Original paper

Prevalence of Helicobacter Pylori Infection in Patients with Type 2 Diabetic

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Abstract

Background: Infection with *Helicobacter pylori* has been recognized as a public health problem worldwide. Patients with diabetes mellitus are more liable to infection. The aim of the study was to determine the prevalence of *Helicobacter pylori* infection in patients with type 2 diabetes mellitus in Erbil City and to find whether *H. pylori* infection associated with higher levels of glycated hemoglobin (HbA1c).

Subjects and Methods: A case-control study was carried out at Laila Kasim Health Centre. Around 150 type 2 diabetes mellitus patients and 50 non-diabetic patients were recruited. The study was conducted between September to November 2020. Blood samples were collected and analyzed for blood sugar, HbA1c and serum used for detection of anti-*Helicobacter pylori* antibody (IgG) by ELISA.

Results: *Helicobacter pylori* infection was detected in 73.3% of Type 2 diabetes mellitus (T2DM) patients and 54% of controls (*P*= 0.01)**.** *Helicobacter pylori* infection was highly prevalent in patients with fair control of blood glucose (HbA1c 83.8%; *P*= 0.007)**.** *Helicobacter pylori infection* was not associated with; duration of T2DM, age, gender, body mass index (BMI), alcohol consumption, dyspeptic symptoms and level of education.

Conclusion: This study found that the significantly higher prevalence of *H. pylori* infection in diabetic patients especially in those with fair control of blood glucose as compared to non-DM individuals, this indicated that the increased levels of HbA1c associated with *H. pylori*.

Key word: *Helicobacter pylori*, Type 2 diabetes mellitus, HbA1c.

Introduction

Helicobacter pylori is a type of bacteria that grows in the stomach, a spiral shape of *H. pylori* allows them to penetrate the stomach lining and upper intestine, it can change the environment around them and reduce its acidity so they can survive, in addition the bacteria protected by mucus and body's immune cells are not able to reach them and not destroyed which lead to stomach problems, responsible for the majority of ulcers in the stomach and small intestine, also it is associated with other important gastrointestinal diseases such as chronic gastritis, gastric adenocarcinoma, and MALT lymphoma which are recognized as a major public health concern in the world[(1).]

Infection with these bacteria occur during childhood but may a symptomatic until they are adult. There are many risk factors that accelerate the infection with bacteria such drinking dirty water and eating food that is not clean or cooked well, share housing with others who are infected with *H. pylori* or live-in overcrowded housing. The infections are thought to spread from one person's mouth to another, they may also be transferred from feces to the mouth [(2)].

Diabetes mellitus (DM) is a chronic disease with increasing prevalence in the world, it is found that *H. pylori* infection has been associated with non-gastrointestinal diseases such as ischemic heart disease, neurologic diseases, and autoimmune thyroid disorders. The association between *H. pylori*

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infection and diabetes mellitus was shown in several studies. Increasing insulin resistance is one of the proposed mechanisms of developing diabetes in patients with *H. pylori* infection, the other mechanisms include increased synthesis of some of the diabetogenic hormones such as leptin that leads to insulin resistance. Furthermore, decreased ghrelin level in patients with *H. pylori* infection leads to reduced energy consumption and weight gain. A significant correlation between microvascular complications of diabetes and helicobacter infection even was shown in some studies, such as microalbuminuria and neuropathy [(3)]. It had been suggested that the *H. pylori* may contribute to the incidence of cardiovascular disease and diabetes through elevations in inflammatory cytokines levels such as C-reactive protein (CRP) and interleukin-6 [(1)]. World Health Organization in 2011 officially recommended that HbA1c ≥ 6.5% as a diagnostic cutoff point for diabetes and American Diabetes Association (ADA) also recommends that HbA1c should be measured in patients with newly developed diabetes, and it plays an important role in the monitoring of diabetes [(4)]. However, the effect of *H. pylori* infection on the glycemic control of diabetes such as fasting plasma glucose, glycosylated hemoglobin (HbA1c), and insulin resistance were observed in some study [(5)].

Reduction of gastrointestinal motility and acid secretion induced by diabetes and thereby induced impairment of cellular and humoral immunity may improve a unique sensibility to *H. pylori*. There are many factors can contribute to *H. pylori* infection to development of diabetes, one of them changed in glucose metabolism may produce chemical changes in the gastric mucosa that promote *H. pylori* colonization. In addition, a significant factor influencing both chronic *H. pylori* infection and Type II Diabetes is lifestyle. Infection with *H. pylori* could delay gastric emptying, that cause a mismatch between the onset of insulin action and absorption of carbohydrates in insulin-dependent with diabetes [(6)]. Some studies reported that there is an increase in the prevalence of *H. pylori* infection among diabetes mellitus patients and this reported was supported with other studies from developed and developing countries. Also, many studies had been documented the relationship between *H. pylori* seropositivity and higher mean HbA1c levels, an indicator of chronic hyperglycemia and they added that *pylori* chronic infection enhance the level of HbA1c and reduces the level of insulin production [(7)]. The aim of present study was to identify the Prevalence of *Helicobacter pylori* infection in patients with type 2 diabetes mellitus in Erbil City.

