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Glycemic Control before and after *Helicobacter pylori* Eradication in Patients with Type 2 Diabetes Mellitus

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Research Article

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Abstract

Background: Diabetes Mellitus Type 2 is considered as a global health problem, the number of diabetic patients is expected to reach 642 million as we approach 2040, diabetic patients usually experience several complications related to macrovascular and microvascular changes, and mostly related to insulin resistance which is partly related to genetic mutation and in part related to other modifiable factors, one of these factors are chronic inflammation and infection. One of the most common chronic infections is *Helicobacter pylori* (*H. pylori*), which causes an increase in inflammatory markers, this raises the suspicion that infection with *Helicobacter pylori* may contribute to the development of diabetes and may affect its control. Many studies have been done on non-diabetic patients to determine the effect of infection with *Helicobacter pylori* on glycemia, thus more studies are needed on diabetic patients to confirm the role of *Helicobacter pylori* chronic infection on glycemic control. Aim: Examine glycemic control in diabetic patients before and after eradication of *Helicobacter pylori* infection. Patients & Method: Glycemic control of 60 diabetic patients with *Helicobacter pylori* infection will be monitored at baseline before eradication of the infection and 3 months after, without change in their diabetic medications. Results: Significant reduction in Fasting blood sugar and HbA1c were noted after *Helicobacter pylori* eradication as well as a decrease in the level of inflammatory markers such as CRP. Conclusion: Improvement in glycemic control after eradication of *Helicobacter pylori* infection.

Keywords: *Helicobacter pylori*, Eradication, Fasting blood sugar, HbA1c.

INTRODUCTION

Diabetes mellitus (DM) is considered a worldwide healthcare challenge. The total number of diabetic patients is increasing causing a burden on healthcare institutes all over the world [1]. Poor glycemic control causes many complications related to macrovascular and microvascular affection which influences the patient's quality of life, the main pathologic feature of these complications is insulin resistance [2]. Some environmental factors may have a role in the development of insulin resistance which are considered modifiable factors that lead to the development of DM. These modifiable factors such as obesity, chronic infection, and chronic inflammation can be avoided to prevent development of DM or at least become therapeutic targets in a trial to achieve glycemic control and avoid many complications [3].

Helicobacter pylori (*H. pylori*) infections are the most common chronic infection affecting people all over the world, especially in developing countries [4]. This gram-negative organism can cause many gastric pathologies such as gastritis, peptic ulcer, or even gastric cancer, and recently it has been involved in many exrtagastric pathologies such as metabolic syndrome, affection of cardiovascular system, immune system, insulin resistance, and obesity [5].

Like any other chronic infection, *H. pylori* causes an increase of inflammatory markers like CRP and tumor necrosis factor α (TNFα) which increase the suspicion that *H. pylori* contributes to the development of insulin resistance and in turn contributes to the development of DM and hyperglycemia [6]. Many studies have been done to find a connection between *H. pylori* infection and glycemia in non-diabetic patients and the results were mostly positive [7], other studies found that *H. pylori* is more prevalent in patients with DM because poor glycemic control increases the incidence of the infection and decrease the compliance to dyspepsia in diabetic patients [8], but whether *H. pylori* infection contributes to hyperglycemia in diabetic patients or not need further studies.

MATERIALS AND METHODS

Study design

A prospective randomized clinical trial was done on 60 patients with *H. pylori* infection and type 2 DM. *H. pylori* infection and eradication was proved by *Helicobacter pylori* antigen in stool, Glycemic control was monitored at the baseline before the eradication of *H. pylori* and 3 months after confirmed eradication.

Glycemic control was monitored by testing Patient's fasting blood sugar and glycated hemoglobin A1c (HbA1c). This study was conducted at the Medical Research Institute, Alexandria University, from Aug 2023 to Dec 2023; the patients were selected from patients with DM routinely following up in the outpatient clinic, and the management plan of diabetes was not changed during the whole period of the study to allow focusing on the effect of *H. pylori* eradication on glycemic control. All patients signed an informed consent, and the study design was approved by the Ethics Committee of Medical Research Institute, which follows the Helsinki Declaration's Requirements.

Patients

Inclusion criteria: DM was diagnosed according to the criteria of the American Diabetes Association [9]. The age of the patients was set to be above 18 years, and their body mass index (BMI) ranged from more than 18.5 to less than 40 kg/m2. All patients had confirmed *H. pylori* infection using *Helicobacter pylori* antigen in stool.

Exclusion criteria: Excluded from the study: DM type1, chronic hepatic and renal impairment, hemoglobinopathies, malignancy, pregnancy and lactation, drug allergy to any medication used during the study, withdrawal during *H. pylori* eradication, antibiotic therapy, a patient who had proton pump inhibitor (PPI) or H2 receptor blocker in the last 3 months.

