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Research Article

A study of *Helicobacter pylori* infection in diabetes mellitus

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ABSTRACT

Background: Helicobacter pylori is the most common bacterial infection in human beings. The aim was to study the association of *Helicobacter pylori* infection in patients of diabetes mellitus. Design of the study was observational analytic cross sectional study.
Methods: A total of 69 subjects were studied. Of these 30 were non diabetics and 39 were diabetics, with disease duration more than 1 year. The serological diagnosis of *H. pylori* was made by Anti- *Helicobacter pylori* antibody test. Antral biopsies of all diabetic patients were taken during endoscopy and subjected to histological examination.
Results: The mean age for the diabetics was 48.9±9.86 years and that of non-diabetics was 47.9±9.16 years. The majority of the subjects belonged to fifth and sixth decades. There was conspicuous male preponderance in both the diabetics and the nondiabetics group, more attributable to the selection bias. Serum samples of all the subjects were tested for the presence of IgG against *Helicobacter pylori*. *Helicobacter pylori* was positive in 40% of non-diabetics and 64.1% of diabetics X^2 = 3.96, p value=0.047 ($p<0.05$) i.e. the prevalence of *Helicobacter pylori* in diabetics is significantly higher than that in non-diabetics. Histological examination of antral biopsies (known to be the gold standard method of diagnosing *Helicobacter pylori*) was performed in all diabetics and comparison of the type of diabetes, duration of diabetes, and level of glycaemia and complications of diabetes were made in patients of diabetes with and without *Helicobacter pylori*. This study showed patients with IDDM had higher positivity (75%) than those of NIDDM (67.6%). The mean duration of diabetes with *Helicobacter pylori* group was 7.85+3.93 years, and higher than that of diabetics without *Helicobacter pylori* which was 5.83±2.52. The mean fasting blood sugar was 192±60.3 mg/dl in diabetics with *Helicobacter pylori* group and was higher than that of diabetics without *Helicobacter pylori* group which was 167±37.1mg/dl. The mean post prandial blood sugar in diabetics with *Helicobacter pylori* group was 318±78.4mg/dl and was more than that of diabetics without *Helicobacter pylori* group in whom it was 280±49.7mg/dl. The two diagnostic modalities viz serological and histological identification of *Helicobacter pylori* correlated well with each other. It was observed that serological diagnosis by Anti- *Helicobacter pylori* antibody test is 80% sensitive and 75% specific.
Conclusions: The prevalence of *Helicobacter pylori* is higher in diabetics than the non-diabetics. The prevalence of *Helicobacter pylori* infection had no significant correlation with duration of diabetes, type of diabetes, glycaemia levels of diabetics and complications of diabetics. The serological diagnosis of *H. pylori* was made by Anti-*Helicobacter pylori* antibody test, by Biochem Immuno systems ITALIA SPA ELAGEN *Helicobacter pylori* IgG Kit. This ELISA technique is 80% sensitive and 75% specific.

Keywords: Association, Complication, Diabetes mellitus, Gastritis, *H. pylori*, Infection

INTRODUCTION

Helicobacter pylorus is the most common bacterial infection in human beings. Diabetics are prone to infections and gastroparesis diabeticorum, leading to bacterial overgrowth in upper GIT. *H. pylori* plays a role in impaired glucose tolerance in adults and it may be potentiated by higher BMI level.[1] Many case-control studies have reported that *H. pylori* infection was significantly associated with DM. *H. pylori* infection is a risk factor for DM.[3,4] Some biological mechanisms may explain the association. First, altered glucose metabolism may produce chemical changes in the gastric mucosa that help to detect *H. pylori* infection.[6] Second, *H. pylori* gastric infection increases secretion of pro inflammatory cytokines, resulting in changes in the structure of insulin receptor interfering with the interaction between its receptor and insulin.[2]

METHODS

This study was carried out in the Department of Medicine. Thirty nine cases of diabetes mellitus admitted in the wards constituted the cases for the present study and thirty non-diabetic subjects who were the attendants of the patients admitted in the department constituted the controls for the present study. They were groped as: Group I: - Non Diabetes controls and Group II: - Diabetes.

