CLINICAL STUDY

Helicobacter Pylori Infection and Vascular Complications in Patients with Type 2 Diabetes Mellitus
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Abstract

Objectives
The present work was designed to study H. pylori infection in type 2 DM, its relation to some clinical; metabolic and radiological markers of atherosclerosis and vascular complications in type 2 DM.

Methods
The study included sixty type 2 diabetic patients and fifteen healthy controls matched with age and sex. Both patients and controls were subjected to full history taking, clinical examination, estimation of BMI, resting ECG. laboratory tests including HbA1C, FBG, Serum creatinine; Lipid profile; fibrinogen assay, ESR; CRP; TNF α; IL-6; IL-1B; H. pylori IgG. 24 hours and urine collection for urinary albumin excretion. Radiological investigations include abdominal ultrasound. Ultrasound on the carotid arteries used in measuring the intima-medial thickness (IMT).

Results
The present study found non significant increase in prevalence of H. pylori infection in type 2 diabetic patients in relation to controls. H. pylori infection had no relation to sex, age of the patients, duration of diabetes, BMI, type of therapy or the degree of diabetic retinopathy. H. pylori infection did not affect levels of FBG, HbA1c and microalbuminuria and caused a significant increase in the level of triglycerides, TNFα, IL-1B, CRP and fibrinogen, decrease in the level of HDL and non significant effect on WBCs count, the levels of total cholesterol, LDL, ESR and IL-6 in type 2 diabetic patients. H. pylori infection does not affect IMT of both Right and Left common carotid arteries. No significant increase of the prevalence of H. pylori infection among diabetic patients with diabetic vascular complications.

Conclusion
There is no significant increase in prevalence of H. pylori infection among type 2 diabetic patients. H. pylori infection is not related to patient age, degree of glycaemic control, IMT or diabetic vascular complications among type 2 diabetic patients. However, H. pylori infection could affect atherosclerotic process through its effects on lipid profile (increase in TG and decrease HDL levels), increase levels of inflammatory cytokines (TNF-alpha and IL-1B) and acute phase reactants (CRP and Fibrinogen).

Key words: H. pylori infection; Type 2 DM, Diabetic vascular complications, IMT, Inflammatory markers, Cardiac risk factors

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Introduction

The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of various organs especially the eyes, kidneys, nerves, heart and blood vessels. At least 80% of the diabetic patients will die predominantly from the consequences of vascular complications. Review of epidemiological studies indicates that classic risk factors for atherosclerosis account for majority but not the entirety of the etiology and pathogenesis of the clinical complications of atherosclerosis, including ischemic heart diseases. The inability of traditional risk factors to completely explain the incidence and trends in cardiovascular diseases has resulted in repeated calls for a search for new risk factors. Infections have been placed among these new putative risk factors. Infection with Helicobacter pylori (H. Pylori; gram negative bacteria) has been epidemiologically linked to some extradigestive conditions, including ischemic heart disease, diabetes mellitus and others. Diabetic patients are at risk of cardiovascular and thrombo-occlusive cerebral diseases. There is a possible relationship between H. pylori infection and cardiovascular or cerebrovascular diseases. The finding that infectious agents are responsible for chronic diseases of unknown cause is not new. Chronic H. pylori colonization may be associated with an increased risk for atherosclerosis. The underlying hypothesis is that H. pylori infection has atherogenic capacities by chronic low-grade activation of the haemostasis cascade.

The association between H. pylori and acute cerebrovascular disease seems to be due to a higher prevalence of more virulent H. pylori strains in patients with atherosclerotic stroke.

Chronic H. pylori infection was associated with a higher risk of stroke due to small artery occlusion and a lower risk of cardio embolic stroke. Chronic H. pylori infection still showed an over all association with ischemic stroke after adjustment of major cardiovascular risk factors. These suggest that chronic H. pylori infection may be a triggering factor that increases the risk of acute ischemic stroke. The present work was designed to study H. pylori infection in type 2 DM, its relation to some; metabolic and radiological markers of atherosclerosis and vascular complications in type 2 DM.

