

Evaluation of Association of *Helicobacter pylori* Infection and Coronary Heart Disease (CHD) among CCU Patients

Mohammad Darvishi¹ and Syyedeh Soma Sadeghi^{2*}

¹Infectious Diseases and Tropical Medicine Research Center (IDTMRC),
AJA University of Medical Sciences, Tehran, Iran.

²General Practitioner, Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran.

<http://dx.doi.org/10.22207/JPAM.10.4.18>

(Received: 13 June 2016; accepted: 19 September 2016)

Presence of some pathogen microorganisms in the body causing or accelerating atherosclerosis is one of the proposed theories in etiology of heart ischemic diseases. This is more probable than other probabilities about the digestive microbes. This study is done in order to evaluate the probability of assistance of the infection caused from *helicobacter pylori* and coronary heart disease in the CCU-admitted patients in Niroo-Havaei Hospital in 2012. The study was done as an observational-analysis case study. In this study 139 patients referred to the Niroo-Havaei Hospital in the year 2012 are brought into the study and the frequency of *helicobacter pylori* infection in the patients with coronary heart disease and patients without that problem was determined and the correlation among suffering from this infection and coronary heart disease was assessed. In this study 60.7% of the patients had coronary heart disease and 61.8% of the patients had *helicobacter pylori* infection which did not demonstrate a significant difference between the two studied groups ($p > 0.05$). Totally according to the results obtained from this study it is inferred that there is no correlation between *helicobacter pylori* infection and coronary heart disease.

Keywords: Coronary Heart Disease, *Helicobacter pylori*, ELISA.

Diseases involved in the range entitled as Acute Coronary Syndrome particularly acute myocardial infarction (AMI) is considered as one of the most prevalent causes of death in many countries including our country, Iran^{1,2}. Coronary heart disease is the major reason of death in industrial countries. Only in USA 900,000 persons are encountered with myocardial infarction yearly. Among them almost 225,000 die because of arrhythmia or heart failure. Epidemiologic investigations have revealed some risk factors increasing the chance of formation of

atherosclerosis in a person. Being old, being male, and family history of atherosclerosis are some of invariable risk factors. Some of the proposed theories in physio pathogenesis of heart ischemic diseases includes presence of some pathogen microorganisms in the body causing or accelerating the atherosclerosis. This is more probable about digestive microbes³. *Helicobacter pylori* is a curved gram negative bacilli living among the stomach mucosa and sometimes duodenum and esophagus. In the developing countries, a broad range of *H. pylori* infection occurs between 80% of the adults^{4,5}. A large variety of diseases has been connected to *helicobacter pylori* infections and eradication of this bacterium has been beneficial⁶. Assessments on comparison trials demonstrate that eradication of the infection (comparing to not to totally healing it) has

* To whom all correspondence should be addressed.
E-mail: soma_sadeghi@yahoo.com

prominent beneficent in the case of peptic ulcers and prevention of relapse. Eradication also prevents the bleeding caused from peptic ulcer. Some non-randomized prospective observational studies support the role of the infection caused from *helicobacter pylori* in lymphoma of lymphoid tissue in the mucosa. These studies also demonstrated that eradication of *helicobacter pylori* causes the long-term quench of low-grade lymphoma in the lymphoid tissue in the mucosa⁷⁻⁹. Collaboration of stomach cancer and *helicobacter pylori* infection has been proven in large scale epidemiologic studies. However; there is no certainty whether the eradication of *helicobacter pylori* reduces the risk factor of stomach cancer or not¹⁰. Although the primary studies showed paradoxical results about the correlation of *helicobacter pylori* infection and ischemic heart diseases, but if this is proven, it is possible to eradicate the living microorganisms using antibiotics easily and consequently reduction of the risk factor of occurrence of acute coronary syndrome¹¹. Lack of credible documents about this matter led the researchers to plan and operate a study about this case. Therefore the evaluation of association of *helicobacter pylori* infection and coronary heart disease among CCU-admitted patients in Niroo-Havaei Hospital in 2012 is done in order to assessment of accuracy of this hypothesis and regarding the importance of this subject.

