

# Helicobacter Pylori Infection in Diabetic Patients

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## **Abstract:**

**Background:** H Pylori infection could be regarded as the commonest infection worldwide, it had been suggested that H pylori infection is more frequent among diabetics.

**Objective:** This study had been designed to define any significant association between diabetes and H pylori infection, to evaluate different demographic features of patients with diabetes mellitus who have H pylori infection, assess any relation between H pylori infection and the metabolic control of diabetes mellitus and to estimate the frequency of different oesophagogastroduodenoscopy findings among diabetic population with H pylori infection.

**Methods:** This study enrolled 50 patients with diabetes mellitus and another 50 non-diabetic patients (as a control group). The patients attended Gastrointestinal unit at Al-Yarmouk Teaching Hospital Baghdad/Iraq during the period between the 1st of March 2004, to the 31st of November 2004. Full history was taken and clinical examination, investigation to assess the glycemic control and esophagogastroduodenoscopy (OGD) had been done to all of them. H pylori status had been detected by positive Rapid Urease test and histopathology and/or ELIZA test for anti-H pylori IgG.

**Results:** This study revealed that 26 diabetic patients (52%) were H pylori positive, while 14 non-diabetic patients (28%) were H pylori positive which is statistically significant ( $X^2=6.0, P=0.01$ ). patients aging 60 year old or more (24 patients, 48% of the sample) 18 of them had positive H pylori status, 20 patients out of the 26 patients with positive H pylori status (76.9%) had poor glycemic control, 84.6% of those with positive H pylori status (22 out of 26 patients) had glycated hemoglobin level of 8% and greater, 61.8% of those with positive H pylori status (16 patients) were diabetic for more than 10 years. 61.5% of those with positive H pylori status had one or more of the chronic diabetic complications, 12 patients had OGD finding consistent with duodenitis, all of them were H pylori positive, OGD examination revealed 20 cases without active disease, 18 of them had negative H pylori status.

**Conclusions:** This study indicates that Helicobacter pylori infection is more common in diabetic patients. Frequency of H pylori infection is higher among elderly diabetics, those with long standing, poorly controlled and with diabetic complications.

**Key words:** Helicobacter pylori, diabetes mellitus

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## **Introduction:**

In 1983, Warren (a biologist) and Marshall (a clinician) described *Helicobacter pylori* (HP). At first, they named the bacterium *Campylobacter pyloridis*<sup>(1)</sup>. Later, it was named *Campylobacter pylori*. Since the first culture of *Helicobacter pylori* 20 years ago, the diagnosis and treatment of upper gastroduodenal disease have changed dramatically.

Peptic ulcer disease is now approached as an infectious disease. The role of H. pylori infection in gastric cancers is increasingly recognized, and its role in other diseases of the gastrointestinal tract is being evaluated<sup>(2, 3)</sup>.

Attention was attracted also by some extragastric diseases, including diabetes mellitus, where the elevated antibodies level against H. pylori was found<sup>(4,5)</sup>.

As many as 75% of patients visiting diabetes clinics will report significant gastrointestinal symptoms<sup>(6,7)</sup>.

Infection with H. pylori occurs worldwide, but the prevalence varies greatly among countries and among population groups within the same country<sup>(8)</sup>.

The 20% prevalence of infection with *H. pylori* among adolescents in the United States (2.5-6.3% in Sweden) in comparison to infection rates exceeding 90% by 5 years of age in parts of the developing world<sup>(9,10)</sup>.

It is just like most enteric infection acquired in childhood and is carried for lifetime in the majority of infected individuals; it causes no symptoms during childhood<sup>(11,12)</sup>.

*H. pylori* infection can be diagnosed by non-invasive methods or by endoscopic biopsy of the gastric mucosa; the selection of the appropriate test depends on the clinical setting<sup>(13,14)</sup>. Non-invasive methods include the urea breath test, serologic tests, and stool antigen assays.

The entire GI tract can be affected by diabetes from the oral cavity and esophagus to the large bowel and anorectal region. Thus, the symptom complex that may be experienced can vary widely<sup>(15)</sup>. Common complaints may include dysphagia, early satiety, reflux, constipation, abdominal pain, nausea, vomiting, and diarrhea. Many patients go undiagnosed and under-treated because the GI tract has not been traditionally associated with diabetes and its complications<sup>(16)</sup>.

This study had been designed to define any significant association between being diabetic and *H. pylori* positive status and to assess the relation between *H. Pylori* infection & metabolic control of diabetes mellitus.