Materials and Methods

Sixty patients of known diabetes type 2, age range of 30-60 years enrolled from outpatient’s clinic of endocrinology unit of Mansoura specialized medical hospital, Mansoura University. The studied cases were enrolled during summer months of 2005. Patients with chronic liver diseases; cardiac diseases; renal impairment; acute medical insults and Patients with other endocrinial diseases were excluded from the study. Fifteen healthy adults of matched age and sex were taken as control group. This descriptive study was approved by the local ethical committee from the Scientific Research at Mansoura University hospital, Egypt. Informed consent was obtained from all subjects before the beginning of the study.

Diabetes mellitus was diagnosed according to the Report of the expert committee on the diagnosis and classification of DM. Both patients and controls were subjected to full history taking with stress upon cardiac risk factors, diabetic history and findings of vascular complications. Full clinical examination was done including cardiac risk factors; blood pressure, resting electrocardiogram, body mass index and (BMI) was calculated according to the following Formula: (Weight) in Kg/(Height)² in meter.

Macrovascular diabetic complications were diagnosed by presence of findings suggestive ischemic heart, peripheral vascular or cerebrovascular diseases. Retinopathy was diagnosed by simple direct ophthaloscope and/or by ophthalmologist. Diagnosis of nephropathy was considered by the presence of persistent albuminuria of 20 to 200 mg/24 hours (microalbuminuria) in at least three occasions in absence of UTI.
Macroalbuminuria was diagnosed when persistent albuminuria equals or exceeds 300 mg/24 hours\textsuperscript{10}. Urinary albumin concentration was measured by Radioimmunoassay.

Laboratory investigations including complete blood picture and HbA1C, fibrinogen assay, ESR; FBG, Liver function tests (SGOT, SGPT, serum albumin); Serum creatinine; Lipid profile; CRP; TNF α; IL-6; IL-1B; and H pylori IgG. 24 hours Urine collection for detection of microalbuminuria. 24-hour collections were used for determination of daily excretions of total albumin. Urinary albumin excretion was measured by Quantitative Turbidimetric Determination of Total Protein. Kits were supplied from Stanbio laboratories, USA. Morning blood samples were collected after a 12 hour fast; 10 ml venous samples were withdrawn and aliquot into tubes under aseptic conditions as follows: sodium fluoride plasma for determination of glucose, serum for determination of the lipid profile (total cholesterol, HDL-C, LDL-C and triglycerides). The EDTA samples were stored on ice (-80) between the time of sampling and centrifugation for determination of Serum Fibrinogen, CRP, IL-6, IL-1β & TNF-alpha levels. A high sensitivity enzyme linked immunosorbent assay (ELISA) was used. Blood picture was done using CEII DYNE 1700 USA blood count analyser. Human Germany supplied prospective kits and reagents for assay of Liver functions tests, Erythrocyte sedimentation rate (ESR) was assessed manually at 1and 2hrs. HbA1C assay done using Quantitative Colorimetric Determination of Glycohema globin in whole blood supplied by Stanbio Laboratory, Texas, USA. The plasma glucose level was measured by an automated enzymatic method on the Hitachi 911 analyzer using Roche Diagnostic’s regents (Indianapolis, IN). Serum levels of total cholesterol, triglyceride, and HDL cholesterol were measured by enzymatic methods using an autoanalyzer (TBA60M; Toshiba, Tokyo, Japan). LDL-cholesterol is calculated using the Friedewald formula\textsuperscript{11} as follows:

$$LDL-C = \text{total cholesterol} - (\text{HDL-C} - \frac{\text{TG}}{2.2})$$

where all quantities are expressed in mmol/L

H. pylori IgG was done using kits supplied by Neo Din Co., Ltd, Seoul, Korea. Radiological investigations include abdominal ultrasound using ultrasonic device power vision 6000, Toshiba by linear probe 8 MHZ. Ultrasound on the carotid arteries was done for all studied cases using B-mode ultrasound. B mode grey scale can be efficiently used in measuring the intima-medial thickness in the common carotid arteries (CCA).