MATERIALS AND METHODS

In this observational-analysis case-control study, 139 patients referring to the Niroo-Havaei Hospital were brought into the study using convenient sampling technique. In this study the input standards include having coronary heart disease or stroke in the studied group, not having coronary heart disease or stroke in the control group, age more than 30 and bleeding intention. The dismiss standards include no intention of bleeding, history of stomach ulcer or gastrointestinal bleeding and recent intake of antibiotics. In this observational study done in 2012, the frequency of *helicobacter pylori* infection in the patients with coronary heart disease and persons without it was determined. Bacterial infection diagnosis is performed based

on radiology, endoscopy, urease test, and disease history^{12,13}. But these techniques are invasive, time consuming, and also their sensitivity is not determined precisely. Nowadays the infection is easily diagnosed using the serologic test of ELISA¹⁴. Since the immune system respond usually starts before clinical signs, the ELISA test provides reliable results by determination of certain antibodies in a short period of time. Different investigations have proven the presence of antibodies against the helicobacter and stomach diseases. There is a clear relationship between serum titer of IgM antibodies and clinical results as increased levels of immunoglobulin is observed in acute gastritis. In this study, this test was used as the rapid screening tests for *helicobacter pylori* infection. In this study different types of infections are divided into 3 categories according to the ELISA results: first category negative samples measured less than 20, second category suspicious samples measured between 20-30 which the test repetition is recommended within few days, and the third category positive measurement higher than 30 which the patient might suffer from helicobacter but necessarily does not prove the presence of disease.

Data analysis

Eventually after gathering demanded data from all the patients, the data were analyzed using SPSS software ver.16. For qualitative variables, frequency and frequency percentage, and for quantitative variables average and standard deviation were calculated. In order to comparison of the two control groups, Fisher's exact test, Chi-Square, and independent t test were employed and significant difference was considered 0.05.

RESULTS

In this study the frequency distribution of sex, age, smoking, and taking alcohol were compared together and assessed in the case and control groups. Statistical test results are presented in the table 1 briefly; where it demonstrating no significant difference between the two studied groups in the case of age, gender, smoking, and alcohol consumption variables and frequency distribution in these 4 variables is equal in two groups of studied patients (P-Value > 0.05).

In the following, the frequency of comorbidities was studied in both groups and then compared together. For comorbidities 5 states of diabetes mellitus (DM), Hypertention (HTN), hyperlipidemia (HLP), and having more than one co-occurring diseases were considered. The results obtained from statistical tests (table 2) revealed that there is a significant difference between the two groups of comorbidities and the frequency distribution of this variable in different cases is different in two groups of patients as the frequency of comorbidities in two groups of patients is significantly higher than control group (P-Value = 0.0001).

Based on the main purpose of designing this study, in the following the correlation of having gastrointestinal infection of helicobacter with coronary heart disease was assessed in two groups of case and control. Descriptive data demonstrated that 51 patients from the case group (60.7%)

suffering from coronary heart disease and 34 patients from the control group (61.8%) had positive results of helicobacter pylori. Analysis results obtained from statistical tests proved that there is no significant difference among the two studied groups (P>0.05). This shows that there is no correlation between coronary heart disease and *helicobacter pylori* infection (table 3).

Researchers evaluated the correlation between a variety of coronary artery diseases (CAD) including Acute Myocardial Infarction (AMI), Unstable Angina (U/A), and Stable Angina (S/A) with *helicobacter pylori* infection. Results of this study demonstrated that 22.6% of the patients had AMI, 76.2% of patients had U/A, and 1.2% had S/A. statistical analysis results obtained from proper statistical tests showed no significant difference between CHD and *H. pylori* infection in the patients (P>0.05) (table 4).

