Japanese Journal of Gastroenterology and Hepatology

Clinical Paper

ISSN: 2435-1210 | Volume 8

Helicobacter Pylori Infections among Patients with Type 2 Diabetes Mellitus in Benghazi, Libya

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Received: 04 Mar 2022
Accepted: 18 Mar 2022
Published: 24 Mar 2022
J Short Name: JJGH

Citation:

Younis, EZ, Helicobacter Pylori Infections among Patients with Type 2 Diabetes Mellitus in Benghazi, Libya. J Gstro Hepato.. V8(11): 1-7

Keywords:

Helicobacter pylori; Diabetes Mellitus; Benghazi; Libya

1. Abstract

1.1. Background: Diabetes Mellitus is the most common endocrine disease, diabetic patients also suffer more frequently from [complicated] infections compared with non-diabetic patients one of them is Helicobacter pylori infection, it is a major health aliment in developing countries.

1.2. Aim of the study: To determine the prevalence of Helicobacter pylori [H. pylori] infection in Type 2 diabetic Patients.

1.3. Methods: A cross sectional study recruited three hundred patient two hundred out of them were type 2 diabetics from Benghazi diabetic center and one hundred healthy individuals or non diabetic patients which served as control group was taken from Benghazi medical center and Elhiaa clinic . Their ages ranged between 25 to 70 years , from the period of 2015 -2019 . All members of the study were investigated for serum H.pylori -IgG by Elisa ,blood glucose levels and HbA1c and Parasitic tests were also done for all patients. Socio demographic characteristics were taken during the interview.

1.4. Results: The results revealed that the overall prevalence of infection with Helicobacter pylori among Type2 diabetic patients were 144 [72.0%] with highly significant difference [p=0.000] compared to 49% of the non-diabetic group. Our results show that there was no statistical difference in H. pylori positivity according to gender smoking history and education level in diabetic and non-diabetic while presence of parasitic infestation and gastrointestinal symptoms in H. pylori positive patients were statistically different between diabetic and non-diabetic group being higher in diabetics. H. pylori was statistically more prevalent in diabetic with higher fasting plasma glucose and HbA1c. Diabetes duration was not predictor for H. pylori infection.

2. Introduction

Helicobacter pylori [H. pylori] plays a major pathogenic role in gastrointestinal diseases, including chronic gastritis, peptic ulcer disease, gastric cancer, and mucosa-associated lymphoid tissue lymphoma [1]. At present, more than One half of the world's population has H. pylori infection, with an estimated prevalence of more than 90% during adulthood in developing countries. This has been attributed to the poor socioeconomic status and overcrowded conditions [2,3]. The only host in which H. pylori causes disease is human. Although it usually has an asymptomatic course during its life span, it is closely associated with gastroduodenal diseases such as gastritis, peptic ulcer, non-ulcer dyspepsia, gastric carcinoma, MALT-lymphoma, hypertrophic gastrolatry [1,4,5,6]. Diabetes mellitus [DM] is a clinical syndrome associated with deficiency of insulin secretion or action. It is considered one of the largest emerging threats to health in the 21st century. It is estimated that there will be 380 million persons with DM in 2025 [7]. Diabetic gastroparesis [DGP] is a common chronic complication of diabetes characterized by decreased gastric motility, delayed gastric emptying, and gastric rhythm disorders, with upper abdominal pain, early satiety, nausea, vomiting, and anorexia as its

main clinical manifestations The presence of H. pylori and diabetes mellitus [DM] is one of the main causes of gastrointestinal diseases [8,9]. The causes of gastrointestinal diseases and dyspepsia remain uncertain and are likely to be infectious and non-infectious agents. Helicobacter pylori [H. pylori], intestinal parasite [IP] and coeliac disease are common causes of dyspepsia [10]. Recently, polymicrobial causes of upper gastrointestinal disorders have gained tremendous clinical significance and the importance of synergism has been identified as significant contributor of dyspepsia [11]. Several studies suggest that there might be a potential link between H. pylori infection and T2D, but still it remains a subject of debate, the role of H pylori infection in T2D still unclear [12, 13, 14], whether it has a pathogenic role or that diabetic patients have increase susceptibility to H .pylori infection. Patients with diabetes mellitus are often affected by chronic infections. Many studies have evaluated the prevalence of H. pylori infection in diabetic patients and the possible role of this condition in their metabolic control. Some studies found a higher prevalence of the infection in diabetic patients and a reduced glycemic control, while others did not support any correlation between metabolic control and H. pylori infection. No previous studies have examined the association between T2D and the prevalence of H. pylori in Benghazi, Libya.