**Statistical Analysis**

Statistical evaluation of all data was done on IBM-PC microprocessor computer using SPSS software for windows (Statistical Package for Social Sciences version 11, USA) for data management and analysis and the excel for figures. Quantitative data were presented as mean ± SD. Quantitative variables with normal distribution were analyzed with a two-tailed, paired Student’s \textit{t} test. ANOVA (F) test with Bonferroni multiple comparisons were used for comparison between more than 2 groups. Qualitative variables such as comparison between proportion & percentage by Chi square with Yates correction as necessary. Pearson correlation coefficient was used to correlate between variables. \textit{P} value under 0.05 was considered statistically significant.

**Results**

The age, sex and body mass index of cases were matched with the control (Table 1). H. pylori was higher in type 2 diabetic patients (38.3\%) compared to the healthy control (20\%), but this difference was statistically non significant (\textit{p} value = 0.581) (Table 1). H. pylori infection had no significant relation to the duration of diabetes (\textit{p}. Value=0.602). The difference in H pylori seropositivity in relation to type of therapy was statistically non significant (\textit{p} value = 0.335) as shown in Table 2.
Table 1: *H. pylori* infection among controls and type 2 diabetic patients with their clinical characteristics (sex; body mass index and diabetic duration)

<table>
<thead>
<tr>
<th>Clinical Data</th>
<th><em>H. pylori</em> +ve</th>
<th><em>H. pylori</em> -ve</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (No; %) (60)</td>
<td>23/38.3%</td>
<td>37/61.7%</td>
<td>0.581</td>
</tr>
<tr>
<td>Controls (No; %) (15)</td>
<td>3/20%</td>
<td>12/80%</td>
<td>NS</td>
</tr>
<tr>
<td>Male (16)</td>
<td>4/25%</td>
<td>12/75%</td>
<td>0.44</td>
</tr>
<tr>
<td>Female (44)</td>
<td>19/43%</td>
<td>25/57%</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>37.16±5.2</td>
<td>31.64±5.1</td>
<td>0.140 (NS)</td>
</tr>
<tr>
<td>Diab. duration (years)</td>
<td>7.9±5.2</td>
<td>7.3±4.8</td>
<td>0.602 (NS)</td>
</tr>
</tbody>
</table>

Comparison between the different groups by using T test for numerical data and Chi square test for percentages. * P: mildly statistically significant (P<0.05). ** P: highly statistically significant (P<0.01). No: number. %: Percentage. NS: non-significant. BMI: Body mass index.

Table 2: *H. pylori* infection among type 2 diabetic patients in relation to anti-diabetic therapy (oral; insulin and combined therapies)

<table>
<thead>
<tr>
<th><em>H. pylori</em></th>
<th>Oral</th>
<th>Insulin</th>
<th>Combined</th>
<th>Total</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>H. pylori</em> +ve (No;%)(100)</td>
<td>7/30.5%</td>
<td>3/13%</td>
<td>13/56.5%</td>
<td>23/100%</td>
<td>0.335</td>
</tr>
<tr>
<td><em>H. pylori</em> -ve (No;%)(100)</td>
<td>10/27%</td>
<td>10/27%</td>
<td>17/45.9%</td>
<td>37/100%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>17/28.3%</td>
<td>13/21.7%</td>
<td>30/50%</td>
<td>60/100%</td>
<td></td>
</tr>
</tbody>
</table>

Comparison between the different groups by using Chi square test for percentages. No: number. %: Percentage. NS: non-significant.

Table 3: *H. pylori* infection among type 2 diabetic patients in relation to some laboratory data (fasting blood glucose; hemoglobin A1C; Microalbuminuria and serum lipids profile)

<table>
<thead>
<tr>
<th>Laboratory Data</th>
<th><em>H. pylori</em> +ve</th>
<th><em>H. pylori</em> -ve</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBG (mg/dl)</td>
<td>331.2±101</td>
<td>289.4±99.6</td>
<td>0.120</td>
</tr>
<tr>
<td>HbA1C% (gm %)</td>
<td>9.2±2.1</td>
<td>8.92±2.1</td>
<td>0.627</td>
</tr>
<tr>
<td>Albuminuria (ug/ml)</td>
<td>108.7±121.7</td>
<td>138.8±122.8</td>
<td>0.357</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>199.6±57.5</td>
<td>214.6±59.5</td>
<td>0.339</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>180.7±64.1</td>
<td>137.6±48.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>29.4±7.3</td>
<td>45.6±8.9</td>
<td>0.01</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>138.1±42.2</td>
<td>144.1±61.2</td>
<td>0.687</td>
</tr>
</tbody>
</table>

Comparison between the different groups by using T test * P: mildly statistically significant (P<0.05). ** P: highly statistically significant (P<0.01). FBG: Fasting blood glucose. HAIC: hemoglobin A1c. HDL: High density lipoprotein. LDL: Low density lipoprotein.