### **Patients and Methods:**

This study enrolled 50 patients with diabetes mellitus; another 50 patients were randomly selected as non-diabetic control group. The patients had been randomly selected from those who had attended Gastrointestinal Disease Unit at Al-Yarmouk Teaching Hospital Baghdad/Iraq during the period between the 1st of March 2004, to the 31st of November 2004. All of the patients were exposed to thorough history taking and physical examination, and had been investigated for assessing their glycemic control.

Oesophagogastroduodenoscopy had been done to all of the patients included in this study. *H. pylori* status had been detected by histopathology and positive biopsy urease test and/or ELISA test for anti-*H. pylori* IgG.

### **Result:**

This study included 50 diabetic patients and 50 non diabetic subjects as a control group. Age of patients had ranged between 12-74 year old ( $41.88 \pm 20.16$  year old). Type 1 diabetes mellitus patients had ages ranged between 12-28 year old ( $21.8 \pm 11.0$  year old), while type 2 patients aged between 25-74 year old ( $55.26 \pm 13.8$ ). The patients aging 60 year old or more (24 patients, 48% of the sample), 18 of them had positive *H. pylori* status. On the other hand, 85.7% of *H. pylori* positive non diabetic patients were younger than 40 year old (12 patients). Table 1 shows patients' distribution according to age and *H. pylori* status.

Fourteen patients (28% of the sample) with type 1 diabetes mellitus and 36 patients (72% of the sample) with type 2 diabetes. 61.1% (22 patients) and 28.6% (4 patients) had positive *H. pylori* status among type 2 and type 1 diabetes mellitus respectively. This study included 18 female patients (36% of the sample), 10 of them (55.6%) had positive *H. pylori* status and 32 male patients, 16 of them (50%) had positive *H. pylori* status as it is shown in Table-2.

The patients who had been enrolled in this study had fasting blood sugar ranging between 105-228 mg/dl ( $167.04 \pm 39.61$  mg/dl) (mean of two readings). Twenty patients out of the 26 patients with positive *H. pylori* status (76.9% of those with positive status) had poor glycemic control. Table-3 shows patients' distribution according to their fasting plasma glucose and *H. pylori* status. Duration of diabetes ranged between 1-20 years ( $9.36 \pm 5.75$  years). 61.8% of those with positive *H. pylori* status (16 patients) were diabetic for more than 10 years. As it is showed in table -4

Thirty six patients with diabetes included in this study (72% of the sample) had one or more of the chronic diabetic complications. 16 of them were *H. pylori* positive (32% of the whole sample, 61.5% of those with positive *H. pylori* status).

Regarding oesophagogastroduodenoscopy (OGD) findings, this study revealed that 12 patients had finding consistent with duodenitis or duodenal ulcer (24% of the whole sample), all of them were H pylori positive (46.2% of those with positive H pylori status. On the other hand, OGD examination revealed 20 cases without active disease (40% of the sample), 18 of them had negative H pylori diagnostic tests (90% of those without active disease, 75% of those with negative H pylori status, and 36% of the whole sample). Table-6 shows patients' distribution according to their OGD findings.

This study revealed that 52% (26 diabetic patients) of the diabetic patients were H pylori positive, while 28% (14 non-diabetic patients) of non-diabetic control group patients were H pylori positive. Statistical analysis using chi square test revealed that there is significant association between being diabetic and having a positive H pylori tests ( $X^2=6.0$ ,  $P=0.01$ ). Table-7 shows patients' distribution according to H-pylori status and the results of statistical analysis.

**Table-1: Patients' distribution according to age and H pylori status**

<b>Age group (Year-old)</b>	<b><i>H pylori status</i></b>							
	<b><i>Diabetics</i></b>				<b><i>Non-diabetics</i></b>			
	<b><i>Positive</i></b>		<b><i>Negative</i></b>		<b><i>Positive</i></b>		<b><i>Negative</i></b>	
	<b><i>No</i></b>	<b><i>%</i></b>	<b><i>No</i></b>	<b><i>%</i></b>	<b><i>No</i></b>	<b><i>%</i></b>	<b><i>No</i></b>	<b><i>%</i></b>
<b>10-19</b>	2	7.7	6	25%	6	42.8%	4	11.1%
<b>20-29</b>	2	7.7	0	0	2	14.3%	12	33.3%
<b>30-39</b>	0	0	0	0%	4	28.6%	8	22.2%
<b>40-49</b>	2	7.7	4	16.7%	0	0%	4	11.1%
<b>50-59</b>	2	7.7	10	41.6%	2	14.3%	6	16.7%
<b>60-69</b>	8	30.8	4	16.7%	0	0%	2	5.6%
<b>70-79</b>	10	38.4	0	0%	0	0%	0	0%
<b>Total</b>	<b>26</b>	<b>100%</b>	<b>24</b>	<b>100%</b>	<b>14</b>	<b>100%</b>	<b>36</b>	<b>100%</b>

