SERUM ANTI-HELICOBACTER PYLORI IGG ANTIBODY TEST AMONG PATIENTS WITH DIABETES: A CROSS-SECTIONAL STUDY

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ABSTRACT

Diabetes patients frequently experience numerous and serious chronic infections because of their weakened cellular and humoral immune systems. Regrettably, there is insufficient information on the prevalence of Helicobacter pylori (H. pylori) infection among diabetics, especially in southern Libya. This study aimed to determine how frequently these bacteria were infected among diabetes patients in various parts of Ubari. This study was conducted on 150 diabetic patients of both sexes, who visited the health centers in different Ubari areas. Their ages ranged from 20 to 80. Analysis of blood serum samples to measure Helicobacter pylori IgG antibodies by the enzymatic immunoassay (ELISA) and the rapid test (cassette rapid test). Biochemistry parameters such as Blood glucose concentration, cumulative glucose, α-amylase, LDH, Serum cholesterol, Triglycerides, LDL, and HDL, as well as the blood group, were also measured. Other data collected was the body mass index. A questionnaire was used to find out some habits, such as smoking, the use of spices in food, and the type and duration of diabetes. Data showed the rate of infection with H. pylori bacteria through immunological testing was 45.33% in both sexes; however, it was significantly higher in males than females, 28% and 17%, respectively. The infection rate was found to be higher in the age group 41–60 years, and there was no significant difference in bacterial infection between patients with type I and type II diabetes (20.7 and 24.7%), respectively. Similarly, there was no effect of body mass index on the rate of infection.

INTRODUCTION

Helicobacter pylori infection has been recognized worldwide as a public health problem affecting nearly 50% of the world's population. It is more prevalent in developing countries than in developed countries, although the prevalence may vary depending on geographic location, age, and socioeconomic status. It is a common infection in patients with diabetes mellitus (DM) (Devrajani et al., 2010).

The relationship between H. pylori and diabetes was first discovered in 1989 by Simon et al., who found that the prevalence of H. pylori infection, using a urease test, in diabetic patients was much higher than in asymptomatic controls (62% vs. 21%). (He et al., 2014). Currently, a lot of evidence seems to suggest that H. pylori infection may be more common in patients with DM than in the general population. However, the exact relationship is not fully understood. Many studies did not find a difference in the incidence rate between diabetic patients and healthy subjects (Amara, 2020; Oluyemi et al., 2012; Alzahrani et al., 2020). Conversely, a significant difference
was found between diabetic patients and healthy subjects in the study conducted in Misrata, Libya (Sariti et al., 2018), Karachi, in Basra, Iraq (AL-Abdul, 2014), Pakistan (Devrajani et al., 2010), Iran (Siavashi et al., 2015) and Turkey (Korkmaz et al., 2011). All five studies concluded that diabetic patients are at higher risk for H. pylori infection. There are several mechanisms that may contribute to this association. One possibility is that H. pylori infection may lead to chronic inflammation in the stomach, which can impair insulin signaling and contribute to insulin resistance (Chen et al., 2015). Another theory is that H. pylori infection may alter the gut microbiota, leading to changes in glucose metabolism and insulin resistance (Mohammadi et al., 2020). Other factors involved are the weakness of cellular and humoral immunity, which enhances the patient's sensitivity to infection with these bacteria, and a decrease in gastrointestinal motility and gastric acidity, which leads to the promotion of bacterial colonization and increases the rate of infection in the viscera, in addition to hyperglycemia that may result in chemical changes in the gastric mucosa promoting colonization of H. pylori (He et al., 2014).