Table 4: Relation of *H. pylori* to the degree of retinopathy among type 2 diabetic patients

<table>
<thead>
<tr>
<th>Fundus Exam</th>
<th><em>H. pylori</em> +ve</th>
<th><em>H. pylori</em> -ve</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Fundus (No;%)(100)</td>
<td>15/65.2%</td>
<td>30/81.1%</td>
<td>0.118 (NS)</td>
</tr>
<tr>
<td>Non-Proliferative DR (No%)</td>
<td>6/26%</td>
<td>4/11%</td>
<td>10/16.6%</td>
</tr>
<tr>
<td>Proliferative DR (No%)</td>
<td>2/8.8%</td>
<td>3/7.9%</td>
<td>5/8.4%</td>
</tr>
</tbody>
</table>

Comparison between the different groups by using Chi square test for percentages. No: number. %: Percentage. NS: non-significant. DR: diabetic retinopathy.
Table 5: Relation of *H. pylori* seropositivity and inflammatory markers in type 2 diabetic patients

<table>
<thead>
<tr>
<th>Inflammatory Markers</th>
<th><em>H. pylori</em> +ve No: 23</th>
<th><em>H. pylori</em> -ve No: 37</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBCs</td>
<td>6.8±1.8</td>
<td>6.8±1.9</td>
<td>0.975</td>
</tr>
<tr>
<td>ESR-1</td>
<td>27.6±17.2</td>
<td>24.8±20.1</td>
<td>0.581</td>
</tr>
<tr>
<td>ESR-2</td>
<td>53.9±29.2</td>
<td>47.9±30.3</td>
<td>0.450</td>
</tr>
<tr>
<td>CRP mg/l</td>
<td>14.8±7.8</td>
<td>9.2±7.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Fibrinogen mg/dl</td>
<td>432±176</td>
<td>283±98</td>
<td>0.001</td>
</tr>
<tr>
<td>TNF-α pg/ml</td>
<td>67.3±8.1</td>
<td>47.3±9.1</td>
<td>0.01</td>
</tr>
<tr>
<td>IL-6 pg/ml</td>
<td>48.2±19.2</td>
<td>52.3±32.1</td>
<td>0.581</td>
</tr>
<tr>
<td>IL-1β pg/ml</td>
<td>19.3±4.1</td>
<td>17.2±3.1</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Comparison between the different groups by using T test * P: mildly statistically significant (P<0.05). ** P: highly statistically significant (P<0.01). WBC: white blood cells. ESR: erythrocyte sedimentation rate. CRP: C- reactive protein. TNF-α: Tumor Necrosis Factor-alpha IL-6: Interleukin-6. IL-1β: Interleukin-1β.

Table 6: Effect of *H. pylori* seropositivity on the carotid Intima Medial Thickness (IMT) of both Right and left common carotid arteries in type 2 diabetic patients

<table>
<thead>
<tr>
<th>Intima Medial Thickness</th>
<th><em>H. pylori</em> +ve No: 23</th>
<th><em>H. pylori</em> -ve No: 37</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right CCA in mm</td>
<td>7.78±1.41</td>
<td>8.16±1.69</td>
<td>0.373</td>
</tr>
<tr>
<td>Left CCA in mm</td>
<td>8.08±1.54</td>
<td>8.21±1.62</td>
<td>0.760</td>
</tr>
</tbody>
</table>

Comparison between the different groups by using T test * P: mildly statistically significant (P<0.05). ** P: highly statistically significant (P<0.01). CCA: common carotid artery.

Table 7: *H. pylori* infection among type 2 diabetic patients with and without macrovascular complications (IHD or stroke).

