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ORIGINAL ARTICLE

ROLE OF HELICOBACTER PYLORI IN DIABETES MELLITUS & ITS COMPLICATIONS

Sherwal B L[1], Bhatnagar M. K[2], Verma A. K[3], Paliwal M[4]

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ABSTRACT: Introduction: Human being are major reservoir of Helicobacter pylori (H. pylori).The organism has been associated with gastritis, peptic ulcer, gastric cancer and many other non-gastrointestinal tract diseases. This study aimed at detection and comparison of anti H. pylori antibodies (IgG) in serum of diabetes mellitus and non-diabetic cases as well as to observe the relationship of anti H. pylori antibodies to complications of diabetes mellitus. **MATERIALS AND METHODS:** The study group included 101 diabetics, diagnosed as per standard criteria. Of the total, 91 were type 2 and 10 were type 1 diabetes mellitus cases. The control group included 30 nos. of age and sex matched healthy subjects. Demographic and clinical information of both groups were recorded. **RESULTS:** Anti H. pylori antibodies (IgG) were found 88.1% in diabetics and 70% in control group and the result was significant statistically ($P<0.05$).The most common manifestation in anti H. pylori antibodies positive cases pyrosis (58.4%) followed by nausea (39%). High positivity of anti H. pylori antibodies were observed in almost all age groups in the diabetic group than the control. However, statistical significant difference was seen only in two age groups. **CONCLUSION:** The result showed that diabetics are more prone to H. pylori infection and need continuous monitoring.

KEYWORDS: Helicobacter pylori, Diabetes mellitus, H. pylori antibody.

INTRODUCTION: The first isolation of Helicobacter pylori in 1982 by Marshal and Warren ushered a new era in gastric microbiology.[1] Human beings are major reservoir of H. pylori infection. Infection with H. pylori leads to gastritis, peptic ulcer, gastric cancer and gastric lymphoma and other non-gastrointestinal tract associations are diabetes mellitus, ischemic heart disease, neurological disorder, hypertension, thyroiditis, dermatological, rheumatological and cerebrovascular disease.[2-4]

Infection of gastric mucosa with H.pylori results in systemic as well as local immune responses, thus enabling serological detection of this organism. The serological tests are non-invasive, relatively rapid, simple to perform, very useful for initial diagnosis of H. pylori infection and are less expensive in comparison to endoscopic biopsy and other tests like histology, culture, 13 carbon urea breath test and PCR.[5]

Diabetes mellitus is the most common endocrine disease, which is characterized by metabolic abnormalities and by long-term complications. Meagre data is available on association of H. pylori with diabetes mellitus and its complications. The aim of the study was detection and comparison of H. pylori antibodies in clinical cases of diabetes mellitus with non-diabetics and to find out the relationship of H. pylori antibodies to complications of diabetes mellitus.

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MATERIAL AND METHODS: A total of 101 diabetic patients diagnosed previously or recently according to the standard criteria as type 1 and type 2 diabetes were included in the study from the department of Medicine at Lady Hardinge Medical College, New Delhi as described by Mayfield et al.[6] The control group consisted of 30 healthy age and sex matched subjects with no history of diabetes, hypertension, cerebrovascular accident, upper gastrointestinal complaint. None of the controls included was on antimicrobial agents, H_2 receptor antagonist or proton-pump inhibitor for at least last 4 weeks.

Age, sex, height, weight, and body mass index of all the participants were recorded. History of gastrointestinal symptoms, viz. pain epigastrium, nausea, vomiting, pyrosis, hematemesis, melena, postprandial abdominal fullness, early satiety, belching, recurrent diarrhoea, alternating diarrhoea and constipation was recorded.

The participants were also enquired for intake of non-steroidal anti-inflammatory drugs, history of treatment of H. pylori infection, use of proton pump inhibitors, H_2 receptor antagonist and antacids. Abdominal examination was done in all patients to specifically look for epigastric tenderness.