Another possible factor that may contribute to increased infection susceptibility is frequent visits to health centers and hospitals, resulting in exposure to different types of germs (He et al., 2014). If a patient with diabetes is suspected to have an H. pylori infection, prompt diagnosis and treatment are important to prevent complications and improve glycemic control (Devrajani et al., 2010). The treatment typically involves a combination of antibiotics and proton pump inhibitors to eradicate the bacteria and reduce inflammation in the stomach. It is important to note that some antibiotics commonly used to treat H. pylori infection, such as clarithromycin, may interact with certain diabetes medications, such as repaglinide, and may require dosage adjustments (Martín-Núñez et al., 2021). The aim of this study is to identify the prevalence of H. pylori bacteria in the sera of diabetic patients in some areas of Ubari. Besides, exploring the relationship between the infection and the levels of HbA1c and FBG. In addition to estimating the percentage of infection according to the type of diabetes, blood group (ABO), and BMI.

METHOD

This study included 150 people, all of whom had diabetes. Their ages ranged between 20 to 80 years. The number of males was 95, while the number of females was 55. Patients were examined in various health centers in Ubari regions, and samples were collected in February 2020. Analysis of fasting blood Glucose (FBG), and HbA1c, as well as conducting the test for the qualitative detection of antibacterial antibodies using the H. pylori antibody; Rapid and Enzyme-linked immunosorbent assay (ELISA). The positive result is when the antibody titer is >1.10. The determination of the blood group (ABO) was also done. Age, residence, gender, duration of diabetes, smoking history, spicy food intake history, and type of diabetes were obtained via filling out a questionnaire. BMI was calculated, with those less than 18.5 were considered underweight, 18.5-25 were considered normal weight, >25-30 were overweight and those >30 were considered obese. The results of this study were analyzed statistically and logically using the Chi-square test, the 2-sample t-test, and the Anova two-way. The value (P > 0.05) was considered significant using the Minitab 16.1 program, and the graphic results were presented.
RESULT AND DISCUSSION

Sex difference

The total number was 150 diabetic patients: 95 (63.3%) males and 55 (36.7%) females (Figure 1A). Out of 95 diabetic male patients, 43 (28.66%) calculated from the total examined were infected with 45.2% calculated from males, and out of 55 diabetic female patients, 25 (16.66%) calculated total examined were infected with H. pylori (had raised IgG titers) (Figure 1B).

![Figure 1A](image1.png)  ![Figure 1B](image2.png)

**Figure 1A.** The total number of males and females **Figure 1B.** The number of infected males and females

Effect of Ages on H. pylori Infection in Diabetic Patients

As can be seen in Figure 2, 51–60 years old is ranked as having the highest infection rate 17 (0.18%) in the male group. The age groups 41–50 and 61–70 were next, each with 10 infected individuals (0.11%). Then, the prevalence numbers for the age range 71–80, >80, and 31–40 were 3 (0.03%), 2 (0.02%), and 1 (0.01%), respectively. Significantly, no individuals between the ages of 20 and 30 were affected.

Similarly, the age range that was most often infected was 51 to 60 (0.24%) in the female group. The age categories 61-70, in which there were 5 (0.09%) infected individuals, were next, followed by 41-50, 71-80, and 20-30, where there were 3 (0.05%), 2 (0.04%), and 1 (0.01%), respectively.
Effect of type of diabetes on H. pylori infection

68 (45.66%) of the total diabetic patients were infected with H. pylori. Of them, 38 (25.33%) were type 2 diabetes, and 30 (20%) were type 1 diabetes (Figure 3).

The relation between the duration of diabetes and H. pylori

As can be seen in Figure 4, 20% of infections occurred when the period of diabetes was 10–14, followed by the periods of 5–9 and 20–24 at approximately 13%. In the other period, there was less infection prevalence.
The Relation Between Fasting Blood Glucose and HbA1c with H. pylori Infection

According to Table 1, 43 infected men and 25 infected women had blood glucose levels between 203.9±12 and 209.2±17, respectively, while HB1c in males and females was 8.51± 0.33 and 8.56± 0.46 respectively.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Infected males</th>
<th>Infected females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SEM</td>
<td>Mean±SEM</td>
</tr>
<tr>
<td>FBG</td>
<td>12±203.9</td>
<td>17±209.2</td>
</tr>
<tr>
<td>HbA1C</td>
<td>8.51±0.33</td>
<td>0.46±8.56</td>
</tr>
</tbody>
</table>

Comparison of Results Between Rapid Test Cassette and ELISA Technique

The number of positive and negative infections using the fast and ELISA procedures is shown in Figure 5. In terms of the outcome, the two alternative procedures were quite comparable. Using the fast and ELISA procedures, there were 67 (44.66%) and 68 (33%) positive infections, respectively.

