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ORIGINAL ARTICLE

Association of helicobacter pylori infection with coronary artery disease and the severity of angiographic lesions

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Abstract

Objective: There are controversies evaluating the association between different strains of *Helicobacter* pylori (HP) and occurrence of coronary arterial disease (CAD). HP may facilitate gastric ulcers and gastrointestinal bleeding. As angiographic lesions of high thrombus burden needs more potent and risky antithrombotic treatment regimens, we aimed to investigate the role of different strains of HP for angiographic lesions with high thrombus burden.

Methods: Medical and drug history of 109 consecutive patients who were candidate for coronary angiography were taken. Blood samples were obtained to measure anti HP (Ig) immunoglobulin G and anti-CagA (cytotoxin-associated gene) IgG antibody. According to angiography reports, participants were divided into three groups. Normal (n = 34), lesions with no thrombus (n=38) and lesions with thrombus (n = 37). To measure the association between CagA positive and less virulan strains of HP with the severity of CAD, ordinal logistic regression tests were used by adjusting age, sex, history of hypertention, diabetes mellitus , dyslipidemia and smoking.

Results: The mean ages of patients with and without CAD were 59±14. The prevalence of seropositivity to HP IgG titer was 69% (n=75). Fifty nine (79%) subject had CagA IgG seropositivity. Positive CagA IgG serology was 67% (n=50) and 44% (n=15) in CAD and control groups respectively. While HP IgG serology wasn't associated with lesion severity; CagA IgG serology was independently associated with lesion severity (OR: 2.4 (1.1-5.6) p=0.03).

Conclusion: Colonization of CagA positive HP was an independent risk factor for angiographic lesion severity.

Keywords: Helicobacter Pylori; coronary arterial disease; atherosclerotic lesion severity

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Introduction

Atherosclerosis represents a prevalent vascular condition that can lead to numerous clinical problems. Among these are coronary artery disease (CAD), ischemic stroke and peripheral tissue necrosis [1,2]. Numerous studies have identified factors such as diabetes, hypertension, smoking, and hypercholesterolemia as significant contributors to the development of atherosclerosis. However, the precise processes that initiate and drive the progression of atherosclerotic plaques are not yet fully understood. Interestingly, atherosclerosis can occur without conventional risk factors. Inflammation plays a key role in CAD pathogenesis, highlighting chronic infections as possible triggers of inflammatory responses. In the last ten years, significant effort has been directed toward researching to uncover potential links between chronic infections and atherosclerosis [3,4]. Several pathogens have been detected within atherosclerotic plaques, leading to the hypothesis that these infectious agents may trigger vascular inflammation through persistent infection or immune-mediated [5,6].

Helicobacter pylori (HP) infection is closely associated with various medical conditions, including peptic ulcer disease, potentially dangerous gastrointestinal bleeding, atrophic gastritis, and gastric cancer [7]. Recent research has also indicated a possible connection between HP infection and CAD. A case-control study found a notably higher rate of seropositivity to HP among patients with coronary artery stenosis, as confirmed through coronary angiography, compared to the general population [8]. Although certain studies have corroborated these findings [9,10], other research shows conflicting evidence regarding the link between HP infection and CAD [11,12]. Factors such as age, smoking habits, and social class, which are related to both HP infection and CAD risk, may contribute to these inconsistent results [4]. On the other hand, investigations examining the impact of more virulent strains of HP particularly those harboring the cytotoxin-associated gene A (CagA) pathogenicity island, have yielded more promising findings. A significant association between infection sustained by those strains and vascular damage have been shown [13].

Effective long-term antiplatelet and antithrombotic treatments are essential for patients with CAD, especially for those presenting with significant thrombus burden in angiographic assessments. In addition to the inflammatory mechanisms involved in atherosclerosis, HP infection has been shown to elevate the risk of gastrointestinal bleeding [14]. The increased cytotoxicity of certain HP strains, coupled with the enhanced risk of digestive tract complications arising from the use of aspirin or dual antiplatelet therapies, underscores the crucial role HP plays in the context of CAD management.

We therefore conducted a cross-sectional study to assess the association between various markers of previous infection with HP (IgG) and angiographically confirmed CAD, controlling simultaneously for a variety of potential confounders. Specifically, we wanted to assess whether chronic infection with HP was associated with angiographic lesion severity and whether this association was related to the presence of the more virulent HP CagA-positive strain. Thus, we will contribute to the literature on the extent of the risk that long-term antiplatelet therapy may pose in ischemic heart disease.

