CORRELATION BETWEEN HIGH SENSITIVITY C-REACTIVE PROTEIN AND CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH HELICOBACTER PYLORI INFECTION

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ABSTRACT

Background

Helicobacter pylori (*H. pylori*) infection in gastric mucosa may cause systemic inflammatory reaction, which increases risk of cardiovascular disease and atherosclerosis.

Objetives

This study aimed to assess the association between *H. pylori* infection and serum high sensitivity C-reactive protein (hsCRP), and carotid intima media thickness.

Patients and Methods

This is a case control study, conducted at Kurdistan center for Gastroenterology & Hepatology from Dec. 2012 to March 2014. One hundred patients with dyspepsia and positive *H. pylori*. 75 (39 males and 36 females) non dyspeptic apparently healthy subject with *H. pylori* negative as control group were assessed. The serum sample tested for *H. pylori* infection and Hs-CRP using ELISA and stool sample examined by using Rapid Immunoassay method to detect *H. pylori* antigens.

Results

The mean hs-CRP level was significantly different ($P<0.01$) between patients and controls. A significant correlation between different tests of *H. pylori* and hs-CRP level was found ($p < 0.01$). A significant correlation was found between hs-CRP level and internal carotid artery (ICA), common carotid artery (CCA) thickness in patients ($p < 0.01$).

Conclusion

H. pylori infection was significantly associated with higher serum hs-CRP.There was significant correlation between hs-CRP and carotid intima-media thickness.

Keywords: *H. pylori, hs-CRP, Carotid Thickness, Sulaimani.*

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INTRODUCTION

Higher levels of inflammatory markers are associated with a higher risk of cardiovascular disease; consistent with the concept that atherosclerosis is an inflammatory process [1]. C-reactive protein is a sensitive indicator of acute and chronic inflammation, and an elevated serum level of CRP in apparently healthy men and women is a predictor of the risk of cardiovascular events or degree of atherosclerosis in patients with coronary artery disease(CAD) [2, 3]. Carotid Intima Media Thickness CIMT is now widely used as an early marker for atherosclerotic disease [4].

High levels of CRP have previously been found to be associated with arterial inflammation, central to the initiation and progression of atherosclerosis [5]. Increased inflammation due to *H. pylori* (cagA) infection may have a significant bearing on the pathogenesis of atherosclerosis, although an association of this infection with CAD is controversial [6, 7]. Kanbay et al., hypothesized that this organism could be a major risk factor for endothelial dysfunction by virtue of its association in the elevation of some proinflammatory cytokines, particularly CRP [8].

Several ways of H pylori testing exist. One can test noninvasively for *H. pylori* infection with a blood antibody test, stool antigen test [9]. However, the most reliable method for detecting *H. pylori* infection is a biopsy check during endoscopy.

This study aimed to examine the association between the *H. pylori* infection and serum hs-CRP, and to assess the relationship between serum hs-CRP and carotids intima thickness.

MATERIALS AND METHODS

This study enrolled 100 patients (54 males and 46 females) with dyspepsia, attending Kurdistan Center of Gastroenterology &Hepatology (KCGH) in Sulaimani city and 75 (39 males and 36 females) non dyspeptic (*H. pylori* negative) apparently healthy subject as control group were assessed, during the period of December 2012 to March 2014. Both groups were comparable regarding mean age, gender, BMI, not diabetic or hypertensive, non smoker and all were below 50 years of age.

Exclusion criteria

1. Pregnant,

2. Who had fever,

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

This study was approved by the Ethical Committee of Faculty of Medicine, University of Sulaimani and Sulaimani directorate of Health. Written informed consent was obtained from the participants.

Five ml venous blood aspirated then centrifuged at 5 000 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),

