HELCOBACTER PYLORI INFECTION AMONG PATIENTS WITH DIABETES MELLITUS

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Abstract
Helicobacter pylori (H. pylori) is a gram-negative bacterium that specifically colonizes the gastric epithelium causing many complications. The link between H. pylori infection and diabetes mellitus (DM) remains controversial. This study was conducted to determine the frequency of H. pylori infection among a group of subjects with DM and to compare it with that of an age and sex-matched group of non-diabetic subjects.

This case control study was conducted in Al-Sadr Teaching Hospital, Basrah, Southern Iraq from January 2013 to September 2014 on 200 subjects aged ≥ 40 years, 100 diabetic and 100 non-diabetic subjects. All subjects were required to submit fresh stool samples which were tested for evidence of H. pylori infection by stool antigen positivity.

Helicobacter pylori infection was detected in 43% of diabetic group and 25% of controls, which was found to be statistically significant (p value=0.007).

In conclusion, the present study suggests that diabetic subjects are at more risk for H. pylori infection in comparison to non-diabetic subjects. This association is found to be higher in those with long duration of DM and those with poor glycemic control.

Introduction
Helicobacter pylori (H. pylori) is a gram negative, spiral shaped pathogenic bacterium that specifically colonizes the gastric epithelium causing chronic gastritis, peptic ulcer disease, and/or gastric malignancy. H. pylori is mainly acquired in childhood by the feco-oral, oro-oral or gastro-oral routes. It has been estimated that up to half of the world’s population harbor the infection in their stomach. The developing world has a higher prevalence rate of infection than the developed world, and it has associated with both gastrointestinal and extra-intestinal complications. H. pylori infection may have an impact on cardiovascular conditions, insulin resistance, and metabolic syndrome potentially mediated by elevations in inflammatory markers such as C-reactive protein (CRP) and Interlukin-6 (IL-6). Elevated levels of inflammatory cytokines may lead to phosphorylation of serine residues on the insulin receptor substrate, which prevents its interaction with insulin receptors, and then inhibits insulin action. Mammalian stomach produces leptin and ghrelin, two hormones involved in energy homeostasis and whose interactions affect obesity, insulin sensitivity, and glucose homeostasis. Increasing evidence indicates that H. pylori is involved in the regulation of these hormones.

The link between H. pylori infection and diabetes remains controversial, as some studies indicate a higher prevalence of infection in diabetic patients, while others report no difference. The relationship between H. pylori and diabetes mellitus was first explored in 1989 by Simon et al who found that the prevalence of H. pylori infection in patients with DM was significantly higher than in asymptomatic controls.
(62% vs 21%). However, the test used for detecting H. pylori was only a rapid urease test, and their comparison did not adjust for age, which is a major confounding factor. Additional supportive data have come from groups in the Netherlands, Italy, Turkey, and Africa. Recently, a meta-analysis conducted by Zhou et al. involved 14080 patients from 41 studies with a total H. pylori infection rate of 42.29%.

Although there is no concrete evidence demonstrating that H. pylori plays a role in diabetes, the possibility for a causal relationship is an intriguing issue deserving discussion. There are several lines of evidence to implicate increased susceptibility to infection in diabetic patients. Among these, impairment of cellular and humoral immunity, reduction of gastrointestinal motility and acid secretion, altered glucose metabolism and increased susceptibility of pathogens as they regularly attend hospital settings.

However, there are also indications that H. pylori infection may contribute to the development of diabetes. Whereas insulin insensitivity is an early phenomenon, pancreatic β-cell function declines gradually over time before the onset of clinical hyperglycemia, the result of many factors that can be influenced by infection, such as insulin resistance (IR), glucotoxicity, lipotoxicity, β-cell dysfunction, chronic inflammation, and genetic and epigenetic factors.

This study aims to determine the frequency of H. pylori infection among a group of subjects with DM and to compare it with that of an age and sex-matched group of non-diabetic subjects.

