

Original Article

Prevalence of Helicobacter Pylori In Type II Diabetes Mellitus

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ABSTRACT

Objective: To determine the prevalence of Helicobacter pylori infection in type 2 diabetes and non-diabetes patients.

Methodology: This case control study was conducted in Microbiology Department, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre Karachi with the collaboration of diabetic clinic of medical and gastroenterology OPD, from June 2019 to November 2019. Known cases of type 2 diabetes mellitus, irrespective of gender, above 30 years of age, and in equal number non-diabetic patients with a history of epigastric burning, epigastric pain, belching, bloating, nausea, vomiting for >1 month were included. Three ml venous blood was taken from antecubital vein after overnight fasting of 8-12 hours for blood sugar fasting. Patients underwent H. pylori Antigen Rapid Test Cassette (Stool). All the data was recorded on self-made proforma. Data was analyzed by using SPSS version 20.

Results: In the diabetic group most of the cases 35.2% were more than 60 years old and in non-diabetic group majority of the cases 44.8% were <50 years. Females were most common in both diabetes non-diabetes groups. A total of 83(79%) of the diabetic group and 54 (51.4%) of non-diabetic were labeled as positive for H. pylori infection (p=0.001). Diabetic patients >50 years of age, were significantly associated with h-pylori infection, (p=0.001), while there was no significant impact found of gender on H-pylori infection (p=0.330).

Conclusion: H. pylori infection in diabetic patients was higher as compared to non-diabetes. Effectiveness of stool antigen method is the best diagnostic tool for the detection of H. pylori infection in diabetic subjects.

Keywords: H-pylori, diabetes, non-diabetes.

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Introduction

In humans, lack of insulin production or insulin resistance leads to a group of metabolic disorders known as diabetes mellitus (DM).¹ It has become one of the most important and serious public health challenges of the twenty-first century.² It is characterized by hyperglycemia which results in abnormalities in carbohydrates, proteins, and lipid metabolism.³ There is a wide range of pathogenic processes which are involved in the development of diabetes mellitus ranging from autoimmune destruction of pancreatic beta cells leads to

decrease insulin production and abnormalities that result in insulin resistance.⁴ Based on pathogenicity DM is usually divided into two forms, Type 1 and Type 2 DM. Type 2 DM mostly appear in adults, although it can be seen in children. In the early stages of this type, insulin is produced and available in the body but cannot be utilized by the body resulting in insulin resistance. This resistance in turn leads to insufficient insulin production. Hence, resistance and deficiency, both are causative factors of Type 2 DM.⁵ Eventually, deficiency of insulin in both types of DM leads to high blood glucose levels which may with time, leads to grave damage to the heart,

kidneys, eyes, nerves, and vessels; and also the cause of autonomic neuropathy which results in gastrointestinal and genitourinary abnormalities (American Diabetes Association, 2014). Around 415 million people, across the globe, were living with diabetes, and with the probability of a rise in the number, there will be 642 million people diagnosed with diabetes in the year 2040.⁶ In Pakistan, according to WHO, 12.9 million persons suffer from diabetes (WHO, 2016) and there will be estimated rise in diabetic cases to 14.5 million in 2025 in Pakistan alone. Furthermore, it is delineated that every year in Pakistan approximately 120,000 thousand people die as a result of type II diabetes and its related complications.⁶ Diabetes mellitus usually remain critically silent in its initial stages however the hyperglycemia itself enough to produce pathophysiological changes at the tissue level.¹ The prediction of its appearance in its undetected stage, by any means could be helpful in the timely diagnosis and management of the disease itself and also the prevention of its complication. It has been observed that among bacterial infections, *Helicobacter pylori* is most common in DM patients particularly in those with poor glycemic control, so the detection of this infection could indicate the future appearance of DM. In uncontrolled DM patients, chronic infections are more common and frequent due to decreased immunity.⁷