**Table-2: Patients distribution according to gender and H. pylori status:**

<b>H. Pylori status</b>	<b><i>Male</i></b>		<b><i>Female</i></b>	
	<b><i>No</i></b>	<b><i>%</i></b>	<b><i>No</i></b>	<b><i>%</i></b>
<b>Positive</b>	16	50%	10	55.6%
<b>Negative</b>	16	50%	8	44.4%
<b>Total</b>	<b>32</b>	<b>100%</b>	<b>18</b>	<b>100%</b>

**Table-3: Patients' distribution according to their fasting plasma glucose and H pylori status.**

<i>Fasting plasma glucose (mg/dl)</i>	<i>H pylori status</i>			
	<i>Positive</i>		<i>Negative</i>	
	<i>No</i>	<i>%</i>	<i>No</i>	<i>%</i>
<b>100-125</b>	6	23.1%	6	25%
<b>126-150</b>	0	0%	0	0%
<b>151-200</b>	14	53.8%	8	33.3%
<b>201-225</b>	4	15.4%	10	41.7%
<b>226-250</b>	2	7.7%	0	0%
<b>Total</b>	<b>26</b>	<b>100%</b>	<b>24</b>	<b>100%</b>

**Table-4: patients' distribution according to duration of diabetes and H pylori status.**

<i>Duration of diabetes (years)</i>	<i>H pylori status</i>			
	<i>Positive</i>		<i>Negative</i>	
	<i>No</i>	<i>%</i>	<i>No</i>	<i>%</i>
<b>1-5</b>	4	15.4%	12	50%
<b>6-10</b>	6	23%	10	41.7%
<b>11-15</b>	8	30.8%	2	8.3%
<b>16-20</b>	8	30.8%	0	0
<b>Total</b>	<b>26</b>	<b>100%</b>	<b>24</b>	<b>100%</b>

**Table-5: Patients' distribution according to their OGD findings**

<i>Age group (Year-old)</i>	<i>H pylori status</i>							
	<i>Diabetics</i>				<i>Non-diabetics</i>			
	<i>Positive</i>		<i>Negative</i>		<i>Positive</i>		<i>Negative</i>	
	<i>No</i>	<i>%</i>	<i>No</i>	<i>%</i>	<i>No</i>	<i>%</i>	<i>No</i>	<i>%</i>
<b>Esophagitis</b>	0	0%	2	8.3%	0	0%	12	33.3%
<b>Duodenitis/duodenal ulcer</b>	12	46.2%	0	0%	6	42.8%	0	0%
<b>Gastritis/gastric erosion/gastric ulcer</b>	6	23.1%	4	16.7%	4	28.6%	8	22.2%
<b>Gastritis &amp; duodenitis</b>	6	23.1%	0	0%	2	14.3%	0	0%
<b>No Active Disease</b>	2	7.6%	18	75%	2	14.3%	16	44.5%
<b>Total</b>	<b>26</b>	<b>100%</b>	<b>24</b>	<b>100%</b>	<b>14</b>	<b>100%</b>	<b>36</b>	<b>100%</b>

**Table-6: Patients' distribution according to H pylori status with the statistical analysis.**

<b>H pylori status</b>	<b>Diabetic patients</b>		<b>Non-diabetic patients</b>	
	<b>No</b>	<b>%</b>	<b>No</b>	<b>%</b>
<b>Positive</b>	26	52%	14	28%
<b>Negative</b>	24	48%	36	72%
<b>Total</b>	<b>50</b>	<b>100%</b>	<b>50</b>	<b>100%</b>
<b>Statistical analysis</b>	<i>Calculated <math>\chi^2=6.0</math>, <math>P=0.01</math> significant difference in the frequency of H pylori infection between diabetics and non-diabetics</i>			

**Discussion:**

This study revealed that there were higher frequency of H pylori positive status among older diabetics who had been included in this study (60-69 year old (30.8% of H pylori positive cases) and 70-79 year old (38.4% of H pylori positive cases)). In contrast, it had been found that 85.7% of non-diabetic control group patients were under the age of 40 years old (see table-1). This finding of higher frequency of H pylori infection among old diabetics could be explained by the fact that elderly diabetics had been diabetics for longer period than younger age diabetics, exposing them to higher risk of chronic diabetic related complications, particularly diabetic autonomic neuropathy which enhances the risk of developing diabetic gastric dysmotility and hence more frequent H pylori infection<sup>(17,18)</sup>. Another important point to be considered in explanation of this finding is that H pylori infection is essentially acquired during childhood, but changes in infection status with time are rare in adults<sup>(19)</sup>.