<table>
<thead>
<tr>
<th>Type 2 DM</th>
<th><em>H. pylori</em> +ve No: 23</th>
<th><em>H. pylori</em> -ve No: 37</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM without MAVC (No/%)</td>
<td>13/30.9%</td>
<td>30/70.1%</td>
<td>0.373</td>
</tr>
<tr>
<td>DM with MAVC (No/%)</td>
<td>10/58.8%</td>
<td>7/41.2%</td>
<td>0.760</td>
</tr>
<tr>
<td>Total (No/%)</td>
<td>23/38.3%</td>
<td>37/61.7%</td>
<td>0.511</td>
</tr>
</tbody>
</table>

Comparison between the different groups by using Chi square test for percentages. No: number. %: Percentage. MAVC: macrovascular complications.

The patients with *H. pylori* seropositivity had significant high triglyceride and low HDL levels than those with negative *H. pylori* (180.7±64.1, 29.4±7.3 versus 137.6±48.4, 45.6±8.9). The patients with *H. pylori* seropositivity had non-significant high FBG and HA1C levels as shown in Table 3. *H. pylori* seropositivity had no relation to the degree of diabetic retinopathy as demonstrated in Table 4.

*H. pylori* infection caused significant increase in the level of Fibrinogen, C reactive protein and some inflammatory cytokines as TNF-alpha and IL.1B as depicted in Table 5. Intima medial thickness of both right and left common carotid arteries were not significantly affected by *H. pylori* seropositivity (Table 6). No significant difference in prevalence of *H. Pylori* infection between diabetic patients with no evidence of macrovascular complications
(30.9%) and those with macrovascular complications (58.8%) as outlined in Table 7.

Figure 1: Inflammatory Markers in type 2 diabetic patients with positive H Pylori versus those with negative H. Pylori.

Figure 2: Macrovascular diabetic complications in type 2 diabetic patients with positive H. Pylori versus those with negative H Pylori.

Discussion

Recent and compelling evidence has shown the significant and independent role of inflammation, insulin resistance and subsequent endothelial dysfunction in the initiation and progression of atherothrombosis, superimposed on traditional risk factors. Infection by Helicobacter pylori has been epidemiologically linked to some extradigestive conditions, including ischemic heart diseases. Diabetic patients are at risk of cardiovascular and thrombo-occlusive cerebral disease. There is a possible relationship between H. pylori infection and cardiovascular or cerebrovascular diseases in diabetic patients.

The present study found non significant increase in the prevalence of H. pylori infection among diabetic patients (38.3%) in relation to control healthy subjects (20%). No association between H. pylori infection among diabetic patients and duration of diabetes, BMI, sex of patients or their age. These findings support that found by Hamed et al, Anastasios et al who found no statistically significant increase in H. pylori seropositivity among diabetic patients and seems to be linked to the presence of atherosclerosis. Therefore, it seems that prevalence of H. pylori infection in diabetes mellitus reflects a balance between possible predisposing conditions (e.g.: gastroparesis diabeticorum) and preventing factors (e.g.: diabetes induced achlorhydria). It is certain that many other factors related to H. pylori colonization of gastric mucosa in diabetes mellitus remain unknown.

The present study found a non significant relation between H. pylori infection and glycaemic control in type 2 diabetic patients as evidenced by levels of fasting blood glucose (FBG), HbA1c and type of therapy (oral, insulin, combined). These findings support that found by Gillum who found that H. pylori infection status was not significantly associated with glycated hemoglobin (HbA1c) in men aged 40-70 years with or without history of diabetes. Also it supports Candelli and co-workers who found that H. pylori eradication in type 1 diabetes doesn’t affect glycaemic control in such patients as evidenced by HbA1c level and daily insulin requirement. This difference may be attributed to differences in type of diabetes or age of patients between the present study and the study done by Begue et al.