Helicobacter pylori is a gram negative spiral, multi-flagellate, bacillus, growing best at an atmosphere of 5% Oxygen with 5-10% CO₂ on blood containing media in vitro.⁸ Worldwide high prevalence of this organism which is about 50% has warranted health care workers and other clinicians about its control in a large population. The prevalence of *H. pylori* in Pakistan is around 92% and *H. pylori* prevalence in DM is 62%.⁹ The association between *H.pylori* infection and DM remains difficult to interpret. Either *H. pylori* induced inflammation is one of the causative factors in the development of DM or poor glycemic control of diabetes predisposes to *H. pylori* infection.¹⁰ In recent years, it has been proposed that certain products from the gut microbiome could cause the induction of tissue metabolic infection by interacting with the host immune system, which in turn is the cause of stimulation of low-grade inflammation that indicates the onset of obesity and diabetes.¹¹ Impaired gastrointestinal motility due to diabetic autonomic neuropathy has been linked to *H.pylori* infection.¹² Impaired glycemic control helps in the colonization of *H. pylori* in the gastric antrum.

Increased blood sugar levels are associated with *H. pylori* infection or may become a cause of reactivation of the silent infection.¹³ *H. pylori* can be held responsible for various gastrointestinal abnormalities like dyspepsia or increase risk of the peptic ulcer which in turn can lead to gastric cancer.¹⁴ Hence, *H. pylori* can become a source of other debilitating diseases in diabetic patients. In previous studies, a strong association has also been observed between *H.pylori* along with cardiovascular conditions and metabolic syndrome which is initiated through endothelial cell damage and recruitment of inflammatory cytokines such as C-reactive protein (CRP) and interleukin-6 (IL-6) (Ramadan et al., 2016). It was observed by jeon et al that *H.pylori* infected persons have more chances of having diabetes mellitus.¹⁵ Some other researchers have also found a significant association between *H. pylori* and DM. In the United Arab Emirates population, a case control study compared to type 2 diabetes mellitus and non-diabetic groups and observed that there was significantly higher *Helicobacter pylori* infection in diabetic obese patients than non-diabetic subjects.¹⁶ A cross-sectional study was performed in Iran which shows the prevalence of HP seropositive was found to be 65.9% in diabetic versus 50.5% in nondiabetics (p= 0.001) this also supports the association of *H.pylori* with DM.¹⁷ A cohort study done on Japanese population suggested that CagA gene positive *H.pylori* had no association with DM.¹⁸ A case control study was done in Hyderabad, according to the high prevalence of *H. pylori* infection in diabetic patients.¹⁹ However, data on the prevalence of *Helicobacter pylori* infection in diabetics is scanty and contradictory. Keeping this in view, the current study is designed to get an idea regarding prevalence of *H.pylori* infection in DM to enhance awareness regarding proper blood glucose monitoring and also encouraging *H. pylori* screening in symptomless subjects with underlying DM, before it becomes a source for development of severe diabetic complications and other diseases.

Methodology

This case control study was conducted in Microbiology Department, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre Karachi with collaboration of diabetic clinic of medical and gastroenterology OPD. Study was completed within 06 months from June 2019 to November 2019. Study technique was non-probability purposive sampling. Ethical permission for the present study was taken by the Institutional Review Board (IRB)

Committee of Jinnah Postgraduate Medical Centre (JPMC), Karachi vide letter NO.F.2-81/2018-GENL/5422/JPMC.

All the known cases of type 2 diabetes mellitus irrespective of gender above 30 years of age and in equal number non-diabetic patients with a history of epigastric burning, epigastric pain, belching, bloating, nausea, vomiting for more than one month were included. All the diabetic and non-diabetic patients who had already taken steroids, non-steroidal anti-inflammatory drugs, immunosuppressive or Helicobacter pylori eradication therapy, patients with GI bleeding history, and who were not willing to be a part of this study were excluded. Sample size was calculated by using EPI software by using the proportion of (HpSA was positive in 73% diabetic cases).¹⁹ Blood samples were obtained from all the patients for the fasting Glucose. 3 ml venous blood was taken from antecubital vein after overnight fasting of 8-12 hours for blood sugar fasting. Patients underwent H. pylori Antigen Rapid Test Cassette (Stool).

