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Association of *Helicobacter pylori* Infection with Type 2 Diabetic Patients in Dohuk Governorate, Iraq

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Abstract

Helicobacter pylori (*H. pylori*) is one of the most common human pathogens in the world. Several studies that have investigated the correlation between *H. pylori* infection and type 2 diabetes mellitus (DM) found that *H. pylori* infection is more frequent in the patients, while the results of other studies were unclear. This paper aims to investigate the interrelation between the infection with *H. pylori* and type 2 DM in Dohuk governorate, Iraq. Eighty four diabetes patients (41 males, 43 females) and 92 healthy controls were involved in this study. *H. pylori* status was assessed in serum samples by using ELISA test. Out of the 84 patients, 65 patients (77.4%) were *H. pylori* positive (+ve) and 19 (22.6%) were *H. pylori* negative (-ve), with the difference being statistically significant. This paper found that diabetes is significantly associated with the infection of *H. pylori* in the studied sample of Iraqi patients.

Keywords: *Helicobacter pylori*, type 2 diabetes mellitus

علاقة الإصابة بالحلزونية البوابية بمرضى داء السكري من النوع الثاني في محافظة دهوك/العراق

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الخلاصة:

البكتريا الحلزونية البوابية هي واحدة من أكثر مسببات الأمراض البشرية شيوعاً في العالم. هناك العديد من الدراسات التي فحصت العلاقة بين الحلزونية البوابية والسكري ووجدت أن عدوى الحلزونية البوابية كانت أكثر شيوعاً في مرضى السكري، بينما كانت نتائج الدراسات الأخرى غير واضحة. تهدف الدراسة الحالية في هذه العلاقة بين عدوى الحلزونية البوابية ومرض السكري من النوع الثاني في محافظة دهوك، العراق. أجريت هذه الدراسة على 84 مريض بالسكري، من بينهم 41 من الذكور و43 من الإناث يعانون من أعراض الجهاز الهضمي و 92 اشخاص اصحاء. تم تقييم حالة الحلزونية البوابية من مصل المرضى والاشخاص الاصحاء عن طريق اختبار ELISA. تم تسجيل ما مجموعه 84 من مرضى السكري في الدراسة، 65 مريضا بنسبة (77.4%) كانت موجبة لفحص الحلزونية البوابية و 19 مريضا بنسبة (22.6%) كانت سلبية لفحص

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الكلزونية البوابية. وقد أشارت النتائج إلى أن هناك علاقة معنوية بين الإصابة بالبكتيريا الكلزونية ومرض السكري من النوع الثاني.

Introduction

In 1982, Marshal and Warren (Australian scientists) first described *Helicobacter pylori* [1], giving it the name of *Campylobacter pyloridis*, which was then changed to *Campylobacter pylori* [2]. *H. pylori* belongs to the Subdivision *Proteobacteria*, Order *Campylobacterales*, Family *Helicobacteraceae*, Genus *Helicobacter*, Species *pylori*.

H. pylori is a Gram-negative bacterium that colonizes the stomach and causes persistent infection. This infection is a global public health problem, affecting more than half of the world's population [3, 4]. It is more frequent in the developing countries, but it differs among countries and among populations in the same country [5].

H. pylori infection, if not treated, persists for the whole life. At the socioeconomic level, poor hygiene and high overcrowding rate can attribute to infections with *H. pylori* [6, 7]. It was estimated that *H. pylori* infected about 4.5 billion individuals all over the world in 2015 [8].

H. pylori is associated with different diseases, including diabetes [9-13], ischemic heart diseases [14], anemia [15], allergic and autoimmune diseases [16, 17], and skin disorders [18].

Type 2 DM (T2DM) is a disease that always affects adults and is responsible of more than 90% of DM cases, being regarded as a serious threat for public health. T2DM is responsible for the death of "3.8 million" of the adult population in the world [19, 20]. Worldwide, it is estimated that 420 million adults (20–79 years) have diabetes, a number that is projected to reach 645 million by 2050 [21].

Most patients of (T2DM) suffer from gastrointestinal tract (GIT) infection symptoms [22]. Hence, diabetic patients are more responsive to bacterial infections in the upper GIT. However, the relationship between DM and *H. pylori* infection is still unclear [23]. (GIT) infection represents a risk factor of stomach carcinoma [24].

This paper aims to investigate the relation between the infection with *H. pylori* and type 2 DM in patients from Dohuk governorate, Iraq.

Patients and methods

Eighty four diabetic patients (41 males and 43 females) were involved in this study, with an age range between 22 and 75 years. Ninety two age-matched healthy controls were also included for comparison purposes. The infection with *H. pylori* was detected in serum of patients suffering from gastrointestinal infection symptoms, as well as of control group, during the period from April 2018 to May 2019 in a private laboratory (AmrLab Medical Laboratories) in Dohuk.

