The Egyptian Journal of Hospital Medicine (January 2024) Vol. 94, Page 1268-1271

Helicobacter Pylori Infection and Glycaemic Control in Egyptian Diabetic Patients with Dyspepsia

Abdallah H.El-Shaat Soliman,Mohamed M.Hegazy, Ahmed M. Ghazy
Department of Hepatology, Gastroenterlogy and Infectious Disease, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
Corresponding author: Abdallah H. Elshaat, **Email**:drabdallah_soliman@yahoo.com
Mobile:01112214486

ABSTRACT

Background: Diabetic patients often experience symptoms that originate from the gastrointestinal tract. Various agents, including gastric motility abnormalities and Helicobacter Pylori (HP) infection, are believed to be responsible for these changes. Limited and controversial data are available on the prevalence of HP in those studied cases & the correlation between HP infection & diabetic control is not well-defined.

Aims: This study aimed to examine the prevalence of HP in diabetic patients with dyspepsia and to evaluate the link between H. Pylori infection and glycemic control. We evaluated the prevalence of HP in type 1 and type 2 diabetic patients with ulcer and non-ulcer dyspepsia (NUD) and their relationship to diabetes (DM) control.

Subjects and Methods: In this study, 150 subjects were selected and were split into three groups: Group 1: type 1 diabetes, group 2 (type 2 diabetes), and group 3 (non- diabetic).Patients were asked for dyspeptic symptoms. Endoscopy of the upper gastrointestinal tract was performed for all patients to confirm or exclude peptic ulcer. HP infection was diagnosed by rapid urease test (RUT) and histopathology (HPE), and glycemic control was measured by fasting (FBS), postprandial blood sugar (PPBS), and Glycated hemoglobin (HbA1c).

Results: HP prevalence in diabetic patients was significantly higher than in the control group and its presence was likely associated with poor glycaemic control.

Conclusions: Diabetics are at high risk of HP infection. HP infection may be related to inadequate glycemic control and should be considered for eradication therapy.

Keywords: H. Pylori, Dyspepsia, Diabetes. Non ulcer dyspepsia.

INTRODUCTION

Dyspepsia is the upper abdominal pain or discomfort that is episodic or persistent. Dyspepsia is reported to happen in nearly 25 % of the population each year, but most affected individuals do not seek medical care [(1)]. Furthermore, dyspepsia accounts for significant healthcare costs and a considerable loss of time from work. A particular etiology is not recognized in about 50% to 60% of patients (i.e., "functional" or NUD).Many of these patients are assumed they have an augmented perception of visceral pains [(1)].

Uninvestigated dyspepsia is the term used to describe study cases that did not have any investigations done but that appear with predominant epigastric pain or discomfort. There are five main reasons for dyspepsia in studied cases that are investigated: medicines, functional dyspepsia, persistent peptic ulcer disease (PUD), gastric reflux (with or without esophagitis), and cancer [(2)].

Table (1): Causes of dyspepsia [(2)]

Iagnostic category	Approximate prevalence
Functional (NUD)	Up to 60%
Dyspepsia caused by structural or biochemical disease	
Peptic ulcer disease	15-25 %
Reflux esophagitis Gastric or esophageal cancer Biliary tract disease, gastroparesis and pancreatitis	5-15% < 2% Rare

The gram-negative spiral flagellate bacillus Helicobacter pylori (HP) is typically found in the stomach epithelium. It may induce the infiltration of inflammatory cells into the gastric mucosa, releasing cytokines that damage distant tissues & cause extra digestive diseases such as ischemic heart disease, autoimmune thyroid disease, iron deficiency anaemia, & neurologic disorders [(3)].

In addition to this, it is also thought to play a direct or indirect role in the pathogenesis of metabolic syndrome, non-alcoholic fatty liver disease, and type 2 diabetes [(4)].The incidence of HP infection differs among nations; the incidence is usually aboutthirty percent in developed countries & up to eighty percent in developing nations [(5)].

