INTRODUCTION

Helicobacter pylori (H. pylori) is a gram-negative, spiral-shaped bacterium that specifically colonizes the gastric epithelium causing chronic gastritis, peptic ulcer disease, and/or gastric malignancy Helicobacter pylori and gastric cancer. Gastroenterol Clin. (14) H. pylori is mainly acquired in childhood by the fecal-oral, oral-oral or gastro-oral route, and has been recognized as a worldwide public health problem that is more prevalent in developing countries. The infection induces an acute polymorphonuclear infiltration in the gastric mucosa, which is gradually replaced by an immunologically-mediated, chronic, predominantly mononuclear cellular infiltration.

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The mononuclear infiltration is characterized by the local production and systemic diffusion of pro-inflammatory cytokines that can affect remote tissues and organic systems. As a result, an increased prevalence of extra-digestive diseases has been reported in those with evidence of H. pylori infection in recent years, including ischemic heart disease Epidemiology of Helicobacter pylori infection (Tan and Goh, 2012). Coronary artery disease (CAD) also known as atherosclerotic heart disease, atherosclerotic cardiovascular disease, coronary heart disease, or ischemic heart disease (IHD), is the most common type of heart disease and cause of heart attacks. (Coronary heart disease". (Lobo, 2008) The disease is caused by plaque building up along the inner walls of the arteries of the heart, which narrows the lumen of arteries and reduces blood flow to the heart. Nowadays the most common risk factors for atherosclerosis process which cause coronary heart diseases (CHD) include diabetes, dyslipidemia, hypertension, and smoking (Onat et al., 2007). The inflammation processes and atherogenesis have many similarities, and the role of an
active inflammatory process in atherosclerosis pathogenesis of the coronary circulation is al growing. Significantly, monocytes and macrophages are recognized as components of atheromatous plaques for several years. The risk of cardiovascular events is associated with increased levels of the acute phase proteins, fibrinogen, C-reactive protein (CRP), and proinflammatory cytokines (Ridker et al., 2000). For this reason, chronic inflammation is considered as a risk factor for CHD, and vascular injury, inflammation, and thrombosis are considered to cause atherosclerosis whereas the stimulus that generates the inflammatory response has remained unclear. (Ridker et al., 2000). The aim of this study was to evaluate the association between HP infection and CAD in suspected patients referred for diagnosis coronary angiography.

**MATERIAL AND METHODS**

**Study Population**

In this cross-sectional study, 140 patients with suspected CAD referred to khartoum Hospital of sudan for diagnosis coronary angiography were prospectively enrolled from January to June 2015 and all of them underwent physical examinations. In data evaluation, age, gender, patient's history (history of hypertension (indicated by systolic blood pressure 140 mmHg, diastolic blood pressure of 90 mmHg, or antihypertensive medication), diabetes mellitus, stroke, CCU admission, cardiac diseases and cardiac failure, renal insufficiency, and smoking (Patients who had stopped smoking for 10 years or less were classified as smokers)), and biochemical parameters (total cholesterol, low density lipoprotein (LDL) cholesterol, and CRP) were recorded.

**Exclusion criteria**

Patients with severe renal (creatinine 2 mg/dL) or hepatic failure, anemia, endocrine or neurological diseases or malignancies, and previous HP infection treatment were excluded.

**Blood sample**

Venous blood samples were obtained and stored at 4°C. Serum was acquired by centrifugation of blood samples at 2000 r/min for 15 minutes, immediately after sampling.

**Inclusion Criteria**

Coronary angiography was performed by femoral artery using Judkins method (Bush et al., 1993). Two experienced cardiologists unaware of the patients’ enrollment reviewed all angiograms. If they did not have the same view, the third cardiologist saw the angiographic film and then, based on angiographic results, patients were divided into two groups with and without coronary artery disease.

**Statistical analysis**

Statistical evaluation of all data was done on IBM-PC microprocessor computer using SPSS software for windows (Statistical Package for Social Sciences version 11, USA) for data management and analysis and the excel for figures. Quantitative data were presented as mean ± SD. Quantitative variables with normal distribution were analyzed with a two-tailed, paired Student's t test. ANOVA (F) test with Bonferroni multiple comparisons were used for comparison between more than 2 groups. Qualitative variables such as comparison between proportion & percentage by Chi square with Yates correction as necessary. Pearson correlation coefficient was used to correlate between variables. P value under 0.05 was considered statistically significant.

**RESULTS**

In this study 140 patients were allocated in two groups according to positive 70 patients) and negative CAD (70patients) all this patients were hp.pylori positive. Detailed division in subgroups with single- and multi vessel CAD (positive CAD) and control group (negative CAD) is presented in Tables 1-2.

**DISCUSSION**

In the new decade, many study evaluated the role of H. pylori infection in extra-digestive disorders and the results was surprising. For examples, one study showed that H. pylori infection decrease the blood pressure value in patients who suffer from hypertension (Danesh et al., 1999). In addition, a few studies have demonstrated the association of some kinds of DLP and H. pylori infection (0Izadi et al., 2012; Vcev et al., 2007). In a case control study, relationship of H. pylori infection with insulin resistance was suggested (Tamer et al., 2009). On the other hand, it was documented that this gram negative bacterium induces the higher levels of some inflammatory biomarkers like CRP and IL-6. (Kowalski, 2001; Wald et al., 1997). Accordingly, H. pylori association with some cardiovascular risk factors has been suggested and also it was shown that this bacterium induces some inflammatory cytokines. In the present study, the role of these risk factors and cytokines were adjusted, therefore, the remained higher chance may be due this adjusting and reveal the independent role of H.pylori infection in atherosclerosis process. One study in a Korean population by Lee et al. (2008) suggested that H. pylori infection is not an independent risk factor for CHD.

