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Evaluation of *Helicobacter pylori* IgG levels in type 2 diabetes mellitus patients

ABSTRACT

Background. Diabetes mellitus (DM) is a common and debilitating chronic disease with increasing prevalence in the world and in Iran. *Helicobacter pylori* (*H. pylori*) is a gram-negative bacillus that causes gastritis and peptic ulcer disease and stomach cancer. It is more common in developing countries. Several studies have shown the possible association between *H. pylori* infection and DM. We performed this study to evaluate *H. pylori* infection in type 2 diabetes mellitus (T2DM) patients in comparison to non-diabetic individuals.

Methods. In a case-control study 99 T2DM patients (aged 31 to 96 years) who referred to Urmia Imam Khomaini hospital and 96 non-diabetic controls were included. Venous blood samples were received from all participants and fasting blood glucose (FBG), HbA_{1c} and serum *H. pylori* IgG levels were measured. For all individuals demographic data, including age, sex and body mass index (BMI) were recorded. *H. pylori* IgG levels greater than 10 U/ml was considered as *H. pylori* infection. *H. pylori* IgG serum levels of all of T2DM patients and control group were compared with each other. Data were analyzed using SPSS version 17. We used independent T-test, Chi-square and Fisher exact test for statistical analysis. The level of significance was considered as p-value < 0.05.

Results. Means age of T2DM patients and control group were 59.77 ± 13.25 and 63.43 ± 13.16 years respectively and there was not significant difference between two groups (p = 0.05). Frequency of positive *H. pylori* serology in T2DM patients was 69.7% and in non-diabetic group was 66.7% and there was not significant difference between two groups in this regard (p = 0.65). Mean ± SE serum *H. pylori* IgG levels in T2DM and non-diabetic subjects was 45.78 ± 4.82 and 44.35 ± 4.83 U/ml respectively (p = 0.83). Mean HbA_{1c} level was significantly higher in T2DM patients compared to control group (8.40 ± 2.02 and 5.29 ± 0.45 respectively, p < 0.001).

Conclusions. According to the results of this study frequency of *H. pylori* infection and also serum *H. pylori* IgG levels in diabetic patients does not differ from non-diabetics subjects. (Clin Diabetol 2020; 9; 3: 179–183)

Key words: diabetes mellitus type 2, *Helicobacter pylori*, *Helicobacter pylori* serology, IgG

Introduction

Diabetes is a common and debilitating chronic disease with increasing prevalence both in the world and in Iran [1–3]. *Helicobacter pylori* (*H. pylori*) is a gram-negative bacillus that causes gastritis and peptic ulcer disease and stomach cancer [4]. It is more common in developing countries [5]. Some studies have shown that *H. pylori* infection has been associated with non-gastrointestinal diseases such as ischemic heart disease, neurologic diseases, and autoimmune thyroid disorders [5–10]. Several studies have shown the association between *H. pylori* infection and diabetes mellitus [5, 11, 12]. The issue of whether *H. pylori* infection causes diabetes or those with diabetes are more likely to develop *H. pylori* infection is still not fully understood [12]. One of the proposed mechanisms of developing diabetes in patients with *H. pylori* infection can be increased insulin resistance [5]. Other

Table 1. Demographic characteristics and laboratory test results of type 2 diabetes mellitus (T2DM) patients and control group

Parameter	T2DM patients (n = 99)	Control group (n = 96)	p value
Age (years)	59.77 ± 13.25	63.43 ± 13.16	0.05
Female (%)	53 (53.5%)	49 (51%)	0.72
Weight [kg]	73.56 ± 14.44	66.54 ± 14.34	0.001
Height [cm]	163.99 ± 9.81	161.02 ± 10.46	0.04
BMI [kg/m^2]	27.45 ± 5.28	25.61 ± 4.47	0.009
HbA$_{1c}$ (%)	8.40 ± 2.02	5.29 ± 0.45	< 0.001
FBG [mg/dL]	201.69 ± 78.71	90.39 ± 24.25	0.001

Data are expressed as mean ± SD. FBG — fasting blood glucose; BMI — body mass index

mechanisms include chronic inflammation, reduced insulin secretion, and increased synthesis of some of the diabetogenic hormones such as leptin that leads to insulin resistance [5]. Furthermore decreased ghrelin level in patients with *H. pylori* infection leads to reduced energy consumption and weight gain [5].

In some studies, there is even a significant correlation between microvascular complications of diabetes and helicobacter infection such as microalbuminuria and neuropathy [13, 14]. In contrast, in some studies, there was no association between *H. pylori* infection and diabetes mellitus found [15].

Given the controversy and limited studies in this field in Iran, we designed this study to investigate the association of *H. pylori* infection with type 2 diabetes.