The mammalian stomach produces leptin and ghrelin, 2 hemostasis energy hormones whose interactions influence obesity, and insulin sensitivity [(6)]. Some studies have shown a high prevalenceof HP infection in diabetic patients. HP infection is correlated with the length of diabetes mellitus (DM), the existence of dyspeptic symptoms, autonomous neuropathy, cardiovascular signs, age, gender, BMI, blood pressure, fasting glucose, and HbA1c. This could be connected to decreased peristaltic activity & stomach motility, chemical changes in the gastric mucosa as a result of nonenzymatic glycosylation, and a decline in diabetic patients' non-specific immunity [(6)].

On the other hand, according to other surveys, DM and HP infection are unrelated. The stomach mucosa's microvascular alterations can provide a hostile

Received: 29/10/2023
Accepted: 27/12/2023

environment for HP development. Certain statistics indicate that there is no correlation between HP infection & diabetic complications like kidney disease &/or microangiopathy. However, other data indicate that virulent HP strains, like the CagA+ gene related to cytotoxins, are linked to microangiopathy, neuropathy, & microalbuminuria in diabetic studied cases. This could be the result of an immunological response to an HP infection that causes endothelium damage [7].

The objectives of this study were to examine the prevalence of HP in diabetic patients with dyspepsia and to evaluate the link between H. Pylori infection and glycemic control.

PATIENTS AND METHODS

This cross-sectional research had been conducted on 150 diabetic studied cases (either type 1 or type 2 DM). Both males and females were involved in the research. All studied cases with an age ranged between 18-70 years old presented with dyspeptic manifestation of more than 3 months at El-Hussein & Sayed Galal Hospitals (Al-Azhar University Hospitals). The patients were divided into 3 groups as shown in table (2).

Table (2): Characteristics of patients grouping enrolled in the study

Groups	Characteristics
Group 1	50 patients with type 1 DM
Group 2	50 patients with type 2 DM
Group 3	50 patient's non-diabetics (Control group)

Full medical history with a detailed history of dyspeptic symptoms and duration, and treatment of DM. Thorough clinical examinations included: BMI using the formula: weight (kg)/height (m^2). Routine laboratory investigation (Full blood count, kidney and liver function tests, lipid profile, FBS, PP-BS and HbA1c). Sonographic examination of the abdomen and pelvis was also done. All patients underwent upper gastrointestinal endoscopy to diagnose or exclude peptic ulcer or any other mucosal disease. Antral biopsies were collected, and placed in a sterile phosphatebuffer. Biopsy tissue was collected by using standard endoscopy, biopsy forcips, and gastroscopies (Olympus GIF Type Q40 – 2300903). The gastric mucosal endoscopic biopsy was placed on agar gel containing urea. Two pH dye indicators were used bromothymol blue and methyl red together with paraben preservative.

Exclusion criteria: Prior treatment for H. Pylori (Within one month), advanced liver cirrhosis, and advanced chronic illness.

Ethical Approval: The study was approved by the Ethics Board of Al-Azhar University and an informed written consent was taken from each participant in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Numbers & percentages were used to describe the qualitative data. The Chi-square test was used to compare several groups concerning categorical variables. The mean & standard deviation were used to characterize the quantitative data. The level of significance was explained by P value in the following ways: $P \leq 0.05$ significant, $P > 0.05$ non-significant, & $P \leq 0.01$ extremely significant.

RESULTS

There were no statistically significant differences in sex, age, and BMI between groups (Table 3).