The present study provides evidences that H. pylori seropositivity was associated with
atherogenic modified lipid profile among patients with type 2 DM. \textit{H. pylori} infection was associated with significant increase in triglyceride level. Significant decrease in HDL level and non significant effect on levels of both LDL and total cholesterol. The present study supports Sung and his co-workers\(^{(19)}\) who found that \textit{H. pylori} infection in healthy Korean adults was associated with atherogenic lipid profile (increase in total cholesterol, triglyceride, LDL cholesterol and decrease in HDL cholesterol) but this study had many limitations (subjects included were healthy, young, self selected and of relatively high socioeconomic status). While in the present study patients were type 2 diabetic aged 30-60 years and of relatively lower socioeconomic status. A lot of studies which provided evidences for association between \textit{H. pylori} infection and atherogenic modified lipid profile were done. A possible association of \textit{H. pylori} infection and the development of coronary heart disease, thrombo-occlusive cerebral disease, or both, in diabetic patients. The importance of this link is highlighted by the possibility of an effective intervention against \textit{H. pylori} infection\(^{19}\).

Eradication of \textit{H. pylori} was found to be associated with significant decrease in CRP, significant increase in HDL and non significant effect on LDL, neither triglycerides nor total cholesterol among healthy people with \textit{H. pylori} infection\(^2\). \textit{H. pylori} infection is associated with cardiovascular risk factors, especially with triglyceride, HDL-cholesterol and apolipoproteins, independently from the presence of peptic ulcer\(^{21}\). Association of \textit{H. pylori} infection with modified atherogenic lipid profile may be due to lipopolysaccharides present in this gram negative bacteria which stimulate the production of many cytokines including tumor necrosis factor alpha (TNF-\(\alpha\)) which inhibit lipoprotein lipase activity leading to mobilization of lipids from the tissues and elevated serum triglycerides, lowered HDL cholesterol levels\(^{22}\).

The present study found significant increase in serum levels of TNF-\(\alpha\) and IL1-B in patients seropositive for \textit{H. pylori} infection than seronegative ones. The presence of these inflammatory cytokines in the serum in association with \textit{H. pylori} infection was demonstrated by a lot of studies. \textit{H. pylori} seropositivity was found to cause increase in serum TNF-\(\alpha\) in human\(^3, 4\) irrespective of the type of strain included. Cag A positive \textit{H. pylori} infection was found to be significantly associated with increased TNF-\(\alpha\) level than Cag A negative one\(^5\). Serum level of IL-1B was found to be significantly associated with \textit{H. pylori} infection in human. A good experimental evidence of association between \textit{H. pylori} infection especially with toxigenic strains (Cag A and Vac A positive) with increased plasma levels of TNF-\(\alpha\) and IL-1B in rats was supplied by Brzozowski et al\(^{26}\). Systemic increase in serum levels of TNF-\(\alpha\) and IL-1B in association with \textit{H. pylori} infection is due to lipopolysaccharides present in this gram negative bacteria.

In the present study significant increase in CRP level was found in association with \textit{H. pylori} infection among type 2 diabetic patients. Oshima et al\(^{27}\) found significant increase in CRP level in non smoker healthy subjects seropositive for \textit{H. pylori} infection. Markus et al.\(^{(28)}\) found significant association between CRP and \textit{H pylori} seropositivity. CRP was also found to be increased in stroke patients seropositive to \textit{H. pylori} infection than seronegative ones and this supports the hypothesis which considers \textit{H. pylori} to be a cause of generalized inflammation, a recognized risk factor for atherosclerosis\(^8\).