Methods

Patients and Control Subjects

Consecutive patients undergoing elective and urgent coronary angiography in the Department of Cardiology, Ankara Training and Research Hospital, Turkey with various manifestations of ischaemic heart disease including the acute coronary syndrome patients were included in the study. All patients were considered potential cases of CAD based on clinical symptoms or findings from non-invasive diagnostic tests such as electrocardiography, a treadmill exercise test, and radionuclide myocardial test. Participation was on a voluntary basis, and written informed consent was obtained from all participants. The study protocol received approval from the ethics committee of the Ankara Training and Research Hospital, Turkey. The inclusion period was from February to August of 2014. A total of 34 patients with acute coronary syndrome and 75 patients with evidence of ischemia (34 patients with normal angiographic coronary arteries) were studied.

The case group was consisted of 75 angiographically confirmed CAD patients who had stable or unstable symptoms. The control group consisted of 34 symptomatic patients admitted to the hospital with angiographically normal coronary arteries. No participant showed clinical signs of connective tissue disease, liver dysfunction, hypothyroidism, severe chronic heart failure or severe renal disease (eGFR < 30 mL/min/1.73 m²) and malignant diseases. Moreover, patients were excluded if they had an acute or chronic infection or inflammation,

had undergone any surgery in the four weeks prior, had a history of upper gastrointestinal tract surgery or coronary artery bypass surgery, were using nonsteroidal anti-inflammatory drugs, or if their data was incomplete. Additionally, none of the 109 participants enrolled in the study irrespective of stable or unstable symptoms had undergone eradication therapy for HP infection or received any antibiotic treatment during the study period.

All subjects underwent standardized interviews conducted by trained interviewers. Demographic information and CAD risk factors were documented for all participants. Participants were asked about medical history, including specific questions related to physician-diagnosed hypertension, diabetes, heart failure and gastro duodenal disease. Furthermore, current medication, socio-demographic data, and lifestyle habits, including smoking and alcohol consumption, were recorded. Individuals with an income below twice the national minimum wage were classified as having a lower socioeconomic status. Education levels were categorized into two groups: those with less than 10 years of education and those with 10 or more years of education.

Cardiovascular risk factors included a family history of CAD in first-degree relatives under 55, hypertension (blood pressure >140/90 mm Hg or use of antihypertensive medication), diabetes (fasting glucose >126 mg/dL or use of antidiabetic drugs/insulin), and hyperlipidemia (LDL cholesterol ≥130 mg/dL or use of lipid-lowering medication). Twenty cigarettes per month were smokers and renal dysfunction was defined as creatinine plasma concentrations of >1.3 mg/dL.

Effort angina was defined as chest pain during walking that was relieved within 10 minutes of stopping, indicated by ST segment depression on a 12-lead ECG during pain, or a positive stress test. Acute myocardial infarction (AMI) diagnosis followed the related Society of Cardiology criteria [15].

Laboratory methods

Blood testing before coronary angiography was evaluated using an auto-analyzer. Blood was centrifuged at 3000*g* for 10 minutes till frozen at -70°C until analysis. Specific anti–HP IgG and Anti-CagA IgG antibodies were measured using a commercial ELISA kit (Radim Diagnostics, Rome, Italy) following the manufacturer's instructions. Titers were classified as positive or negative with a cutoff of 30 UR/mL. The test sensitivity and specificity were 88% and 93.8%, respectively [16].

Determination of CAD

Coronary arteries were demonstrated in the left and right oblique planes with cranial and caudal angulations. Iohexol injections opacified the coronary arteries at each position. Based on the results of coronary angiography, the patients were classified into CAD (including the acute coronary syndrome patients) and control groups. The CAD group was divided further into thrombotic and non-thrombotic groups.

