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Original Article

Biochemistry Section

Lipid Profile in Cardiac Syndrome X: Association with *Helicobacter pylori*

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ABSTRACT

Introduction: Chronic inflammation caused by *Helicobacter pylori* (*H.pylori*) infection has a pathogenic role in Cardiac Syndrome X (CSX). In addition, it has shown that bacterial infection may affect blood lipids.

Aim: To assess if *H.pylori* affects the level of lipid profile in CSX.

Materials and Methods: Eighty-eight CSX patients and 97 healthy controls were enrolled. The Total Cholesterol (TC), Triglyceride (TG), Lipoprotein A (LP{A}), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL), Apoprotein A_1 ($APOA_1$), and Apoprotein B (APOB) was estimated colorimetrically. In addition, the presence of IgG antibody to *H.pylori* was tested in plasma samples by using enzyme linked immunosorbent assay method.

Results: TC, LP{A}, LDL, $APOA_1$ and APOB levels in CSX group were significantly higher than those of the control group ($p<0.05$). But, these parameters in *H.pylori* positive and *H.pylori* negative, among CSX and control groups were not significant.

Conclusion: Increased plasma level of lipid profile and *H.pylori* infection were associated with CSX; it seems that plasma lipid disorders have a significant role in the development of CSX.

Keywords: Angiography, Chest Pain, Infection, Inflammation, Lipoprotein

INTRODUCTION

Upto 30% of patients with chest pain, who undergo coronary arteriography, have completely normal coronary angiograms [1]. Patients with typical anginal chest pain, a positive response to stress testing and normal coronary angiogram are included in the subgroup with diagnosis of Cardiac Syndrome X (CSX) [2]. In the past 40 years, several mechanisms have been suggested to explain both chest pain and ischemic angina-like ST segment depression observed in the CSX patients [3]. Among the suggested pathophysiological mechanisms, endothelial dysfunction has a prominent role [3].

On the other hand, some studies have shown an association between coronary artery diseases including CSX and bacterial infections such as *Helicobacter pylori* (*H.pylori)* infection [4]. The host immune response against *H.pylori* could be determinant for the occurrence of extra-intestinal manifestations; in particular the virulent cytotoxin-associated gene A- positive ($CagA^+$) strain may evoke a more consistent release of cytokines with vasoactive properties [5]. On the other hand, some reports have indicated that the infection can enhance the serum lipid concentrations being also associated with an atherogenic lipid profile [6,7]. In addition, the administration of bacterial endotoxin induces the production of several cytokines, such as Tumour Necrosis Factor α (TNF-α) which increases serum triglyceride level in animals [8]. It is also indicated that lipid profile changes is related to the secretion of inflammatory cytokines by cells chronically infected with gram-negative bacteria such as *H.pylori* [9]. But there is no general consensus since other authors have not confirmed these findings. Therefore, the present study sought to analyse the association between lipid profile, *H.pylori* infection and CSX.

MATERIALS AND METHODS

The study was conducted between September 2009–June 2010.

Study population

CSX patients and apparently healthy controls were evaluated in this case-control study. The CSX group consisted of 88 patients (32 men, 56 women; mean age: 53.8±1.3 year). The patients were recruited from the Department of Cardiology in Urmia University of Medical Sciences (UMSU), Urmia, Iran. All CSX patients had a previously established the diagnosis of classic cardiac syndrome X, with a typical history of exertional angina, an abnormal exercise electrocardiogram and normal results on coronary angiography. Patients with non-cardiac causes of chest pain, such as gastro-intestinal and musculoskeletal disorders and diabetes mellitus were excluded from the study.

For the control group, 97 healthy blood donors (36 men, 61 women; age: 45.7±0.7 years) referred to the Regional Blood Transfusion Organization of the West Azerbaijan province, northwestern of Iran were enrolled. We divided CSX and control groups as *H.pylori* positive *(Hpylori$^+$)* and *H.pylori* negative *(Hpylori$^-$)* subgroups. None of the controls had a previous history of chest pain or acute/chronic diseases. Also, none of them were taking cardiac or non-cardiac medications. The study was approved by the university Research Medical Ethics Committee and all subjects gave written informed consent.