Regarding the relationship between being obese and having a positive H pylori status, this study indicate that the frequency of positive H pylori status in diabetic patients were higher among those being under or normal weight (61.5% of H pylori positive diabetic cases had body mass index  $\leq 25$ ). On the other hand, 71.4% of non-diabetic control group patients, who had positive H pylori status, had body mass index  $>25$ ). The relationship of H pylori and obesity is still under extreme controversy, some studies revealed a positive relationship, while many other studies indicate that the incidence of H pylori is not increased in obese people but the risk of duodenal ulcer is higher in H pylori positive people of high body mass index<sup>(20)</sup>. In addition the finding of higher frequency of H pylori among underweight diabetic could be explained by the well known fact that poorly controlled diabetic would loose their weight eventually.

Poor glycemic control had been found in 76.9% and 84.6% of diabetic patients with positive H pylori status in term of uncontrolled fasting plasma glucose and uncontrolled HbA1c respectively. This finding is in agreement of the findings revealed by Hammer et al in a cohort study enrolling 15,000 patients to define predictors for membership in different common upper gastrointestinal clusters of symptoms among diabetic patients, it had been concluded that poor glycemic control is the strongest predictor for membership in all symptoms clusters<sup>(15)</sup>. In addition, poor short and long term control is associated with higher frequency of diabetic complications particularly autonomic neuropathy and gastropathy. On the other hand, Begue Rodolfo et al, showed that eradication of H pylori infection in patients with type 1 diabetes mellitus might be associated with better glycemic control in term of fasting plasma glucose and HbA1c<sup>(15,16)</sup>.

84.6% of diabetic patients with H pylori infection were found to be diabetics for more than 10 years. Duration of diabetes is the main risk factor, beside the glycemic control, in increasing the risk of chronic diabetes related complications, the important of which here is the autonomic neuropathy and gastropathy that are important predictor for H pylori infection in diabetics<sup>(16,17)</sup>. In addition, new studies, primarily in animals, point to a defect in the enteric nervous system as a

major molecular cause of abnormal gastric motility in diabetes. This defect is characterized by a loss of nitric oxide signals from nerves to muscles in the gut resulting in delayed gastric emptying; an abnormalities that certainly need time with diabetes to develop (18). However, duration of diabetes is important for the development of changes in the microvasculature of the stomach which beside the frequent antibiotic usage because of recurrent bacterial infections had been found to cause significantly lower rate of H pylori eradication in type 2 diabetic patients<sup>(19,20)</sup>.

This study indicates that 61.5% of those with H pylori positive status had one or more of the chronic diabetic complications. This finding is in agreement with the conclusions made by Chnadran et al who concluded that diabetic patients with history of retinopathy, nephropathy, or neuropathy should be presumed to have gastrointestinal abnormalities until proven otherwise

Oesophagogastroduodenoscopy examination of diabetic patients included in this study showed no significant difference in OGD findings between diabetics and non-diabetic control group patients. All of duodenal ulcer/duodenitis patients were H pylori positive; in contrast, 18 out of 20 patients without active disease at OGD examination were H pylori negative. This findings is in agreement with the findings estimated by another similar study done in diabetic outpatients at Kenyatta National Hospital, Nairobi by Wafula et al, they found that 77.5% of diabetic patients with dyspepsia were H pylori positive (52% in this study, which is quite lower percentage), H pylori infection increased with increasing level of HbA1c, with quite similar frequency of OGD findings<sup>(21)</sup>.

### **Conclusions:**

- 1- Helicobacter pylori infection is more common in diabetic patients, with significant statistical association between being diabetic and the acquiring of H pylori infection.
- 2- Frequency of H pylori infection is higher among elderly diabetics
- 3- Duration of diabetes mellitus beside glycemic control is associated with higher frequency of H pylori infection.
- 4- Presence of chronic diabetic complications in its different categories enhances the H pylori infection.
- 5- No significant difference in male to female distribution of H pylori infection.

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