Evidence of Infection with Helicobacter Pylori in Patients With Acute Myocardial Infarction

Dr. Ala Hussain Abbass Haider
Dr. Ahmed Abdul Abbas

Abstract

Background: the role of infection with Helicobacter pylori (H. pylori) as a risk factor for acute myocardial infarction is controversial.

Aim of the study: to assess the association between H. pylori infection and acute myocardial infarction.

Patients and Methods: the IgG seropositivity to H. pylori was assessed in 40 patients with acute myocardial infarction and 39 controls.

Results: in the total study the association was statistically insignificant (80% vs 69.2%, p value:0.2, OR 0.56, 95%CI(0.2-1.5)), but in those below the age of 50 years was significant (100% vs 66.7%, p value: 0.04, OR 2.3, 95%CI(1.4-4.02)). No association was found between H. pylori seropositivity and worsening of the classic coronary risk factors.

Conclusion: this study suggests that H. pylori infection is a risk factor for coronary artery disease in patients below 50 years.

Keywords: Helicobacter pylori, acute myocardial infarction
Introduction

Ischaemia refers to lack of oxygen due to inadequate perfusion of the myocardium, which causes imbalance between oxygen supply and demand. The most common cause of myocardial ischaemia is obstructive atherosclerotic disease of epicardial coronary arteries. Ischaemic heart disease causes more deaths and disability and incurs greater economic costs than any other illness in the developed world. With urbanization in the developing world, the prevalence of risk factors for ischaemic heart disease is increasing rapidly in these regions. Large increases in ischaemic heart disease throughout the world are projected, and it is likely to become the most common cause of death worldwide by 2020.

Patients with ischaemic heart disease fall into two large groups: patients with stable angina secondary to chronic coronary artery disease and patients with acute coronary syndromes. The latter group, in turn, is composed of patients with acute myocardial infarction with ST-segment elevation on their presenting electrocardiogram and those with unstable angina and non-ST-segment elevation myocardial infarction. ST-segment elevation myocardial infarction generally occurs when coronary blood flow decreases abruptly after thrombotic occlusion of a coronary artery previously affected by atherosclerosis. Slowly developing, high-grade coronary artery stenoses do not usually precipitate ST-segment elevation myocardial infarction because of the development of a rich collateral network over time. Instead, ST-segment elevation myocardial infarction occurs when a coronary artery thrombus develops rapidly at a site of vascular injury. This injury is produced or facilitated by factors such as cigarette smoking, hypertension, and lipid accumulation. In most cases, infarction occurs when an atherosclerotic plaque fissures, ruptures, or ulcerates and when conditions (local or systemic) favor thrombogenesis so that a mural thrombus forms at the site of rupture and leads to coronary artery occlusion (1).

H. pylori was found by Marshal and Warren (2) in 1984, and then the bacterium was detected in the gastric mucosa. Numerous studies have reported the association of the bacteria with peptic ulcer, gastric mucosal diseases and gastric cancer. It was reported soon after the discovery of H. pylori that the bacteria are frequently encountered not only in patients with gastropathy but also in healthy individuals. This was because endoscopic examination had been limited to symptomatic patients, and examination in healthy individuals had been difficult. However, since the measurement of serum antibody titers became available, the infection rate in asymptomatic individuals has been indicated to be relatively high. It has also been shown that the infection rate is high (60-80%) in developing countries with poor sanitary conditions and low (30-40%) in advanced western countries, in that age, race, eating habits and geographical and socioeconomic conditions have great influences on the infection rate (3). In Iraq its prevalence had ranged between 42.9% and 67% depending on the method that were used (4). The main route of infection transmission is human to human.