Materials and methods

In this case-control study 99 type 2 diabetes mellitus (T2DM) patients over the age of thirty (aged 31–96 years) who referred to Endocrinology department of Urmia Imam Khomaini hospital and 96 non-diabetic controls were included. Subjects who had autoimmune, infectious or rheumatologic diseases and those taking proton pomp inhibitors within one month before the study as well as patients treated with immunosuppressive drugs were excluded from study.

The subjects in our study had no predominant symptoms of upper gastrointestinal tract involvement and they had not been treated with anti-helicobacter drugs for a month before study initiation. The control group was selected from non-diabetic healthy individuals who referred to the ophthalmology department of Imam Khomaini hospital and did not present any exclusion criteria.

The study began after approval of Urmia University of medical sciences ethic committee and after obtaining written consent from all individuals. Venous blood samples were received from participants in the fasting state for fasting blood glucose (FBG), HbA$_{1c}$ and serum

H. pylori IgG levels. FBG and HbA$_{1c}$ were measured by enzymatic method (Pars Azmun kite, Tehran, Iran) and turbidimetric immunoassay (Aptec kite, Belgium) respectively and serum *H. pylori* IgG level was measured by ELISA method (Pishtazteb kite, Tehran, Iran). For all subjects demographic data, including age, sex weight, height and body mass index (BMI) were recorded. *H. pylori* IgG levels greater than 10 U/ml was considered as *H. pylori* infection. *H. pylori* IgG serum levels of all of T2DM patients and control group were compared with each other. Data were analyzed by independent T-test, Chi-square and Fisher exact tests using SPSS version 17. The level of significance was considered as p-value < 0.05.

Results

Demographic characteristics and laboratory test results of two study groups are demonstrated in Table 1.

As shown in Table 1, there is no statistically significant difference between the two groups in terms of age (p = 0.05). Also, the percentage of female population in the two groups was not statistically significant.

Both FBG and HbA$_{1c}$ mean values were significantly higher in T2DM patients than in control group (Table 1). Frequency of positive *H. pylori* serology in T2DM patients was 69.7% (n = 69) and in non-diabetic group was 66.7% (n = 64) and there was not significant difference between these two groups in this regard (p = 0.65). Mean ± SE (standard error) serum *H. pylori* IgG levels in T2DM and non-diabetic subjects were 45.78 ± 4.82 and 44.35 ± 4.83 U/ml respectively and the difference between these two groups was not statistically significant (p = 0.83).

FBG, HbA$_{1c}$ and BMI mean values did not differ significantly between diabetic patients with and without *H. pylori* infection (Table 2). Also as shown in Table 3 the difference between FBG, HbA$_{1c}$ and BMI mean values was not statistically significant between control subjects with *H. pylori* infection and without it.

Table 2. Glycemic parameters and BMI in diabetic patients with and without *H. pylori* infection

	DM *H. pylori*+	DM *H. pylori*–	p-value
FBG [mg/dL]	191.66 ± 64.33	224.7 ± 102.18	0.05
HbA$_{1c}$ (%)	8.33 ± 1.95	8.55 ± 2.22	0.63
BMI [kg/m^2]	27.47 ± 5.22	27.40 ± 5.49	0.96

DM — diabetes mellitus; FBG — fasting blood glucose; BMI — body mass index

Table 3. Glycemic parameters and BMI in control group with and without *H. pylori* infection

	Control *H. pylori*+	Control *H. pylori*–	p-value
FBG [mg/dL]	92.73 ± 27.86	85.71 ± 13.8	0.1
HbA$_{1c}$ (%)	5.34 ± 0.48	5.19 ± 0.37	0.13
BMI [kg/m^2]	25.83 ± 4.3	25.16 ± 4.85	0.49

FBG — fasting blood glucose; BMI — body mass index

Moreover in the total population of our study, the mean value of BMI was 26.68 ± 4.85 kg/m^2 in *Helicobacter* infected subjects and 26.25 ± 5.25 kg/m^2 in non-infected individuals, and there was no statistically significant difference between these two groups (p = 0.57).

Discussion

Type 2 diabetes mellitus is a common systemic disease with serious complications [1, 2, 16]. In recent years, several studies have examined the association between T2DM and *H. pylori* infection and some of them have confirmed this association but others have not shown any relationship between these two. In the present study, the percentage of T2DM patients with *H. pylori* infection was 69.7% and in the control group it was 66.7% and the difference between these two groups was not statistically significant. Similar to our study in a cross-sectional study conducted by Jafarzadeh et al. on 100 T2DM patients and 100 healthy controls in 2011 in Rafsanjan city of Iran, there was no significant difference between the prevalence of positive *Helicobacter* antibodies (IgG) levels among patients with type 2 diabetes and healthy subjects (76% *vs*. 75% respectively). But in their study healthy individuals compared with diabetic patients, had significantly higher levels of anti-*Helicobacter* IgG antibodies (131.63 ± 11.68 *vs*. 54.43 ± 4.50 U/ml; p < 0.0001) [17]. Our results are consistent with study by Jafarzadeh et al. regarding the similar rate of *H. pylori* seropositivity in the two study groups and lack of association between T2DM and *H. pylori* infection [17]. However, in our study, the mean serum level of anti-*Helicobacter* IgG antibiodies in diabetic patients was higher than in the control group (45.78 ± 4.82

and 44.35 ± 4.83 respectively), but this difference was not statistically significant (p = 0.83).