Subjects and Methods

The study was a case and control, comparison of T2DM and non-diabetic groups done. It is conducted during September to November 2020 in Erbil City in Iraq.

Known diabetic patients with T2DM above 30 years of age selected from Laila Kasim Diabetic Centre in Erbil. Control subject were collected from patients attending Erbil Teaching Hospital for other reasons. One hundred and fifty (150) diabetes mellitus patients and 50 non-diabetic subjects (control) were included. Five ml of peripheral venous blood samples were collected and divided into; 3ml for blood glucose (BIOLABO/ France) and 2ml in anti- coagulated with EDTA for HbA1c level (STAN-BIO/USA), Reference value of HbA1c {(Normal range (4.5-5.6%), Good control (5.7-6.4%), Fair control (6.5-7%), poor control (>7%)}.

The blood was centrifuged to prepared serum for detection of *H. pylori* antibody (IgG) by quantities ELISA (Monobind Inc/ACCU-Bind ELISA Microwells/ USA). Anti *H. pylori* antibody IgG concentration >20 U/ml was considered as positive. The questionnaire used to assess the participants health, social and demographic status. It included questions about; age, gender, body mass index, duration of disease, level of education, alcohol consumption and presence of gastric symptoms for

more than one month. Patients on immunosuppressive drugs, patients with type 1 diabetes mellitus and those have been treated for *H. pylori* infection were excluded from the study. The study was approved by the Research Ethics Committee, Erbil Polytechnic University and the participation was free and voluntarily, both verbal and written consents were taken from the research participants.

Statistical analysis

The 2 groups were evenly matched for age and sex using SPSS version 24 (SPSS. Inc. USA). Frequency and percentage were calculated on 95% confidence interval.

Mean ± SD (standard division) of socio-demographic data was computed. The contingency coefficient test (CCTest) was applied among the categorical variable. The *P-value* ≤0.05 was considered as statistically significant.

Results

The socio-demographic variables showed that the gender, age and BMI have no effects on the prevalence of *H. pylori*, although *H. pylori* infections were more predominant in overweight people (not significant). Alcohol consumption and level of education have no significant relations with prevalence of *H. pylori* too. Prevalence of dyspepsia in patients with *H. pylori* positive and negative groups were not significant (Table 1).

Helicobacter pylori were more predominant in diabetic group 73.3% than in control group 54% (*P value* 0.01) (Table 2).

The duration of diabetes has no relation with *H. pylori* infection (Table 3).

Helicobacter pylori infection was highly significant in patients with fair control of blood glucose (HbA1c 83.8%) (Table 4).

Table 1. Socio-demographic data between *Helicobacter pylori* –positive and *H pylori* –negative with T2DM and non- diabetes patients (n=200)

Variable	***H. pylori* infection Positive (n:137) Mean ± SD**	***H. pylori* infection Negative (n:63) Mean ± SD**	***P-value***
Gender			
Female (n=140)	98 (70%)	42 (30%)	0.48 (NS**)
Male (n=60)	39(65%)	21(35%)	
Age (years)	54.45±11.15	51.84±13.0	0.14 (NS**)
***BMI** (kg/m^2)	29.38±4.61	28.2 ±5.39	0.12 (NS**)
Alcohol consumption			
Yes (n=2) (1%)	1(50%)	1(50%)	0.57 (NS**)
No (n=198) (99%)	136(68.7%)	62(31.3%)	
Level of education			
Illiterate (n=132)	94 (71.2%)	38(28.8%)	0.08 (NS**)
Primary school (n=40)	28 (70%)	12(30%)	
Secondary school (n=18)	10 (55.6%)	8(44.4%)	
University (n=10)	5 (50%)	5 (50%)	
Dyspeptic symptoms			
Present (n=82) (41%)	58 (70.7%)	24 (29.3%)	0.57(NS**)
Absent (n= 118) (59%)	79 (66.9%)	39 (33.1%)	