Clinical data and laboratory investigations.

- Clinical examination
- BMI was assigned according to WHO criteria [10].
- Diagnosis of Hp was confirmed by *Helicobacter pylori* antigen in stool [11].
- C-reactive protein (CRP) was tested as an indication of inflammation [12].
- Fasting blood sugar and HbA1c were used to monitor glycemic control [13].
- Other laboratory investigations: Liver function and renal function tests, and complete blood profile [14].
- Triple therapy was used to eradicate *H. pylori* infection, the medications used were Clarithromycin 500 mg twice daily, Amoxicillin 1000 mg twice daily, and Esomeprazole 20 mg given twice daily for 14 days, UBT was done 3 months after treatment to confirm eradication [15].

Statistical analysis of the data

IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) was used for data analysis. The normality of the distribution of variables was verified by The Kolmogorov- Smirnov test. Normally distributed quantitative variables were compared using a Paired t-test; however, abnormally distributed quantitative variables were assessed using While Wilcoxon signed ranks test. P value was used to test the significance of the results and set at a value < 0.05.

RESULTS

After treatment of *H. pylori* infection, about 50 patients out of 60 had successful eradication, with success rate about 83.3%.

The mean age of diabetic patients at the start of the study was (59.5 ± 12.7) years. As regards male and female distribution, we found that females constituted 56% and males constituted 44%, the average weight of the diabetic patients in the study was around 81.5± 12.3 Kg, with an average BMI of around 29.7±5.1 Kg/m^2. (Table 1).

Table 1: Distribution of the studied cases according to demographic data

n = 50	No. (%)
Gender	
Male	22 (44%)
Female	28 (56%)
Age (year)	
Mean ± SD.	59.5 ± 12.7
Median (Min. – Max.)	60.5 (18.6 – 81)
BMI (Kg/m^2)	
Mean ± SD	29.7±5.1
Median (Min. – Max.)	20 (39-19)

During monitoring of glycemic control both at the baseline of the study and after confirmed eradication of *H. pylori* infection, we found that eradication had a significant effect on all parameters of glycemic control. Fasting blood sugar was higher in diabetic patients at baseline of the study (336.1 ± 202) than after eradication of the infection (187.3 ± 49.4), P= <001. (Table 2, figure 1).

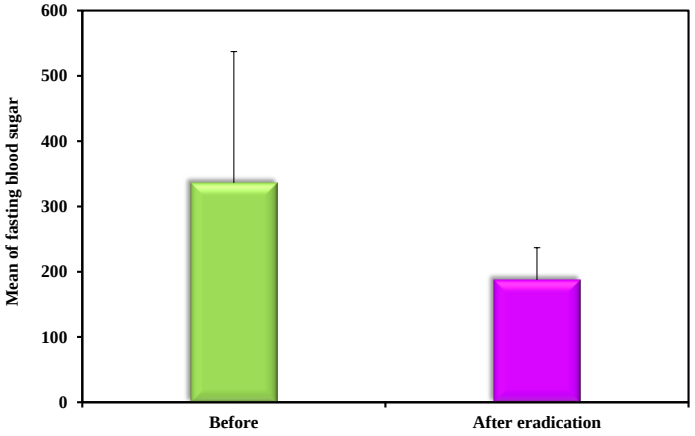

Figure 1: Fasting blood sugar before and after eradication of *Helicobacter pylori*

Table 2: Glycemic control and inflammatory marker before and after *H. pylori* eradication

	Before	After eradication	P
Fasting blood sugar Mean ± SD	336.1 ± 202	187.3 ± 49.4	<0.001*
HbA1c Mean ± SD	8.8 ± 1.3	8.3 ± 1.2	<0.001*
CRP Mean ± SD	1.67 ± 0.44	0.97 ± 0.31	0.004*

Moreover, HbA1c level showed a significant increase in diabetic patients at baseline of the study (8.8 ± 1.3), than after eradication of infection (8.3 ± 1.2), P= <001. (Table 2, figure 2).

Also, inflammatory markers such as CRP showed a significant reduction of its level when *H. pylori* infection had been eradicated, as it was

reduced from (1.67± 0.44) mg/L at baseline to (0.97 ± 0.31) mg/L, after eradication, P= 0.004 (Table 2).