In a study by Bener and colleagues on 210 patients with type 2 diabetes and the same number of non-diabetic patients, a higher percentage of diabetic patients than non-diabetic ones had positive *H. pylori* antibody (IgG) levels (76.7% *vs.* 64.8% respectively, p = 0.01) which is against our study results [18].

In the research conducted by Devrajani et al. on 74 diabetes cases and 74 non-diabetic controls in Pakistan, the percentage of positive *Helicobacter pylori* stool antigen was 73% and 51.4%, respectively and the difference between these two groups in this regard was statistically significant (p = 0.0001). They suggested that patients with diabetes are susceptible to *H. pylori* infection, therefore they recommended screening for *H. pylori* infection in diabetic patients [19].

Furthermore Bajaj et al. in the study on 80 diabetic patients and 80 controls, showed that the prevalence of *H. pylori* infection in diabetic patients is considerably higher than in the control group (77.5% *vs.* 58.3% respectively, p = 0.02). Also, in their study the average HbA$_{1c}$ levels in the diabetic group with *H. pylori* was significantly higher than those without *Helicobacter* infection [20].

Therefore, they suggested that *H. pylori* infection is associated with higher HbA$_{1c}$ levels and inappropriate blood glucose control, but our study results are not consistent with the results of the study by Bajaj et al.

In a study by Zojaji et al. on 85 T2DM patients in Iran, the mean serum HbA$_{1c}$ level 3 months after treatment of *H. pylori* infection was significantly reduced compared to its pre-treatment level, however, fasting blood glucose did not change significantly after treatment compared to the pretreatment state. They

concluded that *H. pylori* eradication has beneficial effects on the glycemic control in diabetic patients [21]. However, Wada and colleagues, in a retrospective study in Japan, showed that treatment of *Helicobacter pylori* infection in T2DM patients does not improve HbA$_{1c}$ levels [22].

Also Vafaeimanesh et al. in the study on T2DM patients who were treated with oral medications showed that *H. pylori* infection therapy has no beneficial effects on blood glucose profiles, in addition they had lower rates of successful response to anti *H. pylori* regimen compared with non-diabetic subjects [23].

The study of Quatrini et al. in Italy, also supports the higher percentage of *H. pylori* infection in diabetic patients population (insulin dependent and non-insulin dependent) compared with non-diabetic subjects (69% and 46% respectively, p = 0.007) [24]. Although the different outcomes of their study comparing to our study may be due to the fact that they used respiratory urease test for the detection of *H. pylori* infection, while we have used ELISA method (anti *H. pylori* IgG levels).

Our study shows that there is no significant relationship between *H. pylori* infection and type 2 diabetes.

H. pylori infection diagnostic tests are classified into two categories of invasive and non-invasive tools and various previous studies have used either one method alone or a combination of several methods [25, 26].

Although urea breath test is more accurate and commonly used as a standard diagnostic test [25, 26], we did not use it because of its high cost and unavailability in our center.

Among the different methods for *H. pylori* infection detection, we used serology (ELISA) becauseof its convenience and availability and its low cost in this study. Although serologic results also usually not influenced by antibiotic or PPI (proton pump inhibitors) treatment [26], we did not include subjects that were taking PPI or anti-helicobacter medications within one month before the study.

One of the limitations of our study is the use of only one method (ELISA) for the diagnosis of *H. pylori* infection. As mentioned earlier given the high cost of respiratory urease test and its unavailability as well as the financial limitations we could not use neither this test nor any additional method such as *H. pylori* fecal antigen test to confirm the diagnosis of *H. pylori* infection.

Another limitation of our study was the lack of assessment of the upper gastrointestinal symptoms in diabetic patients and not considering it as the inclusion criteria, although most of participants were

asymptomatic and did not report any significant upper gastrointestinal symptoms.

Factors such as race, geographic region, economic state, different dietary and drug regimens used to control blood glucose, as well as different diagnostic methods used to detect *H. pylori* infection, can influence the results of different studies.

More prospective studies with long-term follow-up of *H. pylori* infected patients in terms of the risk of type 2 diabetes development are needed. These studies should use more accurate methods or a combination of several diagnostic tools for *H. pylori* infection what can be helpful in revealing the relationship between *H. pylori* infection and diabetes. As well as future research on the role of oral hypoglycemic drugs may be useful in the development of H. pylori infection in diabetic type 2 patients.

Conclusion

Based on the results of this study, it seems that there is no relationship between *H. pylori* infection and type 2 diabetes.

Acknowledgements

Conflict of interest

The authors declare to have no conflict of interest.

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