Using aseptic techniques 4-6 ml of venous blood was collected in sterile vial, which was kept undisturbed for 1-2 hours for clot formation. The serum was transferred into sterile plastic vial and stored at -20°C, for estimation of specific IgG anti H. pylori antibodies by Vir-Elisa Helicobacter pylori IgG antibodies enzyme immunoassay (VIR-ELISA HELICOBACTER PYLORI – IgG Viro Immunolabor Diagnostic Ka GmbH Germany).

The blood samples were also processed for hemoglobin, total leucocytes count (TLC), erythrocyte sedimentation rate (ESR), platelets count and fasting/ postprandial blood sugar. All the diabetic patients in study group were observed for various diabetes mellitus related complications like diabetes retinopathy, nephropathy, neuropathy, coronary heart disease, cerebrovascular accident and diabetic foot.

Data was interpreted using SPSS software. Chi-square test was applied to test the difference between two proportions and P value less than 0.05 was regarded as significant ($P<0.05$).

RESULTS: Of the total 101 diabetic patients, 91 were classified into type 2 and 10 into type 1 type. A total of 71 females (71.3%) and 30 males (29.7%) were included in the study and in control group 20 females (66.7%) and 10 males (33.3%) were included. Female/Male Sex ratio was 70:3 in diabetics and 21:9 in control group.

The mean height in diabetic and control group was 1.56±0.16 metres and 1.59±0.18 meters respectively. The mean weight in diabetic and control groups was 61.5±23.4 and 60.7±12.2 kilograms respectively. However, the body mass index in diabetic and control groups was 25.29 ± 9.10 and 23.91 ± 4.06 kgs/m^2 ($P<0.05$).

Hemoglobin, total leukocyte count, platelets count were comparable in diabetic and control groups. Erythrocytes sedimentation rate (ESR) was found to be significantly elevated in the diabetic group, 32±18 as compared to 22±10 in control group ($P<0.05$). The mean fasting blood sugar in diabetic group was 205±132 mg/dl and in control group 82±10 mg/dl with mean postprandial blood sugar level 266± 153mg/dl and 95± 7 mg/dl respectively (Table-1).

The study included patients from 11 to 80 years with mean age 50.6 ± 26.8 years in diabetics and 47.4±29.6 years in control group. Anti H. pylori antibodies (IgG) were detected in

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89/101 (88.1%) diabetics and in 21/30 (70%) in control group. Except age group 21-30 years, higher seroprevalence of anti H. pylori antibodies were noticed in all age groups of diabetics than the control group (Fig.-1).

Anti H. pylori antibodies positivity rate was 95.8 and 88.9 % in diabetics group and 66.7 and 62.5 % in control group in age group 41-50 & 51-60 years respectively (Table-2). This association was found to be statistically significant (P<0.017) in diabetic patients as compared to controls.

Various gastrointestinal manifestations were observed in both the groups of diabetic patients (seropositive, seronegative). The most common manifestation was pyrosis (58.4%) followed by nausea (39%), pain epigastrium (24.5%), belching (18%), vomiting (15.7%), postprandial abdominal fullness (11.2%), early satiety (5.6%), tenderness epigastrium (2.2%) and recurrent diarrhoea (2.2%). Statistically no significant association was observed in the gastrointestinal manifestation between the seropositive and seronegative diabetic group (P>0.05) (Table-3).

Oral hypoglycemic drugs were commonest mode of treatment followed by proton pump inhibitor, H_2 receptor antagonist, antacid, NSAIDS and insulin in seropositive and seronegative diabetic groups (Table-4). These treatments are comparable to H. pylori negative diabetic patients. No history of eradication for H. pylori was recorded in any of the participants. Statistically the association was not significant (P>0.05). There was no statistically significant difference observed between anti-H. pylori antibodies positive and negative diabetic with complications (Table-5).

