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## Review Article

# ASSOCIATION BETWEEN H.PYLORI AND CORONARY HEART DISEASE AMONG SUDANESE PATIENTS

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**ABSTRACT**

**Background:** Helicobacter pylori (HP) infection is the most common infection in the world and coronary artery disease (CAD) is probably associated with it.
**Objective:** The aim of this study was to evaluate the association between HP infection and CAD in suspected patients referred for diagnosis coronary angiography.
**Methodology:** 140 patients were divided in two group , in the first group there 70 patients (29 female, 41 male ) having h.pylori positive and coronary heart disease . in the second group , which is arrange as acontrol group there were 70 patients having h,pylori positive with out coronary heart disease . this cross –sectional study referred to heart center Enrolled from January to march 2015 and all of them under went physical examination . in data evaluation age , gender , patient history and bio chemical parameters ( total cholesterol , low density lipoprotein (LDL), H.pylori ,and CRP ) were recorded . The serum HP IgG antibody was measured using ELISa`. While other parameters measured using spectorophotometer (MINDARY**.**
**Result: (** mean +,- SD) of serum totalcholestrol ,CRP, LDL in the group which had h.pylori positive and coronary heart disease **(** (175.29-47.975) ,( 21.91-17.799), (107.66-44.565) **)** while in control group which had h,pylori positive with out coronary heart disease **(** (166.00-44.211),(125.47-37.201), (9.13-1.689))
**Conclution:** this study revelaed the serum of total cholesterol, CRP were significantly increase in group which had h.ylori positive and coronary heart disease. while in other group which had h,pylori positive with out coronary heart disease the serum of LDL was significantly increase .



## 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 lumenof 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

### Inclution 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.

**Table 1. Mean +,- SD of serum in study population**

| Parameter | Groups | mean | Std. Deviation | P-Value |
|---|---|---|---|---|
| Total cholesterol | Control | 166.00 | 44.211 | 0.24** |
| | Patient | 175.29 | 47.975 | |
| LDL | Control | 125.47 | 37.201 | 0.01* |
| | Patient | 107.66 | 44.565 | |
| CRP | Control | 9.13 | 1.689 | 0.00* |
| | Patient | 21.91 | 17.799 | |

** Not significant different at the 0.05 level.
* Significant different at the 0.05 level.

## DISCSSUION

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, cytotoxins 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, cytotoxins, 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 hemocysteine concentration which results in damage of endothelial cells (Corrado and Novo, 2005).

Siddiqui *et al*. evaluated the hemocysteine 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*. (Pieni *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) (0Izadi *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.

## REFERENCES

Birnie, D.H., Holme, E.R., McKay, I.C., Hood, S., McColl, K.E.L. and Hillis,W.S. 1998. "Association between antibodies to heat shock protein 65 and coronary atherosclerosis. Possible mechanism of action of Helicobacter pylori and other bacterial infections in increasing cardiovascular risk," *European Heart Journal,* 19(3):387–394.

Bush, C.A., VanFossen, D.B., Kolibash, Jr. A. J. *et al*., 1993. "Cardiac catheterization and coronary angiography using 5 French preformed (Judkins) catheters from the percutaneous right brachial approach: a comparative analysis with the femoral approach," Catheterization and Cardiovascular Diagnosis, 29(4):267–272.

Corrado, E. and Novo, S. 2005. "Role of inflammation and infection in vascular disease," *Acta Chirurgica Belgica,* 105(6):567–579.

Danesh, J., Youngman, L., Clark, S., Parish, S., Peto, R. and Collins, R. 1999. "Helicobacter pylori infection and early onset myocardial infarction: case-control and sibling pairs study," *British Medical Journal*, 319 (7218): 1157–1162.

De Luis, D.A., Avello, A.G., Lasuncion, M.A. *et al*. 1999. "Improvement in lipid and haemostasis patterns after Helicobacter pylori infection eradication in type 1 diabetic patients," Clinical Nutrition, 18(4): 227–231.