An informed consent was taken up from all patients before further work up.

Each case was evaluated with detailed history regarding age, type of diabetes, duration of diabetes, level of blood glucose and medication prescribed to them for control of diabetes with stress given to elicit the clinical symptoms of neuropathy, nephropathy and retinopathy.

Each case was subjected to thorough physical examination. Fundoscopy was carried out to assess the retinopathic changes. The routine investigations included complete blood count, urine analysis for proteinuria, glycosuria, ketonuria and microscopic sediments, Blood Urea, Serum Creatinine, Blood Sugar Fasting and 2 hours after 75 gm of glucose load/standard glucose tolerance test.

The diagnosis of Diabetes Mellitus was based on the criteria: Fasting plasma glucose ≥7 mmol/L (126 mg %) or 2 hours plasma glucose ≥11.1 mmol/L (200 mg %) during an oral glucose tolerance test.

Serological diagnosis of Helicobacter pylori

For serological diagnosis of *Helicobacter pylori* we used Biochem immunosystems Italia S.P.A. Elagen *Helicobacter pylori* IgG.

Endoscopic biopsy

Antral biopsies of all diabetic patients were taken during endoscopy and subjected to histological examination.

Statistical analysis

Descriptive analysis of the collected data will be done and association of various parameters with presence or absence of *H. pylori* infection in patients of diabetes mellitus will be studied.

RESULTS

Table 1: Age distribution of all subjects.

Age Group	Group I	Group II
21 – 30	2	2
31 – 40	3	3
41 – 50	12	18
51 – 60	10	13
61 – 70	3	2
71 – 80	0	1

The majority of diabetics belonged to the age group of 41-60 years and the mean age of this group was 48.9+9.86 years. Among the non diabetics the mean age was 47.9+9.16 years.

Table 2: Depicts sex distribution of subjects under study.

Sex	Group I	Group II
Male	21 (70%)	24 (61.5%)
Female	9 (30%)	15 (38.5%)

In present study 70% of group I and 61.5% of group II were males and rest females.

Helicobacter pylori

Serum samples of all the subjects were taken and subjected to serological test by ELISA KIT for IgG against *Helicobacter pylori*.

Table 3: Prevalence of *Helicobacter pylori* in cases of diabetes and non diabetes.

H.P. status IgG	Group I	Group II	X2 = 3.96 P value = 0.047 (<0.05) i.e. significant)
Positive	12 (40%)	25 (64.1%)	
Negative	18 (60%)	14 (35.9%)	

IgG for *Helicobacter pylori* was positive in 40% of Group I and 64.1% of Group II and the difference was statistically significantly (P value<0.05).

Table 4: Illustrates age distribution of cases of *Helicobacter pylori* infection. Maximum positivity was seen in age group 41 - 60 years in both the groups.

Age Group	Group I		Group II	
	Total	H.P. +ve	Total	H.P. +ve
21 - 30	2	1	2	0
31 - 40	3	1	3	2
41 - 50	12	5	18	13
51 - 60	10	4	123	8
61 - 70	3	1	2	1
71 - 80	0	0	1	1

Table 5: Sex distribution of cases of *Helicobacter pylori* infection. *Helicobacter pylori* was present in 42.8% of group I and 75% of group II males.

Sex	Group I		Group II	
	N	H.P. +ve	n	H.P. +ve
Males	21	9 (42.8%)	24	18 (75%)
Females	9	3 (33.3%)	15	7 (46.7%)

Helicobacter pylori in patients of diabetes mellitus

Among the patients of Diabetes mellitus, antral biopsies from all the patients were subjected to histopathological examination using H+E stain and Giemsa stain and studied for presence and absence of *Helicobacter pylori*. Out of 39 tissue obtained only 38 could be studied as in one case tissue was found to be insufficient and could not be reposed to studies.