DISCUSSION: A total of 101 diabetic patients and 30 healthy subjects were included. The mean age was 50.6 years in diabetics and 47.4 years in control group. Both these groups were age and sex matched. In our study, 88.1% diabetics and 70% control group tested seropositive for anti H. pylori antibodies (P<0.05). Jeon et al in his prospective cohort study also showed that infection of H. pylori leads to an increased incidence of diabetes. Tahir et al also observed that there is higher prevalence of H. pylori in diabetic dyspeptic patients than in non- diabetic. Many other authors have also observed the statistically significant (P<0.05) association of H. pylori with diabetes mellitus.[7-10]

High positivity of anti H. pylori antibodies were observed in almost all age groups in the diabetic group than the control. However, significant difference was seen only in two age groups i.e. 41-50 years (95.8% vs. 66.7%) P<0.05 and 51-60 years (88.5% vs. 62.9%) P<0.05. The similar finding where H. pylori positivity was found to be more in diabetic patients whose age were >18 years was discussed by Chen et al.[11]

Oldenburg et al had also described that seroprevalence of H. pylori is higher in all diabetics age groups except the age group <30 where control group had higher seroprevalence.[10]

The common symptoms observed in H. pylori antibody positive diabetic patients were pyrosis (58.4%), nausea (39.3%) and pain in epigastrium (24.5%). These symptoms were also observed among H. pylori seronegative diabetic patients. Gasbarrini et al. had also reported similar results in a group of 116 diabetic patients and 50 healthy controls.[12]

The reason for increased seropositivity rates in diabetics is not clearly known. Diabetes mellitus patients may be considered immuno-compromised with impaired humoral and cellular immunity, predisposing them to persistent infections. ESR was significantly elevated P<0.05 in diabetic group, this could be due to more widespread infections in diabetic people.

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In the present study, highest seroprevalence of H.pylori was seen in diabetic patients on oral hypoglycemic drugs (70) as compared to patients on insulin therapy, on NSAIDS and on H_2 receptor antagonist. Corroborating our results Ojetti et al observed that there is increase in insulin requirement in H. pylori infected patients.[13]

In this study the diabetes related complications and its association with H. pylori showed no statistically significant difference. De Luis et al had described similar result who observed that diabetic retinopathy, nephropathy and neuropathy are equally distributed in anti H.pylori antibodies positive and negative groups.[14]

Limitations: the one-time study was primarily aimed at finding the incidence of H.pylori infection amongst the given lot of diabetic patients. Therefore, the correlation of H. pylori with glycemic control vis a vis HBA1C and the clinical data on old or new cases of diabetes were not recorded.

It would be premature to conclude, on the basis of current evidence that in Type2 diabetes, diagnosis and treatment of H Pylori a must. Rayner et al has also discussed that intervention to treat and manage H. pylori infection reduce the subsequent incidence of diabetes would require a very large long term prospective study.[15]

CONCLUSION: The study indicates towards the growing need for regular monitoring and specific treatment of H. pylori infection in diabetic patients. However more extensive well-designed cohort studies are needed to definitely conclude the relationship of H. pylori infection with diabetes mellitus and its complications.

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SL. No.	Parameters	Diabetic (101)	Control (30)	S/NS*
1	Sex (Female/Male)	71/30	20/10	-
2	Height (metre)	1.56 ± 0.16	1.59 ± 0.18	NS
3	Weight (Kilograms)	61.5 ± 23.4	60.7 ± 12.2	NS
4	Body Mass Index(Kg/M^2)	25.29 ± 9.10	23.91 ± 4.06	S
5	Hemoglobin gm/dl	11.4 ±2.8	12 ±2.2	NS
6	TLC X 10^9/L	5.2± 0.8	4.8± 0.6	NS
7	ESR mm/Hr.	32 ±18	22 ±10	S
8	Platelets countX10^9/L	250 ±130	300 ±120	NS
9	Blood sugar, fasting/ post prandial	205 ±132/ 266 ±153	82±10/ 95±7	-

