# Lack of association of coronary artery disease with *H.pylori* infection

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## ABSTRACT

**Objectives:** It has been suggested from previous studies that there is an associated increased risk of coronary artery disease (CAD) in patients with *Helicobacter pylori (H.pylori)*. However, others dispute this. We therefore evaluated this hypothesis in a group of patients with confirmed *H.pylori* infection.

**Methods:** A total of 158 patients with dyspeptic symptoms were evaluated by esophago-gastro-duodenoscopy (EGD) in King Khalid University Hospital in Riyadh, Kingdom of Saudi Arabia from May through to June 1997. Endoscopic biopsies and histology as well as culture and serology for *H.pylori* were obtained. In patients with confirmed *H.pylori* a further analysis was performed looking at associated (CAD) or known risk factors for CAD.

**Results:** Among the 158 patients who underwent EGD, 143 patients (90.5%) were found to have *H.pylori* either by culture, histology or serology, or both in a percentage of (31.5%) (77.6%) and (60.8%). There was no evidence of CAD in this group of patients based on history, electrocardiogram (ECG), echocardiography, ECG stress test, dypiridamole thallium scan or coronary angiography. Other known risk factors for CAD were cigarette smoking (12.6%), diabetes mellitus (10.5%), hypertension (1.4%) and hyperlipidemia (2.8%).

**Conclusions:** *Helicobacter pylori* infection does not increase the risk of CAD, and should not be considered as an independent risk factor for CAD. Further, prospective large trial is needed to confirm our finding.

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*Helicobacter pylori (H. pylori)*, which is a well-known major risk factor in the development of peptic ulcer disease, has been claimed to be associated with an increased risk of coronary artery disease (CAD).[1] The hypothesis of an infectious etiology to atherosclerosis in patients with CAD is suggested in a manner similar to gastric mucosal damage induced by *H.pylori*.[2] Infectious agents such as cytomegalovirus, hepatitis A virus, herpes simplex virus one and 2, *Chlamydia pneumoniae (C.pneumoniae)* and others were incriminated as possible causative factors in the pathogenesis of CAD, particularly, in the absence of known risk factors for CAD. Some workers reported that not only infection plays an important role in the incidence of myocardial infarction or death, but also the risk posed by infection is independently related to the pathogen burden.[3] Moreover, the implication of such hypothesis will be supported by prognostic influence of *H.pylori* eradication in the treatment of CAD and prevention of restenosis after percutaneous transluminal coronary angioplasty (PTCA).[4,5]

However, other studies have shown inconsistency of *H.pylori* as a risk factor determining either risk of CAD, acute myocardial infarction or death in patients

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with CAD.[6-8] We conducted this study to evaluate the association of CAD in patients with proven *H.pylori* infection.

**Methods.** This study is a retrospective in design. Data were collected from 158 patients who were referred for esophago-gastro-duodenoscopy EGD in King Khalid University Hospital from May through to June 1997 as of dyspeptic symptoms. All patients had blood samples obtained for *H.pylori* serology immunoglobin (Ig) G and IgA and it was considered positive if IgG, IgA or both were positive. For IgG readings 155-230 u/ml were considered positive, and < 135 u/ml as negative. For IgA readings in the range 50-75 u/ml were considered positive, and <40 u/ml as negative. Endoscopic biopsies were obtained from all patients, samples were sent for culture and histology. Coronery artery disease risk factors data were obtained for diabetes mellitus, hypertension, cigarette smoking and hyperlipidemia. The indications for the tests to determine CAD were directed by the presence or absence of symptoms suggestive of CAD; such as exertional chest pain or dyspnea. The presence or absence of CAD was considered by collecting data from electrocardiogram (ECG), echocardiography, ECG stress test, dypiridamole thallium scan or coronary angiography.

Patients were excluded from the study if serology, culture or histology did not confirm *H.pylori*.

**Results.** The number of patients who had negative *H.pylori* infection and were excluded from the study was 15 (9.5%) out of the 158 patients who were endoscoped. The endoscopic findings were reported as erythema, erosions or ulcer, or both (**Table 1**). *Helicobacter pylori* were confirmed in 143 (90.5%) patients by serology, culture or histology **(Table 2)**. The mean age was 37.8 years ± 15 (range 16-80), and 71 patients (49.7%) were males. Saudi patients were 139 (97.2%) with a mean age of 39.3 years ± 14 (range 16-80). The presence of known risk factors for CAD is shown in **(Table 3)**. There was no evidence of CAD in any patient with *H.pylori* infection by negative history suggestive of angina in 37 patients with a mean age of 22 years. Electrocardiogram was performed on 106 patients who had complained of chest pain or dyspnea, and was normal in 103 patients. Seven patients were reported to have normal left ventricular wall motion on echocardiography and 3 patients had Thallium stress test, 2 reported as normal **(Table 4)**. One patient, who is a 48-year-old lady known to have type II diabetes mellitus and hypertension, had complaints of exertional chest pain associated with shortness of breath. Her clinical examination revealed an obese lady with a body mass index of 34.4 (calculated by weight in kilograms divided by squared height in meters); the rest of the examination was unremarkable. Her laboratory evaluation revealed