Results of histological examination of antral biopsy in cases of diabetes mellitus

Table 6: Sex distribution of H.P. status in cases of diabetes.

Sex	D.M. H.P. Status +ve	D.M. H.P. Status -ve
Male	17	7
Female	8	6

Most of the patients with *Helicobacter pylori* positively were males.

Table 7: Age distribution of *H. pylori* status in patients of D.M. maximum patients of diabetes with *Helicobacter pylori* were in age group 41-50 according to histopathological examination of antral biopsies.

Age	D.M. H.P. Status +ve	D.M. H.P. Status -ve
21 - 30	1	1
31 - 40	3	0
41 - 50	13	5
51 - 60	7	6
61 - 70	2	0

Table 8: *Helicobacter pylori* status in relation to type of diabetes.

Type of diabetes	N	H.P. status +ve
NIDDM	34	23 (67.6%)
IDDM	4	3 (75%)

Among the diabetes IDDM type had higher positivity than those with NIDDM type.

The subjects were further divided into subgroups according to duration of the detection of their diabetes.

Table 9: Duration of diabetes in patients of H.P. positive and negative patients with increased duration of diabetes had more changes of being *Helicobacter pylori* positivity.

Duration of diabetes (years)	D.M. with H.P.	D.M. without H.P.
1 - 5	7	6
6 - 10	14	6
11 - 15	4	0
16 - 20	1	0

Table 10: The mean duration of diabetes was higher in diabetes mellitus with *Helicobacter pylori* than that of diabetes mellitus without *Helicobacter pylori*.

Mean duration of diabetes (years)	D.M. with H.P.	D.M. without H.P.	P (t- test)
	7.85±3.93	5.83±2.52	0.066

Patients were grouped under 3 categories according to the type of anti diabetic treatment taken by them, and relation with H.P. status was seen in Table 11.

Table 11: Type of medication of diabetics with and without *Helicobacter pylori*. Most of the patients in both the groups were on OHA treatment.

Type of medication	D.M. with H.P.	D.M. without H.P.
Insulin	3	1
OHA	15	9
Insulin + OHA	8	2

Table 12: Comparison of mean fasting blood sugar and mean post prandial blood sugar in patients of diabetes with or without *Helicobacter pylori*.

Biochemical parameter	D.M. H.P positive	D.M. H.P. negative	P value (t -Test)
FBS (mg/dl) mean±SD	192±60.3	167±37.1	0.1159
PPBS (mg/dl) mean±SD	318.2±78.4	280±99.7	0.258

In diabetics with *Helicobacter pylori* the FBS and PPBS was 192±60.3 and 318±78.4 respectively.

Table 13: Complication in patients of diabetes with/without *Helicobacter pylori*.

Type of Complications	D.M. with H.P.	D.M. without H.P.	P
Neuropathy	9	5	0.67
Nephropathy	3	2	0.663
Retinopathy	3	1	0.76
Cardiovascular	16	5	0.25

The numbers of complications were more in diabetes with *Helicobacter pylori* in all groups.

Considering Biopsy as the gold standard method, the sensitivity and specificity of ELISA for detection of IgG against *Helicobacter pylori* is calculated and shown in Table 14.

Table 14: Comparison of ELISA IgG against *Helicobacter pylori* with histological examination of *Helicobacter pylori* by antral biopsy.

Type of test		Biopsy (histological)	
		HP+	HP-
ELISA	HP +	21	3
	HP -	5	9

Sensitivity of ELISA test is 80.8% and specificity of ELISA test is 75%.

DISCUSSION

Helicobacter pylori is the most common chronic bacterial infection in the world. It is the most common cause of non-erosive non-specific gastritis. It has been implicated in the causation of gastric and duodenal ulcer, chronic atrophic gastritis, gastric adenocarcinoma, NHL and MALT lymphoma. From this aspect identification of risk groups is increasingly important.

Considering paucity of data on prevalence of *Helicobacter pylori* in India and its association with Diabetes Mellitus, this study was undertaken.