Table 1. Frequency distribution in 4 variables of age, sex, smoking, and alcohol consumption in two groups of studied patients

Group	Age (Mean±SD)	Sex		Smoking		Alcohol consumption	
		Male	Female	Yes	No	Yes	No
Case	63.12±13.70	41	43	18	66	2	82
Control	56.89±11.94	28	27	13	42	4	51
P-Value	> 0.05	> 0.05		> 0.05		> 0.05	

Table 2. Frequency distribution of comorbidities in both groups of patients

Group	Comorbidity					Total	P-Value
	DM	HTN	HLP	>1	Neg		
43	6	15	5	43	15	84	0.0001
4	3	15	9	4	24	55	
47	9	30	14	47	39	139	

Table 3. Statistical data and frequency distribution of *helicobacter pylori* infection in studied patients

Group	HP (<i>helicobacter pylori</i>)			Total	P-Value
	Positive	Equivocal	Negative		
Case	51	18	15	84	0.0001
Control	34	6	15	55	
Total	85	24	30	139	

Table 4. *H. pylori* infection frequency distribution based on the type of CAD of the studied patients

CAD Type		HP			Total	P-Value
		Positive	Equivocal	Negative		
AMI	AMI	11	6	2	19	> 0.05
	U/A	40	11	13	64	
	S/A	0	1	0	1	
	Total	51	18	15	84	

DISCUSSION

Presence of some pathogen microorganisms in the body causing or accelerating atherosclerosis is one of the proposed theories in etiology of heart ischemic diseases (15). This is more probable than other probabilities about the digestive microbes. Although the primary studies showed paradoxical results about the correlation of *helicobacter pylori* infection and ischemic heart diseases, but if this is proven, it is possible to eradicate the living microorganisms using antibiotics easily and consequently reduction of the risk factor of occurrence of acute coronary syndrome. Therefore, in order to evaluate the accuracy of this hypothesis and regarding the importance of the matter we evaluated the association of *helicobacter pylori* infection and coronary heart disease (CHD) among CCU-admitted patients in Niroo-Havaei Hospital in 2012. In this study the serologic results demonstrated that 60.7% of the patients had coronary heart disease and 61.8% of the patients of control group had *helicobacter pylori* infection which did not demonstrates a significant difference between the two studied groups ($p > 0.05$). In a review study done by Tan et al. in Malaysia published in 2012 it was declared that although there have been many studies to evaluate the correlation of coronary heart disease and *helicobacter pylori* infection, but regarding the paradoxes in the results there is a necessity to more studies in this case which proves the importance of our study more than before. In another review study done by Vizzard et al (16). in 2011 it was declared that there is a significant difference between the coronary heart disease and *helicobacter pylori* infection which does not match the results of our study. Proposed mechanisms

about this correlation in the mentioned study include colonization of endothelial cells, a change in fat levels in serum, an increase in coagulability and platelet aggregation and systemic inflammations. In a study done in Iran by Rogha et al. in 2012 it was revealed that there is no significant statistical relationship between the type of coronary heart disease and *helicobacter pylori* infection (17) which matches the results of our study. In another study done by Rogha et al in 2012 it was declared that there is no significant difference between coronary heart disease *helicobacter pylori* infection (18) which does not match the results of our study. In a review study done by Fagoonee et al. in Italy published in 2010, it was declared that the increase of aggregation of leucocytes and platelets and the synergy among them are the most important background mechanism causing the coronary heart disease in patients who already suffer from *helicobacter pylori* infection (19) however in our study no correlation was found among coronary heart disease and *helicobacter pylori* infection. Results of studies done by Zhu et al. in the USA (20) in 2012 demonstrated that there is no correlation between coronary heart disease and *helicobacter pylori* infection which approves the results of our study. Studies of Jin et al (21). in South Korea in 2007 demonstrated that there is a correlation between coronary heart disease and *helicobacter pylori* infection which does not match the results of our study. Studies done by Vcev et al (22). in Croatia in 2007 demonstrated that there is a significant correlation between coronary heart disease and *helicobacter pylori* infection which does not approve the results of our study. Studies of Ikeda et al (23). in Japan in 2013 demonstrated that there is no significant correlation between

coronary heart disease and *helicobacter pylori* infection which matches the results of our study. Studies of Schöttker et al (24). in Germany in 2012 demonstrated that there is no significant correlation between cardiovascular diseases and *helicobacter pylori* infection which is along with the results of our study. The same paradox is seen in other studies as well; Frazer, Ozdogru, Bahar, Aghajani, and Rhatbone did not find any correlation between *helicobacter pylori* infection and coronary heart disease, but in studies done by Rahimi and Rahnama the correlation was significant (25-30).