**Table 1 -** Endoscopic findings for patients with *Helicobacter pylori* infection.

| Findings | Esophagus n (%) | Stomach n (%) | Duodenum n (%) |
|---|---|---|---|
| Erythema | 17 (11.9) | 58 (40.6) | 15 (10.5) |
| Erosion | 7 (4.9) | 22 (15.4) | 18 (12.6) |
| Ulcer | 1 (0.7) | 0 (0) | 10 (7) |

**Table 2 -** Diagnosis of *Helicobacter pylori* infection.

| Esophago-gastro duodenoscopy | Patients 158 (%) |
|---|---|
| Culture (C) | 45 (31.5) |
| Histology (H) | 111 (77.6) |
| Serology (S) | 87 (60.8) |
| All positive (C,H,S) | 20 (13.9) |
| **Total *H.pylori* positive** | **143 (90.5)** |

**Table 3 -** Demographic data and risk factors for coronary artery disease.

| Data | n (%) | KSA (%) | Reference |
|---|---|---|---|
| *H.pylori* | 143 (90.5) | (70-90) | 9 |
| Mean age (range) | 37.8 ± 15 (16-80) | | |
| Saudi | 139 (97.2) | | |
| Non Saudi | 4 (2.8) | | |
| Males | 71 (49.7) | | |
| Cigarette smoking | 18 (12.6) | (21.1) | 20 |
| Diabetes mellitus | 15 (10.5) | (9.7) | 21 |
| Hypertension | 2 (1.4) | (5.4-30) | 21,22 |
| Hyperlipidemia | 4 (2.8) | (9-14) | 23 |
| Coronary artery disease | 0 (0) | | |

**Table 4** - Evaluation of patients with Helicobacter pylori infection for coronary artery disease.

| Parameter | n | (%) | Positive or abnormal | | Negative or normal | |
|---|---|---|---|---|---|---|
| *H.pylori* | 143 | (100) | 143 | | 0 | |
| History of chest pain or shortness of breath | - | | 106 | (74.1) | 37 | (25.9) |
| Electrocardiogram | 106 | (74.1) | 3 | (2.1) | 103 | (72) |
| Echocardiogram | 7 | (4.9) | 0 | (0) | 7 | (4.9) |
| Thallium stress test | 3 | (2.1) | 1 | (0.7) | 2 | (1.4) |
| Coronary angiogram | 1 | (0.7) | 0 | (0) | 1 | (0.7) |

normal lipid profile. She further underwent a thallium stress test (TST) for evaluation of abnormal ECG (inverted T wave in the anterior leads). Her TST was reported as consistent with ischemia. However, CAD was excluded by a normal coronary angiography.

**Discussion.** Our study was conducted to evaluate an association of coronary artery disease in patients with confirmed *H.pylori* infection at a tertiary care hospital in Riyadh, KSA. The prevalence of *H.pylori* among adult population in the Middle East was estimated to be in the range of 70-90%.[9] *Helicobacter pylori* infection is higher among lower socioeconomic classes. In KSA, the higher prevalence of *H.pylori* may be attributed to exposure from workers recruited from lower socioeconomic countries (housemaids, food-handlers for example). This was shown to be true in deployed United States of America military personnel who were found at increased risk of *H.pylori* infection compared with adult populations in western countries due to exposure or overcrowding.[10] It is suggested that *H.pylori* may be hyper-endemic among Arab patients with dyspepsia.[11] Moreover, other factors that may increase the risk of *H.pylori* infection in KSA are smoking, lower educational level, and older age.[12,13]

The data presented in this study showed positive *H. pylori* in 90.5% of dyspeptic patients, a finding consistent with previous studies.[9,11] The presence of *H. pylori* was detected either by serology, culture, or histology. The absence of CAD in these patients is raising a doubt of an association with *H.pylori*. This negative finding is consistent with the finding of other investigators.[6-8,14] Furthermore, in one study, cytomegalovirus and *C.pneumoniae* were found to be prevalent in coronary atherosclerotic lesions when serial analysis is performed, but *H.pylori* was not detectable.[15] A recent study confirmed identification of *H.pylori* deoxyribonucleic acid in atherosclerotic plaques of patients with severe coronary artery disease, which supports the hypothesis that *H.pylori* infection may influence the development of atherosclerosis. These findings may suggest an involvement of *H.pylori* in the progression and instability of plaques in these patients.[16]

Another study reported no significant changes of coronary risk factors after eradication of *H.pylori* infection, and the relationship between *H.pylori* infection and CAD needs to be clarified.[17] Moreover, due to the lack of evidence relating *H.pylori* as a cause for CAD it has been postulated that the relationship between *H.pylori* and myocardial infarction may be due to confounding or co-linearity with socioeconomic status.[18] The association of *H.pylori* and CAD is still debatable as shown by one Japanese study revealing worsening of classic coronary risk factors was not associated with *H. pylori* infection in subjects younger than 55 years. Their results suggested that in younger individuals in Japan, *H.pylori* infection is significantly associated with acute myocardial infarction independent of the classic coronary risk factors.[19] We find the observation that our patients, presented in this study, being of younger age group strengthens our negative finding of a causal relation of *H.pylori* as an independent risk factor for CAD. Probably, the link between *H.pylori* infection and CAD, if found in a particular patient, is the vulnerability of that patient to both illnesses but not an association. Nonetheless, a large prospective trial is needed before a final conclusion can be made to accept or refute this association.

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