ORIGINAL ARTICLE

Comparison of Helicobacter *pylori* seropositivity in individuals with and without type 2 diabetes mellitus - an immunological analysis

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ABSTRACT

Background and Objective: *Helicobacter pylori* (*H. pylori*) infection is common in type 2 diabetic patients who present with symptoms of acid peptic disease (APD). Both cellular and humoral immunity are compromised in T2DM; therefore, patients with diabetes are more susceptible to *H. pylori* infection. The aim of this study was to detect and compare *H. pylori* IgG antibody seropositivity in patients with type 2 diabetes mellitus (T2DM) in comparison with non-diabetic individuals.

Methods: This case-control study was performed at the Pathology Laboratory of Gulab Devi Educational Complex Lahore, Pakistan, from August 2022 to January 2023 comprising 100 patients with type 2 diabetes and 100 matchable non-diabetic individuals with a strong clinical history of APD. After obtaining written consent, blood samples were collected from diabetic and non-diabetic individuals and their blood sugar random (BSR) and glycated hemoglobin (HbA1c) was measured followed by detection of *H. pylori* IgG antibody seropositivity through Enzyme linked immunosorbent assay (ELISA). All the collected data was statistically analyzed by Statistical Package of Social Sciences 26.0.

Results: A total of 63% of the 100 diabetic individuals tested positive for *H. pylori* antibodies with 44% of those having BSR > 201 mg/dl or above with a mean BSR of 235.92 ± 93.42 (p = 0.01). In addition, 58% of diabetics had positive *H. pylori* IgG antibodies whose HbA1c levels were >6.5% with a mean value of 8.71 ± 2.14 (p = 0.033).

Conclusion: *Helicobacter pylori* seropositivity is more prevalent in type 2 diabetic patients as compared to non-diabetic individuals and has a significant association with mean BSR and HbAIC levels.

Keywords: Blood sugar, *Helicobacter pylori,* glycated hemoglobin, type 2 diabetes mellitus.

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Introduction

Gastrointestinal tract infection with *Helicobacter pylori* (*H. pylori*) affects 50% of the world's population and raises the risk of developing chronic inflammation, duodenal and gastric ulcer disease, as well as gastric cancer.[1] These Gram-negative bacteria have a helix form that allows them to pass through the mucous lining of the stomach to infect the gastric mucosa causing chronic inflammation and colonization with subsequent denudation of mucosal lining leading to ulcer formation.[2,3]

Chronic inflammation is the most common underlying pathogenic mechanism of *H. pylori* infection, especially those strains that can also cause the production of vital cytokines such as interleukins (6, 8, 17), and tumor necrosis factor-α.[4,5] Numerous studies have examined the relationship between *H. pylori* infection and persons with type 2 diabetes mellitus.[6-8]

Type 2 diabetes mellitus patients have been reported to be more prone to infections with associated complications. Early detection of gastric infection with *H. pylori*, proper treatment, and avoidance of complications in these patients remain the challenge for the treating physicians. A current study was conducted to determine the frequency of *H. pylori* seropositivity in patients with type 2 diabetes mellitus at a local tertiary care hospital in Lahore, Pakistan.

Methods

A cross-sectional comparative study was conducted over a six-month duration at the Endocrinology and Diabetic Outdoor of Gulab Devi Teaching Hospital Lahore, Pakistan, in collaboration with the Pathology laboratory of Gulab

Devi Educational Complex Lahore, Pakistan. A total of 100 diagnosed cases of type 2 diabetes mellitus and an equal number of matchable but non-diabetic control subjects were included in this study through a non-probability sampling technique. Patients in both groups had a history of acid peptic disease (APD) and none of them had started any treatment for APD. The study variables included were age, gender, blood sugar random (BSR), HbA1c, and *H. pylori* IgG seropositivity by Enzyme Linked Immunosorbent Assay (ELISA). Relevant clinical history was recorded in the relevant proforma. The inclusion criteria included diagnosed cases of type 2 diabetes mellitus according to HbA1c and BSR levels of both genders between the age group of 18-60 years. Pregnant females, patients on antibiotic or *H. pylori*-eradication therapy for APD, patients with uncontrolled diabetes mellitus, patients having type 1 diabetes mellitus, or any co-morbid immune disorders were excluded.

After taking written informed consent, a 3 cc blood sample was collected from both groups to measure *H. pylori IgG* antibodies by using a commercial ELISA test kit (IBL International, Germany). The optical density was determined using a microplate reader at 450 nm. Cutoff index values of >1.2 were considered positive, values <0.8 were considered negative, and values from 0.8 to 1.2 were considered indeterminate.

Statistical analysis

All the collected data were statistically analyzed by using Statistical Package of Social Sciences (SPSS) 26. 0 (SPSSA Inc. Chicago, IL). Pearson chi-square test and Fisher's exact probability statistics were applied to obtain associations between different variables (quantitative as age, mean BSR, mean HBAIC while qualitative as gender, clinical symptoms, and IgG seropositivity by ELISA). A *p*-value of ≤0.05 was taken as significant.