Normal coronary artery has been defined as absence of angiographically visible atherosclerotic plaques, thrombi, ectasia, myocardial bridging, or congenital coronary artery anomalies. Abnormal coronary artery has been defined as stenosis of at least one major epicardial coronary vessel. The assessment of stenosis severity is based on the percentage decrease in the vessel's diameter. Abnormal angiograms were categorized as one, two, or three vessel disease based on the presence of stenosis greater than 50% in a significant epicardial vessel. Additionally, the severity of visual lesions was classified according to their thrombotic characteristics. Thrombotic lesions included intraluminal, rounded filling defects that were largely detached from the vessel wall, evidence of embolization from this material, haziness of the lesions, irregular shapes with poorly defined edges, intraluminal staining at sites of total occlusion, and other filling defects that did not correspond with calcification.

Statistical analysis

Demographic and clinical characteristics in patients and control subjects were compared in a descriptive way. We employed the Shapiro-Wilk test to evaluate the normality of numeric variables. The Student *t* test, and the chi-square ($\chi 2$) tests (or Fisher's exact test if any expected cell count was <5) were used to compare baseline characteristics, HP serology, and the presence of CAD. Comparisons of parametric values among the normal, thrombotic and non-thrombotic groups were performed by 1-way analysis of variance (ANOVA). Tukey Honest Significant Difference (HSD) was used as a post hoc test for multiple comparisons between the groups. Binary regression was used to investigate the relation between HP serostatus and coronary disease, while accounting for any confounding variables including age, sex, smoking, hypertension, hyperlipidemia and diabetes mellitus. Results are expressed mean±SD, percentages and as odds ratio (OR) with 95% confidence intervals (CI) as appropriate.

Proportional-odds ordinal logistic-regression models

Table-1. Main Characteristics of Our Study Group

	Overall (n=109)	CAD (n=75)	Control (n=34)	*p*-value
Age, (years)	59±14	62±13	53±12	**0.001**
Female, n (%)	45 (41)	28 (37)	17 (50)	0.21
Family history of CAD, n (%)	64 (59)	51 (68)	13 (38)	**0.003**
Socioeconomic status, n (%) Low Middle-High	 38 (35) 71 (65)	 25 (33) 50 (67)	 13 (38) 21 (62)	0.62
School education <10 years, n (%)	52 (48)	38 (51)	14 (41)	0.36
Diabetes, n (%)	46 (42)	41 (55)	5 (15)	**<0.0001**
Hypertention,n (%)	67 (61)	57 (76)	10 (29)	**<0.0001**
Dyslipidemia, n (%)	54 (49)	46 (61)	8 (23)	**<0.0001**
Current smoker, n (%)	58 (53)	45 (60)	13 (38)	**0.03**
Daily alcohol consumption, n (%)	26 (24)	21 (28)	5 (15)	0.13
Heart failure, n (%)	22 (20)	22 (29)	0 (0)	**<0.0001**
Renal dysfunction, n (%)	16 (15)	15 (20)	1 (3)	**0.015**
Gastroduodenal disease, n (%)	55 (50)	37 (49)	18 (53)	0.73
Income level, n (%) Poor Medium-Good	 38 (35) 71 (65)	 25 (33) 50 (67)	 13 (38) 21 (62)	0.62
Helicobacter pylori IgG seropositivity, n (%)	75 (69)	51 (68)	24 (71)	0.78
CagA IgG seropositivity, n (%)	65 (60)	50 (67)	15 (44)	**0.026**
Helicobacter pylori IgG titer	53.8±45.6	54.2±46.1	52.7±45.1	0.87
CagA IgG titer	81.6±89.7	92.4±91.8	57.6±81.1	0.06

CAD; Coronary arterial disease Data are expressed as mean±SD or number (%).

were used to assess the independent association of a positive antibody titer against HP with multiple severity categories of CAD, while simultaneously controlling for age, sex, smoking, history of hypertension,

Table-2. Relationship Between Helicobacter Pylori CagA Seropositivity and The Severity of Coronary Atherosclerotic Lesions

	Overall (n=109)	CagA IgG seropositive (n=65)	CagA IgG seronegative (n=44)	*p*-value
CAD, n (%)	75 (69)	50 (77)	25 (57)	**0.03**
CAD type, n (%) Stable CAD ACS	 75 (69) 34 (31)	 44 (68) 21 (32)	 31 (70) 13 (29)	0.76
Number of arteries with lesions, n (%) 1 2 3	 24 (22) 21 (19) 28 (26)	 13 (20) 14 (21) 21 (32)	 11 (25) 7 (16) 7 (16)	0.14
Thrombotic lesion, n (%)	37 (34)	26 (40)	11 (25)	0.07

ACS; Acute coronary syndrome, CAD; Coronary Arterial Disease.