Patients with diabetes mellitus are prone to infection and gastroparesis diabeticorum may lead to bacterial overgrowth in upper GIT. Also infection with *Helicobacter pylori* induces gastric inflammation leading to increase in cytokines, which could be deleterious for the control of the glycaemia of patients with diabetes.

The present study aimed at detecting the prevalence of *Helicobacter pylori* infection in patients of diabetes, and non- diabetes. For this we took 69 subjects. After detailed history and examination they were divided into two groups, among them 30 were non-diabetics and 39 were diabetics. The majority of subjects belonged to the age group of 41-60 years and the mean age of diabetics group was 48.9±9.86 years and of non-diabetics was 47.9±9.16 years.

The majority of subjects were males i.e. 70% in non-diabetics and 61.5% in diabetics. This could be more attributed to the selection bias than any significant statement as the prevalence of diabetes among male as compared to female.

From all the 69 subjects serum samples were taken and subjected, to ELISA test for IgG against *Helicobacter pylori* by Biochem Immunosystems Italia S.P.A. Elagen *Helicobacter pylori* IgG. IgG for *Helicobacter pylori* was positive is 40% of non-diabetics and 64.1% o diabetics X^2 =3.96, p value=0.04 (<0.05) i.e. the prevalence of *Helicobacter pylori* is diabetics is significantly higher than that in non-diabetics. A study showed that 61% of NIDDM patients had *Helicobacter pylori* infection.[7] Prevalence of *Helicobacter pylori* was found to be significantly higher in diabetic patients than in controls.[8] *Helicobacter pylori* infection was higher is IDDM children than the healthy controls.[9] *Helicobacter pylori* sero prevalence was higher than age matched controls in the diabetics.[10] Literature available regarding the prevalence of *Helicobacter pylori* in diabetics vis-a-vis controls is contradictory and indecisive. Further studies are required to reach any definite conclusion.

The prevalence of *Helicobacter pylori* in diabetic subjects was 64.1% in the present study. The prevalence of *Helicobacter pylori* colonization among diabetics as reported in world literature varies between 37% to 85%.[11,12] It has been reported that various drugs, including anti-ulcerants, antiemetics and antispasmodics in addition to antibiotics may interfere with the detection of *Helicobacter pylori* by rapid urease test. It is logical to presume that these drugs may effect detection by other methods also.

On studying the prevalence of *Helicobacter pylori* infection in relation to age. The prevalence was found to be higher in 5th& 6th decade, in both the non diabetics and diabetic group (40.9%) and (67.7%) respectively. Thus suggesting a late acquisition of the infection, which was concurrent with the observations.[13] Sero prevalence of *Helicobacter pylori* among IDDM patients aged <24 year was significantly higher than controls and corresponding rate among IDDM aged >24 years was significantly lower than control.[6]

An early age of acquisition of infection in the developing countries has been seen.[14,15] In factin most under developed countries an endemic of *Helicobacter pylori* goes unchecked and most adults are infected.[16] The prevalence rate was found to be increased with all age groups until 60-70 years.[17] But factual relation of *Helicobacter pylori* infection to age remains inconclusive

in the present study, as the number of subjects in the study was small.

When the prevalence of *Helicobacter pylori* infection among males and females were assessed, it was found that the males had higher positivity, both in Diabetics (75%) and non-diabetics (42.8%). This apparently suggests a male predilection for *Helicobacter pylori* infection.

A higher prevalence of *Helicobacter pylori* infection was found in diabetic women than in control women (80% vs 37.37%, p<0.01), whereas there was no difference between males.[18] Thus in all probability the infection has no gender preference, and the same is supported by similar findings.[14]

Histological examination of antral biopsies (taken during endoscopy) in all diabetics was done (except one whose tissue sample was not sufficient), The level of glycaemia, duration of diabetes, type of diabetes and complications in patients of diabetes were compared according to positivity and negativity shown by this histological examination as this is the gold standard method known so far.

