The Egyptian Journal of Hospital Medicine (January 2022) Vol. 86, Page 963-967

Association of Helicobacter pylori Infection and Severity of Coronary Artery Atherosclerosis in Patients with Suspected Coronary Artery Disease

Hamdy Abdel Azeem[1], Mohamed S. Zaghlol[2], Mohamed M. Elawady [3] and Majid Darraj [4]

[1] Cardiology Department, Faculty of Medicine, [3] Hepatogastroentrology and Infectious Diseases Department, Al-Azhar University, Cairo, Egypt

[2] Clinical Pathology Department, Faculty of Medicine, Al-Azhar University, Assuit, Egypt,

[4] Internal Medicine Department, Faculty of Medicine, Jazan University, KSA

Corresponding author: Mohamed Zaghlol,

E mail: Zaghlol_msz@yahoo.com, Mobile phone: 01006560985

ABSTRACT

Background: There is a strong correlation between Helicobacter pylori (HP) infection and coronary artery disease (CAD). There is also a strong correlation between HP infection and the severity of coronary artery atherosclerosis in patients with CAD. Our study determined the association of HP infection and severity of coronary artery atherosclerosis in patients with suspected CAD. **Methods:** A prospective study of 100 individuals who had coronary angiography for coronary atherosclerosis was conducted. Body mass index (BMI), blood pressure, blood cholesterol, blood glucose, leukocyte count, hemoglobin, and urea breath test were all done on the patients. Coronary angiograms were graded based on vascular and angiographic severity scores. **Results: Triglyceride, (**TG), Low Density Lipoprotein (LDL), C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), vessel score, and angiographic severity score all showed high correlations with Gensini score. There was a substantial association between vessel score and TG, LDL and angiographic severity score. It was found that angiographic severity score has a substantial positive link to a person's BMI; LDL; CRP; ESR, and vessel score. **Conclusion:** Although HP infection has been linked to an increased risk of coronary artery disease (CAD), established risk variables outweigh their potential impact.

Key words: Atherosclerosis, Coronary artery disease, Helicobacter pylori, Inflammation.

INTRODUCTION

As the most frequent infection in the world, Helicobacter pylori (HP) contribute to the development of digestive system diseases, particularly in poor nations [(1)]. H. Pylori has long been suspected of causing a wide spectrum of illnesses that are not related to gastrointestinal issues. Gastritis, peptic ulcers, gastric MALTOMA (mucosa associated lymphoid tissue lymphoma), and adenocarcinomas of the stomach in the esophagus are among the many conditions linked to H. pylori [(2)]. The illness has also been linked to thrombocytopenia and iron deficient anemia [(3)].

Angina, myocardial infarction, and heart failure are all symptoms of coronary artery disease [(4)]. Cardiovascular disease (CVD) is exacerbated by hyperlipidemia, smoking, diabetes, inactivity, and the male gender [(5)].

The proinflammatory cytokines (IL-8, IL-7, IL-15, IL-18), acute phase proteins, fibrinogen and C-reactive protein all have a role in cardiovascular disease [(6)]. Thrombosis and inflammation are both thought to be factors to atherosclerosis, although the fundamental source of inflammation remains a mystery [(7)].

Several studies have linked H. pylori, the bacteria that cause stomach ulcers, to CAD. There was an increased risk of H. pylori infection in people with angiographically-diagnosed heart disease (CAD) [(8)]. H. pylori antibody seropositivity was shown to be more prevalent in those with coronary artery calcification than those without CAD, according to researchers [(9)].

This study, which focused on patients with known or suspected heart disease, to find a relationship between HP infection and coronary atherosclerosis.

PATIENTS AND METHODS

This was a prospective cross-sectional study done in Alemeis Hospital and Alhayat National Hospital, Jazan, KSA and was conducted on 100 patients suffering from coronary atherosclerosis as confirmed by coronary angiography.

We excluded those with spastic angina pectoris, infectious diseases within two weeks of the catheterization, heart failure (Killip Class = 2) after an acute myocardial infarction, hepatic dysfunction, cardiovascular diseases, familial hypercholesterolemia, thyroid dysfunction, adrenal dysfunction, or mental illness that would have precluded informed consent from participating in this research.