Table-3. General Characteristics of Our Study Group According to Angiographic Lesion Severity

	Control n=34	Non-thrombotic n=38	Thrombotic n=37	*p*-value
Age, (years)	53±12	62±14	63±14	**0.003 * †**
Female, n (%)	17 (50)	15 (39)	13 (35)	0.43
Family history of CAD, n (%)	13 (38)	25 (66)	26 (70)	**0.01**
Socioeconomic status, n (%) Low Middle-High	 13 (38) 21 (62)	 8 (21) 30 (79)	 17 (46) 20 (54)	0.07
School education <10 years, n (%)	14 (41)	17 (45)	21 (57)	0.38 †‡
Diabetes, n (%)	5 (15)	22 (58)	19 (51)	**<0.0001 †‡**
Hypertention,n (%)	10 (29)	30 (79)	27 (73)	**<0.0001 †‡**
Dyslipidemia, n (%)	8 (23)	24 (63)	22 (59)	**0.001 †‡**
Current smoker, n (%)	13 (38)	22 (58)	23 (62)	0.10
Daily alcohol consumption, n (%)	5 (15)	10 (26)	11 (30)	0.30
Heart failure, n (%)	0 (0)	11 (29)	11 (30)	**0.002 †‡**
Renal dysfunction, n (%)	1 (3)	8 (21)	7 (19)	0.06
Gastroduodenal disease, n (%)	18 (53)	22 (58)	15 (40)	0.30
Helicobacter pylori infection, n (%)	24 (71)	25 (66)	26 (70)	0.88
CagA IgG seropositivity, n (%)	15 (44)	24 (63)	26 (70)	**0.03 *§**
H. Pylori IgG titer	53±45	59±49	49±42	0.75
CagA IgG titer	57±81	97±99	87±85	0.15
CAD type, n (%) Stable CAD ACS	 34 (100) 0 (0)	 25 (66) 13 (34)	 16 (43) 21 (57)	**<0.0001 †‡**

ACS; Acute coronary syndrome, CAD; Coronary Arterial Disease. Values are expressed as mean ± standard deviation. *p<0.05 between non-thrombotic and control groups, § p<0.05 between thrombotic and control groups, †p<0.01 between thrombotic and control groups, ‡p<0.01 between non-thrombotic and control groups.

hyperlipidemia and diabetes. This approach fits a uniform log cumulative odds of progression across our three categories of severity as a function of a positive antibody titer against HP at admission and other covariates. The proportional odds assumptions were met for these regression models. A P-value ≤0.05 was considered statistically significant. Statistical tests were two-sided. All analyses were performed with IBM SPSS 14 (SPSS Statistics version 14, IBM Corp).

Results

Study population

The main characteristics of our study group are summarized in Table 1.

Patients showing CAD at coronary angiography presented more frequently with arterial hypertension, hypercholesterolemia, and diabetes mellitus as compared with controls, and were more frequently current smokers. Control subjects were slightly younger; and showed higher HDL cholesterol levels.

Approximately sixty-nine percent of the patients (69%) had CAD by coronary angiography, 69% had SAP and 31% had acute coronary syndrome (ACS). Thrombotic coronary lesions were detected in 34% of patients (Table 2).

General characteristics of our study patients stratified into three groups according to angiographic lesion severity are shown in Table 3.

Patients with normal coronary arteries were younger, had lower rate of comorbidities and family history of CAD compared to other groups.

HP Infection

The prevalence of seropositivity to HP (IgG titer) was 69% (n=75) and 59 (79%) subject had CagA IgG seropositivity. HP CagA IgG antibody titers in females and males were 92.8±88.9 vs. 73.7±90.2, respectively (p=0.3). There was no association between age groups and both of the HP serostatus. The prevalence of seropositivity to HP (IgG titer) was not significantly different between the CAD and control groups but CagA IgG seropositive patients were more likely to have CAD (Table 1 and 3). The percentage of seropositivity to HP CagA IgG in HP IgG seropositive patients according to angiographic lesion severity is shown in Figure-1.