In the present study during the analysis of the prevalence of *Helicobacter pylori* with the type of diabetes, it was found that subjects with IDDM had higher positivity than those with NIDDM (75% vs 67.6%). This is statistically insignificant and the numbers of subjects were too small to come to any definite conclusion. The observation of the present study was comparable to the works who have reported that there is no significant correlation of the type of diabetes with *Helicobacter pylori*.[9,19]

In the present study the prevalence of *Helicobacter pylori* infection among diabetes increased with the duration of disease, reaching almost 100% with duration exceeding 10 years. Mean duration of diabetes in diabetics with *Helicobacter pylori* was 7.85±3.93 and in diabetics without *Helicobacter pylori* was 5.83±2.522. That is though this mean duration was more in diabetes with *Helicobacter pylori*, yet the difference was not statistically significant (p= 0.66). In separate studies, the prevalence of *Helicobacter pylori* infection was directly related to the duration of diabetics.[9,10,13] This conclusion seems logically appropriate as both age and diabetes increase the *Helicobacter pylori* colonization, but interestingly a prospective study observed no significant difference between the newly diagnosed and older diabetics.[12] However there was no connection between frequency of the infection and duration of diabetes.[19]

On comparing blood sugar level, mean fasting blood sugar in diabetics with *Helicobacter pylori* was 192±6.03mg/dl and so more than that of diabetics without *Helicobacter pylori* in who mean was 167±37.1mg/dl. But the difference was not statistically significant (p 0.1159). Similarly on comparing post prandial blood sugar the mean level in diabetics with *Helicobacter pylori* was 318±78.4mg/dl and was more than that of diabetics without *Helicobacter pylori* in whom it was 280±99.9mg/dl. The difference was again statistically non-significant (p=0.258). The present study is concordant with most of the world literature, where no significant correlation of diabetic control with *Helicobacter pylori* status was reported.[9,13] Glycosylated HbA1c level was higher is infected children than the level found in non-infected subject.[20] *Helicobacter pylori* infection may lead to lower fasting plasma glucose concentration among females.[21]

When comparison of type of medication was done in patients of Diabetes mellitus with and without *Helicobacter pylori* most patients in both the groups were found to be on OHA. In patients with *Helicobacter pylori* total number of patients on insulin were 11 (8 were also on OHA) and 15 on OHA alone. No significant difference was seen between those on insulin and OHA.

Comparisons of various complications in patients of diabetes mellitus with and without *Helicobacter pylori* were done. Though the number of complications of each type i.e. neuropathy, nephropathy, retinopathy and cardiovascular were proportionally higher is patients of diabetes with *Helicobacter pylori* than among those of diabetes without *Helicobacter pylori* yet the difference was not found to be significant in any of these. CAD was more prevalent in diabetic patients with than without *Helicobacter pylori* and history of thrombo-occlusive cerebral disease was also more frequent in *Helicobacter pylori* positive diabetic patients, but other complications such as peripheral arteriopathy, advanced nephropathy, neuropathy or retinopathy were no differently distributed according to serological status.[21]

The limitations of the present study were many. The number of subjects was small, many unknown selection bias and confounding factors were present and the study was hospital based. Thus the interpretation and significance of conclusion derived from the study is difficult to assess.

CONCLUSION

- The prevalence of *Helicobacter pylori* is higher in diabetics than the non-diabetics.
- The prevalence of *Helicobacter pylori* infection had no significant correlation with duration of diabetes, type of diabetes, glycaemia levels of diabetics and complications of diabetics.
- The serological diagnosis by Anti- *Helicobacter pylori* antibody test by Biochem Immunosystems ITALIA SPA ELAGEN *Helicobacter pylori* IgG Kit by ELISA technique is 80% sensitive and 75% specific as calculated by taking histological examination of antral biopsies as the gold standard method.

But the present study had many limitations and the above mentioned points need to be investigated further in large scale, well planned case control studies, while making arrangement of eliminate possible confounding factors and selection bias, to come to any logical and equivocal conclusion.

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