Procedure: Wearing protective clothing such as laboratory coats, disposable gloves and eye protection when specimens were being tested. Allowed the test, specimen, buffer to reach room temperature prior to testing. Assay was performed within 6 hours after stool collection to obtain best results. Stool specimen approximately 50mg (equivalent to ¼ of a pea) was aspirated from stool container with the help of applicator and then transferred in specimen collection tube which contained buffer was shaken vigorously to mix the stool and extraction buffer and tube was left for 2 minutes. Test cassette was removed from the pouch, 2 drops of extracted specimen were transferred on specimen well (S) of the cassette, air bubbles were avoided in the specimen well (S), timer was started and result was watched after 10 minutes of each specimen.

Result was considered as positive when there is the appearance of both T (Test) and C (Control) lines of the H. pylori antigen in stool. All the data was recorded on self-made proforma. Data was analysed by using SPSS version 20. Categorical variables were computed in form of frequency and percentage. Chi-square test was applied and a p-value <0.05 was considered as significant.

Results

In the diabetic group most cases 35.2% were more than 60 years old and in non-diabetic group majority of the cases 44.8% belonged to age group between 41 to 50 years. There were 27.6% males and 72.4% were females

in the diabetic group, while 28.6% were males and 71.4% were females in non-diabetic group. Findings were statistically significant (p<0.01). Table I

In the diabetic group 89.5% of patients had Bloating, 89.5% had Burning, 88.6% subjects had Epigastric pain, 67.6% had Belching, 63.8% had Nausea, 36.2% had Flatulence and 24.8% had Vomiting. Whereas in non-diabetic group 71.4% had Bloating, 74.3% had Burning, 68.6% subjects had Epigastric pain, 66.7% had Belching, 37.1% had Flatulence, 36.2% had Nausea and 15.2% had Vomiting. There was a significant association obtained for Epigastric pain, Nausea, Bloating, and Burning with diabetes and non-diabetes dyspeptic patients. These symptoms were found more in the diabetic population (p=0.001). Table II

According to regarding HpSA a total of 83(79%) of diabetic group and 54 (51.4%) in non-diabetic were labeled positive for H. pylori infection indicating a significant difference (p=0.001). Table III

Diabetic patients >50 years of the age, were significantly associated with h-pylori infection, (p=0.001), while there was no significant impact found of gender on H-pylori infection (p=0.330). Table IV

Table I: Age and Gender comparison among both groups (n=205)

Variables	Study group				p-value	
	Diabetes		Non Diabetes			
	Dyspeptic (n=105)		Dyspeptic (n=105)			
	n	%	n	%		
Age Group (Years)	30 - 40	16	15.2	38	36.2	0.001
	41 - 50	27	25.7	47	44.8	
	51 - 60	25	23.8	20	19.0	
	>60	37	35.2	0	0.0	
Gender	Male	29	27.6	30	28.6	0.87
	Female	76	72.4	75	71.4	

Table II: Association of Gastrointestinal symptoms with studied groups (n=210)

Clinical presentation	Study group		p-value
	Diabetes	Non-Diabetes	
	Dyspeptic (n=105)	Dyspeptic (n=105)	
	n (%)	n (%)	
Epigastric pain	93(88.6)	72(68.6)	<0.01*
Flatulence	38(36.2)	39(37.1)	0.88
Belching	71(67.6)	70(66.7)	0.87
Nausea	67(63.8)	38(36.2)	<0.01*
Vomiting	26 (24.8)	16(15.2)	0.08
Bloating	94(89.5)	75(71.4)	<0.01*
Burning	94(89.5)	78(74.3)	<0.01*

Table III: Prevalence of H.Pylori (on HpSA) among diabetes and non-diabetes dyspeptic cases (n=210)

Parameters	Group		p-value
	Diabetes Dyspeptic (n=105)	Non Diabetes Dyspeptic (n=105)	
	n(%)	n(%)	
HpSA Positive	83(79.0)	54(51.4)	<0.01*
HpSA Negative	22(21.0)	51(48.6)	