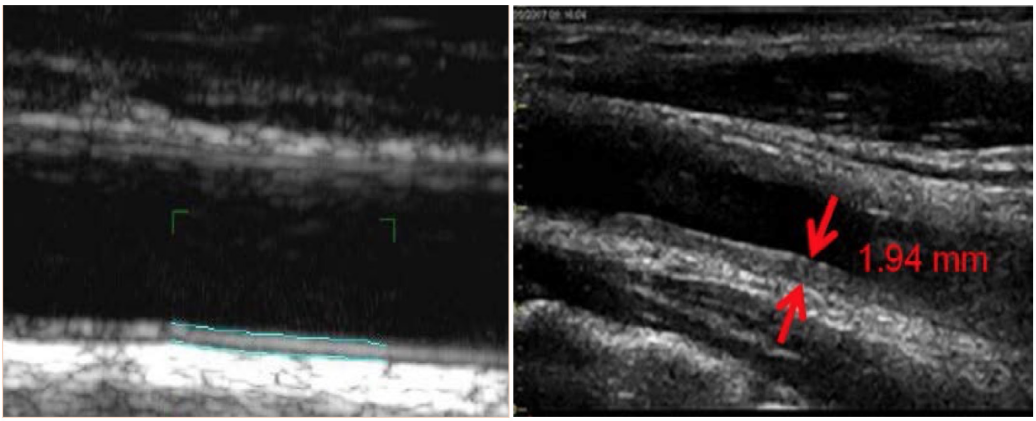
Hs-CRP was measured based on immunoenzymometric assay (Monobind Inc., Accu-Bind ELISA kit, hs-CRP: 3125-300, USA) . Normal range as follows: Low risk: <1.0 mg/L, Average risk: 1.0 ~ 3.0 mg/L, High risk: >3.0 mg/L.

Stool Antigen test: Stool specimens were taken in reference laboratory and tested using the stool antigen test kits (Rapid Immunoassay method, Coris Bioconcept C-1019, Belgium).

Endoscopy: After fasting overnight, esophago-gastro-duodenoscopy was performed with an Olympus videoscope, 4 gastric biopsies (from antrum and body) were taken from each patient. Biopsies were sent to the laboratory in formalin solution for histological examination using (Hematoxylin and eosin stain and modified Giemsa stain).

All of the 3 tests were performed for each patient. When the results of at least 2 tests were positive, *H. pylori* infection was considered to be positive.

All Patients were evaluated by a single expert for both internal carotid (IC) and common carotid (CC) intima media thickness (CIMT) 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 hyperextended neck and rotated away from the imaging transducer. Both carotid arteries were scanned. IMT measurement at a distance of at least 5 mm below the distal end of CCA, IMT measured at end-diastole (R wave), 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, Figure 1.



(a) **(b)**

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

According to European Society of Cardiology (ESC), Intima-media thickness values of more than 0.9 mm should be considered abnormal [10].

All data were analyzed using Excel and SPSS (Version 21 software) computer program. 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 $p \leq 0.05$ was considered statistically significant.

RESULTS

Both groups of *H. pylori* seropositive (patients) and seronegative (control) groups were comparable in mean age and gender ($p>0.05$).

The mean hs-CRP among patients and controls were (1.57 + 1.34) and (0.53 + 0.21) mg/L respectively, with highly significant difference ($p< 0.01$), Table 1.

A positive correlation between hs-CRP level and different types of *H. pylori* tests was found, which was statistically significant ($p < 0.01$), Table 2.

A moderate correlation between hs-CRP level and ICA, CCA thickness in patients was found ($r = 0.375$), ($r = 0.364$) respectively, which is statistically significant ($p < 0.01$), Figure 1 & 2 respectively.

Table 1. Hs-CRP level in patients and control.

Investigation	Patients	Controls	p value
	Mean ±SD	Mean± SD	
hs-CRP (mg/L)	1.57±1.34	0.53±0.21	< 0.01

Table 2. Relationship between hs-CRP and different *H. pylori* tests in patients.

hs-CRP (mg/L)	Correlation coefficient (r)	p value
H. pylori IgG(Au/ml)	0.447	< 0.01
H. pylori IgA (Ndx)	0.266	< 0.01
Stool Ag	0.324	< 0.01
Biopsy	0.468	< 0.01

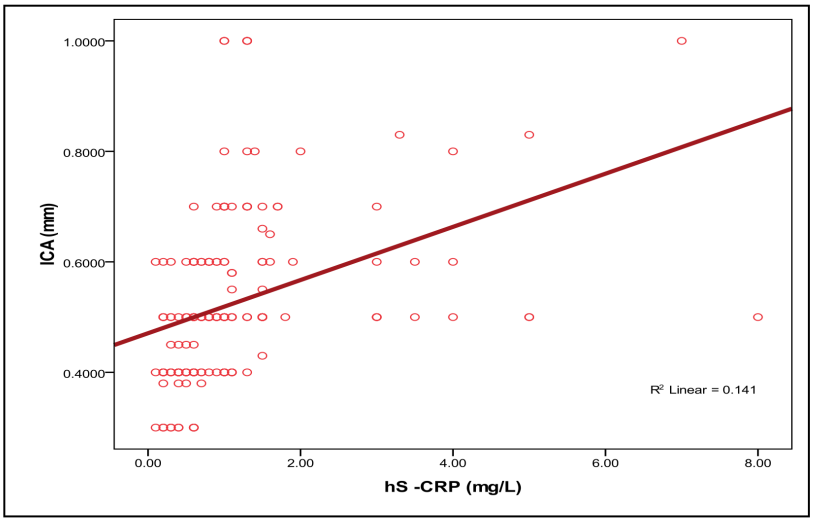


Figure 2. Relationship between hs-CRP level and ICA thickness in *H. pylori* positive patients.

