Prevalence of *Helicobacter pylori* Infection among Type 2 Diabetes Mellitus

**Abstract**

**Background:** Several conducted studies have reported a higher and more frequent *Helicobacter pylori* infection rate in type 2 diabetes mellitus (T2DM). The aim of this study was to investigate the prevalence and its association between *H. pylori* infection and T2DM. **Materials and Methods:** A case and control study was conducted based on 529 T2DM patients and 529 control. *H. pylori* was assessed by Serum anti-*H. pylori* immunoglobulin G (IgG) and IgA. Furthermore, patients were investigated for fasting blood glucose (FBG) levels, glycosylated hemoglobin (HbA1c), serum cholesterol, and other biochemistry parameters. **Results:** The findings showed a positive significantly higher antibody titer for *H. pylori* infection (IgA > 250) in diabetic patients (50.7%) compared to controls (38.2%) (*P* = 0.001). Similarly, *H. pylori* infection for IgG > 300 titer was higher in T2DM patients (73.5%) compared to controls 61.8% (*P* = 0.01). Further, the mean values were statistically significant diabetes with *H. pylori* infection for IgG > 300 titer and IgA > 250 titer, regarding Vitamin D, HbA1C (*P* > 0.01), FBG, calcium, creatinine, total cholesterol, LHDL, triglyceride levels, uric acid, bilirubin, thyroid-stimulating hormone (TSH), and systolic and diastolic blood pressure. The diabetic patients showed higher prevalence rate of symptoms than controls included: hypertension (14.3%), vomiting (15.5%), muscular symptoms (35.2%), bloating/distension (13.2%), abdominal pain (17%), nausea (9.6%), anemia (17%), kidneys (20.8%), chronic bronchitis (14.7%), gastrointestinal (23.8%), and diarrhea (20.4%). **Conclusions:** The current study revealed that *H. pylori* infections were significantly higher in diabetic patients compared to controls. Furthermore, T2DM patients infected with *H. pylori* positive reported a higher prevalence rate of symptoms than *H. pylori* negative.

**Keywords:** Diabetes, glycosylated hemoglobin, *Helicobacter pylori* infection, immunoglobulin, immunoglobulin A, immunoglobulin G

**Introduction**

*Helicobacter pylori* infection is one of the most common chronic infections worldwide and the relationship between *H. pylori* infection and diabetes patients has been investigated by several authors.[1,4] The high prevalence of *H. pylori* infection among diabetes mellitus and metabolic syndrome patients has been documented in detailed.[5,9] More recently, it has been reported that by tracing anti-*H. pylori* antibodies in patients with diabetes mellitus and the occurrence of symptoms such as digestive problems in >75% of these patients, it can be concluded that there is a relationship between this bacterium and type 2 diabetes mellitus (T2DM).[10] Furthermore, several studies reported that the prevalence of *H. pylori* infection was found to be a significantly higher risk in people with diabetes than in controls.[3,5,11]

The objective of the current study is to determine the prevalence and its association of *H. pylori* infection with T2DM in the Turkish population.

**Materials and Methods**

**Study design**

This case and control study consisted of patients aged between 30 and 70 who visited diabetes, endocrinology, gastroenterology, or outpatient clinics. The sample size was based on matched 529 T2DM patients and 529 controls. Written informed consent was obtained from all individuals prior to enrolling in the study.

**How to cite this article:** Bener A, Ağań AF, Al-hamaq AO, Barisik CC, Öztürk M, Ömer A. Prevalence of *Helicobacter pylori* infection among type 2 diabetes mellitus. Adv Biomed Res 2020;9:27.

**Received:** 30 November 2019  
**Revised:** 09 March 2020  
**Accepted:** 14 April 2020  
**Published:** 27 July 2020

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Selection of type 2 diabetic mellitus patients

Case patients were considered to have T2DM if they had a history of DM and were currently taking any oral medications for diabetes. DM was defined as individuals with the fasting plasma glucose ≥7.0 mmol/l or 75-g oral glucose tolerance test with 2-h plasma glucose ≥11.1 mmol/l or glycosylated hemoglobin (HbA1c) >6.5%[12,13] and by the International Diabetes Federation.[14]

Selection of controls

The controls aged 30–70 years were identified from a community consisting of a sample of 529 controls who visited the outpatient clinics for any reason other than T2DM and were selected randomly.