Table IV: Age and gender association with H.Pylori (on HpSA) among Diabetes Dyspeptic Patients (n=105)

Characteristics	Diabetic HpSA (n=105)		p-value
	Positive (n=83)	Negative (n=22)	
	n(%)	n(%)	
Gender	Male	21(25.3)	0.330
	Female	62(74.7)	
Age Group (Years)	30 - 40	9(10.8)	0.001
	41 - 50	17(20.5)	
	51 - 60	23(27.7)	
	>60	34(41.0)	

Discussion

Diabetes mellitus (DM) is a chronic condition which embroils many organ systems of the body including the gastrointestinal system. Moreover, diabetic patients are prone to various bacterial infections including H. pylori infection. Prevalence of H. pylori in third world countries is much higher as compared to developed nations which may be because financially deprived countries have poor socioeconomic status, health problems, and issues of overcrowded conditions and environmental pollution.²⁰ In Pakistan the H. pylori prevalence is up to 74.4%.²¹ Therefore, in an underdeveloped country like Pakistan the estimation of H. pylori prevalence and its diagnosis by a feasible diagnostic test in the diabetic population needs to be reviewed. Hence, this study was projected to assess the prevalence rate of H. pylori in diabetic dyspeptic type 2 diabetes mellitus and non-diabetic dyspeptic patients based on detection of anti H. pylori stool antigen (HpSA) in stool, to get accurate figures of H. pylori prevalence in diabetes mellitus which in turn would help in better management of both conditions and we found seroprevalence of H. pylori infection was 79.0% in diabetic patients and 51.4% in non-diabetics, (p<0.01). Our results of prevalence rate by HpSA are favored by a study done on H. Pylori detection by HpSA in diabetic patients, who also found the prevalence rate of infection around 73%.¹⁹ In another study done in Iran, the reported prevalence of H. pylori was 60% in diabetic dyspeptic patients and 26.6% in non-diabetic dyspeptic patients with a significant p-value of 0.001.²² The reason for the highest prevalence in both groups could be due to the higher H. pylori prevalence rate in Pakistan and in this study all the suspected cases were included.

Moreover, in the current study the H. pylori positivity rate was recorded to increase with advancing age. In diabetic dyspeptic group the highest H. pylori prevalence was above the age of 60 years. However, in non-diabetic group, the prevalence was highest (55.6%) in the age group of 41-50 years and it decreased with increasing age, being 31.5% in 51-60 years of age group. Another cross-sectional study conducted in the Chinese population reported high prevalence of H. pylori infection in diabetic patients who were above 65 years of age and females, thus confirming the association of H. pylori with diabetes mellitus and old age.²³ In the line with our finding regarding the age group of non-diabetic dyspeptic patients (41-50 years) having the highest H. pylori prevalence and a decreasing trend in prevalence with increasing age, an Iranian study also detected mean age of 48±16.8 years as having the highest occurrence of H. pylori infection which decreased with age.²⁴ Early detection of any disease is the mainstay to control its development towards complications. For detection of H. pylori infection, several invasive and noninvasive techniques are present. Invasive methods require endoscopic intervention, making it unacceptable by many patients especially children. Several invasive and noninvasive techniques have been used to diagnose H. pylori and many of them have been implemented in current practice. However, in diabetics, the detection of active infection by HpSA is more effective than serum IgG method. This finding is under a previous study which proclaimed that IgG specific serology is not an affirmative test for ongoing infection. It further concluded that stool antigen test stands high with sensitivity and specificity of 94.1% and 91.8%, respectively for the detection of H. pylori bacilli.²⁵ On the other hand H. pylori stool antigen test is acceptable with excellent sensitivity and specificity and a high participation rate to screening.²⁶

Conclusion

After this study concluded that the prevalence of H. pylori infection in diabetic patients was higher. Effectiveness of stool antigen method is the best diagnostic tool for detection of H. pylori infection in diabetic subjects. These findings would helpful for the health policy makers in designing appropriate health programs for timely detection and eradication of H. pylori infection in diabetic patients.

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