Figure 4. Effect of duration of diabetes on H. pylori infection

Figure 5. The Number of Positive and Negative Infections with the Rapid and ELISA
Serum Anti-Helicobacter pylori IGG Antibody Test Among Patients with Diabetes: A Cross-Sectional Study

Titer of H. pylori IgG

As can be seen in Figure 6, the most common titer (a quarter of the cases) was in the range of 2.01-3, followed by the range > 9.01, which was about 0.18%. Then the range was 5.01-6, 3.01–4, and 8.01–9. The range of 4.01–5 and 6.01–7 have an equal percentage (0.09), and the lowest percentage was in the range of 8.01–9.

![Figure 6. Titre H. pylori Infection](image)

Effect of blood group on H. pylori infection

90 (59.99%) of the study participants were O+, and 40 (26.66%) of them had H pylori infection. Another common blood type was A+, which accounted for 33 (21.9%) cases, of which 16 (10.66%) had infections. Next, the blood types B+ and AB+ were 14 (or 9.3%) and 7 (or 4.66%), respectively. Six patients (5.33%) gave blood samples for the uncommon blood types A-, B-, AB-, and O-, and two (2% of them) had H. pylori infection (Figure 7).

![Figure 7. Effect of Blood Group Types on H. pylori Infection](image)

Geographical distribution of infected and non-infected diabetic cases in different areas of Obari city

The accompanying graph, No. 8, revealed that 33 (22%) of the infected individuals were from Germa, making up 64 (42.66%) of the total group. In Gragra, which is in second place with
Serum Anti-*Helicobacter pylori* IGG Antibody Test Among Patients with Diabetes: A Cross-Sectional Study

a score of 46 (30.66), there were 8 more non-infected persons than diseased ones. Remarkably, there was just one afflicted patient from Gria who was involved.

![Figure 8](image)

**Figure 8.** Effect of Type of Diabetes on H. pylori infection

**Relation to spicy food**

The total number of patients consuming spicy food was 95 (0.63%), of which 0.28 were infected and 0.35 were uninfected. However, when comparing the incidence of infected diabetic patients who always consumed spices with those who sometimes or never did, the incidence was high in those regularly consuming spices (0.28%), and the average rate in patients who didn't eat spices was 0.12%, with the lowest infection rate. In patients who sometimes eat spices at a rate of (0.05%), (Figure 9).

![Figure 9](image)

**Figure 9.** Effect of Spicy Food
**Distribution of H. pylori infection in smokers and non-smokers diabetic men**

As shown in Figure 10, only 5 (11.63%) of the 43 infected people were smokers. On the other hand, out of 52 non-infected persons, only 9 (17.31%) were smokers.

**Effect of body mass index**

In the infected male group, most of the patients were normal weight (48.2%), followed by overweight (37%), and underweight (6.6%). Though, in the uninfected male group, most of the patients were overweight (62.9%), followed by normal weight (51.7%). and the underweight (3%). While in the infected and non-infected female groups, most of the patients were overweight (58.9% and 41%), followed by normal weight (4.3% and 5.6%), respectively. There was no infection in the underweight infected group, while the uninfected underweight was 1%, (Figure 11).