**Patients and Methods**

This case control study was conducted in Al-Sadr Teaching Hospital, Basrah, Southern Iraq from January 2013 to September 2014 on 200 subjects aged ≥40 years who were divided into two groups:

Group 1: consisted of 100 subjects known to have DM and on anti-diabetic medications (81 on oral and 19 on insulin), Group 2: consisted of 100 non-diabetic subjects, for whom samples of venous blood were sent for fasting blood sugar to rule out the possibility of undiagnosed DM by readings <7 mmol/L according to American Diabetic Association. All subjects were required to submit fresh stool samples which were tested for evidence of H. pylori infection by stool antigen positivity with the immunoassay-based Rapid Strip HpSATM according to the manufacturer’s instructions (from CTK Biotech, Inc), since it has high sensitivity (94%) and specificity (94%) and is potentially very helpful in diagnosing active and repeated H. pylori infection.

Glycated haemoglobin (HbA1c) was ordered for all diabetic subjects, and according to the result, they were subdivided into 3 groups: group (A) with HbA1c<7, group (B) with HbA1c 7-10 and group (C) with HbA1c>10. The frequency of H. pylori infection was then measured among each group.

**Exclusion criteria:**
1. Newly diagnosed cases of DM and those with a history of less than 2 years duration.
2. Subjects on antibiotics and/or proton pump inhibitors.
3. Subjects with GIT bleeding.
4. Subjects with haemoglobinopathies.
5. Subjects with a history of renal failure, chronic liver disease, malignant disease or on immunosuppressant agents. Statistical analysis was done by using the SPSS V 19 multilingual software. P value less than 0.05 was considered to be significant.
Results

Both 2 groups (diabetic and non-diabetic) were matched in view of age and gender as there was no significant statistical difference. The mean age±SD of group 1 subjects was 55.7±10.2 years, while that of group 2 subjects was 57.6±10.9 years. The P value was 0.203 [Table I].

Table I: Demographic distribution of studied groups

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male No. (%)</td>
<td>40 (40%)</td>
<td>48 (48%)</td>
<td>88 (44%)</td>
</tr>
<tr>
<td></td>
<td>Female No. (%)</td>
<td>60 (60%)</td>
<td>52 (52%)</td>
<td>112 (56%)</td>
</tr>
<tr>
<td>Mean age ± SD yr.</td>
<td>55.7±10.2</td>
<td>57.6±10.9</td>
<td>-----</td>
<td>0.203</td>
</tr>
</tbody>
</table>

H. pylori was positive in 68 (34%) subjects of the studied population, 43 of them were in group 1, and 25 in group 2, which was found to be statistically significant (Odds Ratio= 2.26, $x^2=7.2$, $df=1$, $P=0.007$). [Table II].

Table II: Frequency of HpSA positive cases in studied groups

<table>
<thead>
<tr>
<th></th>
<th>Group1 No.</th>
<th>Group2 No.</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HpSA +ve</td>
<td>43</td>
<td>25</td>
<td>68 (34%)</td>
</tr>
<tr>
<td>HpSA -ve</td>
<td>57</td>
<td>75</td>
<td>132 (66%)</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>200 (100%)</td>
</tr>
</tbody>
</table>

Odds Ratio= 2.26, $x^2=7.2$, $df=1$, $P=0.007$

Among group 1, the mean HbA1c of subjects with HpSA positive was 10.18 (±0.28)%, while that for those with HpSA negative was 8.5(±2.09)%. This difference was found to be statistically significant (P value<0.001). Furthermore, by subdividing the diabetic subjects into group A, B and C depending on HbA1c level, it was found that the percentage of infected subjects with H. pylori was the highest (73%) among group C (HbA1c>0), (31%) among group B (HbA1c 7-10), and the lowest (25%) among group A (HbA1c<7), as demonstrated in figure 1.

Figure 1: Percentage of HpSA positive subjects among each HbA1c group
In addition, H. pylori infection was found to be significantly higher among those with long duration DM (>5 years) as compared with those with short duration DM (2-5 years), as demonstrated in Table III.