Laboratory Assays

A 5-ml tri-sodium-citrated blood sample was obtained from each subject and centrifuged at 2000×*g* for 15 minutes. Plasma was aliquoted and stored at –80°C until analysis. Anti-*H.pylori* immuno-globulin-G (IgG) concentration was evaluated with a commercial enzyme-linked immunosorbent assay. (ELISA; Glob anti-HP/IgG, Milan, Italy) according to the manufacturer's instruction (sensitivity 96.5% and specificity 98.6%). Also, plasma lipid profile, which include Total Cholesterol (TC), Triglyceride (TG), Lipoprotein A (LP{A}), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL), Apoprotein A_1 ($APOA_1$), and Apoprotein B (APOB), were measured enzymatically (Pars Azmon, Iran).

STATISTICAL ANALYSIS

The data were analysed by SPSS 16.0 software. Data were shown as mean ± standard error of mean.

The differences between the groups and subgroups were interpreted on the basis of independent-samples *t*-test and for qualitative data on the basis of chi-square test. A p-value less than 0.05 were considered statistically significant.

RESULTS

[Table/Fig-1] shows the demographic characteristics and lipid profile of the CSX and control groups. Significant lipid profile differences emerged at the t-test from the comparison of CSX with controls in TC, LDL-C, HDL-C, $APOA_1$, APOB, and LP{A} levels. But TG levels are not significant.

On the other hand, anti- *H.pylori* antibody was diagnosed in 82 (93.2%) in CSX patients and 56 (57.7%) individuals in control group (p=0.001). Change in the mean amount of lipid profile in *H.pylori*$^+$ group of CSX in comparison with *H.pylori*$^-$ group was not significant except HDL-C levels. In addition, lipid profile assessment in control group showed that these parameters in *H.pylori*$^+$ patients were not significant [Table/Fig-2].

Variable	CSX	Controls	p-value
gender(male/female)	32/ 56	36/ 61	0.916
Age (years)	53.8±1.3	45.7±0.7	0.001
BMI* (kg/m^2)	27.2±0.5	26.1±0.3	0.070
TC (mg/dl)	157.0±4.5	118.3±4.5	<0.001
TG (mg/dl)	149.0±7.6	131.0±10.9	0.187
LDL-C (mg/dl)	91.4±3.0	68.4±2.1	<0.001
HDL-C (mg/dl)	36.3±0.9	28.4±0.9	<0.001
$APOA_1$ (mg/dl)	120.6±1.4	106.5±1.5	<0.001
APOB (mg/dl)	97.5±2.6	77.1±2.2	<0.001
LP[A] (mg/dl)	42.2±5.7	25.2±4.5	0.019

[Table/Fig-1]: The main demographic characteristics and lipid profile of CSX and control groups.
*BMI(body mass index), total cholesterol (TC), triglyceride (TG), lipoprotein A (LP[A]), low density lipoprotein (LDL), high density lipoprotein (HDL), apoprotein A_1 (APOA1), and apoprotein B (APOB)

	CSX			Control		
Lipid profile	*H.pylori*$^+$ (n=82)	*H.pylori*$^-$ (n=6)	p	*H.pylori*$^+$ (n=56)	*H.pylori*$^-$ (n=41)	p
TC (mg/dl)	157.2±4.7	158.7±17.3	0.937	121.1±4.7	114.4±6.0	0.374
TG (mg/dl)	151.9±8.0	109.5±14.8	0.162	127.6±9.4	135.7±22.5	0.717
LDL-C (mg/dl)	91.6±3.1	94.3±9.9	0.823	71.7±2.9	63.9±2.9	0.066
HDL-C (mg/dl)	35.9±0.9	43.00±5.3	0.044	29.4±1.3	27.1±1.2	0.216
$APOA_1$ (mg/dl)	120.2±1.5	125.8±10.3	0.326	108.3±2.3	104.1±1.6	0.170
APOB (mg/dl)	97.8±2.7	93.5±8.0	0.675	80.5±2.9	72.3±3.3	0.064
LP[A] (mg/dl)	43.2±6.0	28.3±11.7	0.511	29.6±7.1	19.2±4.4	0.259