The information collected for each patient included the variables of sex, age, *H. pylori* test result, body mass index (BMI), DM test result (fasting plasma glucose level), history of diabetes drugs use, family history of diabetes, and glycosylated Hb (HbA1c) level. The symptoms of gastric infection with *H. pylori* are characterized by abdominal cramps and discomfort, followed by diarrhea, nausea, vomiting, fever, loss of appetite, muscle aches, dehydration, headache, bloody or black stools, and weight loss.

Laboratory examinations were performed on blood samples of fasting patients for at least 8 hours. Samples were collected and stored at 4°C. Serum was separated by using a centrifuge at 1800 rpm for 18 min. The serum samples were tested for fasting plasma glucose level, HbA1c level, and *H. pylori* infection [25, 26]. The level of anti- *H. pylori* immunoglobulin G antibody was measured using enzyme-linked immunosorbent assay (ELISA) kit (Euroimmun, PerKinElmer, USA).

Statistical analyses were performed using Prism 8 statistics software (GraphPad Software, San Diego, UC). Continuous variables were expressed as mean \pm SD. Categorical variables were expressed as n (%). The chi square (X^2) test was selected to evaluate the relations among categorical variables, with reports of the corresponding p-values. A p-value lower than 0.05 was regarded as indicating statistically significant difference. ELISA test was used as a suitable method of the serodiagnosis for *H. pylori* infection, by measuring the levels of anti-*H. pylori* immunoglobulin G antibody, which was tested for finding the association between *H. pylori* infection and type 2 diabetes.

Results

Among the 84 patients, 51.2% (n=43) were females and 48.8% (n=41) were males. The range of age for the patients was 22-75 years, with a mean \pm SD of 54.35 \pm 9.36 years.

The present study shows that the percentage of female diabetic patients is higher than that of males.

Total prevalence of *H. pylori* in the blood of patients under study was 65/84 (77.4%). Our results show a statistically significant difference between the patients and control groups with regards to *H. pylori* infection rate (Table 1).

Table 1- Prevalence of *Helicobacter pylori* infection in diabetic and non- diabetic patients (control group)

<i>H. pylori</i> infection	T2DM patients No. (%)	Non- diabetic subjects (control) No. (%)	Total	P-value
Positive	65 (77.4)	54 (58.7)	119	0.006
Negative	19 (22.6)	38 (41.3)	57	
Total	84 (100)	92 (100)	176	

The results showed no significant male preponderance in exposure to the infection with *H. pylori* (33/65; 50.8%), compared with female infection rate (32/65; 49.2%), as listed in Table 2.

Table 2- Distribution of *H. pylori* infection according to gender

Sex	<i>H. pylori</i> (+) No. (%)	<i>H. pylori</i> (-) No. (%)	Total	P-value
Female	32 (49.2)	11 (57.9)	43 (51.2)	0.344
Male	33 (50.8)	8 (42.1)	41 (48.8)	
Total	65 (100%)	19 (100%)	84 (100%)	

In the present paper, 22.62% (n=19) of the diabetic patients were negative to *H. pylori* infection and, whereas 77.38% (n=65) were positive (Figure 1).

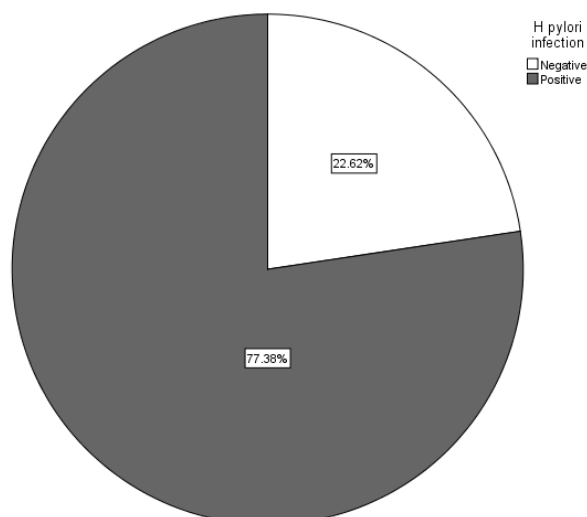


Figure 1-Percentage of *H. pylori* infection (negative and positive) among DM patients.

The rate of higher infection of *H. pylori* was observed in the group of patients with age range of 50 – 59 years (n=25, 38.5%), followed by the age groups of 40 – 49 years, 60 - 69 years, and 70+ years (n=19, 29.2%; n=16, 24.6%; n=3, 4.6%, respectively). The lower infection was recorded among patients with age of 20 – 39 years (n=1, 1.5%) (Table 3). Statistically, no significance was detected in terms of differences in infection rate according to age (p value = 0.4).

The infection *H. pylori* was not significantly related with the variables of history of diabetic treatment, HbA1c level, family history of diabetes, and BMI. Information related to the GIT infection symptoms and history of gastric surgeries are listed in Table 4.