Although several classic risk factors for the development of coronary artery disease have been identified (ie hypertension, hypercholesterolaemia, cigarette smoking, diabetes mellitus, and marked obesity), they only explain half of all patients with coronary artery disease (CAD) (5). In an effort to better identify patients with CAD, several markers of risk, including infectious agents, have been proposed for screening programs. H. pylori infection has been associated with a higher risk to develop ischaemic heart disease (6-8), although the results are controversial (4,9-11). The elucidation of the nature of the relation between this infection and ischaemic heart disease is of major public importance for the prevalence of the infection and the possibility to treat it by antibiotics and acid suppressive drugs.
The role of infection in the pathogenesis of atherosclerosis is still a matter of debate and the underlying processes responsible for any association also remain unclear, but it may be mediated through direct effects of H. pylori on the arterial wall, including smooth muscle cell proliferation, lipid accumulation, endothelial dysfunction, and local inflammation, or indirect effects mediated in the circulation through chronic inflammation, cross-reactive antibodies, or alterations in the classic coronary risk factors (diabetes mellitus, hypertension, body mass index, and lipid metabolism). However, correlations between H. pylori infection and coronary risk factors remain controversial.

In this study, patients with acute myocardial infarction were studied and compared with control group for H. pylori seropositivity. Because the association of coronary risk factors with CAD tends to be stronger in younger individuals than in older individuals, subgroup analysis was performed based on age. Furthermore, the association between H. pylori infection and changes in the classic coronary risk factors was studied.

Aim of the study
To assess the association between helicobacter pylori infection and acute myocardial infarction.

Patients and Methods
Patient and control Subjects
Patients included in this study were 40, had been taken from those who admitted to the coronary care unit in Mirjan teaching hospital with acute ST-segment elevation myocardial infarction between December 2006 and May 2007. A 12 leads ECG was done for each patient and diagnosis of acute myocardial infarction depends on the history of ischaemic chest complaint and ECG changes (ST-segment elevation followed by abnormally persistent Q-wave) as cardiac enzymes were unavailable at the time of the study. Control subjects were 39 volunteers, had no history of coronary artery disease, and matching patients for age, sex and presence of coronary risk factors (diabetes mellitus, hypertension, smoking and family history). Patients and controls subjects with history of peptic ulcer and chronic dyspepsia had been excluded from the study.

Laboratory Methods
Patients and controls provided venous blood samples that were centrifuged and the serum tested for the presence of IgG antibody by direct agglutination test (by using ACON® Laboratories, Inc. San Diego, CA 92121, USA) which has a sensitivity of 99% and specificity of 86.7% when compared with biopsy/ELISA according to the manufacturer. Measurements of total serum cholesterol, high-density lipoprotein cholesterol and triglycerides concentrations were performed in the hospital laboratory.

Coronary risk factors
Estimation of body mass index (BMI) was done by self measurement of weight and height (BMI=weight kg/height m²), patients and controls were considered to have diabetes mellitus if they had a history of diabetes mellitus on treatment or fasting blood glucose ≥7 mmol/l and hypertension if they had a history of hypertension on treatment, or systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, smoking was defined as current or ex-smoker, and patients and controls were asked about the presence of family history of coronary artery disease.
Statistical analysis
All data were coded and tabulated and entered to the computer using statistical
package for social sciences (SPSS14), difference between variables measured by using
t-test and association between variables measured by using Chi-square test. P value <
0.05 considered as a level of significance.

Results
32 (80%) out of 40 patients with acute myocardial infarction appeared to have
positive results to H. pylori, while 27 (69.2%) out of 39 control subjects had positive
results to H. pylori, which was not significant (p value: 0.2, OR 0.56, 95%CI(0.2-1.5)).
In those below the age of 50 years, all patients, their number was 11 (100%), had
positive results to H. pylori, while 8 (66.7%) out of 12 control subjects had positive
results to H. pylori, which was significant (p value=0.04, OR 2.3, 95%CI(1.4-4.02)),
while in those of 50 years and more , 21 (72.4%) out of 29 patients had positive results
to H. pylori and 19 (70.4%) out of 27 control subjects had positive results to H. pylori
which was not significant (p value=0.55, OR 0.9,95%CI(0.28-2.88)), (Table 1).