*BMI: Body Mass Index, ** NS: Not significant

Table 2. Prevalence of *H. Pylori* in T2DM and non-diabetes patients

Patients	***Helicobacter pylori* infection**		**Total (No.%)**
	Positive (No.%)	**Negative (No. %)**	
***T2DM**	110 (73.3%)	40(26.7%)	150 (75%)
Non- diabetes	27 (54%)	23 (46%)	50 (25%)
Total	137 (68.5%)	63 (315%)	200 (100%)
CC test	***P-value* = 0.01 (HS**)**		

*T2DM: Type two diabetes mellitus, ** HS: Highly significant

Table 3. Distribution of *H. Pylori* in T2DM in relation to duration of illness

Duration of illness group/ years	*Helicobacter pylori* infection		Total (No.%)
	Positive (No.%)	Negative (No.%)	
1-2 years	21(67.7%)	10(32.3%)	31(20.7%)
>2 years	89(74.8%)	30(25.5%)	119(79.3%)
Total	110 (73.3%)	40 (26.7%)	150 (100%)
CC test	*P-value* = 0.42 (NS*)		

* NS: Not significant

Table 4. Frequency of *H. Pylori* in T2DM and non-diabetes patients in relation to HbA1C

HbA1c	*Helicobacter pylori* infection		Total (No.%)
	Positive (No.%)	Negative (No.%)	
Normal range (4.5-5.6%)	34 (53.1%)	30(46.9%)	64 (32%)
Good control (5.7-6.4%)	17 (68%)	8 (32%)	25 (12.5%)
Fair control (6.5-7%)	31 (83.8%)	6 (16.2%)	37(18.5%)
Poor control (>7%)	55(74.3%)	19(25.7%)	74 (37%)
Total	137 (68.5%)	63 (31.5%)	200 (100%)
CC test	*P-value* = 0.007 (HS*)		

***** HS: Highly significant

Discussion

The most important cause of gastritis and peptic ulcer in humans is Helicobacter pylori infection, and the potential links between a variety of extra-gastroduodenal manifestations and H. pylori infection have been reported by many studies [4].

The role of gender as a risk factor for H. pylori infection is still unknown; our study showed that H. pylori infection was more common in females (70%) than in males (65%) (not significant), which, is in concordance with other results [3,8]. As gender concerned, Mabeku et al., (2020) reported that although the difference was not significant but dyspeptic women were at a slightly higher risk than dyspeptic men to develop diabetes [7].

Higher prevalence in women in our society could be explained by the fact the women are responsible for food preparation and spend most of their times in the kitchen in our society.

When considering the age of our participants the results showed that the majority of patients with H. pylori infection in both groups were more than 50 years of age (not significant), this result was similarly to Mabeku et al., (2020) who reports that old people are more affected by T2DM than young ones independently of their dyspeptic status [7]. Our study showed that most patients with *H. pylori* infection in both groups were more than 50 years of age (not significant). This was similarly to Mabeku *et al.,* (2020) how noticed that many dyspeptic diabetic patients belonged to 55–64 years age group and he concluded that this age group were more infected than their corresponding non-diabetic age group [7]. Lim and his colleagues (2018) reported that *H. pylori* Seropositivity tended to increase with age 60-69 years old. Therefore, the results of the present study indicate that the significant difference could be explained by the older age of those infected and the higher prevalence of diabetes in the elderly [9]. Wang *et al*., (2019) found that the prevalence of *H. pylori* infection reach peak at age group of 51-60 and he also added that a significant predictor for *H. pylori* infection was age [10]. From analysis of previous studies revealed that the prevalence of *H. pylori* infection increased by age manner, and it might be a potent risk factor.

Helicobacter pylori infection was higher (27.5%) in obese people in both groups (diabetic and non-diabetic), This result is in accord with data of the literature which reported by Alzahrani *etal*.,(2020) who found that highest percentage was in in obese participants of both groups [8]. However Mabeku *etal*.,(2020) stated that obese patients having *H. pylori* + ve significantly more

affected by diabetic mellitus. According to some studies [7]. Manoranjan, (2020) suggested that an increased incidence of *H. pylori* colonization may be associated with obesity [6]. The primary etiological cause of Type 2 Diabetes Mellitus is obesity and to prevent most obese subjects with impaired glucose tolerance from contracting the disease is a weight loss that determined through clinical trials.

In present study when we analyzed participants according to Alcohol consumptions and level of education there were no significant differences between individuals with and without *H. pylori* infection, similarly finding reported by other study [11]. Priyadarshini *et al*., (2018) and Bello *et al.*, (2018) found an increase in the risk of chronic *H. pylori* infection with low level of education, including poor health education and more tendency to living in an environment that predisposes to fecal contamination of food and water [12,13]. Alcohol consumption may compromise the living conditions of *H. pylori* in the stomach due to that alcohol has strong antimicrobial activity that stimulates gastric acid secretion which could impact the *H. pylori* load through lowering the pH in the stomach.