CagA IgG titers in SAP and ACS groups were 75.2±85.9 vs.95.6±97.4; p>0.05 respectively. Patients with positive CagA IgG serology were more likely to be females and to have lower socioeconomic status. Diabetes mellitus, heart failure and gastro-duodenal disease were the most prevalent comorbidities in the CagA IgG seropositive group than the seronegative group (Table-4).

Predictors of CAD and lesion severity

Table 5 presents the results of univariable and multivariable logistic regression analyses in which the association between HP CagA IgG serostatus and CAD was adjusted for age,sex and for a variety of other potential confounders.

The OR for CAD given a positive HP CagA status remained to be statistically significant after adjustment for cardiovascular risk factors and other confounding factors. The association between HP CagA IgG serostatus and angiographic lesion severity was also assessed. In fully adjusted analyses HP CagA IgG serostatus was independently associated with lesion severity in addition to gender, hypertention and smoking (OR: 2.4, 95% CI: 1.1-5.6, *p*=0.03). CagA IgG serostatus was not a predictor of CAD type (OR: 1.1, 95% CI: 0.5-2.6, *p*=0.76).

Discussion

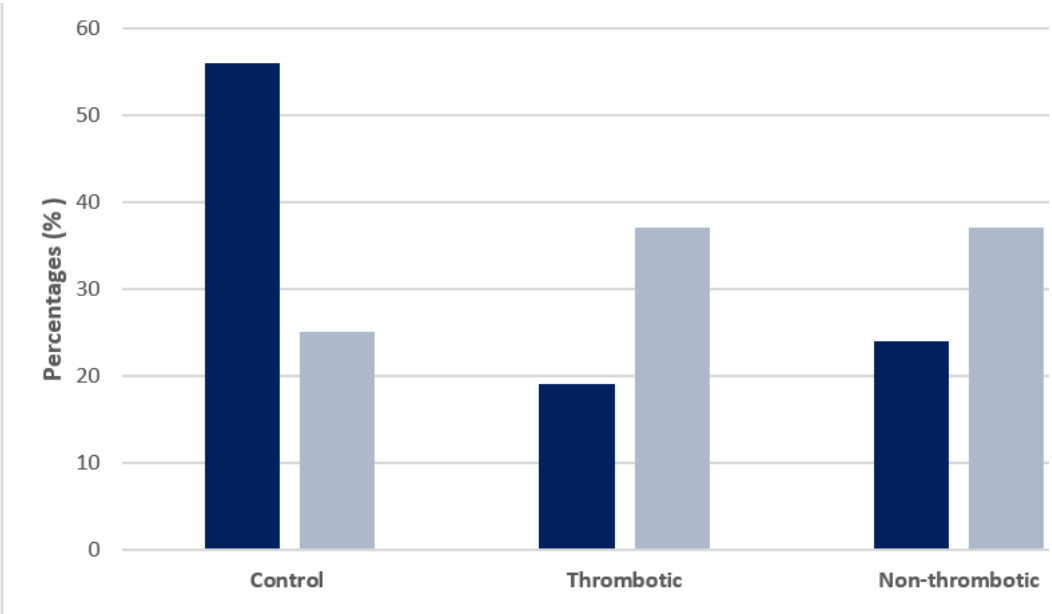

Figure-1: The percentage of seropositivity to HP CagA IgG in HP IgG seropositive patients according to angiographic lesion severity

In our study we have not demonstrated an association between serologic evidence of HP infection and angiographic evidence of CAD. On the other hand we found moderate associations between CagA IgG seropositivity to HP and the presence of angiographically confirmed CAD and lesion severity, which persisted to be statistically significant

Table-5. Univariate and Multivariate Logistic Regression Analysis of the Association Between The Confounding Multiple Variables and CAD.