The present study found significant increase in fibrinogen level in \textit{H. pylori} positive diabetic patients in comparison to negative patients. The same results were found by Schumacher, et al\(^{29}\) among patients with coronary heart disease. Zito et al\(^{30}\) found an increase in level of plasma fibrinogen in \textit{H. pylori} infected individuals even after controlling of possible confounding factors related to either infection or fibrinogen. The intima-medial thickness (IMT) of the carotid arteries is a marker of early atherosclerosis and the available epidemiological data indicate that increased IMT at or above 1mm
represents a risk for myocardial infarction and or cerebrovascular disease. So, IMT was assessed in the present study (in both right and left common carotid arteries just 1cm before bifurcation) and its relation to \textit{H. pylori} was examined. The present study found a non significant difference in IMT of both CCAs in relation to \textit{H. pylori} seropositivity among diabetic patients. Folsom et al\textsuperscript{32} found that \textit{H. pylori} seropositivity was not associated with increased IMT of carotid artery measure of subclinical atherosclerosis among patients with CHD. Markus et al \textsuperscript{28} found that \textit{H. pylori} infection was not associated with increased IMT among normal individuals. Koksal et al\textsuperscript{33} found non significant difference in the IMT of carotid arteries between \textit{H. pylori} positive and negative groups of patients who were identical in terms of sex distribution, smoking pattern, glucose, cholesterol, ESR, triglycerides, LDL, HDL, systolic and diastolic blood pressure levels. The lack of relation between \textit{H. pylori} seropositivity and IMT of CCAs may be due to interference of multiple other risk factors in the process of atherosclerosis. These risk factors may be more related and affecting the progression of atherosclerosis than \textit{H. pylori} seropositivity. However, virulence of \textit{H. pylori} strain may be another possible factor that may lead to atherosclerosis which in not included in our study.

The present study found non significant relation between \textit{H. pylori} seropositivity and microvascular complications (degree of retinopathy and nephropathy as indicated by level of microalbuminuria) or prevalence of macrovascular complications (IHD and cerebrovascular diseases). Tasi and Huang\textsuperscript{35} found non significant association between \textit{H. pylori} infection and angiographically documented coronary heart disease. Bielanski\textsuperscript{36} performed an epidemiological study in which no any clear correlation between \textit{H. pylori} infection and IHD was found. Biagi, et al\textsuperscript{37} found no positive association between seroprevalence of \textit{H. pylori} infection and CHD. On the other hand, \textit{H. pylori} infection might be one of the risk factors of atherosclerosis thorough inflammation (fibrinogen) and modulation of glucose and lipid profiles, which may be prevented by low antibiotics. Also, \textit{H. pylori} seropositivity is a potential risk factor for increased brachial-ankle pulse wave velocity levels\textsuperscript{39}. Majka et al\textsuperscript{40} demonstrated higher prevalence of \textit{H. pylori} infection in patients with ischemic stroke. Also, some studies revealed no consistent associations of \textit{H. pylori} infection with diabetes prevalence but it was associated with CHD prevalence\textsuperscript{41}. The differences between previous studies and the present one may be due to predominant effect of cardiovascular risk factors in diabetic patients than direct effect of \textit{H. pylori} infection. Another explanation is the role of toxigenic strains of \textit{H. pylori} infection (Cag A and Vac A strains) which were proved to be highly related to IHD and atherosclerotic plaque instability\textsuperscript{43}. These toxigenic strains were not examined in the present study.

Epidemiologic study has suggested possible atherogenic roles for \textit{H. pylori}. \textit{H. pylori} infection is associated with arterial stiffness determined by pulse wave velocity in patients with type 2 diabetes mellitus\textsuperscript{44}. The importance of this link is highlighted by the possibility of an effective intervention against \textit{H. pylori} infection.

It is concluded that, there is no significant increase in prevalence of \textit{H. pylori} infection among type 2 diabetic patients. \textit{H. pylori} infection is not related to age of the patients, their sex, BMI, duration of diabetes nor to the degree of glycaemic control. \textit{H. pylori} infection has no direct relation to atherosclerosis (IMT) or vascular (micro and macrovascular) complications among type 2 diabetic patients. However, \textit{H. pylori} infection may increase atherosclerotic plaque formation, plaque instability and incidence of arterial thrombosis among these patients making them more prone to acute ischemic events. These effects are mediated through modification of lipid profile (increase in TG and decrease HDL levels), increase levels of inflammatory cytokines (TNF-alpha and IL-1B) and acute phase reactants (CRP and Fibrinogen).

Due to the above mentioned results and conclusion of the present study, many relations need to be clarified in the future.
studies. Effect of *H. pylori* on various clinical, chemical, radiological changes in diabetic patients presented with acute complications especially ischemic events needs clarification and studies. The relations especially the direct relation of *H. pylori* infection to atherosclerotic plaque formation and plaque instability in patients with DM can be studied in the future. Finally, larger number of patients, form of *H. pylori* infection (acute or chronic) and presence of virulent strains are important aspects which need to be considered as much as possible.

**References**