Biochemistry data

These individuals were also investigated for fasting blood glucose levels (FBG), HbA1c, serum cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), urea, creatinine, and the presence of other comorbid conditions.

Helicobacter pylori serology

Blood samples were taken from the peripheral veins of the individuals. The serum specimens were obtained from all cases and controls for H. pylori serology test from the participants. Immunoglobulin G (IgG) and IgA classes of anti-endomysial antibodies (EMAs) were measured with enzyme-linked immunosorbent assays (ELISAs) (CeliAK EmA human IgG and IgA, generic assays (GA) GmbH, Dahlewitz, Germany). H. pylori was assessed by measuring IgG and IgA among T2DM patients and the control group.[15] A individual was considered to be positive for H. pylori if IgG and IgA anti-H. pylori antibody titers were >300 and >250, respectively.[15]

The SPSS computer software (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp) was used for the statistical analysis. Student t-test was used to ascertain the significance of differences between the mean values of two continuous variables. Chi-square and Fisher exact tests were performed to test for differences in the proportions of categorical variables between two or more groups. Odds ratio and their 95% confidence intervals were calculated using Mantel–Haenszel test. One-way analysis of variance was employed for the comparison of several group means. The cutoff value for determining significance was chosen as 0.05.

Results

The demographic and clinical characteristics of investigated case patients and controls are shown in Table 1. The findings showed significant differences between T2DM patients compared with controls with respect to their age in years, body mass index (kg/m²), household income, sheesha smoking, smoking habit, family history of hypertension, metabolic syndrome, coronary heart disease (CHD), and nephropathy.

In the present study, over 60% of the patients had received H. pylori eradication therapy and about 22% had active infections. Most patients had routine follow-up as recommended by physicians.

Table 2 gives the magnitude of H. pylori infection among T2DM and controls. A positive antibody titer for H. pylori infection (IgA > 250) was found significantly higher in T2DM (diabetes [50.7%] vs. control [38.2%]), (P < 0.001). Similarly, H. pylori infection for IgG > 300 titer was higher in T2DM patients (73.5%) compared to controls subjects (61.8%) (P < 0.001).

Table 3 presents the clinical and biochemistry characteristics of T2DM and controls with H. pylori infection. As shown in Table 3, the mean values were significantly higher in T2DM with H. pylori infection for IgG > 300 titer, regarding Vitamin D (P < 0.001), HbA1C (P < 0.001), FBG (P < 0.001), calcium (P = 0.002), creatinine (P = 0.025), total cholesterol (P < 0.001), HDL (P = 0.048), triglyceride levels (P < 0.001), uric acid (P < 0.001), bilirubin (P = 0.015), TSH (P < 0.001), systolic blood pressure (P < 0.001), and diastolic (P < 0.001) blood pressure. Similarly, a positive antibody titer for H. pylori infection (IgA > 250) was found significantly higher in diabetic patients compared to controls.

Table 4 shows symptoms and diseases among T2DM patients with H. pylori infection. The T2DM patients infected with H. pylori positive reported statistically significant higher prevalence rate of symptoms than H. pylori negative: hypertension (20.1% vs. 12.1%), vomiting (21.1% vs. 10.7%), muscular symptoms (47.8% vs. 19.5%), bloating/distension (18.0% vs. 9.3%), abdominal pain (23.1% vs. 13.6), chronic bronchitis (20.1% vs. 10.7%), nausea (13.1% vs. 5.7%), anemia (23.1% vs. 11.4%), kidneys (28.9% vs. 15.7%), gastrointestinal (GI) (32.4% vs. 20.7%), and diarrhea (27.8% vs. 17.9%).