All patients' demographic information, including their age, gender, history of chronic illnesses (such as hypertension, diabetes, heart failure, stroke, and chronic kidney disease), and their use of tobacco products or other substances of abuse, was collected.

An examination gown was put on the patients after they removed their shoes and shirts for the procedure. A wall-mounted stadiometer allowed us to measure height to the tenth of a centimeter. Weighing was done using a hospital balance beam scale to within 0.1 kg of the actual weight. The person's weight in

Received: 22/09/2021
Accepted: 20/11/2021

kilograms divided by the square of height in meters yielded the BMI (m^2).

Automated blood analyzers measured hemoglobin, total leukocyte count, and thrombocyte count in all patients admitted to the coronary unit. Enzymatic techniques were used to assess total cholesterol, triglyceride, HDL-c, LDL-c, creatinine, FBG, ESR (Westergren method) , and CRP (immunoturbidimetry).

As part of H. pylori's enzyme increased ammonia production, urea is broken down into ammonia and carbon dioxide by an enzyme called urease. It is seen that carbon dioxide exhaled during the experiment is urea, a combination of radioactive nitrate and nitrogen, which is consumed [(9)]. Patients with H. pylori were categorized into two groups: HP positive and HP negative, based on this test

Coronary angiography

The Judkins method and Kodak 35 mm cine film at 30 frames per second were utilized to cannulate the coronary arteries with 5F catheters. One minute later, computer-assisted coronary angiography was used to identify the existence of coronary stenosis from multiple projections after an intracoronary injection of isosorbide dinitrate (2.5 mg/ml solution over 20 seconds).

Scoring of coronary angiograms

Coronary angiograms were scored according to vessel score and Angiographic severity score.

Gensini score: description of a Coronary Artery Disease Scoring and Retrieval System (Cardscores). The system was intended to take into account: 1- Geometrically increasing severity of lesions: 25, 50, 75, 90, 99 and 100% diameter reduction; 2- cumulative effect of multiple lesions; 3- lesion location; 4- influence of collaterals; 5- vessel graftability.

Coronary Score:

• **Severity score** – With each step in the 25 – 50 – 75 – 90 – 99 – 100% diameter reduction progression, the impact on flow doubles in accordance with Poiseuille's law. As a result severity scores for lesions in this progression were assigned the values 1 – 2 – 4 – 8 – 16 – 32.

• Region multiplying factors for coronary segments were designated to express the relative amount of myocardium supplied by a diseased segment (see diagram)

• Collateral factor – The severity score adjustment for collaterals is indicated on the right side of the table below. The adjustment is reduced by the extent of disease in the vessel that is the source of collaterals (left column).

Gensini Score Calculation: severity score X the segment location multiplying factor X Collateral adjustment factor [(10)].

Vessel score: This was the number of vessels with a significant stenosis (50% or greater reduction in lumen diameter). Scores ranged from 0 to 4, depending on the number of vessels involved. Left main artery stenosis was scored as single-vessel disease.

Angiographic severity score: number of coronary artery segments with a stenosis ≥50%, according to the American College of Cardiology/American Heart Association's 16 segments model of the coronary tree [(11)].

Ethical approval:

The study was approved by the Ethics Board Alemeis Hospital and an informed written consent was taken from each participant in the study after reviewing the research materials and expressing their willingness to participate. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Statistical analysis was done using IBM© SPSS© Statistics version 23 (IBM© Corp., Armonk, NY, USA) and JMP® version 10 (SAS© Institute Inc., Cary, NC, USA). Continuous numerical variables were described as mean and standard deviation (SD), groups were compared using the independent-samples t-test. Categorical data was presented as number and percentage and Fisher's exact test was applied to compare groups.

RESULTS

Table (1) showed that the two groups were comparable regarding demographic data, comorbidities and medication distribution without statistically significance.