Variables	Univariate OR (95% CI)	*P* value	Multivariate OR (95% CI)	*P* Value
Age	1.0 (1.02-1.08)	**0.001**	1.04 (0.98-1.1)	0.21
Female gender	0.6 (0.3-1.3)	0.21	0.2 (0.05-0.72)	**0.02**
School education <10 years	1.5 (0.6-3.3)	0.36	-	-
Lower socioeconomic status	1.2 (0.5-2.8)	0.62	-	-
Hypertention	7.6 (3.0-18.8)	**<0.0001**	6.8 (1.7-26.4)	**0.005**
Diabetes mellitus	6.9 (2.4-20)	**<0.0001**	2.7 (0.7-10.3)	0.15
Dyslipidemia	5.1 (2.0-12.9)	**<0.0001**	1.9 (0.5-7.5)	0.34
Current smoker	2.4 (1.1-5.6)	**0.037**	4.5 (1.3-16.2)	**0.02**
Family history of CAD	1.3 (0.6-2.9)	0.6	-	-
Daily alcohol consumption	2.2 (0.8-6.6)	0.14	-	-
CagA IgG seropositivity	2.5 (1.1-5.8)	**0.028**	3.6 (1.1-12.3)	**0.04**
Helicobacter pylori IgG seropositivity	0.89 (0.36-2.14)	0.79	-	-

CAD; Coronary arterial disease.

after controlling for a variety of potential confounders.

As a widespread global infection, HP impacts over half of the world's population [7]. In Turkey, a developing country, seroprevalence of HP IgG is between 41% to 83% [17]. Our seropositivity rates were consistent with the previous findings. We found, 79% seropositivity for HP CagA IgG. In previous research, almost all strains isolated from samples collected in East Asian countries tested positive for CagA, in contrast to only about half of the strains from Western countries displaying CagA positivity [17]. This research found no significant variation in the rate of HP IgG seropositivity based on age or gender. However, CagA IgG seropositivity was notably higher in females compared to males. This finding is different from the study of Jafarzadeh et al. [18] that CagA positivity was more prevalent in males.

Although, some studies found HP infection as being one of the risk factors for CAD, separate from diabetes mellitus, dyslipidemia, and hypertension; existing research on the connection between HP infection and stable, chronic cardiac conditions has produced inconsistent findings [19,20]. These conflicting findings might be attributed to the varying methodologies employed in these studies. These studies primarily relied on Enzyme-linked Immunosorbent Assay (ELISA) tests to detect HP IgG antibodies, which can indicate a current or past infection but do not confirm an active HP infection. Kowalski et al [21] discovered that subjects with CAD were significantly more likely to test seropositive for both HP and CagA IgG antibodies compared to the control group. Conversely, Sandifer et al. [22], demonstrated a negative correlation between the death rate from CAD and the seroprevalence of HP antibodies. Additionally, other studies have not confirmed any relationship between HP infection and the progression of CAD [23]. However, these authors did not examine the significance of anti-CagA seropositivity, which is known to be a marker for a heightened potential to trigger a systemic immune response. This inconsistency may partly be explained by Pasceri et al.'s hypothesis that only cytotoxic, CagA-positive H. pylori strains might be associated with CAD [13,24]. CagA seropositivity, as opposed to CagA seronegativity, has been shown to be linked with an increased susceptibility to CAD [13,24]. Furthermore, in a cross-sectional study

conducted by Niccoli et al [25], the anti-CagA antibody titer emerged as the sole independent predictor of the extent of coronary atherosclerosis. In our study, the rate of anti-CagA antibody seropositivity was consistent with the aforementioned studies, and this group alone demonstrated a significant association with CAD.

Another controversial subject is the relation between HP infection and unstable forms of cardiac syndromes. Such a significant, positive association between CagA IgG seropositivity and the occurrence of ACS was confirmed in a meta-analysis [26]. Similarly no significant relation was demonstrated between HP IgG seropositivity and the risk of acute myocardial infarction and stroke among 29,876 middle-aged Japanese patients in 12 year period. Only CagA IgG seropositivity exhibited a trend toward correlation with acute myocardial infarction [27]. In contrast, a relatively small study reported the higher seroprevalence of HP IgG in ACS patients than the control group while CagA IgG seroprevalence was similar in both groups [18]. These studies primarily utilized Enzyme-linked Immunosorbent Assay (ELISA) tests to detect HP IgG antibodies, which indicate current or past infection but do not confirm ongoing infection. This discrepancy between the investigations may be attributed to cohort heterogeneity due to the presence of probable active HP infection rate. In studies concerning the relationships between HP seropositivity and ACS, the CAD patients were frequently followed in relation to ACS occurrence. After ACS, being on acute infection period by HP can be responsible for platelet aggregation and local inflammation within the vascular wall that diminish along with plaque stabilization during subsequent weeks. The significant association of HP seropositivity with the risk of only short-term outcomes, rather than long-term outcomes; may emphasize the importance of acute infection in unstable forms of cardiac syndromes [28]. Although our analysis did not reveal any significant differences between stable and unstable cardiac syndromes based on pathogen HP serology, we did find a higher prevalence of thrombotic lesions in cases that were CagA seropositive. Unfortunately, we are unable to assess the potential influence of acute HP infection on our results.