3. Aim of the study

Prevalence of Helicobacter pylori infections among Patients with Type 2 Diabetes Mellitus and to assess concomitant co-infection of intestinal parasites and H. pylori, and associated risk factors of adult upper gastrointestinal symptomatic patients in Benghazi, Libya.

4 Materials and Methods

4.1. Study design and patients: A cross sectional case control study recruited two hundred type 2 diabetics [124 females and 76 males] from Benghazi diabetic center and one hundred non-diabetic individuals [73 females and 27 males] which served as control group was taken from Benghazi medical center and Elhiaa clinic their ages ranged between 25 to 70 years from the period of 2015 -2019. All members of the study were investigated for serum *H.pylori* - IgG by Elisa , blood glucose levels and HbA1c and Parasitic tests were also done for all patients. Socio demographic characteristics were taken during the interview study population. Each case was evaluated with detailed history regarding age, type of diabetes, duration of diabetes, level of blood glucose and medication prescribed to them for control of diabetes. The diagnosis of Diabetes Mellitus was based on the criteria, fasting plasma glucose, mg/dL and HbA1c > or = 6.5.

4.2. Samples

Each participant provided a blood and stool sample, The blood samples were examined serologically for Helicobacter *H. pylori* immunoglobulin G [IgG] antibodies using ELISA [Enzyme–Linked Immunosorbent Assay] KIT for IgG against *Helicobacter pylori*. also The *H. pylori* antigen was detected in the stool samples. All collected stool samples were coded and screened for intestinal parasites by using direct wet mount using 0.85% sodium chloride solution as recommended by standard guideline [15,16], also we used modified Ziehl-Neelsen staining technique for detection of oocysts of opportunistic coccidial intestinal parasite- *Cryptosporidium* spp, *Isospora belli* and *Cyclospora cayetanensis* [17].

4.3. Statistical analysis

Descriptive analysis of the collected data using SPSS version 17 statistical package . Acomparison of the frequency and association of various parameters with presence or absence of *H. pylori* infection between cases and controls was performed by chi-square test.

4.4. Results

The present study was carried out on three hundred patients comprising two hundred diabetic patients Type 2 and one hundred were non-diabetic [control group].

The results revealed that the overall seropositivity of *H. pylori* infection among diabetic patients was [72.0%] higher than non diabetic [control group] [49.0%] (Table 1).

The results showed that there was a significant difference between *Helicobacter pylori* infection among diabetic patients and non-diabetic [P=0.000]. Odds ratio for acquiring *Helicobacter pylori* infections for Diabetic and Non diabetic was =3.01 which mean that diabetics have three-fold increase in risk for *Helicobacter pylori* infections compared with non-diabetics. The prevalence of *H. pylori* infection among different age groups [years] of diabetic patients is presented in (Table 2) , The results revealed that the highest prevalence rate [89.7%] was observed in age group of 55-46 years followed by age group ≥56 and age group 20-35 , years old at prevalence rates [87.5%] and 70.9% respectively. Low prevalence rate was recorded among age group 36-45 years old at 65.5 %. Age had a significant influence on the prevalence of *H. pylori* infection among diabetic patients [P= 0.03]. The highest prevalence of *H . pylori* infection among different age groups of non diabetic patients was detected among age groups ≥56 years old at 82.4% followed by age groups 46-55 , 36-45 , and 20-35 years old at prevalence rates 52.9 %, 42.4% , 27.3 %, respectively. Age had no significant influence on the prevalence of *H . pylori* among non-diabetic patients [P= 0.568]. The results revealed that the prevalence rate was higher in males 58[76.3%] than in females 86[69.4%] in diabetic patients with non significant difference [P=.287] was found between gender and diabetes status. On the other hand, the prevalence rate of *H. pylori* in non diabetic was higher in females 37[50.7%] than in males 9[33.3%]. There was no significant difference was detected between gender [P = .122]. The relationship between prevalence of *H. pylori* infection among diabetic and non diabetic and sex is presented in (Table 3). The results showed that the prevalence rate of *H. pylori* positivity in individuals with higher academic qualifications was high in both diabetic patient and non diabetic 32[80%] , 5 [71.4%] respectively, but with no statistical differences between *H. pylori* infection and diabetic and non diabetic (Table 4).