Characteristics of the study population
Table 2 shows the characteristics of patients and controls as a total and those below 50
years, it shows no significant difference between patients and controls except in
triglyceride in the total study population and total serum cholesterol for those below 50
years.

Table 1 Incidence of seropositivity to H. pylori IgG antibody in patients and controls
subgroups according to age

<table>
<thead>
<tr>
<th></th>
<th>Seropositivity to IgG antibody</th>
<th>p value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients n(%)</td>
<td>Controls n(%)</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>32(80%)</td>
<td>27(69.2%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Age&lt;50 years</td>
<td>11(100%)</td>
<td>8(66.7%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Age≥50 years</td>
<td>21(72.4%)</td>
<td>19(70.4%)</td>
<td>0.55</td>
</tr>
</tbody>
</table>
Table 2 Characteristics of patients and controls

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (mean ±SD)</td>
<td>57±12</td>
<td>56.3±10.1</td>
<td>0.47</td>
</tr>
<tr>
<td>Male n(%)</td>
<td>33(82.5)</td>
<td>30(76.9)</td>
<td>0.36</td>
</tr>
<tr>
<td>Diabetes mellitus n(%)</td>
<td>9(22.5)</td>
<td>7(17.9)</td>
<td>0.41</td>
</tr>
<tr>
<td>Hypertension n(%)</td>
<td>7(17.5)</td>
<td>5(12.8)</td>
<td>0.39</td>
</tr>
<tr>
<td>Smoking n(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not</td>
<td>18(45)</td>
<td>23(59)</td>
<td></td>
</tr>
<tr>
<td>Ex</td>
<td>2(5)</td>
<td>5(12.8)</td>
<td>0.106</td>
</tr>
<tr>
<td>Age (&lt;50 years)</td>
<td>41.9(5.7)</td>
<td>44.3(2.7)</td>
<td>0.47</td>
</tr>
<tr>
<td>Male (%)</td>
<td>10(90.9)</td>
<td>11(91.7)</td>
<td>0.73</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>2(18.2)</td>
<td>0</td>
<td>0.21</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>2(18.2)</td>
<td>0</td>
<td>0.21</td>
</tr>
<tr>
<td>Smoking n(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not</td>
<td>6(54.5)</td>
<td>8(66.7)</td>
<td>0.41</td>
</tr>
<tr>
<td>Ex</td>
<td>0</td>
<td>1(8.3)</td>
<td>ND</td>
</tr>
<tr>
<td>Age (&lt;50 years)</td>
<td>27±4.7</td>
<td>26.2±3.4</td>
<td>0.62</td>
</tr>
<tr>
<td>Male (%)</td>
<td>5.6±1.5</td>
<td>3.7±0.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>1.2±0.3</td>
<td>1.0±0.4</td>
<td>0.38</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>1.7±0.4</td>
<td>2.2±1.2</td>
<td>0.17</td>
</tr>
</tbody>
</table>

Comparison of demographic and classic coronary risk factors by H. pylori seropositivity in patients and control
There was no significant association between H. pylori seropositivity and any of the coronary risk factors in both patients and controls groups (Table 3). Table 3 Comparison of demographic and classic coronary risk factors in patients and controls by H. pylori seropositivity in the total study.
<table>
<thead>
<tr>
<th></th>
<th>Not</th>
<th>Ex</th>
<th>Current</th>
<th>Family history (%)</th>
<th>BMI (mean±SD)</th>
<th>T.S.Ch.mmol/L (mean±SD)</th>
<th>HDL Ch. mmol/L (mean±SD)</th>
<th>TG. mmol/L (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>40.6</td>
<td>62.5</td>
<td>59.3</td>
<td>9.4</td>
<td>25.7(4.1)</td>
<td>4.7(1.3)</td>
<td>1.19(0.4)</td>
<td>1.6(0.5)</td>
</tr>
<tr>
<td></td>
<td>6.3</td>
<td>_</td>
<td>0.47</td>
<td>0.87</td>
<td>24.2(3.4)</td>
<td>4.7(1.2)</td>
<td>1.4(0.3)</td>
<td>1.3(0.4)</td>
</tr>
<tr>
<td></td>
<td>0.65</td>
<td></td>
<td>11.1</td>
<td>0.65</td>
<td>26(3.6)</td>
<td>5.0(1.8)</td>
<td>1.3(0.6)</td>
<td>2.7(2.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.87</td>
<td>16.7</td>
<td>9.1</td>
<td>25.2(4.2)</td>
<td>4.0(0.8)</td>
<td>1.09(0.4)</td>
<td>1.9(0.7)</td>
</tr>
</tbody>
</table>