CONCLUSION

According to the results obtained from this study it can be inferred that there is no significant difference between *helicobacter pylori* infection and coronary heart diseases. However; according to the differences in results obtained from different studies maybe it is hard to declare a certain opinion about this relationship. In the end, it is proposed that more studies should be performed in order to affirm the obtained results of this study with larger population size.

REFERENCES

- Lihoui M, Boughzala E, Ben Farhat M, Ammar H, Chaouech A, Jemaa R, et al. [Distribution of cardiovascular risk factors in coronary patients in Sahel Tunisia]. 2007.
- Fakhrzadeh H, Bandarian F, Adibi H, Samavat T, Malekafzali H, Hodjatzadeh E, et al. Coronary heart disease and associated risk factors in Qazvin: a population-based study. 2008.
- Ghayour Mobarhan M, Sahebkar A, Parizadeh SMR, Moohebbati M, Tavallaie S, RezaKazemi Bajestani SM, et al. Antibody titres to heat shock protein 27 are elevated in patients with acute coronary syndrome. *International journal of experimental pathology*. 2008; **89**(3):209-15.
- De Falco M, Lucariello A, Iaquinto S, Esposito V, Guerra G, De Luca A. Molecular Mechanisms of *Helicobacter pylori* Pathogenesis. *Journal of cellular physiology*. 2015; **230**(8):1702-7.
- Roma E, Miele E. *Helicobacter pylori* Infection in Pediatrics. *Helicobacter*, 2015;20 Suppl 1: 47-53.
- O'Connor A, Gisbert JP, O'Morain C, Ladas S. Treatment of *Helicobacter pylori* Infection 2015. *Helicobacter*. 2015; **20** Suppl 1:54-61.
- Suerbaum S, Michetti P. *Helicobacter pylori* infection. *The New England journal of medicine*. 2002; **347**(15):1175-86.
- Feldman R. Epidemiologic observations and open questions about disease and infection caused by *Helicobacter pylori*. Achtman M, Serbaum S *Helicobacter pylori: Molecular and Cellular Biology* Wymondham: Horizon Scientific. 2001: 29-51.
- Wotherspoon AC. *Helicobacter pylori* infection and gastric lymphoma. *British medical bulletin*.1998; **54**(1):79-85.
- Lee Y-C, Liou J-M, Wu M-S, Wu C-Y, Lin J-T. Eradication of *Helicobacter Pylori* to Prevent Gastroduodenal Diseases: Hitting more than One Bird with the Same Stone. *Therapeutic Advances in Gastroenterology*. 2008; **1**(2):111-20.
- Song Z, Brassard P, Brophy JM. A meta-analysis of antibiotic use for the secondary prevention of cardiovascular diseases. *Canadian Journal of Cardiology*. 2008; **24**(5):391-5.
- Patel SK, Pratap CB, Jain AK, Gulati AK, Nath G. Diagnosis of *Helicobacter pylori*: What should be the gold standard? *World Journal of Gastroenterology : WJG*. 2014; **20**(36):12847-59.
- Uotani T, Graham DY. Diagnosis of *Helicobacter pylori* using the rapid urease test. *Annals of Translational Medicine*. 2015; **3**(1):9.
- Miftahussurur M, Yamaoka Y. Diagnostic Methods of *Helicobacter pylori* Infection for Epidemiological Studies: Critical Importance of Indirect Test Validation. *BioMed Research International*. 2016; 2016: 4819423.
- Honarmand H. Atherosclerosis Induced by *Chlamydia pneumoniae*: A Controversial Theory. *Interdisciplinary Perspectives on Infectious Diseases*. 2013; 2013: 941392.
- Vizzardi E, Bonadei I, Piovanelli B, Quinzani F, Ricci C, Lanzini A, et al. *Helicobacter pylori* and ischemic heart disease. *Panminerva medica*. 2011; **53**(3):193-202.
- Rogha M, Nikvarz M, Pourmoghaddas Z, Shirneshan K, Dadkhah D, Pourmoghaddas M. Is *helicobacter pylori* infection a risk factor for coronary heart disease? *ARYA atherosclerosis*. 2012; **8**(1):5.
- Rogha M, Dadkhah D, Pourmoghaddas Z, Shirneshan K, Nikvarz M, Pourmoghaddas M. Association of *helicobacter pylori* infection with severity of coronary heart disease. *ARYA Atheroscler*. 2011; **7**(4):138-41.
- Fagoonee S, De Angelis C, Elia C, Silvano S, Oliaro E, Rizzetto M, et al. Potential link between *Helicobacter pylori* and ischemic heart