Table (3): Comparison between the three studied groups regarding RUS and Histopathological findings for H. pylori

	Group I		**Group II**		**Group III**		**P1 P2 P3**
	No	%	No	%	No	%	
Rapid urease test (RUS)							0.4120
No	36	72.0	37	74.0	48	96.0	0.0004*
Yes	14	28.0	13	26.0	2	4.0	0.0009*
Histopathologial findings for H.pylori							0.4155
No	34	68.0	35	70.0	47	94.0	0.0004*
Yes	16	32.0	15	30.0	3	6.0	0.0008*

Of the 150 studied cases diagnosed by history, laboratory, & endoscopic examination to diagnose with dyspepsia (ulcer and non-ulcer dyspepsia). They were divided into 3 groups,each group 50 patients (Type 1 DM, type 2 DM and non-diabetic control group). HP infection was more significant in diabetic than in non-diabetic group. Regarding RUT test and HPE findings for H. Pylori, there was a statistically significant difference between group I (type 1 DM), III (non-diabetic) and group II (type 2 DM), III (P2, P3 < 0.05). While, there was no statistically significant difference between diabetic group I, II (P1 > 0.05). Regarding FBS and PPBS, there was a statistically significant difference between H.pylori positive and negative groups (P value < 0.05). Regarding HbA1c, there was a statistically significant difference (P < 0.05).

Table (4): Shows a highly statistically significant increase in HbA1c, FBS, and PP-BS in H. pylori-positive compared with H. pylori-negative groups (P<0.001)

	H pylori positive	H pylori negative	*P* value
HbA1C(mg/dl)	8.32± 2.91	5.4± 1.52	< 0.05
FBS(mg/dl)	3.67± 0.33	128.3± 5.78	< 0.05
PP-BS(mg/dl)	319.8± 16.05	182.93± 7.67	< 0.05

DISCUSSION

Dyspepsia is a common health problem in general as well as in diabetic patients. The cause of dyspepsia in diabetic mellitus is complex. Dyspepsia in diabetic studied cases might be caused by autonomic neuropathy, delayed stomach emptying, HP infection, inadequate glycemic management, peptic ulcer, GERD, etc… [8].

HP is a common bacterial infection that has been implicated to cause gastrointestinal and non-gastrointestinal disorders. Patients with DM are more susceptible to infection and gastroparesis diabeticorum, which may contribute to bacterial overgrowth in the upper gastrointestinal tract hence the need for this study toidentify at-risk groups and to consider whether the presence of HP affects control of DM in these patients [9]. There is ongoing debate over the relationship between H. pylori infection & diabetes, with some research finding a higher prevalence of infection in those with the disease & others finding no difference [4].

In our work, we found that HP infection was common among diabetics. HP infection was more prevalent in dyspeptic patients in diabetic groups (groups I, and II) than in non-diabetic (control) group. In our work, the level of HbA1c was higher in groups I, and II than in group III, which may suggest that HP can play a role in poor control of DM.

In our study, all patients were subjected to endoscopy to diagnose or exclude the presence of peptic ulcer or any other mucosal disease. NUD or functional dyspepsiais diagnosed according to Rome IV criteria for the definition of functional dyspepsia. HP infection was tested by RUT and HPE examination of the specimens taken at endoscopy to confirm or exclude the presence of HP Infection.

The connection between HP infection & diabetes is up for debate. According to several research, persons with diabetes who have type 1 or type 2 DM have a significant prevalence of HP infection. Our results are in agreement with **Candelli *et al.*** [10], who reported that the prevalence of H. pylori infection was increased in diabetics (24%) than in controls of similar age, sex, and socioeconomical status after 3 years of follow-up, the reinfection rate was higher in diabetic patients. In contrast, other studies indicated that the prevalence of HP infection is the same in diabetic & non-diabetic individuals, irrespective of the kind, course, & severity of dyspeptic symptoms in diabetic studied cases [11]. **Xia *et al.*** [12] reported too that no significant difference in HP infection among diabetics and non-diabetic control groups.

In general, we discovered no significant difference between group I and group II regarding HP infection but there was a significant difference between group III (non-diabeticgroup). Both RUT and HPE have been considered the gold standard method for the detection of HP with sensitivity of both tests (95%) in most papers but in our work, we discovered that HPE was slightly more sensitive than RUT.