Discussion

Our objective was to explore the association between H. pylori infection and T2DM. The current study revealed that H. pylori prevalence was significantly higher in T2DM patients than in controls (50.7% vs. 38.2% for IgA > 250 titer and 73.5% vs. 61.8% for IgG > 300 titer). This is consistent with the previously reported studies.[4,10,16-21] Most recently, a meta-analysis suggested a trend toward more frequent H. pylori infections in T2DM patients.[3] Meanwhile, the impact of H. pylori and T2DM was explored in Bener et al.’s study[3] which stated that the prevalence of H. pylori infection rate in T2DM patients revealed higher than in controls. In a study conducted in Italy, H. pylori infection was detected in 69% of the patients with diabetes.[22] This is confirmative with the present study.
The association of *H. pylori* infection is made to a number of gastrointestinal and extra-GI diseases which has changed the approach for diagnosis among the various medical fields, and in most studies, *H. pylori* infection has been linked with T2DM.\[1-10,16\] According to a most recent study in Pakistan, it was observed that *H. pylori* infection was commonly seen among type 2 diabetic group (79%) in comparison to nondiabetic group (21%). This is consistent with the present study. A significant association implied that there stands an association between *H. pylori* infection and diabetes. The results are in line with another study conducted in Pakistan where hyperglycemia due to diabetes was regarded as a predisposing factor *H. pylori* colonization and reported that 73% of the patients having *H. pylori* infection were diabetic and 51% were nondiabetic.\[1,16\] Furthermore, another study performed in Africa reported that 88% of the diabetic and 67% of the nondiabetic patients were found to have a positive status for anti-*H. pylori* antibodies.\[18\] This is again confirmative with the current study.

In fact, worldwide, about over 4 million death patients had T2DM as well as many previous ones showed a high correlation between *H. pylori* infection and T2DM.\[2-10,18\] Many important factors are considered in the development of *H. pylori*-associated gastroduodenal diseases, including...
some risk factors such as environmental-related factors, hygiene, age, gender, and genetic susceptibility.\cite{5}

*Helicobacter pylori* infection plays an important role in the development of GI complications and has a significant role in systemic inflammation. It has some extraGI manifestations like endocrine diseases. In a study conducted in Iran,\cite{8} the prevalence of *H. pylori* seropositive was 65.9% in diabetic versus 50.5% in controls, and the difference was statistically significant. Similarly, in another study in Iran, the rate of *H. pylori* was significantly higher in diabetic patients compared to controls, 55.8% versus 44.2%, respectively.\cite{2} The prevalence of *H. pylori* infection in T2DM patients with obesity has been higher than the control group in Qatar (24% versus 27.5%). This is consistent with the current study. Among the patients referring to diabetes clinics, as many as 75% of them report significant GI symptoms.\cite{18-20} More recently, a study conducted on diabetic patients in Iran\cite{2} showed that *H. pylori* infection increases the prevalence of metabolic syndrome through an increase in insulin resistance, this consistent with the current study.

| Table 2: Prevalence of *Helicobacter pylori* infection in the studied type 2 diabetes mellitus and healthy controls |
|---------------------------------------------------------------|
| Characteristic | T2DM patients (n=529), n (%) | Control subject (n=529), n (%) | P     |
|----------------|---------------------------------|---------------------------------|-------|
| IgA > 250 titre |                                 |                                 |       |
| *H. pylori* positive | 268 (50.7) | 202 (38.2) | <0.001 |
| *H. pylori* negative | 261 (49.3) | 361 (61.8) |       |
| *H. pylori* positive by gender | | | |
| Male | 173 (64.5) | 91 (45.0) | 0.001 |
| Female | 95 (35.5) | 111 (55.0) | 0.001 |
| IgG > 300 titre | | | |
| *H. pylori* positive | 389 (73.5) | 327 (61.8) | 0.001 |
| *H. pylori* negative | 140 (26.5) | 202 (38.2) |       |
| *H. pylori* positive by gender | | | |
| Male | 216 (55.5) | 166 (50.8) | 0.209 |
| Female | 173 (44.4) | 161 (49.2) | 0.200 |