- disease: does the bacterium elicit thrombosis? *Minerva medica*. 2010; **101**(2):121-5.
20. Zhu J, Quyyumi AA, Muhlestein JB, Nieto FJ, Horne BD, Zalles-Ganley A, et al. Lack of association of *Helicobacter pylori* infection with coronary artery disease and frequency of acute myocardial infarction or death. *The American journal of cardiology*. 2002; **89**(2):155-8.
 21. Jin S-W, Her S-H, Lee J-M, Yoon H-J, Moon S-J, Kim P-J, et al. The association between current *Helicobacter pylori* infection and coronary artery disease. *The Korean journal of internal medicine*. 2007; **22**(3):152-6.
 22. Vèev A, Nakiæ D, Mrðen A, Mirat J, Balen S, Ružić A, et al. *Helicobacter pylori* infection and coronary artery disease. *Collegium antropologicum*. 2007; **31**(3):757-60.
 23. Ikeda A, Iso H, Sasazuki S, Inoue M, Tsugane S, Group JS. The combination of *Helicobacter pylori*-and cytotoxin-associated gene-A seropositivity in relation to the risk of myocardial infarction in middle-aged Japanese: The Japan Public Health Center-based study. *Atherosclerosis*. 2013; **230**(1):67-72.
 24. Schöttker B, Adamu MA, Weck MN, Müller H, Brenner H. *Helicobacter pylori* infection, chronic atrophic gastritis and major cardiovascular events: a population-based cohort study. *Atherosclerosis*. 2012; **220**(2):569-74.
 25. Rathbone B, Martin D, Stephens J, Thompson JR, Samani NJ. *Helicobacter pylori* seropositivity in subjects with acute myocardial infarction. *Heart*. 1996; **76**(4):308-11.
 26. Mohammad Darvishi, Katayoun Ziari, Hossein Mohebbi, Kamyab Alizadeh. Association between iron deficiency anemia and *Helicobacter pylori* infection among children under six years in Iran. *Acta Medica Iranica* 2015. **53**(4):220-224.
 27. Rahnema B, Zadegan N, Fatahi E, Samadikhah J. Survey on the association of seropositivity of *Helicobacter pylori* IgG with acute myocardial infarction. *Journal of Kerman University of Medical Sciences*. 2001:73-66.
 28. Khodayar Ghorban, Mehrnoosh Shanaki, Naser Mobarra, Mehdi Azad, Jahanbakhsh Asadi, Reza Pakzad, Hassan Ehteram. Apolipoproteins A1, B, and other prognostic biochemical cardiovascular risk factors in patients with beta-thalassemia major. *Hematology* 2016 Mar 25; **21**(2):113-20.
 29. Fraser A, Scragg R, Cox B, Jackson R. *Helicobacter pylori*, *Chlamydia pneumoniae* and myocardial infarction. *Internal medicine journal*. 2003; **33**(7):267-72.
 30. Ozdogru I, Kalay N, Dogan A, Inanc MT, Kaya MG, Topsakal R, et al. The relationship between *Helicobacter pylori* IgG titre and coronary atherosclerosis. *Acta cardiologica*. 2007; **62**(5):501-5.