Original Article

Effect of Helicobacter Pylori Eradication on Glycemic Control in Type 2 Diabetes Mellitus

Neveen Rashad Mostafa Abdelkader [1], Abeer Ahmed Mohamed Ali [2]

[1]Department of Internal Medicine, [2]Department of Chemical Pathology, Medical Research Institute, Alexandria University, Egypt

ABSTRACT:

Background*: One of the most common infection worldwide is Helicobacter pylori (H pylori) infection, it causes many gastrointestinal disorders, including gastritis, gastric ulcers, and gastric malignancy.(1) Nowadays, diabetes mellitus is a major public health problem, as the number of diabetic patients all over the world is expected to rise to 642 million by 2040.(2) H pylori infection is associated with many extra digestive diseases. It has been suggested that there is a relation between H pylori infection and diabetes mellitus type 2 (T2DM).(3) A number of recent studies, have tried to find the relation between H pylori infection and diabetes, and whether the eradication of H pylori has an effect on glycemic control or not, but the results were conflicting.(4)* ***Objective:*** *Study the effect of H pylori eradication on glycemic control in type 2 diabetics.* ***Patients & Method:*** *Sixty type 2 diabetic subjects were confirmed to have H pylori infection by urea breath test, and their glycemic control was tested at baseline and 3 months after eradication.* ***Results:*** *Fasting blood sugar, HbA1c levels, and CRP were significantly reduced after H pylori eradication.* ***Conclusion:*** *H pylori infection affect blood glucose level and its eradication may improve glycemic control.*

Keyword: **H. Pylori, Glycemic Control, T2DM**

INTRODUCTION:

H pylori is a microaerophilic, gram negative organism, that causes many gastrointestinal diseases such as chronic gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue lymphoma, and gastric cancer. H pylori is also involved in other extra digestive system affection such as cardiovascular and immune systems, recently it was found to be involved in insulin resistance and obesity.(5)

T2DM is now considered as a pandemic as it is responsible for death of about 3.8 million patients yearly worldwide.(6) Chronic hyperglycemia in diabetic patients may cause dysfunction in other systems like renal, cardiovascular and nervous system, and this is the main cause of death in those patients.(7) Insulin resistance, chronic inflammation, reduced insulin secretion, glucotoxicity and lipotoxicity are all pathogenic mechanisms involved in diabetes(3), if a relationship between H pylori and T2DM is proved, there will be new methods for prevention and treatment options for diabetes.

A number of studies has tried to find the link between H pylori infection and diabetes, and whether the eradication of the bacteria has an effect on the blood glucose level, or not, but the results were conflicting.(4)

PATIENTS:

Type 2 diabetic subjects were randomly selected from those who were registered at our outpatient clinic or admitted to our inpatient wards. During selection, diabetes was diagnosed and confirmed according to the diagnostic criteria established by the American Diabetes Association at the time of the study, (8) and no change in their diabetes treatment protocol during the study

Inclusion criteria:

Patients with T2DM above 18 years of age, with 18.5 > body mass index (BMI) < 40 kg/m^2, and confirmed to have H pylori infection were involved in the study.

Exclusion criteria:

Individuals with any of the following were excluded: type one diabetes, chronic liver or renal disease, hematological disorders, malignancy, pregnant and lactating women, allergy to any of the drugs used in the study, withdrawing from H pylori treatment during the study, current antibiotic therapy, H2 receptor blockers therapy, or proton pump inhibitors therapy in the preceding 12 weeks.

METHODS:

Study design

This study design was a prospective randomized clinical trial and conducted on 60 type 2 diabetic subjects proved to have H pylori infection by urea breath test, their fasting blood sugar and glycated hemoglobin A1c (HbA1c) were measured at baseline, and after 3 months from treatment with H. pylori triple therapy and confirmed eradication, their fasting blood sugar and HbA1c were assessed again.

The study was conducted at Medical Research Institute, Alexandria University, during the period from January 2021 to May 2021; the subjects enrolled in the study were selected from diabetic population routinely attending the outpatient clinic or admitted to the inpatient wards for follow up and treatment of their diabetes. All procedures A written informed consent, was obtained from every subject; and all procedures were approved by the Ethics Committee of our institute.

- Thorough clinical examination.
- BMI was calculated as body weight in Kg divided by height in m^2 according to WHO criteria.[9]
- Urea breath test was done using a 100-mg of 13C-urea given with a meal, breath samples were tested at baseline and after 30 minutes. The test was considered positive when the relative amount of 13CO2 increased > 4.0 δ 13CO2 ppm. [10]
- C- reactive protein (CRP) was assessed as a marker of inflammation.[11]
- Glycemic control was assessed by fasting blood sugar and glycated hemoglobin A1c (HbA1c).[12]
- H. pylori eradication treatment done by using triple therapy for 14 days (Esomeprazole 20 mg given twice daily + Clarithromycin 500 mg twice daily + Amoxicillin 1000 mg twice daily). Eradication was confirmed after 3 months from the end of treatment. Negative test means successful eradication.[13]

Statistical analysis of the data

Data Datawere fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). The Kolmogorov- Smirnov test was used to verify the normality of distribution of variables.