TABLE 1: Comparison of various Parameters between Diabetic and Control Group

*S/NS: Significant/Non-significant

SL. No.	Age Group	Diabetic group		Control group		S/NS*
		Total	Positive (%)	Total	Positive (%)	
1	11-20	2	2(100)	1	1(100)	NS
2	21-30	6	5(83.3)	3	3(100)	NS
3	31-40	15	14(93.3)	6	5(83.3)	NS
4	41-50	24	23(95.8)	6	4(66.7)	S
5	51-60	27	24(88.9)	8	5(62.5)	S
6	61-70	18	15(83.3)	4	2(50.0)	NS
7	71-80	9	6(66.3)	2	1(50.0)	NS
	Total	101	89(88.11)	30	21(70)	S

TABLE 2: Age-wise Distribution of number of Positive Cases of anti-H. pylori Antibodies (IgG) among the Diabetic Group and Control Group

*S/NS: Significant/Non-significant

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Sl. No.	Cases (n)	Anti H. Pylori antibodies positive		Anti H. Pylori antibodies negative		S/NS*
		Total	%	Total	%	
1	Pain epigastrium n=23	22/89	24.5	1/12	8.3	NS
2	Tenderness epigastrium n=2	2/89	2.2	-	12	NS
3	Nausea n=40	35/89	39.3	5/12	41.7	NS
4	Vomiting n=15	14/89	15.7	1/12	8.3	NS
5	Pyrosis n=58	52/89	58.4	6/12	50	NS
6	Post prandial abdominal fullness n=13	10/89	11.2	3/12	25	NS
7	Early satiety n=6	5/89	5.6	1/12	8.3	NS
8	Belching n=17	16/89	18	1/12	8.3	NS
9	Recurrent diarrhoea n=2	2/89	2.2	-	12	NS

TABLE 3: Comparison of Gastrointestinal Complaints and anti-Helicobacter pylori Antibodies in Diabetic Group

*S/NS: Significant/Non-significant

Sl. No.	Cases using various drug therapy = n	Anti H. Pylori antibodies positive		Anti H. pylori antibodies negative		S/NS*
		Total	%	Total	%	
1	Currently on Insulin therapy n=31	29/89	32.6	2/12	16.7	NS
2	Currently on oral hypoglycemic drugs n=70	60/89	67.4	10/12	83.3	NS
3	H/O use of NSAIDS n=45	39/89	43.8	6/12	50.0	NS
4	H/O use of PPI, H_2 receptor antagonist, antacids n=55	49/89	55.1	6/6	50.0	NS

TABLE 4: Comparison between Drug Therapies and anti-H. pylori antibodies in Diabetic Group

*S/NS: Significant/Non-significant

Cases (n)	Anti-H. pylori antibodies			
	Positive	%	Negative	%
Diabetic retinopathy (54)	48/89	53.93	6/12	50
Diabetic nephropathy (34)	30/89	33.70	4/12	33.33
Diabetic neuropathy (89)	78/89	87.64	11/12	91.66
Coronary heart disease (93)	82/89	92.13	11/12	91.66
Cerebrovascular accident (12)	10/89	11.23	2/12	16.66
Diabetic foot (8)	7/89	7.86	1/12	8.33

TABLE 5: Comparison between anti-H. pylori antibodies & Diabetic Complications

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AUTHORS:

1. Sherwal B. L.
2. Bhatnagar M. K.
3. Verma A. K.
4. Paliwal M.

PARTICULARS OF CONTRIBUTORS:

1. Director, Profesor, Department of Microbiology, Lady Hardinge Medical College & Associate Hospital, New Delhi, India.
2. Professor, Department of Medicine, Lady Hardinge Medical College & Associate Hospital, New Delhi, India.
3. Specialist, Department of Microbiology, Lady Hardinge Medical College & Associate Hospital, New Delhi, India.
4. Senior Resident, Department of Medicine, Lady Hardinge Medical College & Associate Hospital, New Delhi, India.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Verma A. K,
Specialist, Department of Microbiology,
National Institute of TB & RD,
New Delhi – 110030.
Email: akv_680@yahoo.co.in

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