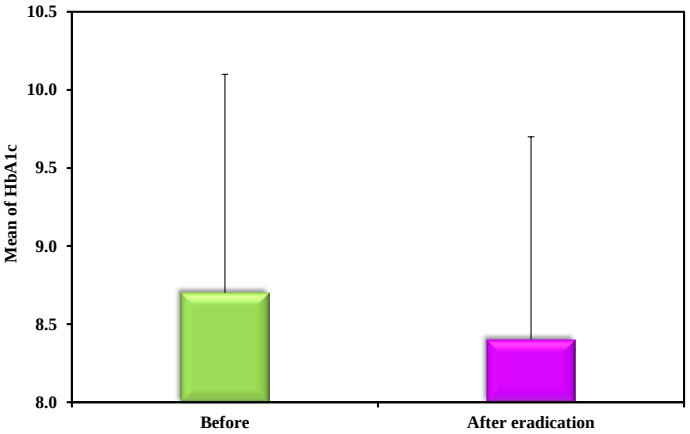

Figure 2: HbA1c level before and after eradication of *Helicobacter pylori*

DISCUSSION

H. pylori infection is the most common infection chronically affecting nearly half of the population worldwide [16]. The reduced function of the gastrointestinal tract in elderly people is mainly due to atrophic gastric mucosa, decreased activity of digestive enzymes, and increased incidence of *H. pylori* infection as the infection rate increases by 0.3-1% every year [17]. In the present study *H. pylori* was prevalent in patients aged 46-72 years of age; this is due to increased age of diabetic patients in the study.

Gender differences in *H. pylori* infection have been studied before, Kooffreh-Ada; et al [18] found that the rate of *H. pylori* infection was more in male patients while Ezugwu R, et al [19] found that the infection rate was higher in females. Other studies found no gender difference in *H. pylori* infection [20]. In our study, there was a higher prevalence of *H. pylori* infection in female patients (56%) than in male patients (44%).

H. pylori infection is associated with high levels of inflammatory markers like tumor TNFα, interleukin-6, and CRP, that's why there may be a relation between *H. pylori* infection and insulin resistance. Therefore, there may be an association between the infection and hyperglycemia in diabetic patients [21].

CRP is a molecular protein that is synthesized in the liver mediated through stimulation by interleukin 6 and TNF α. High levels of CRP is found in obese, diabetic patients, smokers, and patients with coronary artery disease [22]. Masayuki [23], in his study found higher CRP levels in the group of patients with current *H. pylori* infection than those with never, or previous infection group. Other studies found increased levels of CRP in *H. pylori* infected diabetic patients than in diabetics without infection. However, some studies didn't find any change in CRP after *H. pylori* eradication [24]. In our study, there was a decrease in CRP levels after *H. pylori* had been eradicated; this is because of the reduced chronic inflammatory state after eradication.

H. pylori induce signaling of c-Jun/miR-203/SOS3 pathway causing insulin resistance in the liver [25]. In addition, *H. pylori* infection alters gastric hormone secretion causing a reduction of ghrelin production and elevation of leptin production, these lead to insulin resistance, altered insulin secretion, and affection of glycemic control [26].

In a study done in Japan, the prevalence of *H. pylori* was higher in patients with insulin resistance than in patients without insulin resistance provided that the confounding factors were adjusted [27]. However, in a Lebanese study on 308 subjects, they didn't find any relation between *H. pylori* infection and insulin resistance or metabolic syndrome; subsequently, *H. pylori* eradication didn't improve the metabolic state [28].

Moreover, *H. pylori* eradication can improve glycemic control, many studies reported a reduction in both fasting blood sugar and HbA1c after eradication, and they attributed that to the decrease in pro-inflammatory cytokines [29,30], also in Zojaji [31], study eradication of *H. pylori* improved HbA1c level and metabolic profile in diabetic patients, but in a study done on diabetic and non-diabetic patients, they found no significant change in HbA1c or fasting blood glucose after eradication of infection [32].

In a cross-sectional study, the cohort used a two-step diagnostic approach of *H. pylori* infection, they investigated the effects of *H. pylori* eradication on HbA1c level and anti-diabetic medications 3 months after *H. pylori* eradication, they found that patients with diabetes with current *H. pylori* infection needed higher glycemic treatment doses to achieve controlled glycemia and that *H. pylori* eradication reduced HbA1C levels, and improved glycemic control [33].

Similarly, in our study, we found a significant reduction in both fasting blood sugar and HbA1c levels 3 months after *H. pylori* eradication, also there was a decrease in CRP level, which led us to conclude that the improved glycemic control is attributed to *H. pylori* eradication and elimination of the cause of inflammation and its associated mediators and cytokines which affect glucose metabolism.

CONCLUSION

It may be important to check for *H. pylori* infection in diabetic patients and to encourage its eradication; as it can help improve glycemic control in type 2 diabetes mellitus.

Conflict of Interest

The authors declare no conflicts of interest.

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