\*H. pylori*: *Helicobacter pylori*, T2DM: Type 2 diabetes mellitus

| Table 3: The baseline clinical and biochemistry characteristics of type 2 diabetes mellitus and controls with *Helicobacter pylori* infection |
|---------------------------------------------------------------|
| Variables | IgA > 250 | | IgG > 300 | |
| | T2DM (n=268), mean±SD | Control (n=202), mean±SD | P | T2DM (n=389), mean±SD | Control (n=327), mean±SD | P |
| Age (years) | 49.80±15.58 | 48.77±13.55 | 0.028 | 50.22±15.07 | 47.79±13.67 | 0.026 |
| BMI (kg/m²) | 27.82±4.78 | 27.29±4.83 | 0.235 | 27.75±4.75 | 26.95±4.77 | 0.024 |
| BMI >30 (%) | 26.9 | 25.2 | 0.117 | 27.0 | 21.3 | 0.008 |
| Fasting serum Vitamin D (g/dL) | 18.71±5.97 | 27.04±6.52 | 0.001 | 15.21±5.97 | 23.75±6.89 | 0.001 |
| Hba1c | 7.29±0.90 | 5.13±0.83 | 0.001 | 7.37±0.94 | 5.09±0.63 | 0.001 |
| Blood glucose (mmol/L) | 7.31±0.94 | 6.24±0.75 | 0.001 | 7.34±0.97 | 6.28±0.95 | 0.001 |
| Calcium (mmol/L) | 1.79±0.88 | 2.05±0.71 | 0.038 | 1.72±0.67 | 1.99±0.91 | 0.002 |
| Creatinine (mmol/L) | 63.78±15.19 | 67.25±16.90 | 0.178 | 60.98±12.65 | 65.08±13.12 | 0.025 |
| Total cholesterol (mmol/L) | 4.76±1.06 | 3.18±1.05 | 0.001 | 4.74±1.03 | 3.20±1.10 | 0.001 |
| HDL cholesterol (mmol/L) | 1.71±0.52 | 1.75±0.55 | 0.985 | 1.55±0.38 | 1.57±0.35 | 0.967 |
| LDL cholesterol (mmol/L) | 1.91±0.51 | 2.17±0.93 | 0.036 | 1.93±0.80 | 2.13±0.88 | 0.048 |
| Triglyceride (mmol/L) | 2.03±0.47 | 1.16±0.66 | 0.868 | 1.95±0.64 | 1.19±0.68 | 0.001 |
| Uric acid (mmol/L) | 262.04±84.48 | 308.49±91.26 | 0.001 | 265.22±83.07 | 291.48±85.94 | 0.001 |
| Bilirubin (mmol/L) | 8.25±4.03 | 10.88±4.67 | 0.001 | 8.53±4.14 | 10.72±4.58 | 0.001 |
| TSH serum (mmol/L) | 2.73±0.97 | 2.00±0.95 | 0.001 | 2.68±1.00 | 1.98±0.97 | 0.001 |
| Blood pressure Systolic | 129.07±15.70 | 124.64±15.24 | 0.002 | 129.39±15.55 | 125.69±14.29 | 0.001 |
| Diastolic | 78.80±9.06 | 76.40±8.26 | 0.003 | 78.65±9.26 | 75.80±7.30 | 0.001 |

BMI: Body mass index, Hba1c: Glycosylated hemoglobin, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TSH: Thyroid-stimulating hormone, T2DM: Type 2 diabetes mellitus, SD: Standard deviation
Furthermore studies in Pakistan,\(^1,\)\(^10\) in Qatar,\(^5\) in Iran,\(^2,\)\(^6,\)\(^8,\)\(^10\) in Italy\(^21\) and in China,\(^19,\)\(^22\) revealed significantly high risk of infection among Diabetes than in control. This is consistent with the current study, in which \(H. \text{pylori}\) infection was found a statistically significantly high prevalence rate of T2DM compared to the control group.

### Conclusions

The current study suggests that \(H. \text{pylori}\) infection is one of the risk factors that may be considered as a marker in the evaluation of diabetic patients. This study revealed that \(H. \text{pylori}\) infections were higher in diabetic patients compared to controls. The T2DM patients infected with \(H. \text{pylori}\) positive reported a higher prevalence rate of symptoms than \(H. \text{pylori}\) negative.

### Acknowledgment

This work was generously supported and funded by the Qatar Diabetes Association, Qatar Foundation. The authors would like to thank the Istanbul Medipol University for their support and ethical approval (Research Protocol and IRB# 10840098-604.01-01-E.8421 and Research Protool and IRB# 10840098-604.01-01-E.3193).

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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