation of arteries may promote the atherosclerotic cascade, induces a long standing low-grade persistent inflammation stimulus [31].

5. Conclusion

H. pylori infected people have increased CIMT and T. cholestrol, TG and LDL-C and decreased HDL-C levels that create an atherogenic lipid profile which could promote atherosclerosis.

Competing Interests

None.

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