Potent combined and long-term antithrombotic therapies are the mainstay of treatment in ACS, particularly in those with lesions of high thrombus burden. One of the hypothesized mechanisms connecting HP infection to the development of ACS is the stimulation of thrombotic processes through the perpetuation of a low-level chronic inflammatory response. [29]. By observing an association between CagA IgG seroprevalence and lesion severity according to the presence of thrombogenic lesions, we have confirmed this finding. The involvement of HP infection in causing gastrointestinal (GI) bleeding is well documented. Furthermore, GI bleeding following ACS is linked to higher rates of morbidity and mortality [30]. In patients with CAD who are on dual antiplatelet therapy, better outcomes will be influenced by effective prevention of both ischemic events and bleeding complications. At present, it is recommended that patients at risk undergo HP testing and receive eradication therapy as a preventative measure against primary gastrointestinal bleeding [31,32].

The higher prevalence of HP infection in lower socioeconomic groups can be attributed to the greater percentage of infected individuals in developing countries (up to 82.5% of the general population) compared to developed countries (less than 20% of the general population) [17,33]. Low socioeconomic status is a known risk factor for atherosclerosis [33]. Studies indicating a connection between HP infection and CAD without accounting for socioeconomic factors are considered to be biased, as no link between HP seropositivity and future AMI has been detected among individuals of similar socioeconomic backgrounds [34]. In our study although we detected higher rates of low socioeconomic status in CagA IgG seropositive group, no effect of socioeconomic status was found on CAD.

It has been proposed that the link between CAD and HP infection is influenced by shared risk factors that predispose individuals to both conditions [30,35]. Diabetes mellitus, a significant contributor to the rise in CAD cases, is associated with a higher prevalence of HP infection [35]. A recent meta-analysis conducted by Wang et al [36] demonstrated a stronger correlation between HP infection and type 2 diabetes mellitus compared to type 1 diabetes mellitus. The association has been attributed to the delayed gastric emptying caused by autonomic diabetic neuropathy, which facilitates bacterial colonization of the gastric mucosa Tobacco smoking, a significant risk factor for atherosclerosis, has been suggested as a key factor in promoting HP transmission and exacerbating its detrimental effects on gastro-duodenal mucosa and extragastric manifestations, including ACS [30,37]. On the other hand, Brown [38] showed in his review that the majority of studies have not found tobacco use or alcohol consumption to be risk factors for HP infection. In our study while history of Diabetes mellitus, heart failure and gastroduodenal disease were the covariates associated with positive

CagA IgG serostatus, dyslipidemia, smoking and alcohol consumption were not associated with it. In fact, the relation between HP CagA IgG seropositivity and CAD remained to be significant even after adjustment for potential confounding factors. While HP infection may not be as significant a risk factor for CAD as traditional risk factors, even a slight increase in risk could have notable epidemiological consequences. This might be clinically important as the infection can be eradicated by specific antibiotic treatments [39].

Limitations

This is a cross-sectional investigation that establishes an association between HP CagA seropositivity and CAD but not causality. Therefore, CagA seropositivity may not directly cause CAD or lesion severity, but instead serves as a marker for an unknown risk factor. Consequently, the study's conclusions should be viewed as preliminary and hypothesis-generating. In addition, we didn't assess active HP infection based on the examination of biopsy specimens obtained during endoscopy or HP stool antigen and ^{13}C-urea breath tests. Even if an active HP infection is not confirmed in seropositive patients, the possibility remains that the atherogenic impact of the infection, once triggered, may continue. Additionally, the duration of infectivity and the impact of HP infection on inflammatory and autoimmune responses were not taken into account.

Conclusion

These findings underscore the clinical significance of previous research that identified a connection between more virulent HP strains and more severe CAD, although the exact mechanism remains unclear. In this context, eradication and gastroprotective treatment of ischemic heart patients with more virulent H. pylori strains and receiving antiplatelet therapy will come to the fore in clinical practice.

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