Paired t-test was assessed for comparison between two periods for normally distributed quantitative variables, While Wilcoxon signed ranks test was assessed for comparison between two periods for abnormally distributed quantitative variables. Significance of the obtained results was judged at value < 0.05.

RESULTS: According to the above mentioned inclusion/exclusion criteria, 60 H. pylori positive type 2 diabetic subjects were involved in the study, 50 subjects had successful eradication and completed the study with success rate 83.3%.

The demographic data of H. pylori positive diabetic subjects at baseline were: age (59.6 ± 12.8) years, and gender (58%females and 42%males), waist 96.8±11.6 (cm), weight 81.6±12.4 (Kg), BMI 29.8±5.2 (Kg/m2).

H. pylori eradication had an effect on parameters of glycemic control, as we found that fasting blood sugar was significantly higher in diabetic subjects before H pylori eradication (336.0 ± 201), than after H pylori eradication (187.2 ± 49.5), P= <001. (Table I)

HbA1c level was significantly higher in diabetic subjects before H pylori eradication (8.7 ± 1.4), than after H pylori eradication (8.4 ± 1.3), P= <001. (Table I)

CRP was reduced by the H. pylori treatment, as it was higher in diabetic subjects before H pylori eradication (1.6 ± 0.43), than after H pylori eradication (0.98 ± 0.30), P= 0.004 (Table I).

Table I: Blood sugar control and CRP before and after eradication of Helicobacter pylori

	Before	After eradication	P
Fasting blood sugar Mean ± SD	336.0 ± 201	187.2 ± 49.5	<0.001*
HbA1c Mean ± SD	8.7 ± 1.4	8.4 ± 1.3	<0.001*
CRP Mean ± SD	1.6 ± 0.43	0.98 ± 0.30	0.004*

DISCUSSION:

The relation between H pylori infection and diabetes is still under investigation. Generally, the prevalence of H pylori infection in older age is more than that in younger age group this was found in many previous studies,[14] in our study H pylori was prevalent in diabetic subjects between 46-72 years of age, this is because most of the diabetic patients were in the older age group, and it is known that the rate of infection increases 0.3-1% per year.[15]

Distribution of H pylori in this study showed more prevalence in female diabetic subjects (58%) in comparison to the male diabetic subjects (42%), in agreement with studies done by Ghadimi [16] and Marusic.[14]

Colonization of the stomach with H pylori causes a state of low grade inflammation which is the main pathogenic mechanism in gastric complications such as, chronic gastritis, peptic ulcer, and lymphoma, but it is also a contributing factor in extra gastric complications such as cardiovascular, neurological, autoimmune, thyroid and hepatic diseases.[17] This low grad inflammatory state is mediated through upregulation of many cytokines such as CRP, tumor necrosis factor α (TNF α), and interleukins.[18]

CRP is a protein that is synthesized in the liver after stimulation by interleukin 6 and TNF α, increased levels of CRP is usually found in obesity, diabetes, smoking, and coronary artery disease.[19] In the study of Masayuki,[20] CRP was higher in the group of patients that had current H pylori infection than in never, or past infected group of patients. Some studies found higher CRP levels in H pylori positive diabetics than in H pylori negative diabetics,[21] other studies found no change in CRP level after H pylori eradication.[22] In the present study, CRP level was reduced after H pylori eradication, confirming that the state of low grade inflammation was also reduced after eradication.

H pylori also induce hepatic insulin resistance through signaling of c-Jun/miR-203/SOS3 pathway.[23] In asymptomatic Japanese subjects, infection with H pylori was more in those with insulin resistance than in those without resistance, after adjustment of all confounding factors.[24] However, in a study on 308 Lebanese subjects there was no association between H pylori infection with insulin resistance and metabolic syndrome, and concluded that eradication of infection will not affect the metabolic state.[25] In addition, H pylori infection alters secretion of gastric hormones, as it reduces gherlin production and increases leptin production, these changes lead to development of insulin resistance, and abnormal insulin secretion, which in turn affect glycemic control in diabetic patients.[26]

It was reported that eradication of H pylori can improve glycemic control, several studies showed reduction of fasting blood sugar and decrease in HbA1c after eradication, and attributed these results to decrease in pro-inflammatory factors.[27, 28]

In the study of Zojaji, H pylori eradication improved mean HbA1c and metabolic states of diabetic patients.[29] On contrary, De Luis in 2001 didn't find any change in HbA1c level after H pylori eradication.[30] In a study on 141 diabetic patients and 142 non diabetic subjects; there was no change in fasting blood glucose or in HbA1c after H pylori eradication.[31]

In the present study, There was significant reduction in the fasting blood sugar and in HbA1c levels after 3 months of H pylori eradication, together with the reduction in CRP level, which means that the cause of better glycemic control after H pylori eradication can be due to elimination of the source of inflammation and its subsequent mediators and cytokines that affect glucose metabolism.

CONCLUSION:

Helicobacter pylori eradication can improve glycemic control in uncontrolled diabetic patients, and it may be beneficial for diabetic patients to be checked for H pylori infection and to encourage eradication.

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