Original Article

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

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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%) ($P < 0.001$). Further, the mean values were statistically significant diabetes with *H. pylori* infection for IgG > 300 titer and IgA > 250 titer, regarding Vitamin D, HbA1C ($P < 0.001$), 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.

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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.[5]

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/m^2), 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 ($P < 0.001$), LHDL ($P = 0.048$), 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[5] 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.

Table 1: Sociodemographic and clinical characteristics of studied type 2 diabetes mellitus patients and controls (*n*=1058)

Variables	T2DM patients (*n*=529), *n* (%)	Controls (*n*=529), *n* (%)	*P*
Age groups (years)			
<40	134 (25.3)	124 (23.4)	0.664
40-49	123 (23.3)	140 (26.5)	
50-59	145 (27.4)	142 (26.8)	
>60 and above	127 (24.0)	123 (23.3)	
Gender			
Male	261 (49.3)	267 (50.5)	0.712
Female	268 (50.7)	262 (49.5)	
BMI (kg/m^2)			0.008
Normal (<25)	140 (26.5)	182 (34.5)	
Overweight (29-30)	246 (46.5)	233 (44.2)	
Obese (>30)	143 (27.0)	112 (23.3)	
Physical activity 30 min/day			
Yes	141 (26.7)	159 (30.1)	0.220
No	388 (73.3)	370 (69.9)	
Household income			
Low	168 (31.8)	140 (26.4)	0.014
Medium	264 (49.9)	257 (48.7)	
High	97 (18.3)	132 (24.9)	
Sheesha smoking			
Yes	96 (18.7)	75 (14.2)	0.047
No	430 (81.3)	454 (85.8)	
Cigarette smoking			
Never	419 (79.2)	401 (75.8)	0.013
Current smoker	80 (15.1)	72 (13.6)	
Past smoker	30 (5.7)	56 (10.6)	
Family history of hypertension			
Yes	119 (22.5)	84 (15.9)	0.006
No	410 (77.5)	445 (84.1)	
Metabolic syndrome ATP - III			
Yes	138 (26.1)	65 (12.3)	0.001
No	391 (73.9)	464 (87.7)	
CHD			
Yes	82 (15.5)	53 (10.0)	0.008
No	447 (84.5)	476 (90.0)	
Family history of nephropathy			
Yes	80 (15.1)	22 (4.2)	0.001
No	449 (84.9)	507 (95.8)	

CHD: Coronary heart disease, BMI: Body mass index, T2DM: Type 2 diabetes mellitus, ATP: Acute thrombocytopenic purpura

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

Table 2: Prevalence of *Helicobacter pylori* infection in the studied type 2 diabetes mellitus and helthy controls

Charecteristics	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 charecteristics 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/m^2)	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	291.49±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

some risk factors such as environmental-related factors, hygiene, age, gender, and genetic susceptibility.[5]

H. 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,[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.[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.[18-20] More recently, a study conducted on diabetic patients in Iran[2] showed that *H. pylori* infection increases the prevalence of metabolic syndrome through an increase in insulin resistance, this consistent with the current study.

A study, which has been performed in India,[4] reported that CHD was more prevalent in people with diabetes with *H. pylori* infection than those without *H. pylori* (57%).

Table 4: The comparison reported symptoms and diseases among between the parameters of two groups of seropositive diabetic patients with seronegative diabetic patients (*n*=529)

	IgG > 300 titre				
disease/symptoms	**T2DM with *H. pylori* positive (*n*=389), *n* (%)**	**T2DM with *H. pylori* negative (*n*=140), *n* (%)**	**OR**	**95% CI**	***P* (signficant)**
Hypertension	78 (20.1)	17 (12.1)	1.81	1.03-3.19	0.038
Vomiting	82 (21.1)	15 (10.7)	2.25	1.23-4.40	0.007
Muscular symptoms	186 (47.8)	45 (19.5)	1.73	1.14-2.61	0.009
Bloating or distension	70 (18.0)	13 (9.3)	2.14	1.16-4.01	0.018
Abdominal pain,constipation	90 (23.1)	19 (13.6)	1.91	1.12-3.28	0.017
Chronic bronchitis	78 (20.1)	15 (10.7)	2.09	1.16-3.77	0.003
Nausea	51 (13.1)	8 (5.7)	2.49	1.15-5.88	0.020
Anemia	90 (23.1)	16 (11.4)	2.33	1.31-4.13	0.003
Kidneys	110 (28.9)	22 (15.7)	2.11	1.28-3.51	0.003
Gastrointestinal	126 (32.4)	29 (20.7)	1.83	1.16-2.90	0.009
Diarrhea	108 (27.8)	25 (17.9)	1.77	1.08-2.87	0.021

H. pylori: *Helicobacter pylori*, T2DM: Type 2 diabetes mellitus, OR: Odds ratio, CI: Confidence interval

Furthermore studies in Pakistan,[1,16] in Qatar,[5] in Iran,[2,6,8,10] in Italy[21] and in China,[19,22] revealed significantly high risk *H. Pylori* of infection among Diabetes than in control. This is consistent with the current study, in which *H. pylori* infection was found a statistically significantly high prevalence rate of T2DM compared to the control group.

Conclusions

The current study suggests that *H. 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. pylori* infections were higher in diabetic patients compared to controls. The T2DM patients infected with *H. pylori positive* reported a higher prevalence rate of symptoms than *H. pylori negative.*

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Conflicts of interest

There are no conflicts of interest.

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