Various other studies also found That diabetic studied cases received a higher prevalence of HP infection [13]. **Rosenstock *et al.*** [13], found that HP was more prevalent in diabetics than in non-diabetics. However, **Gulcelik *et al.*** [14] did not support an association between HP infection & diabetes.

Different theories explain the increased prevalence of HP among diabetic patients. 1st, diabetes makes it more difficult for the body to map humoral & cellular immunity, making a person more vulnerable to HP infection [15]. Secondly, it diminishes gastrointestinal motility & stomach acid output, thereby elevating colonization & bacterial infections [16]. Third, changes in the metabolism of glucose can alter the chemical production of the gastric mucosa, which ultimately leads to the colonization of more bacteria[15].

The demographic results of this survey showed that the age of the patients in the three studied groups ranged from 23 to 68 years, and the mean age in the three groups was around 47 years. On comparing the three groups, they were matched regarding age and gender. These results were important in eliminating the effect of age and sex on the outcome. In our study the onset of diabetes in the threegroups showed a mean value of 32 years and the duration of diabetes in the three studied groups was 14.2 years, there was no substantial divergence between the two studied groups regarding the onset of diabetes or duration of diabetes. The two diabetic groups were similar regarding clinical data. By these results we eliminate the effect of risk factors of duration of diabetes on the incidence of HP infection.

The causal relationship between Hp infection & diabetes is difficult to find out. One hypothesis is that since HP infection is generally acquired in childhood & diabetes later in life, Hp can directly or indirectly increase inflammatory mediators like interleukin & tumour necrosis factor α, which increase HbA1c level [17]. **Vafaeimanesh *et al.*** [18] found a relationship between HbA1c & HP infection in patients with diabetes and without diabetes. The third national health & nutrition assessment survey, conducted in 2004 on American men between the ages of forty & seventy, did not discover a consistent correlation between the prevalence of diabetes or the HbA1c level & HP infection. We don't know whether HP eradication

improves glycaemic control or not, in that respect are several controversial reports suggesting this theory.

Our findings demonstrated a substantial correlation between H. pylori infection & HbA1c level, with HbA1c in the H. pylori-positive group being significantly greater than that of the H. pylori-negative group. Our results agree with **Chen and Blaser** [(19)], who reported that H. pylori infection was positively associated with HbA1c levels through a large-scale cross-sectional analysis, which indicated a role of H. pylori in impaired glucose tolerance in adults. In contrast, **Gillum** [(20)], reported that The presence of H. pylori infection did not substantially correlate with HbA1c in men forty to seventy years old regardless of whether they had a history of type 2 diabetes.

CONCLUSION

HP infection is more prevalent in diabetics either type 1 or type 2. Furthermore, there was a significant correlation found between H. pylori and elevated HbA1c. Thus, we demand future research with large size to evaluate the impact of H. pylori eradication in glycemic control of diabetes & the impact of glycemic control on reinfection with H. pylori.

- **Consent for Publication:** All authors accepted.
- **Availability of data and material:** Available
- **Competing interests:** None
- **Funding:** No fund
- **Conflicts of Interest:** The authors declared no conflicts of interest regarding the publication of this paper.