Table 3- Distribution of *H. pylori* infection according to the age of diabetic patients.

Age group	<i>H. pylori</i> (-) N=19 No. (%)	<i>H. pylori</i> (+) N=65 No. (%)	P-value
20-29	1 (5.3%)	1 (1.5%)	0.4
30-39	0 (0.0%)	1 (1.5%)	
40-49	2 (10.5%)	19 (29.2%)	
50-59	9 (47.4%)	25 (38.5%)	
60-69	5 (26.3%)	16 (24.6%)	
70+	2 (10.5%)	3 (4.6%)	

Table -4- : Relationship between *H. pylori* infection and several variables.

Variables	Results	<i>H. pylori</i> (-) Total No.=19 No. (%)	<i>H. pylori</i> (+) Total No.=65 No. (%)	P-value
History of diabetic drug (H of D)	Negative	7 (36.8%)	26 (40.0%)	0.512
	Positive	12 (63.2%)	39 (60.0%)	
HbA1c*	Negative	11 (57.9%)	28 (43.1%)	0.3
	Positive	8 (42.1%)	37 (56.9%)	
Family history of diabetes (FHD)	Negative	6 (31.6%)	32 (49.2%)	0.136
	Positive	13 (68.4%)	33 (50.8%)	
Body mass index (BMI)	Negative	16 (84.2%)	57 (87.7%)	0.4
	Positive	3 (15.8%)	8 (12.3%)	
Gastro infection tract symptoms	Negative	11 (57.9%)	50 (76.9%)	0.092
	Positive	8 (42.1%)	15 (23.1%)	
History of gastric surgeries	Negative	14 (73.7%)	57 (87.7%)	0.132
	Positive	5 (26.3%)	8 (12.3%)	

* "HbA1c: average level of blood sugar over the past 2 to 3 months"
[HbA1c: <5.1-6.4%=(Negative); 6.5-9%=(Positive)]

Discussion

Our study found that the percentage of female diabetic patients is higher than that of males (51.2% vs. 48.8%), with no statistical significance of the difference. Similarly, Boyuk *et al.* observed percentages of 36.6% of males and 63.4% of females in individuals with the same disease [27, 28]. Several factors, including dietary habits, culture, and differences in lifestyle may contribute to the higher prevalence of diabetes and obesity among female patients [29].

Diabetic patients are affected by gastrointestinal bacterial infections. Our study tested whether diabetes is possibly accompanied by infection of *H. pylori*. We examined the prevalence of infection with *H. pylori* in T2DM patients and found that the infection rate was significantly higher in T2DM patients than with non T2DM. Similarly, some studies have also found higher spread of *H. pylori* infection in DM patients compared with healthy individuals or with non DM patients [30-34], while others did not support such correlation [35-37].

The defect of diabetic patients' immunity (both humoral and cellular) in response to *H. pylori* infection can be interpreted by the reduction of both acid secretion and gastrointestinal motility, which promote *H. pylori* colonization [38]. This also increases the rate of infection in the gastrointestinal system [39]. Moreover, diabetes induces changes in the metabolism of glucose and, therefore, alters the chemical reactions in the gastric mucosa, encouraging the colonization of *H. pylori* [40].

Also, we found a slight non-significant difference in the prevalence of *H. pylori* infection between female and male patients. These findings support those reported However, Chen *et al.* found an identical percentage of infection prevalence (20%) in males and females of an adult population from Taiwan [41].

In terms of age, there was no significant difference in the prevalence of *H. pylori* infection among all age groups of patients. However, the distribution of *H. pylori* infection was higher among age group patients 50 to 59 years. These findings are in concordance with those of Bajaj *et al.*, who had reported that the maximum patients were in the age group 51-60 years and 41-50 years [42,43]. In contrast to these findings, another investigation showed that *H.*

pylori seropositivity is associated with age, where about 80% of diabetic patients were in the age of lower than 50 years [44,45,46].

In the present study, we found that the infection of *H. pylori* was not significantly related with HbA1c level in T2DM patients. In contrast to these findings, Bajaj *et al.* and Hsieh *et al.* found a significant relationship between *H. pylori* infection and HbA1c level of T2DM patients [43, 47].

Furthermore, other studies reported that among the patients attended to diabetes clinics, as many as 75% of them suffered from a significant gastrointestinal tract infection symptoms [48, 49].

Nam and co-workers found no relation between *H. pylori* infection and family history of diabetes and BMI [50], which is in agreement with our study findings.

In conclusion, our study investigated the relation between T2DM and *H. pylori* infection in Dohuk governorate. Overall, the prevalence of *H. pylori* infection was observed to be significantly higher in patients with type 2 diabetes as compared to patients without diabetes. The findings of the current study support the association of diabetes with *H. pylori* infection.

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