The results showed that among T2DM participants 40% [80/200]

were have parasitic infestation and the relation between diabetic status and the risk parasitic infestation was strongly significant [χ^2 =17.64, df=1, P=0.000, Odds ratio 3.5, CI = 1.94-6.4] at the same time the results showed that the intestinal parasite [IP] infection among patient with *H. pylori* IgG positive were 81.2% [65/144]. Which is higher than the *H. pylori* IgG negative group 56.3% [9/46], analysis showed statistically significant association between intestinal parasite [IP] and *H. pylori* infection among T2DM [P=000] and control group [P= 0.02] (Table 5). From the total of 200 T2DM we found out only 144 and from this the most common parasite species found in T2DM individuals infected with parasites *Cryptosporidium parvum* and *Entamoeba coli* with the highest prevalence at 26.2% [17] in both followed by *Giardia lamblia* 10[15.4%] , *Entamoeba hartmanni* 8[12.3%], *Entamoeba histolytica /E. dispar* 7[11.0%], *Isospora belli* 4[6.2%] and *Blastocystis hominis ,Enterobius vermicularis* 1[1.5%] in both while among control group the prevalence *of intestinal* parasites among *H. pylori* IgG positive were high detect *Entamoeba histolytica / E. dispar* 6[66.7%] followed by *Giardia lamblia and Blastocystis hominis* 2[22.2%],1[11.1%] respectively (Table 6). The prevalence of *H. pylori* infection is higher in individuals with Type 2 diabetic who do not smoke, and in contrast among control group the *H. pylori* infection were equal in smoker and nonsmoker [33.3%] Nevertheless, no statistically significant association was found [P=.407 DM and. p=.303 (Table 7). As shown in (Table 8), the most common symptoms associated with *H. pylori* infections among T2DM were Abdominal pain+ diarehea [30.5%] , followed by Patients with Abdominal pain, Constipation , diarehea , dyspepsia and Nausea [27.8% , 15.3% ,11.8% , 10.4%,4.2%] respectively with a significant difference p=.046* found between *Helicobacter pylori* [*H. pylori*] infection and T2DM Patients While among control group the high infection with *H.pylori* detected among Patients with Abdominal pain [87.0%] and no *Helicobacter pylori [H. pylori]* detection among Patients with Constipation , Nausea , the Patients with Dyspepsia, No Symptoms, Diarehea , Abdominal pain+ diarehea were [13.0% , 10.9%,8.7% and 4.35%] respectively with high significant difference between Helicobacter pylori [*H. pylori* infection and control group[X^2= 17.185 [a] ; df= 1 ; p=.000*** (Table 8). As shown in (Table 8), the most common symptoms associated with *H. pylori* infections among T2DM were Abdominal pain+ diarehea [30.5%] , followed by Patients with Abdominal pain, Constipation , diarehea , dyspepsia and Nausea [27.8% , 15.3% ,11.8% , 10.4%,4.2%] respectively with a significant difference p=.046* found between *Helicobacter pylori* [*H. pylori*] infection and T2DM Patients While among control group the high infection with *H.pylori* detected among Patients with Abdominal pain [87.0%] and no *Helicobacter pylori [H. pylori]* detection among Patients with Constipation , Nausea , the Patients with Dyspepsia, No Symptoms, Diarehea , Abdominal pain+ diarehea were [13.0% , 10.9%,8.7% and 4.35%] respectively with high significant difference between Helicobacter pylori [*H. pylori* infection and control group[X^2= 17.185 [a] ; df= 1 ; p=.000***] (Table 8). Frequency of symptoms associated with *H. pylori* infection among the type 2 diabetes mellitus patients and non-diabetic control subjects Interestingly. Patients with fasting glucose 126or more they have higher prevalence of *H. pylori* positivity compared with those with fasting blood sugar of less than 126 and and the difference was statistically significantly [X2 40.212a df ; 1 p=.0.000] . (Table 9) show these results. In accordance to finding the prevalence of *H. pylori* positive was found to be more in patients with poor glycemic control having HbA1C > 8 %, among the 144 *H. pylori* -positive patients, 97[67.4%] were found to have HbA1c >8 % and 35 patients [24.3%] had HbA1c 7.1-8% . %, and only 12 [8.3%] were found to have HbA1c >7% and there were statistically significant difference among HbA1c level and T2DM with *H. pylori*-positive patients [X2 38.427a df ; 1 p=.0.000]. (Table 10). There was no significant difference between *H.pylori* infection according to duration of the detection of their diabetes.[X2 .158a df ; 1 p=.691] (Table 11).

Table 1: Overall prevalence rate of *Helicobacter pylori* infections among examined patients ,DM & Non DM (n=300).

