THE PATIENTS OF TYPE II DIABETES MELLITUS AND HELICOBACTER PYLORI INFECTION

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Abstract:
Among the human being Helicobacter pylori is the most common bacterial infection. This study has a specific aim to associate Helicobacter pylori infection in patients of diabetes mellitus. The basic design of the study was observational methodical cross sectional. Sixty Nine subjects were studied from which, 30 were non diabetics and 39 were diabetics, and their disease was 1 year or more old. The serological diagnosis of Helicobacter pylori was made according to the test of Anti- Helicobacter pylori antibody. All diabetic patients' Antral biopsies specifically were taken during endoscopy.

It was specifically observed that the diabetics mean age was 48.9 ± 9.86 years and on the contrary of non-diabetics was 47.9 ± 9.16 years. Subject's majority belonged to fifth and sixth decades. There was conspicuous male preponderance in both the diabetics and the non-diabetics group, more attributable to the selection bias. The samples of serum for almost all the subjects were examined for the presence of IgG against Helicobacter pylori. In 40% subjects the Helicobacter pylori was positive particularly in non-diabetics and 64.1% of diabetics $X2= 3.96$, p value=0.047 ($p<0.05$) which was the prevalence of Helicobacter pylori in diabetics is prominently greater as compared with non-diabetics. Histological analysis of antral biopsies 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 deprived of Helicobacter pylori.

According to this study IDDM patients had greater positivity (75%) as compared with those of NIDDM (67.6%). The mean duration with Helicobacter pylori of diabetes group was $7.85+3.93$ years, and greater than that of diabetics deprived of Helicobacter pylori which was 5.83 ± 2.52. The fasting blood sugar's mean was 192 ± 60.3 mg/dl in diabetics with the group of Helicobacter pylori and was greater than that of diabetics deprived of 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 higher than that of diabetics deprived of Helicobacter pylori group in whom it was 280 ± 49.7mg/dl. The 2 diagnostic modalities viz serological and histological recognition of Helicobacter pylori associated well with each other. It was revealed that serological diagnosis by Anti- Helicobacter pylori antibody test is 80% sensitive and 75% particular.

The Helicobacter pylori prevalence is greater in diabetics than the non-diabetics. The Helicobacter pylori infection prevalence had no important connection 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: *Correlation, Barriers, Diabetes mellitus, Gastritis, H. pylori, Infection.*

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INTRODUCTION:

Helicobacter pylorus is the most common bacterial infection in human beings. Diabetics are inclined to infections and gastroparesis diabeticorum, leading to bacterial overgrowth in upper GIT. Helicobacter pylori specifically play a specific in impaired glucose tolerance in adults and it may be potentiated by greater body mass index level. Many case-control studies have reported that Helicobacter pylori infection was prominently associated with DM. Helicobacter pylori infection is a risk factor for DM. Some biological mechanisms may explain the association. Initially, the altered glucose metabolism significantly generates some chemical alterations in the gastric mucosa which supports to identify Helicobacter pylori infection. Secondly, Helicobacter 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 (Abboud and Khalek, 2017).

METHOD DATA COLLECTION:

The Data collected from King Abdullah Teaching Hospital Mansehra, including 42 patients in positive HAV Antibodies: 29% of them were children (Aged 10-15 years) while remaining 13% patients were adults aged 16-50 years. Accordingly, in contrary to data collected from housed where most of the people were IgG positive (386%), data from hospital represents that Igm was positive in 40/42 (%) patients. This is because almost all patients who present to hospital are symptomatic and have acute hepatitis "A".

According to this study, 39 cases of diabetes mellitus conceded in the wards constituted the cases for the present study and thirty non-diabetic subjects who the attendants of the patients admitted in the department were constituted the controls for the present study (Abboud and Khalek, 2017).

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 (AL-Kazazz, 2016).

Each case was subjected to thoroughphysical analysis. 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 (Begue et al., 2017).