BMI: body mass index, T.S.Ch.: total serum cholesterol, HDL Ch.: high density lipoprotein cholesterol, TG.: triglyceride

**Discussion**

Previous studies have shown an association between previous infection with Chlamydia pneumoniae or H. pylori and the presence of CAD or the risk for an acute coronary event. However, the underlying processes responsible for an association between infectious agents and atherosclerotic diseases remain unclear. Various potential mechanisms, as mentioned, had been proposed, including alteration in classic coronary risk factors, so examination of the association between H. pylori infection and changes in the classic coronary risk factors was done and there were no detrimental effect of H. pylori infection on the classic coronary risk factors, which was consistent with a meta-analysis of 18 studies that involved 10,000 people and which also did not find a strong correlation between H. pylori seropositivity and coronary risk factors.

A causal role for H. pylori infection in the pathogenesis of acute myocardial infarction could not be confirmed in this study. In subjects aged <50 years, IgG seropositivity to H. pylori was significantly associated with the onset of acute myocardial infarction. Therefore, direct and/or indirect effects may be important causative factors. First, it has been suggested that chronic direct infection of arteries with H. pylori contributes to the development of atherosclerosis. H. pylori has been detected not only in gastric mucosa but also in human atherosclerotic plaques and the expression of intercellular adhesion molecule-1 is higher in plaques containing H. pylori than in those which do not. Therefore, local vessel inflammation caused by the presence of H. pylori in plaques may be associated with the development of atherosclerosis. Second, it has been suggested that H. pylori increases the risk of myocardial infarction through the promotion of an enhanced systemic inflammatory response. H. pylori seropositivity is associated with increased concentrations of systemic markers of inflammation (i.e., fibrinogen, C-reactive protein) and inflammatory cytokines (i.e., IL-6 and tumor necrosis factor). Systemic markers of inflammation are associated with the onset of myocardial infarction and inflammatory cytokines are believed to activate or injure vascular smooth muscle cells and endothelial cells. Therefore, systemic inflammation from H. pylori infection may be associated with the development of atherosclerosis. This study had several limitations common to case-control studies. In particular, the possibility that unrecognized population stratification of relevant factors influenced the findings cannot be excluded, specifically the socioeconomic status which is known to affect both the prevalence of H. pylori infection and the risk of CAD.
Because the present study examined IgG seropositivity to H. pylori, which can reflect a previous infection, as urea breath test is not available, IgG seropositivity to H. pylori may not reflect an active infection.

Another limitation is that this study does not provide information about the mechanism by which H. pylori plays a role in CAD, so the association of IgG seropositivity to H. pylori and the risk of acute myocardial infarction needs to be confirmed in further prospective studies, and in antibiotic treatment studies for H. pylori eradication, especially in younger individuals.

Conclusion and recommendations
1-this study showed that IgG seropositivity to H. pylori is significantly associated with acute myocardial infarction in patients below the age of 50 years.
2-there were no significant association between H. pylori seropositivity and classical coronary risk factors.
3-these findings can be of particular relevance to direct specific interventions for primary prevention of the disease.
4-given the intrinsic limitations of case-control studies and the relatively small size of the study for interaction analysis, larger prospective studies with the use of antibiotics are necessary to confirm and extend these results

References