In their study, method of data adjusting were different from our study and prothrombin time, activated partial thrombin time, CRP, and fibrinogen were used for adjusting. Also, an upper gastrointestinal endoscopy for diagnosis of H. pylori infection was used, so these differences in methods of two studies probably justifies these different findings. Mechanisms which were suggested as responsible for the possible association of H. pylori infection and CHD are as follows: (Danesh et al., 1999; Tamer et al., 2009; Strachan et al., 1998).
Firstly, damaging influence of H. pylori and its products like cytokines, cytoxins on coronary endothelium; secondly, activation of immune mechanisms by this bacteria which react with the nuclei of monocytes in atherosclerotic vessel wall and cytoplasm of fibroblast-like cell in atherosclerosis plaques; thirdly, H. pylori induces releasing of nitric oxide by vascular endothelium interferes with fibrinogen level which cause the reduction of the normal capacity of muscular relaxation and lead to vasoconstriction and adverse hemodynamic balance; finally, this infection elevates thromboxane which is measured as TXB that results in platelets activation. This study and other studies suggest this hypothesis that HP can be associated with CAD or even consider it as a risk factor that plays a role in atherosclerosis plaque formation (Rogha et al., 2012; Vcev et al., 2007).

HP infection has been suggested to influence the development of atherosclerotic changes in coronary arteries, indicating a damaging effect of this bacterium or its products (e.g., cytokines, endotoxins, cytoxins, and other virulence factors) on the coronary endothelium. On the other side, chronic HP infection is known to increase the pH level of the gastric juice and to decrease ascorbic acid levels, both of which will cause folate absorption reduction. Low folate hampers the methionine synthase reaction. This will increase blood homocysteine concentration which results in damage of endothelial cells (Corrado and Novo, 2005).

Siddiqui et al. evaluated the homocysteine level in CAD patients with HP infection and found no difference (Siddiqui et al., 2009). Also, large population-based studies suggested the relation between the CRP levels and risk of coronary artery disease (Corrado and Novo, 2005). The association between HP infection and plasma levels of CRP, has been investigated by Pienjzek et al. (Pienjzek et al., 1999). Also, Gastric infection with HP may also induce the synthesis of acute phase reactants and activate immune mechanisms due to cross-reacting antibodies to HP and heat shock protein (HSP 60/65) with endothelial-derived HSP 60/65 (Mendall et al., 1996; Birnie et al., 1998). Mendall et al. found a strict. Also some studies suggest the coagulability stimulation caused by HP. Niemelä et al. and de Luis et al. have demonstrated that HP infection causes thrombotic protein changes (Niemelä et al., 1996; De Luis et al., 1999). The association between HP infection and fibrinogen has been investigated by Pienjzek et al. (1999). One interesting hypothesis is stimulated platelet aggregation by Helicobacter pylori. Results showed that some HP strains are able to bind to the von Willebrand factor to interact with glycoprotein Ib and to induce platelet aggregation in humans and HP may eventually affect IHD by eliciting thrombosis (Fagoonee et al., 2010).

Also, Elizalde shows that circulating platelet aggregates and activated platelets were also detected in HP infected patients (Elizalde et al., 2010). Also it seems that CHD is one of the extra gastrointestinal diseases and some studies showed its association with HP infection (Jin et al., 2007; Danesh et al., 1999). The role of inflammation mechanism in the pathogenesis and progression of coronary artery disease has been increasingly explored but still remains to be elucidated. Epidemiological studies based on serological findings have suggested an association between chronic HP infection and atherosclerosis, although controversies exist. In Izadi et al.'s study on 105 patients under CABG, PCR test result was positive Helicobacter species for 31 (29.5%) specimens from coronary artery atherosclerotic plaques. Also in serologic tests 25 (23.8%) were positive for HP immunoglobulin A (IgA) and 56 (53.3%) were positive for anti-HP immunoglobulin G (IgG) (0Zadi et al., 2012). This study and other studies suggest this hypothesis that HP can be associated with CAD or even consider it as a risk factor that plays a role in atherosclerosis plaque formation (9, 19). We found a positive association between HP infection and CAD. This is similar to Rogha et al.'s study which found a positive association between HP seropositivity and CAD in 112 patients candidate for coronary angiography (OR 3.18, 95% CI = 1.08–9.40) (Rogha et al., 2012). Also, Vcev et al. showed this positive association (Vcev et al., 2007). The results of this study showed a higher seroprevalence of HP infection in patients with CAD compared to controls (78.8% versus 58.3%).

In our study, HP seropositive patients had different risk factors which were observed in other studies. Seropositivity rates for HP were significantly higher in patients with coronary artery disease than in controls. In contrast, Rogha et al. did not confirm the association between HP and CAD. They studied 105 subjects and found that HP infection and CagA Ab were not significantly higher compared to the patients with severe and mild CHD ( = 0.28 and = 0.68, resp.). Colonization of CagA positive HP did not significantly associate with severity of CHD (OR = 1.05, 95% CI = 0.33–3.39) (Rogha et al., 2012). In our study, like Tamer et al. and Siddiqui et al.'s study, the CRP level was higher in CAD patients. In Tamer et al.'s study, CRP level was different among patients with and without CAD but HP infection did not differ in both groups (Tamer et al., 2009).

Conclusion

According to our study, HP seropositive patients are at higher risk for CAD and the number of their involved arteries is greater. Given the high prevalence of HP infection and as coronary artery disease is the major cause of mortality in this population, this issue is of importance and in case of proving this causal relationship, we can avoid mortality due to CAD2.4.

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