Although, most of the carriers (70.7%, P value 0.5) for *H. pylori* among both groups were complaining of dyspepsia but not significant and this result corroborates with others [14] and this might be that our population includes a high number of symptom free

The association between *H. pylori* infection and diabetes mellitus have been investigated by some studies and whether *H. pylori* infection causes diabetes or those with diabetes are more likely to develop *H. pylori* infection were clarified. Increased synthesis of leptin that is diabetogenic hormones lead to insulin resistance thereby increased insulin resistance one of the proposed mechanisms of developing diabetes in patients with *H. pylori* infection, however decreased level of ghrelin in patients with *H. pylori* infection leads to reduced energy consumption and weight gain [3].

In our study the percentage of *H. pylori* in diabetic patients (73.3%) were highly significant (p<0 001) compared to non-diabetic patients (54%), the result was good agreement with other study how showed that *H. pylori* seropositivity was found to be 73.11% in diabetic mellitus patients, while in control group it was 58.05% ($p = 0.0279$) [7]. Other studies reported that the percentage of T2DM patients with *H. pylori* infection was 69.7% [3].

Previous studies in their meta-analysis and systematic review suggested that association between *H. pylori* infection and diabetes was positive and they indicated from the results that the association between them was statistically significant [1].

Alzahrani with his colleagues (2020) reported that the prevalence of *H. pylori* infection in type 2 diabetics ranges from 30% to 78% [8].

Mabeku *etal*.,(2020) found in his sample population that (64.87%) were *Helicobacter pylori* seropositive and he confirmed that patients from diabetic group were significantly more *H. pylori* infected compared to those from the non-diabetic group and he added that this because poverty, malnutrition, poor hygiene and unaffordable heath care[7].

Some gastrointestinal problems such as dyspepsia, etc., also worsening the blood glucose levels and metabolic control by decrease levels of immunity increase risk of *H. pylori* infections [6].

The present study demonstrated that *H. pylori* prevalence not affected by the duration of the disease of T2DM ((Table 3). It is increased with time of the illness, 74.8% were holding *H. pylori* who were diabetic for more than 2 years while only 67.7% were positive for *H. Pylori* when the disease was less than 2 years (no significant), similar results reported by others [1,8].

To assess the diabetic status of our dyspeptic sample population, the level of glycated hemoglobin (HbA1c) was used, which results from the non-enzymatic glycosylation of hemoglobin and reflect the integrated blood glucose level for the past 3–4 months.

The relationship between *H. pylori* infection and HbA1c level among the study population is illustrated in Table (4), from this table, infected participants had significantly higher percentage HbA1c levels compared to those who were uninfected (p = 0.007). This result was in consistent with the results of other studies, for example, the study done by Abolfazl Ghasemi *etal*., (2020) suggested that *H. pylori* infection is associated with higher HbA1c levels and inappropriate blood glucose control [(3)]. Also, Mansori *et al*., (2020) revealed that the prevalence of *H. pylori* and serum HbA1c levels statistically significant [(1)]. Alzahrani, *et al*., (2020) reported that *H. pylori* seropositivity was associated with higher mean HbA1c levels, in particular CagA positivity and this association persisted even after excluding individuals with a history of diabetes and controlling for potential confounders, and he recommended that proper screening of *H. pylori* infection together with regular monitoring of blood glucose and HbA1c levels for the early detection of glucose dysregulation and the prevention of type 2 diabetes mellitus[(8)]. Mansori *et al*., (2020) revealed that to impair any association between *H. pylori* infection and glucose regulation it is important subject the fasting glucose levels to daily changes such as diet and physical activity [(1)].

Regarding blood HbA1c levels, Mabeku *et al*., (2020) noticed a significantly higher increase in blood HbA1c level in the group having *H. pylori* positive and from his study he revealed that *H. pylori* chronic infection enhance the level of HbA1c and reduces the level of insulin production, in addition he expected that the incidence rate of high level of HbA1c would be higher in *H. pylori* endemic area [(7)].

Conclusions

This study found that the significantly high prevalence of *H. pylori* infection in diabetic patients especially in those with fair control of blood glucose as compared to non-DM individuals and an increase in intensity of HbA1c blood level was obtained when having *H. pylori* infection. This indicates that the increased levels of HbA1c associated with *H. pylori.*

Routine screening of diabetic patients for *Helicobacter pylori* is recommended.

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