H.P. status IgG	*Helicobacter pylori* positive	*Helicobacter* pylori negative	Total
Diabetic	144(72.0%)	56(28.0%)	200
Non diabetic	49(49.0%)	51(51.0%)	100
Total	193(64.3%)	107(35.7%)	300
P value	X2= 15.370a ; df= 1 ; P=0.00		

Table 2 : Illustrates age distribution of *Helicobacter pylori* infection among DM & Non DM

Age	Diabetic		Non diabetic	
	H. pylori positive	Number of diabetic patients	*H. pylori* positive	**Number of non diabetic patients**
25-35	56(70.9%)	79	9 (27.3%)	33
36-45	55(65.5%)	84	14(42.45)	33
46-55	26(89.7%)	29	9 (52.9%)	17
56-70	7(87.5%)	8	14(82.4%)	17
Total	144	200	46	100
p-value	X2 = 14.203a; df= 3 ; p=0.03(DM)		X2 = 2.022a ; df= 3 ; p=.568 (nonDM)	

Table 3: The prevalence of *Helicobacter pylori* according to gender of the study subjects

Gender	Diabetic		Non diabetic	
	H. pylori positive	Number of subjects	*H. pylori* negative	Number of subjects
Male	58(76.3%)	76	9(33.3%)	27
Female	58(76.3%)	124	37(50.7%)	73
Total	144	200	46	100
p-value	X2= 1.133a ; df= 1 ; p=. 287		X2= 2.389a; df= 1; p=.122	

Table 4 : Relationships between the prevalence of *H. pylori* infection and Education

Education	Diabetic		Non diabetic	
	H. pylori positive	No .exam	*H. pylori* positive	No .exam
University and higher	32(80%)	40	5(71.4%)	7
Middle	95(70.9%)	134	3(27.3%)	11
Lower	17(65.4%)	26	38(46.3%)	82
Total	144	200	46	100
P value	$X^2$2.538[a] ; df = 3; p=.468		X^2= 3.379[a]; df = 2; p=.185	

Table 5: Prevalence of *Helicobacter pylori (H. pylori)* and parasite among diabetic and Non diabetic

Helicobacter pylori (H. pylori)	Diabetic			Non diabetic		
	Parasitic infection n=80	**Non Parasitic infection n=120**	**Total exam**	**Parasitic infection**	**Non Parasitic infection**	**Total exam**
H. pylori positive	65(81.2%)	79(65.8%)	**144**	9(56.3%)	37(80.4%)	**46**
H. pylori negative	15(18.8%)	41(34.2%)	**56**	7(43.8%)	47(87.0%)	**54**
Total	80	120	**200**	16	84	**100**

Table 6: Prevalence of *Helicobacter pylori (H. pylori)* and Types of parasitic infection among diabetic and Non diabetic

Intestinal parasite		H. pylori infection	Intestinal parasite	H. pylori infection
Non parasitic infected	120	79	84	37
Types of parasitic infection	N=80	45.1%((144\65	N=16	9(19.6%)
Blastocystis hominis	1.3%(1)	1(1.5%)	6.3%(1)	1(11.1%)
Entamoeba histolytica / E. dispar	12.5% (10)	7(11.0%)	10))62.5%	6(66.7%)
Giardia lamblia	12.5% (10)	10(15.4%)	(2)12.5%	2(22.2%)
Entamoeba coli	26.3% (21)	17(26.2%)	0 % (0)	0(0.0%)
Cryptosporidium parvum	21.3% (17)	21.3% (17)	0 % (0)	0(0.0%)
Entamoeba hartmanni	11.3% (9)	8(12.3%)	0 % (0)	0(0.0%)
Isospora belli	6.3% (5)	4(6.2%)	0 % (0)	0(0.0%)
Dientamoeba fragilis	3.8% (3)	0(0.0%)	0 % (0)	0(0.0%)
Ascaris Lumbricoides	0(0.0%)	0(0.0%)	19 % (3)	0(0.0%)
Enterobius vermicularis	1.3 % (1)	1(1.5%)	0 % (0)	0(0.0%)
Total	200	144	100	46

Table 7 : The prevalence of of *Helicobacter pylori (H. pylori)* infection and Smoking

Cigarette Smoking	Diabetic		Non – Diabetic	
	H. pylori positive	No .exam	*H. pylori* negative	No .exam
Smoker	32 (72.7%)	44	7(33.3%)	21
Non Smoker	26(81.3%)	32	2(33.3%)	6
Total	58	76	9	27
P value	X^2= 1.800[a] ; df= 2 ; p=.407		X^2= 2.389[a]; df= 2; p=.303	

Table 8: Frequency of symptoms associated with H. pylori infection among among the type 2 diabetes mellitus patients and non-diabetic control subjects

HbA1C	H. pylori positive	No .exam
<7	12(8.3%)	37
7.1-8	35(24.3%)	49
>8	97(67.4%)	114
Total	144	200

Table 9: Comparison of fasting blood sugar in patients of T2DM with or without Helicobacter pylori.