Table 1: Demographic and clinical characteristics

Variable	***HP positive*** *(n=60)*	***HP negative*** *(n=40)*	***p***
Age (years)	54.8 ± 6.28	53.13 ± 5.89	0.185
BMI (kg/m²)	28.13 ± 5.89	27.64 ± 6.15	0.690
Sex, *n (%)*			
Male	35 (58.3%)	21 (52.5%)	0.565
Female	25 (41.7%)	19 (47.5%)	
Comorbidities, *n (%)*			
Smoking	26 (43.3%)	15 (37.5%)	0.561
Hypertension	37 (61.7%)	19 (47.5%)	0.162
Diabetes mellitus	24 (40%)	13 (32.5%)	0.447
Hyperlipidemia	35 (58.3%)	17 (42.5%)	0.121
Medications, *n (%)*			
ACEIs or ARBs	29 (48.3%)	17 (42.5%)	0.566
β-blockers	36 (60%)	18 (45%)	0.141
Calcium channel blockers	21 (35%)	13 (32.5%)	0.796
Statins	44 (73.3%)	28 (70%)	0.716

** Qualitative data were represented as frequencies and relative percentages.*

** Quantitative data were expressed as mean ± SD.*

Total cholesterol, triglycerides, LDL, CRP and ESR were significantly higher in HP positive patients compared to HP negative patients. Moreover, Gensini score was significantly higher in HP positive patients compared to HP negative patients while vessels score, and angiographic severity score were comparable in both groups without statistically significant difference (Table 2).

Table 2: Laboratory parameters

Variable	HP positive (n=60)	HP negative (n=40)	p
RBS (mg/dl)	130.4 ± 23.16	122.47 ± 19.46	0.077
TC (mg/dL)	190.93 ± 38.85	174.6 ± 25.47	0**.021**
Triglycerides (mg/dL)	142.36 ± 39.71	127.5 ± 26.41	0**.040**
LDL (mg/dL)	129.67 ± 4.23	112.84 ± 3.61	0**.015**
HDL (mg/dL)	44.4 ± 6.17	46.51 ± 6.55	0.105
Creatinine (mg/dL)	0.76 ± 0.1	0.813 ± 0.2	0.283
Uric acid (mg/dL)	6.78 ± 1.35	6.42 ± 1.06	0.159
ESR (mm/hr)	45.45 ± 3.74	15.6 ± 2.21	**<0.001**
CRP (mg/L)	39.01 ± 2.74	8.7 ± 1.13	**<0.001**
EF %	49.6 ± 4.94	49.18 ± 2.66	0.884
Gensini Score	67.2 ± 3.51	51.91 ± 8.39	**0.045**
Vessel score	2.23 ± 0.838	2.01 ± 0.768	0.187
Angiographic severity score	4.35 ± 1	3.42 ± 1	0.052

* All variables were presented as mean ±SD, RBS:Random blood sugar, TC:Total cholesterol, LDL:Low Density Lipoprotein, HDL:High Density Lipoprotein, ESR:Erythrocyte Sedimentation Rate, CRP:C- Reactive Protein

There was a significant positive correlation between Gensini score with TG, LDL, CRP, ESR, vessel score and angiographic severity score. Meanwhile, there was a significant positive correlation between vessel score with TG, LDL, and angiographic severity score. Moreover, there was a significant positive correlation between angiographic severity score with BMI, LDL, CRP, ESR, and vessel score (Table 3).

Table 3: Correlations

	Gensini Score		**Vessel score**		**Angiographic severity score**	
	r	P	r	P	r	P
Age	0.213	0.147	0.118	0.541	0.573	0.569
BMI	0.132	0.179	0. 221	0.397	**0.265**	**0.033**
TC	-0.264	0.072	-0.209	0.104	-0.245	0.057
Tri-glycerides	**0.302**	**0.027**	**0.393**	**0.012**	0.239	0.074
LDL	**0.316**	**0.024**	**0.339**	**0.020**	**0.295**	**0.039**
HDL	-0.293	0.387	-0.241	0.364	-0.267	0.106
CRP	**0.344**	**0.018**	0.229	0.091	**0.492**	**0.009**
ESR	**0.351**	**0.016**	-0.217	0.103	**0.365**	**0.021**
Vessel score	**0.296**	**0.032**	---		**0.281**	**0.041**
Angio-graphic severity score	**0.513**	**0.007**	**0.281**	**0.041**	----	

Older age, DM, Gensini score, vessel score, angiographic severity score and HP positivity were found to be significantly associated factors with coronary artery atherosclerosis severity (Table 4).