[Table/Fig-2]: Lipid profile of *H.pylori*$^+$ and *H.pylori*$^-$ in CSX and control groups.
*Total cholesterol (TC), triglyceride (TG), lipoprotein A (LP[A]), low density lipoprotein (LDL), high density lipoprotein (HDL), apoprotein A_1 (APOA1), and apoprotein B (APOB)

DISCUSSION

CSX is associated with a wide range of clinical characteristics which may reflect differences in aetiology and outcome. Several pathophysiologic mechanisms have been suggested for CSX. Inflammation, endothelial dysfunction, impaired pain perception, abnormal response to vasodilator stimuli and insulin resistance are among the suggested aetiologies of CSX [2,10]. Also, dyslipidemia leads to meaningful increase in the development of cardiac disorders include CSX. In our study, there was an increase in lipid profile of CSX patients versus controls. But, the increase in HDL-C level of CSX patients may be due to contraceptive drugs consumption. A few reports suggested that contraceptives increase the level of HDL-C [11,12].

Additionally, there are several possibilities for the mechanism underlying a causal role of *H.pylori* infection in endothelial dysfunction [13]. In other words, *H.pylori* may cause chronic inflammation and immune response with the release of some cytotoxic substances which are mainly responsible for systemic manifestations of *H.pylori* [14]. On the other hand, Lanza *et al*., showed that increase in C-reactive protein and interleukin-1 receptor antagonist, two systemic inflammatory factors, in CSX patients compared to healthy individuals, suggesting the possible pathogenic role of low grade inflammation in patients with CSX [15]. Moreover, the association of infection with CagA- positive *H.pylori* strains and CSX was confirmed in some studies. A case-control study of 60 CSX patients and 60 healthy controls found that the prevalence of CagA-positive strains was higher in patients than controls in a previous study. So it was concluded that *H.pylori* and prominently its CagA$^+$ strain infection causes chronic inflammation and increases the generation of various inflammatory metabolites such as cytokines. Increase in these factors may lead to endothelial dysfunction which is the most prominent cause of the CSX [5,16]. On the other hand, previous studies have showed that serum triglyceride and HDL-cholesterol levels can change during the acute phase of bacterial infection [6]. These alterations promote atherogenesis, which have been attributed to the action of bacterial lipopolysacchride. Some studies showed the casual relationship between changes in lipid profile and inflammatory cytokines produced by cells chronically infected with Gram-negative bacteria such as *H.pylori* [9]. But, the association between *H. pylori* infection and serum lipid profiles is still controversial and this study finding did not confirm the existence of an association between *H. pylori* infection and lipid modulation.

LIMITATION

This study had potential limitations that should be mentioned. In the present study, there was not any significant difference in lipid profile between *H.pylori*$^+$ and *H.pylori*$^-$.Variation in HDL levels could not be compared as sample size was limited in *H.pylori*- and *H.pylori*+ of CSX group. The other limitation of this study was lack of a healthy age matched group, to compare with CSX patients. Hence, the conclusions on the lipid profile differences of CSX patients with healthy subjects could not be ascertained.

CONCLUSION

The present study found an increase in the lipid profile in CSX group. So, it can be concluded that the lipid disorders may play a role in the development of CSX. Increased lipid profile and chronic infection are related with CSX. But we could not find any relationship between *H.pylori* infection and lipid profile in CSX and control group. However, other co-factors might be involved in the lipid modulation along with the strain of *H. pylori* including host genetic and environment factors. The results of this study might be a substrate for clinical differentiation of CSX and other cardiovascular disorders and for more comprehensive planning for diagnostic tests.

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