Fasting serum glucose, mg/dL	Diabetic	
	H. pylori positive	*H. pylori* negative
< 126	15(10.4%)	29
≥126 mg/dL	129(89.6%)	27
Total	144	56

Table 10: Comparison of HbA1c levels with presence of H. pylori positive in Type 2 DM

Duration of Diabetes Mellitus(year)	H. pylori positive	H. pylori negative	Total
Less than 5yr (n=144)	40(27.8%)	14	54
n=54	-74.10%		
≥5 (n=144)	104(72.2%)	42	146
n=146	-71.25		
Total	144	56	200

Table 11: Duration of type 2 diabetes in patients of H.pylori . positive and negative patients with increased duration of diabetes had more changes of being Helicobacter pylori positivity.

Symptoms	% from total *H.Pylori* positive 144	% from Diabetic with Symptoms	% from total *H.Pylori* positive (46)	% from non diabetic with Symptoms
No Symptoms	0 (0.0%)	0 (0.0%)	5 (10.9%)	5/20 (25%)
Abdominal pain+ diarehea	44 (30.5%)	44/45 (97.8%)	2(4.35)	2/3 (66.7%)
Nausea	6 (4.2%)	6/7(85.7%)	0(0.0%)	0/1 (0.0%)
Abdominal pain	40 (27.8%)	40/62(64.5%)	40(87.0%)	40/50 (80%)
Dyspepsia	15 (10.4%)	15/25(60%)	6 (13.0%)	4/17 (35.3%)
Diarehea	17 (11.8%)	17/35(48.6%)	4(8.7%)	4/4(100%)
Constipation	22 (15.3%)	22/26(84.6%)	0(0.0%)	0/5 (0.0%)
p-value	X^2= 3.982[a] ; df= 1 ; p=.046* p=.407		X^2= 17.185 [a] ; df= 1 ; p=.000*** P=.303	

5. Discussion

The prevalence of HP infection detected in the present study was [72.0%] among T2DM subjects, this is a higher in comparison with non –diabetic control [49.0%] with high significant difference [P=0.000] result is in agreement with previous studies [18-21]. In contrast, other studies showed that *H. pylori* infection is not associated with DM, so that there is no significant difference in the prevalence of *H. pylori* infection between diabetics and non-diabetic control groups [22-24]. On the other hand, on the previous study, we found that HP eradication in patients with diabetes was lower than non diabetic subjects [25]. Although, some studies have not supported this association [26]. The present study found the prevalence of Helicobacter pylori seropositive infection in relation to age. The prevalence was found to be higher in in older age group 55-46 and ≥56 years in both the diabetic and non diabetics group [89.7%] and [82.4%] respectively, this difference may be explained to the differences in the immune response among different age group thus suggesting a late acquisition of the infection, which was concurrent with the observations [27,28]. But factual relation of *Helicobacter pylori* infection to age remains inconclusive [28]. Surprisingly, the results showed no significant difference between males and females [p<0.05] in both diabetic and non-diabetic males had higher prevalence rate than Females in diabetic patients. On the other hand, this finding disagree with previous results [29,30]. DM is a major and growing health problem in most countries and an important cause of prolonged ill health and early death The individuals suffering from DM become immune compromised and prone to bacterial and parasitic infections [31,32]. Intestinal parasites have gained attention as important opportunistic pathogens responsible for clinically important infections in immune-compromised patients [31,32]. In the present study, the results showed that DM condition has a significant risk factor for acquiring parasitic infections. However, this differs from the findings of Nazligul *et al* [33] report where non-DM individuals had a significantly higher prevalence of intestinal parasitic infections. However, there was high statistically significant difference in the levels of HbA1c, fasting serum glucose among type 2 diabetes mellitus *with H. pylori* infection [p=.0.000]. this result agreement with *previous* reports [34]. The present study showed that no statistically significant correlation was found between *H. pylori* infection and duration of diabetes, [p=.691] this result agreement with [35-38]. There was no any significant difference in H. *pylori* prevalence according to Smoking history either in diabetic nor in non-diabetic We note that there was no diabetic with *H. ployri* positivity without Symptoms while 20/100[20%] of non-diabetic *H.ployri* positivity were a Symptomatic.

6. Conclusion

Helicobacter pylori infections among Type 2 diabetic Patients was higher than non-diabetic in Benghazi, Libya.

7. Acknowledgement

This research was supported and funded by Department of medical laboratory in Higher institute of medical. Benghazi, Libya. The authors are grateful to the members of the medical laboratory institute and the students which they aid in the collection of samples.

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