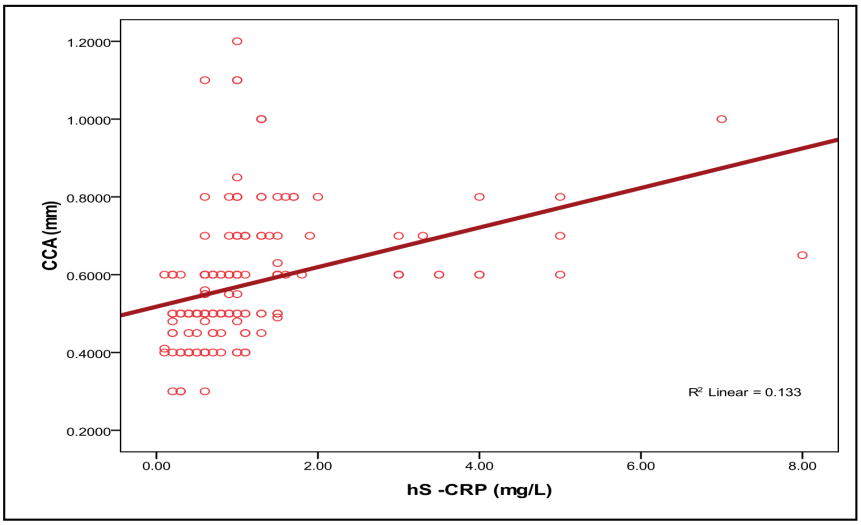


Figure 3. Relationship between hs-CRP level and CCA thickness in *H. pylori* positive patients.

DISCUSSION

In this study, serum levels of hs-CRP were higher in *H. pylori*-infected patients than in control group. These observations are consistent with findings of other studies [7, 11, 12]. Other studies demonstrated that serum levels of hs-CRP were significantly reduced after eradication of *H. pylori* [13, 14]. The mechanisms responsible for induction of CRP synthesis in *H. pylori* infections remains to be determined [15].

However, the higher concentration of hs-CRP in the *H. pylori*-infected group may be because of induction of subclinical micro-inflammatory reactions by *H. pylori* while low concentration of hs-CRP in the healthy *H. pylori*-negative group might represent physiological status [11].

In this study, there was a significant correlation between hs-CRP and different types of *H. pylori* tests, this can be explained by that the CRP is a sensitive indicator of acute and chronic inflammation [16].

CRP is a marker of inflammation and infection of the gastric mucosa with *H. pylori*, which causes an inflammatory reaction [10]. CRP is an acute-phase protein which has been identified as a marker of inflammation that can be used for diagnosis and follow-up of some inflammatory diseases [15]. Moreover, CRP is a phylogenetically highly conserved plasma protein; with homologous invertebrates and many invertebrates that participate in the systemic response to inflammation. Its rapid increase in synthesis within hours after tissue injury or infection suggests that it contributes to host defense and that it is part of the innate immune response [17].

In this study, there was a significant correlation between hs-CRP level and ICA, CCA thickness in patients. This is consistence with other studies that suggested there was relation between the levels of CRP and risk of coronary disease [18]. Two other studies have suggested that serum concentrations of CRP were significant predictors of coronary heart disease even after adjusting for conventional risk factors for coronary heart disease, including serum lipid levels, smoking status and BMI [19, 20]. Injury to the vessel wall and the associated inflammatory response are now generally recognized as essential components of atherogenesis [21].

C-reactive protein has been identified as an independent risk factor for cardiovascular disease and can also be regarded as a valuable tool for estimation of at risk populations [22] and has a role in pathophysiology of plaque development/ progression in CAD patients [23].

It has also been reported that measurement of serum levels of CRP using a high-sensitivity assay (hs-CRP) can reveal subclinical inflammatory states which may reflect vascular inflammation [16, 22]. Jafarzadeh et al. reported that serum levels of hs-CRP were significantly higher in patients with ischemic heart disease than in a healthy control group [24]. Chronic infection as *H. pylori* has been proposed as a possible causative agent in the development of acute coronary syndrome [15, 25].

In conclusion, *H. pylori* infection was significantly associated with higher serum hs-CRP.There was significant correlation between hs-CRP level and Carotid intima- media thickness.

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