Research Article

Elevated hsCRP levels signal increased risk of future cardiovascular disease independent of lipid profile in H. pylori infection

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ABSTRACT

Background: There are reports that Helicobacter pylori (H. pylori) infection leads to changes in serum lipid profile and high sensitivity C-reactive protein (hsCRP) levels, but role of H. pylori in causing increased risk of cardiovascular disease remains a topic of debate.

Methods: A case control study was conducted, in subjects without pre-existing atherosclerotic disease. We studied 72 otherwise healthy subjects in the age group of 20 to 60 years. All subjects underwent gastroduodenoscopy and H. pylori infection status was assessed by rapid urease test.

Results: There were no statistical differences in serum total cholesterol, triglyceride, high density lipoprotein cholesterol, low density lipoprotein cholesterol levels or total cholesterol/HDL cholesterol ratios between cases and controls. However, serum hsCRP (high sensitivity C-reactive protein) levels were significantly higher in cases as compared to controls (P <0.05).

Conclusion: The results of this study showed that H. pylori infection does not modify serum lipid levels; however, it leads to a rise in hsCRP, an important risk factor for atherosclerosis. It can be concluded that H. pylori infection may contribute to atherogenesis through the state of chronic inflammation, which is evidenced by elevated hsCRP levels.

Keywords: Helicobacter pylori, Cholesterol, HDL cholesterol, LDL cholesterol, Triglyceride, C-reactive protein

INTRODUCTION

Infection with Helicobacter pylori (H. pylori), a gram negative bacterium, is the most widespread infection in the world. Prevalence in India is more than 80% in population above 20 years of age.1 Colonization of gastric mucosa with H. pylori is known to be associated with upper gastrointestinal disorders, including gastric carcinoma and gastric cancer.

Altered levels of serum Total Cholesterol (TC), Low Density Lipoprotein cholesterol (LDL-c), triglycerides (TG), High Density Lipoprotein cholesterol (HDL-c) and high sensitivity C-reactive protein (hsCRP) are known risk factors for cardiovascular disease, stroke and metabolic syndrome.2 hsCRP measurement is now accepted as useful for risk assessment of future cardiovascular events.3

Some studies suggest that H. pylori infection leads to elevated levels of serum TC, LDL-c, TG and hsCRP and decreased levels of HDL-c.4,22 This is refuted by other studies.23-30

The effect of H. pylori infection on serum lipid profile and hsCRP levels remains a matter of debate. Many of
these studies were carried out on western populations, in subjects with pre-existing coronary artery disease.

The purpose of this study was to investigate the influence of H. pylori infection on cardiovascular risk factors (lipid profile and hsCRP levels) in relatively younger Indian subjects without pre-existing atherosclerotic disease. This would presumably help in devising strategies for prevention of future atherosclerotic events in this group.

METHODS

Study subjects

Our study consisted of both male and female subjects attending the gastroduodenoscopy clinics of the departments of internal medicine and surgery at B. J. govt. medical college, Pune. Many subjects were excluded according to the following criteria: 1) Patients below 20 years and above 60 years of age, 2) Hypertensive or diabetic patients, 3) Patients with altered kidney and liver function indices, 4) Smokers and alcoholics, 5) Patients with previous history of ischaemic heart disease or thyroid disorders, 6) Patients on drug therapy known to alter lipid indices (e.g. β-blockers, OC pills), and 7) Patients receiving antihyperlipidemic therapy. Finally, a total of 72 subjects, both male and female, were included in the present study. 36 H. pylori infected cases and an equal number of age and sex matched controls without H. pylori infection were to be selected.

Data collection

Information regarding underlying diseases, medication history and addiction to alcohol or smoking was recorded using a standardised questionnaire.

Hypertension and diabetes were ruled out by searching for physician reports, lab findings or use of antihypertensive or antidiabetic medications. 5 ml of venous blood was obtained from each participant after an overnight fast (≥12 hours).