Eeskandarian, R., Ghorbani, R., Shiyasi, M., Momeni, B., Hajifathalian, K. and Madani, M. 2012. "Prognostic role of Helicobacter pylori infection in acute coronary syndrome: a prospective cohort study," *Cardiovascular Journal of Africa*, 23(3): 131–135.

Elizalde, J.I., Gomez, J., Panés, J. *et al*. 2010. "Platelet activation in mice and human Helicobacter pylori infection," *The Journal of Clinical Investigation*, 100(5): 996–1005.

Fagoonee, S., De Angelis, C., Elia, C. *et al*. 2010. "Potential link between Helicobacter pylori and ischemic heart disease: does the bacterium elicit thrombosis?" *Minerva Medica,*101(2): 121–125.

Gasbarrini, A., Franceschi, F., Cammarota, G. Pola, P. and Gasbarrini, G. 1998. "Vascular and immunological disorders associated with Helicobacter pylori infection," Italian *Journal of Gastroenterology and Hepatology,* 30(1):115–118.

Huang, J.Q., Zheng, G.F., Sumanac, Irvine, K.E.J. and Hunt, R. H. 2003. "Meta-analysis of the relationship between cagA seropositivity and gastric cancer," *Gastroenterology*, 125( 6): 1636–1644.

Izadi, M., Fazel, M., Sharubandi, S.H. *et al*., 2012. "Helicobacter species in the atherosclerotic plaques of patients with coronary artery disease," *Cardiovascular Pathology*, 21(4): 307–311.

Jia, E.Z., Zhao, F.J., Hao, B. *et al*. 2009. "Helicobacter pylori infection is associated with decreased serum levels of high density lipoprotein, but not with the severity of coronary atherosclerosis," Lipids in Health and Disease, 8(59):100-120.

Jin, S.W., Her, S.H., Lee, J.M. *et al*., 2007. "The association between current Helicobacter pylori infection and coronary artery disease," *Korean Journal of Internal Medicine*, 22 (3):152–156.

Khodaii, Z., Vakili, H., Ghaderian, S. M. H , Najar, R .A. and Panah, A.S.T. 2011. "Association of Helicobacter pylori infection with acute myocardial infarction," Coronary Artery Disease, 22(1): 6–11.

Kowalski, M. 2001. "Helicobacter pylori (H. pylori) infection in coronary artery disease: influence of H. pylori eradication on coronary artery lumen after percutaneous transluminal coronary angioplasty. The detection of H. pylori specific dna in human coronary atherosclerotic plaque," *Journal of Physiology and Pharmacology,* 52(1): 3–31.

Lobo, R. A. 2008. "Inflammation, coronary artery disease, and hormones," *Menopause,* 15 (6):1036–1038.

Mendall, M.A., Patel, P., Ballam, L., Strachan, D. and Northfield, T.C., 1996. "C Reactive protein and its relation to cardiovascular risk factors: a population based cross sectional study," British Medical Journal, 312 (7038):1061–1065.

Niccoli, G., Franceschi, F. and Cosentino, N. *et al*., "Coronary atherosclerotic burden in patients with infection by CagA-positive strains of Helicobacter pylori," Coronary Artery Disease,2010;21(4): 217–221.

Niemelä, S., Karttunen, T., Korhonen, T. *et al*., 1996. "Could Helicobacter pylori infection increase the risk of coronary heart disease by modifying serum lipid concentrations?" Heart, 75(6):573–575.

Onat, I., Sari, *A.,* Onat, I., Sari, G. and Hergenç, *et al*., 2007. "Predictors of abdominal obesity and high susceptibility of cardiometabolic risk to its increments among Turkish women: a prospective population-based study," Metabolism, 56, ( 3): pp. 348–356.