Table 4: Multivariate regression analysis to determine the potential factors associated with coronary artery atherosclerosis severity

	OR	**Sig.**	**95% Confidence Interval**
Age	1.063	**0.002**	1.021 - 1.122
Male gender	2.264	0.164	0.649 – 4.164
DM	0.913	**0.003**	0.716 - .943
HTN	2.046	0.466	0.837 – 7.232
Gensini Score	1.012	**0.006**	0.816 - 1.035
Vessel score	2.233	**0.046**	0.495 – 3.642
Angiographic severity score	2.014	**0.034**	0.730 - 3.193
HP positive	3.641	**0.021**	1.326 – 7.161

DM: Diabetes mellitus, HTN:Hypertension,HP :Helicobacter Pylori

DISCUSSION

In our study the included HP positive subjects mean age was 54.8 years with mean BMI of 28.13 kg/m^2. Males represented 58.3% of all patients in HP positive group. On the other hand HP negative group mean age was 53.13 years with BMI of 27.64 kg/m^2 and males represented 52.5% of all subjects in this group. In a similar study by **Vafaeimanesh *et al.*** [8] mean age reached up to 59.4 years and BMI up to 27.7 kg/m^2 in patients suffering from coronary atherosclerosis. Mean age of control group reached 49.9 years and mean BMI was 31.6 kg/m^2. Males represented about half of the two groups.

In our study the two groups were comparable regarding demographic data, comorbidities and medication distribution without statistically significance. Also **Jukic *et al.*** [12] reported that there was no significant difference between HP positive and negative groups regarding demographic characteristics.

HP positive individuals had considerably increased levels of total cholesterol, triglycerides, LDL, CRP, and ESR than HP negative patients in our research. Furthermore, HP positive patients had a substantially higher Gensini score than HP negative patients, although vessels and angiographic severity scores were equivalent in both groups without statistically significant differences. Close to our findings **Vafaeimanesh *et al.*** [8] reported that there was significant difference among included study groups regarding ESR, CRP, HDL and creatinine. However, there was no statistical difference regarding TG, total cholesterol and LDL. Another study by **Jia *et al.*** [13] was against our results as it reported that there was statistical difference among included groups regarding HDL only. There was no statistical difference among included subjects regarding cholesterol, TG or LDL. Also along with our results **Jukic *et al.*** [12] reported a significant difference between HP positive and negative groups regarding TC and HDL levels.

Differences in the definition of coronary artery disease (CAD), selection bias in controls, detection methods for HP, imaging methods and scoring systems used to estimate CAD severity may explain why different findings have been made about the relationship between HP infection and the severity of coronary artery disease.

According to our study, the Gensini score has a substantial association with TG, LDL, CRP, ESR, vessel score, and angiographic severity score. In the meanwhile, TG, LDL, and angiographic severity score all have a strong positive relationship with the vessel score. To make matters worse, BMI, LDL, CRP, ESR and vessel score all had a substantial positive connection with angiographic severity score. Along with our results **Jukic *et al.*** [12] reported a significant positive correlation between Gensini score with LDL and CRP.

Our study reported that older age, DM, Gensini score, vessel score, angiographic severity score and HP positivity were found to be significantly associated factors with coronary artery atherosclerosis severity. Along with our results **Vafaeimanesh *et al.*** [8] reported that age, HDL and ESR were found to be significantly associated factors with coronary artery atherosclerosis severity. **Jia *et al.*** [13] reported that Helicobacter pylori infection is related to considerable reduction in high-density lipoprotein (HDL) levels, but not with an increase in coronary atherosclerosis severity.