Total cholesterol, HDL cholesterol and triglycerides were measured by enzymatic methods using an automated chemistry analyzer (ERBA XL 640). 31-34 LDL cholesterol was calculated using the Friedewald equation. 35 Total cholesterol by HDL cholesterol ratio between the 2 groups (P >0.05). However, hsCRP levels were significantly elevated in H. pylori infected as compared to non-infected group (Table 1).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>H. pylori non-infected group (n=36)</th>
<th>H. pylori infected group (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>37.97 ± 11.21</td>
<td>38.94 ± 10.91</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>66.7</td>
<td>66.7</td>
</tr>
<tr>
<td>Chronic alcoholic/smoker</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>175.1 ± 36.4</td>
<td>170.5 ± 36.6</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>132.9 ± 39.0</td>
<td>128 ± 42.9</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>42.14 ± 3.65</td>
<td>40.77 ± 4.72</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dl)</td>
<td>106.3 ± 34.5</td>
<td>104.2 ± 31.9</td>
</tr>
<tr>
<td>Total cholesterol/HDL ratio</td>
<td>4.18 ± 0.9</td>
<td>4.21 ± 0.88</td>
</tr>
<tr>
<td>hsCRP (mg/L)*</td>
<td>0.17 ± 5.07</td>
<td>0.43 ± 4.54</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± standard deviation. *geometric mean, †P <0.05

H. pylori, Helicobacter pylori; HDL, high density lipoprotein; LDL, low density lipoprotein; hsCRP, high sensitivity C-reactive protein

Rapid urease test

All study subjects underwent a rapid urease test in the endoscopy room. The method used for rapid urease test for the detection of pre-formed urease enzyme was as per described by Arvind et al. 36,37

One biopsy sample was introduced in the rapid urease test solution in the endoscopy room. Development of a dark pink colour from the initial pale yellow was checked at 1 min, 5 min, ½ hour, 1 hour and 3 hours. If during these 3 hours the colour changed to pink, then rapid urease test was recorded as being positive for H. pylori infection.

Statistics

Data are presented as mean values with standard deviations. The continuous variables were compared using the Student’s unpaired t-test. All the calculations were done using Microsoft Office excel 2007. A two tailed P-value of less than 0.05 (P <0.05) was considered to be statistically significant.

The study protocol was approved by the institutional ethics committee of B. J. Govt. medical college, Pune.

RESULTS

Among the 72 subjects, 36 subjects were positive and 36 were negative for H. pylori infection by rapid urease test. There were no significant differences in lipid profile or total cholesterol by HDL cholesterol ratio between the 2 groups (P >0.05). However, hsCRP levels were significantly elevated in H. pylori infected as compared to non-infected group (Table 1).

Table 1: Characteristics of study participants.
DISCUSSION

H. pylori infection leads to chronic inflammation of the gastric mucosa. This leads to systemic release of inflammatory cytokines, one of the contributory factors of atherosclerosis. Alteration in lipid profile is another consequence of this systemic inflammatory state. Hence, H. pylori infection may lead to increase in risk of coronary artery disease. It is well documented that a rise in inflammatory cytokine-interleukin 6 is primarily responsible for a rise in hsCRP production by the liver.\textsuperscript{38} Our study also shows a statistically significant increase in hsCRP levels in H. pylori infection.\textsuperscript{(P = 0.01)} Raised hsCRP levels have been shown to be associated with higher risk of cardiovascular events.

It is observed that H. pylori infection is not associated with changes in lipid profile in our study population, which consists of young Indians. In contrast to various studies which postulate a change in lipid profile in H. pylori infection,\textsuperscript{4,22} the present study shows that levels of TC, LDL and TG are reduced in H. pylori infection, even though the decrease is not statistically significant. Levels of HDL cholesterol are also reduced in H. pylori infection, even though this did not reach statistical significance. (P = 0.17) The TC/HDL ratio was found to be weakly higher in cases as compared to controls.

It was shown that subjects with raised levels of hsCRP but low levels of LDL cholesterol are at a greater risk of future cardiovascular events than subjects with low levels of hsCRP but raised levels of LDL cholesterol.\textsuperscript{39} This shows that H. pylori infection may lead to a significant increase in the risk for future cardiovascular disease, independent of any effect on serum lipid levels.

In one study, strains of H. pylori carrying the cytotoxin associated gene A (cag A) have been found to be more pathogenic in terms of raising serum lipid levels as compared to strains lacking it.\textsuperscript{21} while another study refutes this.\textsuperscript{8} One limitation of our work is that the cag A status of the bacterium was not taken into account in our study; this needs to be assessed in future studies.

As a conclusion, the results of this study suggest that H. pylori infection is associated with elevated hsCRP levels, an important risk factor for atherosclerosis, independent of lipid profile. Eradication of H. pylori may help in preventing atherosclerosis by eliminating the cause of systemic inflammation, which is responsible for the cytokine release leading to an atherogenic state.

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Ethical approval: The study was approved by the institutional ethics committee of B. J. govt. medical college, Pune and with the Helsinki declaration of 1975 that was revised in 2000

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