**Figure 10.** Distribution of H. Pylori Infection in Smokers and Nonsmokers Diabetic Men

**Figure 11.** Distribution of infected and non-infected patients with H. pylori infection according to body mass index (kg/m2) BMI
Serum Anti-*Helicobacter pylori* IGG Antibody Test Among Patients with Diabetes: A Cross-Sectional Study

The biochemistry characteristics of diabetes mellitus and *Helicobacter pylori* infection

<table>
<thead>
<tr>
<th>Biochemistry Parameters</th>
<th><em>Helicobacter pylori-infected</em></th>
<th><em>Helicobacter pylori non-infected</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>9.8 ± 4.3 **</td>
<td>5.4 ± 3.3</td>
</tr>
<tr>
<td>Uric acid (mmol/L)</td>
<td>0.31 ± 0.07</td>
<td>0.28 ± 0.06</td>
</tr>
<tr>
<td>α-amylase</td>
<td>45 ± 10</td>
<td>60 ± 6</td>
</tr>
<tr>
<td>S- LDH (IU/l)</td>
<td>551 ± 222 **</td>
<td>272 ± 93</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.5 ± 1.3</td>
<td>4.8 ± 1.1 *</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>1.5 ± 0.5 *</td>
<td>1.1 ± 0.6</td>
</tr>
<tr>
<td>High-Density Lipoprotein (HDL) (mmol/L)</td>
<td>1.4 ± 0.3</td>
<td>1.4 ± 0.2</td>
</tr>
<tr>
<td>Low-Density Lipoprotein (LDL) (mmol/L)</td>
<td>3.3 ± 0.2</td>
<td>3.0 ± 0.2</td>
</tr>
</tbody>
</table>

According to the results obtained in this study, the prevalence of *H. pylori* in diabetic patients in Ubari was 45.33%, which is a high percentage. This percentage was higher than a study done in the city of Jeddah, Saudi Arabia, which was conducted on type II DM patients, and reached 26.9% (Alzahrani et al., 2020), and Nigeria, which was equal to 18% (Oluyemi et al., 2012). While it was lower than the percentage recorded in a study done in Benghazi in 2012 (about 50.5%) (Lemziany, 2012), in Sana, Yemen, in 2020 (49%) (Al-Awadhi et al., 2020), the Amara study in Alexandria, (69%) (Amara, 2020), a study done in Misurata (71.28%) (Sariti et al., 2018), and the Gaza Strip’s study (70.5%) (Mazen et al., 2013). On the other hand, the infection rate was higher in Germa at about 22%, then in Qaraqra with a rate of 12.66%, followed by Takrebeh with a rate of 6.66%, Tosh with a rate of 3.33%, Qurayyah with a rate of 1%, and Al-Fujeij, where there was no infection. Bener et al. (2007) indicated that the different infection rates between countries may be due to the epidemiology of this bacteria (Bener et al, 2007).

In this study we found that there was a difference between men and women in the infection rate (28% vs. 17%). This was in agreement with a study conducted in Iran, which found that the overall prevalence of *H. pylori* infection was 59.6%, with a higher rate in men (69.6%) than in women (49.6%) (Malekzadeh et al., 2004). A similar study in Saudi Arabia showed that the...
prevalence in men (79.5%) and in women (70.6%) (Al-Mofarreh et al., 2010), as well as a study done in Nigeria (15.6% vs 10.9%) (Oluyemi et al., 2012). Contrariwise, there was some studies that have found no significant difference in the H. pylori infection rate between men and women. For instance, a study in Spain (39.2% vs. 38.5%) (Aguilar-Garcia et al., 2014). It is important to note that the prevalence of H. pylori infection may vary depending on various factors other than gender.

Additionally, the prevalence of H. pylori infection can vary depending on various factors, including age. Our study showed that most of the patients were in the age range of 41–60 years. Studies have shown that the prevalence of H. pylori infection increases with age, with higher rates found in older adults compared to younger individuals. For example, a study conducted in Japan found that H. pylori infection was 34.4% among individuals aged 20–29 years, but increased to 66.2% among those aged 70–79 years (Miwa et al., 2020). Similarly, a study in Korea reported that the prevalence of H. pylori infection was 40.6% in individuals aged 20–29 years, but increased to 72.9% in those aged 60–69 years (Kim et al. 2013). Several studies have also shown that early childhood is a critical period for H. pylori acquisition. In many developing countries, the infection is acquired during childhood, and the prevalence of infection remains high throughout adulthood. However, in developed countries, the prevalence of H. pylori infection decreases with increasing age, reflecting changes in living conditions and hygiene practices over time (Malfertheiner et al., 2017).