**Table III:** Frequency of H. pylori infection in relation to duration of DM in group 1 according to time of diagnosis

<table>
<thead>
<tr>
<th>Duration Of DM (yr.)</th>
<th>HpSA +ve No.(%)</th>
<th>HpSA -ve No.(%)</th>
<th>Total No.(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-5</td>
<td>12 (24.0)</td>
<td>38 (76.0)</td>
<td>50 (100.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>&gt;5</td>
<td>31 (62.0)</td>
<td>19 (38.0)</td>
<td>50 (100.0)</td>
<td></td>
</tr>
</tbody>
</table>

Regarding the frequency of H. pylori infection among group 1 as related to the type of therapy, no significant difference was found between those on insulin and those on oral therapy, as demonstrated in Table IV.

**Table IV:** Frequency of H. pylori infection in relation to type of DM therapy in group 1

<table>
<thead>
<tr>
<th>Type of therapy</th>
<th>HpSA+ve No.(%)</th>
<th>HpSA-ve No.(%)</th>
<th>Total No.(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>oral</td>
<td>36 (44.4)</td>
<td>45 (55.6)</td>
<td>81 (100.0)</td>
<td>0.54</td>
</tr>
<tr>
<td>insulin</td>
<td>7 (36.8)</td>
<td>12 (63.2)</td>
<td>19 (100.0)</td>
<td></td>
</tr>
</tbody>
</table>

Among the studied population, the mean age for subjects with HpSA positive was 57.9 (±11.1) years, while that for those with HpSA negative was 56.07 (±10.3) years. This difference found to be statistically not significant (P value =0.24). Twenty five from 88 males (28.4%) in the studied population were HpSA positive, while 43 from 112 females (38.3%) were HpSA positive. This difference was found to be statistically not significant. [Table V].

**Table V:** Frequency of H. pylori infection in relation to gender and age in studied population

<table>
<thead>
<tr>
<th>Gender</th>
<th>HpSA +ve No.(%)</th>
<th>HpSA –ve No.(%)</th>
<th>Total No.(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>25 (28.4)</td>
<td>63 (71.6)</td>
<td>88 (100%)</td>
<td>0.139</td>
</tr>
<tr>
<td>Female</td>
<td>43 (38.3)</td>
<td>69 (61.7)</td>
<td>112 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

**Discussion**

Patients with diabetes mellitus are often affected by chronic infections. Many studies have evaluated the prevalence of H. pylori infection in diabetic patients and the possible role of this condition in their metabolic control.

The present study found that diabetic patients are more prone to acquire H. pylori infection (P=0.007) (statistically significant); similar results were also detected in studies conducted at Japan, Netherlands, Italy, Turkey, and Africa. There are several lines of evidence to implicate increased susceptibility to infection in diabetic patients. Firstly, a diabetes-induced
impairment of cellular and humeral immunity may enhance an individual’s sensitivity to H. pylori infection. Secondly, diabetes-induced reduction of gastrointestinal motility and acid secretion may promote pathogen colonization and infection rate in the gut. Thirdly, altered glucose metabolism may produce chemical changes in the gastric mucosa that promote H. pylori colonization. Finally, individuals with diabetes are more frequently exposed to pathogens than their healthy counterparts as they regularly attend hospital settings.

The mean HbA1c among diabetics with HpSA positive was significantly greater than H. pylori-negative diabetics [10.18(±0.28)% vs 8.5(±2.09)%, P value=0.001]. Similar results were obtained from NHANES III to NHANES 1999–2000. In contrast to these findings Gillum et al., found that H. pylori infection status was not significantly associated with HbA1C in men aged 40-70 years with or without history of type 2 diabetes. However, a study by Sargyń et al. showed that the mean age was 56 years. Most of the H. pylori related diseases are associated with male gender, the role of gender as a risk factor for H. pylori infection is still debated. This study showed that 25/88 (28.4%) of males in the studied populations were infected with H. pylori, while 43/112 (38.3%) of females were infected. However, this difference was found not to be significant. Another study conducted by Catherine showed that males were predominant to have H. pylori infection in adults as a global and homogeneous phenomenon. On the other hand, in another study the H. pylori infected females were predominant as compared to males.

Conclusion: The present study suggests that diabetic patients are at more risk for H. Pylori infection in comparison to non-diabetic population. This association is found to be higher in those with long duration of DM and those with poor glycemic control.
References: