Association of Helicobacter Pylori Infection with Diabetes Mellitus in Baquba-Diyala Province

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ABSTRACT:

BACKGROUND:

Infection with *H. pylori* has been recognized as a public health problem worldwide**.** Studies to address the association of *H. pylori* infection with diabetes mellitus (DM) had yielded controversial results.

OBJECTIVE:

To figure out the association between *H. pylori* infection and DMtype 1 and 2 in Baquba city, Iraq .

PATIENTS AND METHODS:

This cross-sectional case control study was conducted in Baquba-Diyala province for the period from August 2015- March 2016. 82diabetic patients (67 with type 2 and 15 with type 1) and 23 healthy non-diabetic individuals were enrolled. The DM patients include 45 (54.9%) females and 37(45.1%) males. The mean age ±SD of type 2 DM patients was51.37± 10.84 years,while the mean age ±SD of patient with type 1 DMwas 23.66 ± 6.99 years. The patients were collected from the outpatient clinic of Baquba General Teaching Hospital according to the WHO definition criteria of the DM. Blood samples were collected, sera were separated and tested for the presence of anti-*H. pylori*IgG antibody using the commercially available Enzyme- linked immunosorbant assay kit.Statistical analyses were done using the Statistical Package for Social Science (SPSS) Version 18, and P value < 0.05 was considered significant.

RESULTS:

The results showed that the anti- *H. pylori* positivity rate among patients with diabetes mellitus and controls was 35.2% and 9.5% respectively, with statistically insignificant difference (p= 0.54). The anti- *H. pylori*positivity rate was slightly higher in type 2 DM than in type 1 DM (29.5 % *vs* 5.7 %, p=0.9).Diabetic male had insignificantly higher positivity rate compared to female ((29.5% *vs*26.8, p= 0.096%). Furthermore, higher positivity rate was found in the age group 30-50 years.

CONCLUSION:

The anti-*H. pylori*positivity rate is insignificantly higher among diabetes mellitus patients; particularly type 2 diabetes mellitus than non-diabetic individuals in Baquba cit, Iraq .

KEYWORDS: diabetes mellitus, helicobacter pylori, insulin resistant

INTRODUCTION:

The*H. pylori*, is a Gram's negative, microaerophilicbacterium found in the stomach, and may be present in other parts of the body (Cotticelli*et al*., 2006).Infection with *H. pylori* has been recognized as a public health problem affecting approximately 50% of the world population with more prevalence in developing countries (Leja*et al*., 2016). *H.pylori* infection has been associated with both gastrointestinal and extragastrointestinal conditions such as peptic ulcer, gastric cancer and cardiovascular disease (Cong *et al*., 2014; Goni and Franceschi, 2016). As one of the most common chronic bacterial infections in the world, it coupled with the susceptibility of diabetic patients to a wide range of infections as a result of chronic elevation of blood glucose level and impairment of immune functions (Agrawal*et al*., 2010; Marietti*et al*., 2013). Researchers have hypothesized an association between infection with *H. pylori* and diabetes mellitus (Devrajani*et al*., 2010; Zhou *et al*., 2013; Feng*et al*., 2013). On the contrary, other discordant studies have failed to confirm this hypothesis t (Ugwu*et al*., 2007; Jafarzadeh*et al*., 2013).

Although there is no concrete evidence demonstrating that *H. pylori* play a role in diabetes, the possibility for a causal relationship is an intriguing issue. There are several lines of

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evidence to implicate increased susceptibility to infection in diabetic patients. Firstly, a diabetes-induced impairment of cellular and humoral immunity may enhance an individual's sensitivity to *H. pylori* infection (Lassenius*et al*., 2011). Secondly, diabetes-induced reduction of gastrointestinal motility and acid secretion may promote pathogen colonization and infection rate in the gut (Jeon*et al*., 2012). Thirdly, altered glucose metabolism may produce chemical changes in the gastric mucosa that promote *H. pylori* colonization (Marietti*et al*., 2013). Individuals with diabetes are more frequently exposed to pathogens than their healthy counterparts as they regularly attend hospital settings. Ultimately, *H. pylori* infection was significantly increased the prevalence of metabolic syndrome through an increase in insulin resistance (Vafaeimanesh*et al*., 2016).

PATIENTS AND METHODS:

This cross-sectional case control study was conducted in Baquba-Diyala province for the period from August 2015- March 2016 to explore the *H. pylori* positivity rate among patients with diabetes mellitus type 1 and 2. Eighty two diabetic patients and 23 normal healthy non-diabetic individuals were enrolled in this study. The diabetic group includes 67 patients (38 females and 29 males) with type 2 and 15 patients (7 females and 8 males) with type 1DM.The mean age ±SD of patientwith type 2 DM was 51.37± 10.84 years, with age range 32-85 years, while the mean age ±SD of patient with type 1 DMwas 23.66 ± 6.99 years with age range 12-34 years.The control group comprised of 11 females and 12 males, the mean age ±SD 28.56 ±15.36 and the age range of control group comprised (18-42 years).Those patients were collected from the outpatient clinic of Baquba General Teaching Hospital according to WHO definition criteria of the DM (Seino *et al*., 2010). Blood sample was collected from all participants, sera were separated and tested for the presence of anti-*H. pylori*IgG antibody using the commercially available Enzyme- linked immunosorbant assay kit (Biotech.USA). Staistical analyses were done using the Statistical Package for Social Science (SPSS) Version 18 .

RESULTS:

The frequency distribution of numbers of patients and control groups was shown in table (1).

Table 1: Frequency Distribution of Study Groups by Gender.

Sex	Study groups			Total (%)
	DM type 1 (%)	DM type 2(%)	Control group (%)	
Female	7 (6.7)	38 (36.2)	11 (10.5)	56 (53.3)
Male	8 (7.6)	29 (27.6)	12 (11.4)	49 (46.7)
Total	15 (14.3)	67 63.8)	23 (21.9)	105 (100)

Results in Table (2) revealed the *H. pylori* infection rate in DM patients and non-diabetic healthy control was 37(35.2) and 10 (9.5) respectively. Although the infection rate was higher in DM patients, the difference was statistically insignificant P = 0.054.

Table 2: H. pylori infection rate among the study groups.

Study groups	H. pylori infection		Total (%)
	Positive (%)	Negative (%)	
DM patients	37(35.2)	45 (42.9)	82 (78.1)
Control group	10 (9.5)	13 (12.4)	23 (21.9)
Total	47(44.8)	58 (55.2)	105 (100)

Pearson Chi-square = 0.020, P= 0.54 [NS]

The *H. pylori*positivity rate among patients with DM type 1, type 2 and control group were 6 (5.7%), 31 (29.5%), and10 (9.5%) respectively. The differenceamong the study groups was statistically insignificant (P= 0.9), table (3).

Table 3: *H. pylori* Infection Rate According To The Type of DM.

Study groups	*H. pylori* infection		Total (%)
	Positive (%)	Negative (%)	
DM type 1	6 (5.7)	9 (8.6)	15 (14.3)
DM type 2	31 (29.5)	36 (34.3)	67 (63.8)
Control group	10 (9.5)	13 (12.4)	23 (21.9)
Total	47 (44.8)	58 (55.2)	105 (100)

Pearson Chi-Square = 0.21, P = 0. 9[NS]

The rate of *H. pylori*infection among DM patients according to gender was illustrated in table (3). 22 (26.8%) of females and 25 (30.4%)of males were positive. Although the infection rate was higher in males compared to females, however, the difference was statistically insignificant (P= 0.4).

Table 3: H. pylori infection rate among DM patients by gender.

Gender	*H. pylori* infection		Total (%)
	Positive (%)	Negative (%)	
Female	22 (26.8)	15 (18.2)	37 (45.1)
Male	25(30.4)	20(24.3)	45 (54.9)
Total	47 (57.3)	35 (42.7)	82 (100)

Pearson Chi-Square = 0.096, P= 0.4 [NS]

Table (4) showed the *H. pylori* infection rate among DM patients according to age groups.The age range of control group comprised patiens was (18-42). Although the infection rate was higher in the age group 30-50 years compared to other age groups; However, the differences was statistically insignificant (P= 0.19).

Table 4: H. pylori infection rate among DM patients by age groups.

Age groups (Ys)	*H. pylori* infection		Total (%)
	Positive (%)	Negative (%)	
< 30	5 (6.1)	6 (7.3)	11 (13.4)
30-50	24 (29.3)	13 (15.9)	37 (45.1)
➢ 50	18 (21.9)	16 (19.5)	34 (41.5)
Total	47 (57.3)	35 (42.7)	82 (100)

Pearson Chi-square = 3.34, P= 0.19 [NS]

DISCUSSION:

Since the discovery of *H. pylori*, a variety of epidemiological studies, therapeutic trials, and case reports have evaluated the direct or indirect involvement of this bacterium in the pathogenesis of various extragastric disorders particularly DM.The present study found higher *H. pylori* infection rate in diabetics patients compared to non-diabetics healthy individuals (35.2% *vs*9.5%; p = 0.54). In spite of that, the study did not support a strong association between *H. pylori*infectionas determined by the presence of anti-*H. pylori*IgG and DM.Worldwide studies covering the link between *H. pylori* infection and diabetes remains controversial, as some studies indicate a higher prevalence of infection indiabetic patients (Ojetti*et al*., 2010;Feng *et al*., 2013; Hsieh *et al*., 2013; Yang *et al*., 2014) , while others report no differences (Ugwu*et al*., 2007; Jafarzadeh*et al*., 2013; Tamura *et a*l., 2015). In a large meta-analyses study covering forty-one studiesrevealed a significantly higher infection rate of *H. pylori* in patients with type 2 DMcomparedto control group (Zhou *et al*., 2013).Similar meta-analyses included thirty-seven case-control studies and 2 cohort studies suggest a relationship between *H. pylori* infection and the risk of DM and diabetic nephropathy (Wang *et al*., 2013). Moreover, a strong association between diabetic nephropathy, diabetic retinopathy and neuropathy with *H. pylori*infection was also reported(Agrawal et al., 2010).These discrepancies reported concerning the association of *H. pylori* and diabetes are likely due to inconsistencies in the methods used

to define *H. pylori* positivity and diabetic status, the limited sample sizes, and adjustments for potential confounders such as age and socioeconomic status (Cong *et al*., 2014). In addition, the accuracy of self-reported data on medical history depends on the subjects' knowledge and understanding of the relevant information, their ability to recall, and their willingness to report which also may change over time(Dai *et al*., 2015).

Several studies have documented that gastrointestinal inflammation caused by *H. pylori* can influence the absorption of glucose and lipids, which are also abnormal in diabetes mellitus. Type 2 DM, formerly known as non-insulin-dependent diabetes mellitus or adult-onset diabetes, is a metabolic disorder that is characterized by high levels of blood glucose resulting from insulin resistance and relative insulin deficiency (Polyzos*et al*., 2011; Vafaeimanes*et al*., 2016).Data regarding the mechanisms underlying the pathogenesis of diabetes are complex, and there are some indications that *H. pylori* infection may contribute to the development of diabetes. Whereas insulin insensitivity is an early phenomenon, pancreatic β-cell function declines gradually over time before the onset of clinical hyperglycemia, the result of many factors that can be influenced by infection, such as insulin resistance, glucotoxicity, lipotoxicity, β-cell dysfunction, chronic inflammation, and genetic and epigenetic factors (Lasseniu*set al*., 2011; Buzas, 2014). *H. pylori* infection is known to be involved in the pathogenesis of insulin resistance, and the growing awareness of its role in diabetes is important for the early detection of glucose dysregulation and prevention of T2DM in high-risk communities (Ojetti*et al*., 2010; Cong *et al*., 2014). Additionally, an effective *H. pylori* eradication results significantly lowered in diabetic patients than in controls, most likely because of the large use of antibiotic in DM subjects, causing selection of resistant *H. pylori* strains and moreover, re-infection after bacterial eradication,although rarely observed in the general population, seems to be more frequent in diabetic patients than in controls (Ojetti*et a*l., 2010; Marietti*et al*., 2013; Cong *et al.*, 2014).

The present study also found that the *H. pylori* positivity rate was insignificantly higher among type 2 DM compared to type 1 (29.5 % Vs 5.7 %, P = 0. 9). Theseresults are in agreement with the majority of previous studies from various other regions of the world (Zhou *et al*., 2013; Hsieh *et al*., 2013;Osman *et al*., 2016). However, glycemic control was significantly better in type 1DM patients who were negative for *H. pylori* infection compared to their counterparts (Dai *et al*., 2015).

CONCLUSION:

Although the current data are unable to provide concrete evidence that *H. pylorus* plays a role in diabetes mellitus, however the possibility cannot be ruled out.

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