Pellicano, R., Oliaro, E., Mangiardi, L. *et al*. 2000. "Ischemic cardiovascular disease: correlation with Helicobacter pylori infection," *Minerva Cardioangiologica,* 48(12):467–473.

Pienizek, P., Karczewska, E., Duda, A., Tracz, W., Pasowicz, M. and Konturek, S.J. 1999. "Association of Helicobacter pylori infection with coronary heart disease," *Journal of Physiology and Pharmacology,* 50(5): 743–751.

Rahman, M.A., Cope, M.B., Sarker, S.A., Garvey, W.T. Chaudhury, H.S. and Khaled, M.A. 2009. "Khaled Helicobacter pylori Infection and inflammation: implication for the pathophysiology of diabetes and coronary heart disease in Asian Indians," *Journal of Life Sciences,* 1(1): 45–50.

Ridker, P. M., Hennekens, C.H., Buring, J.E. and Rifai, N. 2000. "C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women," *The New England Journal of Medicine,* 342 (12) : 836–843, 2000.

Rogha, M., Nikvarz, M., Pourmoghaddas, Z., Shirneshan, K., Dadkhah, D. and Pourmoghaddas, M. 2012. "Is Helicobacter pylori infection a risk factor for coronary heart disease?" ARYA *Atheroscler*, 8(1): 5–8.

Rožanković, P. B., Rožanković, Huzjan, A.L., Čupić, H., Benčić, I.J., Bašić, S. and Demarin, V. 2011. "Influence of CagA-positive Helicobacter pylori strains on atherosclerotic carotid disease," *Journal of Neurology,* 258( 5) :753–761.

Sawayama, Y., Hamada, M., Otaguro, S. *et al*. 2008. "Chronic Helicobacter pylori infection is associated with peripheral arterial disease," *Journal of Infection and Chemotherapy*, 14(3): 250–254.

Siddiqui, N.R., Garvey, W.T. and Khaled, M.A. 2009. "H. pylori-induced higher C-reactive protein in obese African Americans," *Artery Research,* 3(1): 39–42.

Strachan, D.P., Mendall, M.A., Carrington, D. *et al*., 1998. "Relation of Helicobacter pylori infection to 13-year mortality and incident ischemic heart disease in the caerphilly prospective heart disease study," Circulation, 98( 13): 1286–1290.

Suzuk, I. H., Franceschi, F., Nishizawa, T. and Gasbarri, N. 2011. A, "Extragastric manifestations of Helicobacter pylori infection," *Helicobacter*, 16(1): 65–69.

Tamer, G.S., Tengiz, I., Ercan, E., Duman, C., Alioglu, E. and Turk, U.O. 2009. "Helicobacter pylori seropositivity in patients with acute coronary syndromes," *Digestive Diseases and Sciences*, 54(6): 1253–1256.

Tan Goh K.L, Tan K. L. and Goh H.J. 2012. "Extragastrointestinal manifestations of Helicobacter pylori infection: facts or myth? A critical review," *Journal of Digestive Diseases,* 13( 7): 342–349

Vcev, A., Nakic, D. and Mrden, A. *et al*. 2007. "Helicobacter pylori infection and coronary artery disease," *Collegium Antropologicum*, 31(3):757–760.

Vizzardi, E., Bonadei, I. and Piovanelli, B. *et al*. 2011. "Helicobacter pylori and ischemic heart disease," Panminerva Medica,; 53( 3): 193–202.

Wald, N.J., Law, M. R., Morris, J.K. and Bagnall, A.M. 1997. "Helicobacter pylori infection and mortality from ischaemic heart disease: negative result from a large, prospective study," *British Medical Journal*, 315( 7117): 1199–1201.

Zhang, S., Guo, Y., Ma, Y. and Teng, Y. 2008. "Cytotoxin-associated gene-A-seropositive virulent strains of Helicobacter pylori and atherosclerotic diseases: a systematic review," Chinese Medical Journal,; 121(10) 946–951.

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