In the study by **Jin *et al.*** [14] HP infection was found in 30.7% of the healthy control group and 40.6% of the CAD group, although the difference was not statistically significant. According to **Wald *et al.*** [15] there was no correlation found between HP seropositivity and coronary heart disease. Despite the fact that HP does not appear to induce CAD, a 13-year research by **Strachan and colleagues** [16] indicated that those with HP had a higher death rate (OR = 1.52 (95% CI, 0.99 to 2.34)). **Tsai and Huang** [17] found larger tendency for HP positive in CAD patients with more severe vascular disease, which is along with our findings.

CONCLUSIONS

HP infection may have potential impact and relation with atherosclerotic CAD. In the multifactorial pathogenesis of CAD, traditional risk factors surpass potential impact of HP infection.

Declarations:

Consent for Publication: I confirm that all authors accept the manuscript for submission

Availability of data and material: Available

Competing interests: none

Funding: No fund

Conflicts of Interest: The authors declare no conflicts of interest regarding the publication of this paper.

REFERENCES:

1. **Diaconu S, Predescu A, Moldoveanu A *et al.* (2017):** Helicobacter pylori infection: old and new. Journal of medicine and life, 10(2):112.
2. **Burucoa C, Axon A (2017):** Epidemiology of Helicobacter pylori infection. Helicobacter, 22: e12403.
3. **Lopes A, Vale F, Oleastro M (2014):** Helicobacter pylori infection-recent developments in diagnosis. World journal of gastroenterology: WJG., 20(28):9299.
4. **Darvishi M, Sadeghi S (2016):** Evaluation of association of Helicobacter pylori infection and coronary heart disease (CHD) among CCU patients. Journal of Pure and Applied Microbiology, 10(4): 2621-6.
5. **He C, Yang Z, Lu N (2014):** Helicobacter pylori—an infectious risk factor for atherosclerosis? Journal of atherosclerosis and thrombosis, 25775.
6. **Rezaee-Zavareh M, Tohidi M, Sabouri A *et al.* (2016):** Infectious and coronary artery disease. ARYA atherosclerosis, 12(1):41.

7. **Rožanković P, Huzjan A, Čupić H *et al.* (2011):** Influence of CagA-positive Helicobacter pylori strains on atherosclerotic carotid disease. Journal of neurology, 258(5):753-61.
8. **Vafaeimanesh J, Hejazi SF, Damanpak V *et al.* (2014):** Association of Helicobacter pylori infection with coronary artery disease: is Helicobacter pylori a risk factor? https://www.ncbi.nlm.nih.gov/pubmed/24574896
9. **Park M, Choi S, Kim D *et al.* (2011):** Association between Helicobacter pylori seropositivity and the coronary artery calcium score in a screening population. Gut and liver, 5(3):321.
10. **Gensini G (1975):** Chapter x. The pathological anatomy of the coronary arteries of man. In: Gensini GGMD, ed. *Coronary arteriography*. Mount Kisco, New York: Futura Publishing Co., 271-274.
11. **Scanlon P, Faxon D, Audet A *et al.* (1999):** ACC/AHA guidelines for coronary angiography: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Coronary Angiography) developed in collaboration with the Society for Cardiac Angiography and Interventions. Journal of the American College of Cardiology, 33(6):1756-824.
12. **Jukic A, Bozic D, Kardum D *et al.* (2017):** Helicobacter pylori infection and severity of coronary atherosclerosis in patients with chronic coronary artery disease. Therapeutics and clinical risk management, 13: 933.
13. **Jia E, Zhao F, 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(1): 1-7.
14. **Jin S, Her S, Lee J *et al.* (2007):** The association between current Helicobacter pylori infection and coronary artery disease. The Korean journal of internal medicine, 22(3), 152.
15. **Wald N, Law M, Morris J *et al.* (1997):** Helicobacter pylori infection and mortality from ischaemic heart disease: negative result from a large, prospective study. Bmj., 315(7117): 1199-1201.
16. **Strachan D, Mendall M, 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.
17. **Tsai C, Huang T (2000):** Relation of Helicobacter pylori infection and angiographically demonstrated coronary artery disease. Digestive diseases and sciences, 45(6): 1227-1232.