There is some evidence to suggest that the prevalence of H. pylori infection may differ between individuals with type 1 and type 2 DM. However, the findings have been inconsistent across studies. In our study, we showed no significant difference (Type II, 25.33% vs. Type I, 20%), and this was in agreement with a study in China (type 1 62.7% and type 2 59.4%) (Solmaz G, et al., 2014). However, some studies have suggested that individuals with type 1 may have a higher prevalence compared to those with type. For instance, a study conducted in Turkey found that the prevalence of H. pylori infection was significantly higher in individuals with type 1 (61.8%) compared to those with type 2 (34.4%) (Sari et al., 2009). Another study in Egypt reported a higher prevalence of H. pylori infection in children with type 1 (83.3%) compared to those with type 2 (48.1%) (Chen et al., 2019). In contrast, the Dore et al. (2001) study showed that H. pylori infection is more common in type 2 than in type I. It is important to note that the relationship between H. pylori infection and diabetes is complex and may be influenced by various other factors.

On the other hand, there is some evidence to suggest that there may be an association between the duration of diabetes and the presence of H. pylori infection. In our study, there was no significant difference, and this came in agreement with the study conducted in Turkey and found that the duration of diabetes and blood glucose levels did not differ with infection with H. pylori (Demir et al., 2008). Conversely, Wang et al. (2018) study found that individuals with H. pylori infection had a longer duration of diabetes compared to those without H. pylori infection. The study concluded that H. pylori infection may contribute to the development and progression of diabetes and that screening and treatment of H. pylori infection may help to improve glycemic
control in individuals with diabetes. Similarly, Li et al. (2019) study found the prevalence of H. pylori infection was higher in individuals with long-standing diabetes compared to those with newly diagnosed diabetes. The study also found that individuals with H. pylori infection and long-standing diabetes had a higher incidence of diabetic complications, such as neuropathy, nephropathy, and retinopathy, compared to those without H. pylori infection. Although the duration of H. pylori infection itself is not known to have a direct effect on diabetes, it is possible that the chronic inflammation and immune activation associated with H. pylori infection may contribute to the development and progression of diabetes in individuals who are predisposed to the disease.

On the other hand, there is some evidence to suggest that H. pylori infection may have an impact on fasting blood glucose (FBG) and cumulative glucose (Hb1c) levels (Chen et al., 2012 and Zhou et al., 2019). In our study, there was no significant difference in the FBG and HbA1c between infected and non-infected patients, and this came in agreement with a study of Alzahrani et al. (2020) and Oluyemi et al. (2012), which showed that there is no relationship between infection with bacteria and these variables. Similarly, the results were consistent with the study in Tanta, Egypt, which found that the HbA1c, FBG, and infection with H. pylori bacteria were not significant (Esheba and Nagy, 2016). Conversely, Wang et al. (2012) study found that patients with H. pylori infections had significantly higher FBG levels compared to those without infection. The study found that H. pylori infection was associated with an increased risk of impaired glucose tolerance and type II DM. Another study found that patients with H. pylori infections had higher Hb1c compared to those without the infection. The study suggested that H. pylori infection may contribute to glucose metabolism disorders and insulin resistance (Oksanen et al., 2010).

Both ELISA and rapid tests are diagnostic tests used to detect the presence of H. pylori bacteria in the stomach. Elisa detects the presence of antibodies in the blood sample and is considered more accurate than a rapid test as it has a lower rate of false positives. However, the result takes longer to obtain, a few days to a week and requires specialized equipment and trained personnel. On the other hand, a rapid test detects the presence of H. pylori antigens in a stool sample. The results are available within a few minutes and can be performed by non-medical personnel in a doctor's office or clinic. However, rapid tests are less accurate than Elisa tests and may produce false positive or negative results. The results of our study showed that the percentage of H. pylori infection in the rapid test cassette was 44.67%, while that of the ELISA test was 45.33%, which indicates no significant difference between the two tests. Moreover, the most common titer (a quarter of the cases) was in the lowest range of 2.01-3, followed by the highest range of > 9.01, which was about 0.18%.