REFERENCES

1. **Ofman J, Etchason J, Fullerton S *et al.* (1997):** Management strategies for Helicobacter pylori–seropositive patients with dyspepsia: clinical and economic consequences. Ann Intern Med.,126: 280–91.
2. **Talley N, Vakil N, Moayyedi P (2005):** American Gastroenterological Association technical review on the evaluation of dyspepsia. Gastroenterology, 129: 1756–1780.
3. **Draz U, Rathore R, Butt N *et al.* (2018):** Presence of pre-diabetes in Helicobacter pylori positive versus Helicobacter pylori negative patients having dyspepsia. J Pak Med Assoc., 68: 939–941.
4. **Vaishnav B, Shaikh S, Bamanikar A *et al.* (2018):** A study of relationshipof Helicobacter pylori infection with glycemic control and insulin resistance in adults with type 2 diabetes mellitus. Natl J Integr Res Med., 9: 92–97.
5. **Agrawal R, Sharma R, Garg D *et al.* (2010):** Roleof Helicobacter pylori in causation of diabetic gastropathies and non- gastrointestinal complications in type 2 diabetes. J. Indian Med Assoc., 108 (3): 140-3.
6. **Bener A, Micallef R, Afifi M *et al.* (2007):** Association between type 2 diabetes mellitus and Helicobacter pylori infection. Turk. J. Gastroenterol., 18 (4): 225-229.
7. **Demir M, Gokturk H, Ozturk N *et al.* (2008):** Helicobacter pylori prevalence in diabetes mellitus patients with dyspeptic symptoms and its relationship to glycemic control and late complications. Dig Dis. Sci., 53 (10): 2646 –9.
8. **Outlioua A, Badre W, Desterke C *et al.* (2020):** Gastric IL-1β, IL-8, and IL-17A expression in Moroccan patients infected with Helicobacter pylori may be a predictive signature of severe pathological stages. Cytokine, 126: 154893.
9. **Malaty H (2007):** Epidemiology of Helicobacter pylori infection. Best Pract Res Clin Gastroenterol., 21: 205–214.
10. **Candelli M, Rigante D, Schiavino A *et al.* (2012):** High reinfection rate of Helicobacter pylori in young type 1 diabetic patients: a three-year follow-up study. Eur Rev Med Pharmacol Sci., 16: 1468–1472.
11. **Papamichael K, Papioannou G, Karga H *et al.* (2009):** Helicobacter pylori infection and endocrine disorders: Is there a link? World J Gastroenterol., 15 (22): 2701–2707.
12. **Xia H, Talley N, Kam E *et al.* (2001):** Helicobacter pylori infection is not associated with diabetes mellitus, nor with upper gastrointestinal symptoms in diabetes mellitus. Am J Gastroenterol., 96: 1039–1046.
13. **Rosenstock S, Jørgensen T, Andersen L *et al.* (2000):** Association of Helicobacter pylori infection with lifestyle, chronic disease, body-indices, and age at menarche in Danish adults. Scand J Public Health, 28: 32–40.
14. **Gulcelik N, Kaya E, Demirbas B *et al.* (2005):** Helicobacter pylori prevalence in diabetic patients and its relationship with dyspepsia and autonomic neuropathy. J Endocrinol Invest., 28: 214 7.
15. **Nodoushan S, Nabavi A (2019):** The Interaction of Helicobacter pylori Infection and Type 2 Diabetes Mellitus. Advanced Biomedical Research , 8: 15.
16. **Jeon C, Haan M, Cheng C *et al.* (2012):** Helicobacter pylori infection is associated with an increased rate of diabetes. Diabetes Care, 35: 520–525.
17. **Nam S, Park S, Lee S *et al.* (2019):** Helicobacter pylori eradication in patients with type 2 diabetes mellitus: Multicenter prospective observational study. SAGE Open Medicine, 7: 1 7.
18. **Vafaeimanesh J, Rajabzadeh R, Ahmadi A *et al.* (2013):** Effect of Helicobacter pylori eradication on glycaemia control in patients with type 2 diabetes mellitus and comparison of two therapeutic regimens. Arab J Gastroenterol., 14: 55–58.
19. **Chen Y, Blaser M (2012):** Association between gastric Helicobacter pylori colonization and glycated hemoglobin levels. J Infect Dis., 205: 1195–1202.
20. **Gillum R (2004):** Infection with Helicobacter pylori, coronary heart disease,cardiovascular risk factors, and systemic inflammation: The Third National Health and Nutrition Examination Survey. J Natl Med Assoc., 96: 1470–1476.