Results

Out of 100 diabetic patients, 37% were males and 63% were females with a mean age of 47.9 ± 9.5 years whereas out of 100 non-diabetic controls, 51% were males and 49% were females with a mean age of 42.20 ± 10.02 years. A total of 63 diabetic patients and 42 non-diabetic individuals tested positive for *H. pylori* antibody. On considering the gender, the distribution of *H. pylori* positivity in diabetic patients was 27% in males and 36% in females. According to recorded risk factors for acquiring *H. pylori* infection among diabetic patients and non-diabetic individuals, no significant association was found (Table 1). However, a significant association between BSR ($p = 0.01$), HbA1c ($p = 0.033$), and *H. pylori* seropositivity was seen among the diabetic patients.

Discussion

Helicobacter pylori is a human-specific bacterium that causes chronic gastritis that may lead to gastric cancer.[9] The common symptoms of *H. pylori*-associated APD include abdominal pain, heart burn, nausea, and vomiting associated with multiple gastrointestinal and extra gastrointestinal diseases that have dramatically changed the diagnostic approach in numerous fields of medicine. Moreover, *H. pylori* infection has been linked with T2DM.[6,10] Researchers report a higher frequency of *H. pylori* infection in individuals with diabetes mellitus.

The present study included 200 subjects out of which 100 were non-diabetic individuals with a mean age of 42.20 ± 10.019 years whereas another 100 non-diabetic individuals with a mean age of 47.9 ± 9.5 years were included. The results of the present study correspond with a study conducted in the United Arab Emirates that revealed a mean age of 48.1 ± 7.9 years in type 2 diabetes mellitus patients with *H. pylori* infection. *Helicobacter pylori* seropositivity was detected in 27% of male and 36% of female diabetic patients

Table 1. *Clinical features of 100 diabetics and non-diabetics individuals with risk of developing H. pylori infection.*

Clinical features	T2DM	Non-diabetics	Odds ratio (OR)	Confidence interval 95%	*p*-value*
Weight loss	84	36	0.926	0.306-2.799	0.892
Numbness of hands and feet	75	16	2.639	0.556-12.526	0.208
Hypertension	52	41	0.602	0.268-1.351	0.217
Nausea/vomiting	28	7	3.833	0.800-18.377	0.074
Diarrhea	23	14	0.516	0.107-2.494	0.403
Constipation	17	25	0.908	0.269-3.093	0.878
Anemia	21	13	1.830	0.503-6.658	0.354

*Fisher's exact probability statistics.

in the current study which is similar to the findings of Bener et al.[11,12] who reported a higher incidence of *H. pylori* in females, indicating that there is an ongoing debate on the gender distribution of this illness.

In our study, we found out that the diabetes patients (63%) had a higher prevalence of *H. pylori* infection than the non-diabetics (42%). Furthermore, we explored that there exists a significant association between *H. pylori* infection and BSR and serum HbA1C levels. These results correspond with a study conducted in Iran where *H. pylori* seropositivity was significantly higher in diabetic patients as compared to non-diabetics (55.8% *vs.* 44.2%, respectively).[10] Another research conducted in Libya concluded similar results when compared with the current study where 72% of T2DM patients were seropositive for *H. pylori* as opposed to 49% non-diabetic individuals.[13] *Helicobacter pylori* is more frequent in T2DM patients because they experience rapid progression in their gastric colonization and inflammation on the basis of low immunity and, thus, have more prominent and earlier reported complaints such as dysphagia, reflux, constipation, abdominal pain, nausea, vomiting, and diarrhea. In addition, this bacterium causes various hormonal imbalances in the body, which decreases its sensitivity to insulin and results in insulin resistance, which in turn causes escalated inflammation.[14,15] The diabetic patients of the current study with *H. pylori* infection reported similar clinical symptoms however the OR between the clinical symptoms and risk of acquisition of *H. pylori* was insignificant. Another study showed that age, gender, alcohol consumption, dyspepsia, level of education, duration of T2DM, or body mass index were not significantly associated with *H. pylori* infection.[16]

In the present study, out of 100 diabetic individuals, *H. pylori* seropositivity was detected in 44% of diabetics with BSR > 201 mg/dl or above, and in 58% of diabetics with HbA1c level > 6.5% or above. The results of the current study correspond with a study conducted in Egypt that concluded substantially greater levels of HbA1c in the *H. pylori*-positive group when compared with the *H. pylori*-negative group.[17] Recently a study done at King Edward Medical University, Lahore, Pakistan, showed an increased frequency of *H. pylori* infection in pre-diabetes which is in contrast to the findings of the present study in which *H. pylori* infection was more common in diabetics whose HbA1c > 6.5% or above.[18]

There are several techniques to detect *H. pylori* infection including mucosal biopsy, rapid urease test, serum *H. pylori* antibodies, and stool antigen test. ELISA is considered a rapid and reliable technique and has been reported in various studies to examine *H. pylori* infection in serum[10] or stool[13] samples with high sensitivity and specificity.

Conclusion

Helicobacter pylori seropositivity is higher in type 2 diabetic patients with APD as compared to non-diabetic individuals. This seropositivity is also strongly associated with blood glucose and HBA1C levels in patients with type 2 diabetes mellitus.

Limitations of the Study

The major limitation of the study is that the seropositivity could not be compared to other *H. pylori* detection techniques used in a standard clinical setting.

Conflict of interest

None to declare.

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Ethical approval

The study was approved by Institutional Ethics Committee dated 10th March, 2021.

Authors' contributions

JN, GA, MA: Substantial contributions in conception and drafting of the manuscript, critical intellectual input to the manuscript, approval of the final version of the manuscript to be published.

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