There have been some studies that suggest a possible link between blood group and susceptibility to H. pylori infection (Makiyama et al., 2017). The histo-blood group carbohydrate portion of the blood group has been suggested to influence the risk of acquiring this pathogen through effects on adhesion to the gastric mucosa (Yahav, J., et al. (2012). Specifically, people with blood type O may be more resistant to H. pylori infection, while people with blood type A may be more susceptible (Jafarzadeh et al. 2014). In our study, most of the samples (60%) were from blood group O+, and this result was in agreement with the literature, in which the dominant
species in the community is the O+ species (Gaidaa Baqir et al., 2016). Out of this O+ group, 40 samples were positive for bacteria at a rate of 26.67%, followed by blood group A+ with 33 cases. This relationship was inconsistent with Jafarzadeh et al. (2014) while agreeing Chakrani et al. (2018). Gaidaa Baqir et al. (2016) and Kanbay et al. (2005). Therefore, more research is needed to confirm this association and understand the underlying mechanisms involved.

On the other hand, Spicy food consumption has been thought to exacerbate the symptoms of H. pylori infection (Peleteiro, 2018), but the evidence for this is mixed. Some studies have suggested that capsaicin, the compound that gives chili peppers their spiciness, may promote the growth of H. pylori and increase the risk of developing gastric cancer (Genta, 2006). However, other studies have not found a significant association between spicy food consumption and H. pylori infection or its complications (Ma et al., 2014). The result of our study showed that there was a significant difference between those eating spices (0.28 percent), and those who didn't eat spices (0.12 percent). These results are consistent with Shar et al. (2022) in Pakistan, which showed H. pylori infection is more common in those who eat spicy foods than in those who don’t. Thus, it is recommended that individuals with H. pylori infection avoid spicy and acidic foods, as they may increase symptoms such as abdominal pain, bloating, and heartburn. It is also recommended that these individuals follow a healthy diet that is low in fat and includes plenty of fruits, vegetables, and whole grains.

Moreover, smoking and H. pylori infection are significant risk factors for a range of health problems. Although our study showed no clear relation between the prevalence of H. pylori and smoking, several studies have suggested that smoking may increase the risk of H. pylori infection (Ogihara et al., 2020) and this may be due to the damaging effect of smoking on the lining of the stomach. Additionally, H. pylori infection may exacerbate the harmful effects of smoking on the stomach lining, potentially increasing the risk of ulcers, gastritis, and stomach cancer. Thus, individuals who smoke and are infected with H. pylori may be at increased risk of developing these conditions. Quitting smoking and seeking treatment for H. pylori infection are both important steps in reducing the risk of associated health problems.

On the other hand, we studied the relationship between body mass index and H. pylori infection and found no significant association. Different studies have found a potential association between BMI and H. pylori infection. Some studies have suggested that individuals with a higher BMI may have a lower risk of H. pylori infection, while others have found a higher risk (Dore et al., 2001; Ma et al., 2012; Sayehmiri et al., 2015). As well, research has found that H. pylori infection may affect BMI. In some studies, it may be associated with a lower BMI (Ferrández et al., 2018), while in others have found the opposite (Bener et al., 2007, Cohen and Muhsen, 2012, Park et al., 2015). It is important to note, however, that the evidence for this association is not consistent, and further research is needed to fully understand the relationship between BMI and H. pylori.
CONCLUSION

Our study shows the rate of infection with H. pylori bacteria in Ubari was high; significantly higher in males than females. The infection rate was found to be higher in the age group 41–60 years, and there was no significant difference in bacterial infection between patients with type I and type II diabetes. Similarly, there was no effect of body mass index, spicy, or smoking on the rate of infection. It is important to note that the relationship between H. pylori infection and diabetes is complex and may be influenced by various factors, including age, ethnicity, and other comorbidities. More research is needed to better understand the relationship between H. pylori infection and diabetes.

REFERENCE


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