Inclusion Criteria

- All female heads houses having age 18-60
- All members of female headed houses aged 10-50 years

Exclusion Criteria

- All male headed house
- All people who were not native of members
- Members who were not giving the consent for blood sample collection

Serological diagnosis of Helicobacter pylori
In Helicobacter pylori, specifically for serological diagnosis 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 analysis.

Statistical analysis
A particular 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 – All Subjects Age Distribution

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

Source: (Begue et al., 2017)

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%)

Source: (Begue et al., 2017)

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 =
Positive	12 (40%)	25 (64.1%)	0.047
Negative	18 (60%)	14 (35.9%)	(<0.05) i.e. significant)

Source: (Begue et al., 2017)

IgG for Helicobacter pylori was positive in 40% of Group I and 64.1% of Group II and the difference was statistically prominently (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 I		Group II	
Group	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

Source: (Begue et al., 2017)

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%)

Source: (Begue et al., 2017)

Helicobacter pylori in patients of diabetes mellitus
Among the patients of Diabetes mellitus, antral biopsies from all the patients were subjected to histopathological analysis 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 analysis of antral biopsy in cases of diabetes mellitus
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 analysis 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

Source: (Begue et al., 2017)

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%)

Source: (Begue et al., 2017)

Among the diabetes IDDM type had greater 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

Source: (Begue et al., 2017)

Table – 10 The mean duration of diabetes was greater in diabetes mellitus with Helicobacter pylori than that of diabetes mellitus deprived of 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

Source: (Begue et al., 2017)

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 deprived of 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

Source: (Begue et al., 2017)

Table – 12 Comparison of mean fasting blood sugar and mean post prandial blood sugar in patients of diabetes with or deprived of 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

Source: (Begue et al., 2017)

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/deprived of 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

Source: (Begue et al., 2017)

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 analysis of Helicobacter pylori by antral biopsy

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

Source: (Begue et al., 2017)

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

DISCUSSION:

The most common chronic bacterial infection in the globe is famously known as Helicobacter pylori; particularly it is the most general reason of non-erosive non-specific gastritis. It has been concerned in duodenal and gastric causation, chronic atrophic gastritis, gastric adenocarcinoma, NHL and MALT lymphoma. Diabetes mellitus patients are prone to infection and gastroparesis diabeticorum which further indicate to bacterial overgrowth in upper GIT (Fedorchenko and Martynuk, 2018).

The Helicobacter pylori infection further persuades the gastric inflammation leading to elevate in cytokines, which could be deleterious for the management of the glycaemia of patients with diabetes. This specific research aimed at detecting of Helicobacter pylori infection prevalence in patients of diabetes, and non- diabetes (Fedorchenko and Martynuk, 2018).

As mentioned above for this purpose there were 69 subjects, and after observing the analysis and history they were divided into two groups, among them thirty were non-diabetics and 39 were diabetics. The major age group of the subjects was 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. Most of the subjects were males (70% in no 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 (Güvener et al., 2017) .

From all the sixty-nine subject's 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% of diabetics X 2 =3.96, p value=0.04 (<0.05) i.e. the prevalence of Helicobacter pylori is diabetics is prominently greater than that in non-diabetics (Güvener et al., 2017).

The research observed that NIDDM 61% patients had Helicobacter pylori infection and Helicobacter pylori prevalence was originated to be prominently greater in diabetic patients than in controls. Helicobacter pylori infection was greater is IDDM children than the healthy controls. Helicobacter pylori sero prevalence was greater than age matched controls in the diabetics. Literature available regarding the prevalence of Helicobacter pylori in diabetics vis-à-vis controls is contradictory and indecisive (Güvener et al., 2017).

There was 64.1% of Helicobacter pylori prevalence in diabetic subjects and the Helicobacter pylori prevalence establishment among diabetics as reported in world literature vary between 37% to 85%. Further it has been reported that various drugs, including anti-ulcerants anti-emetics and anti-spasmodics in

addition to anti-biotics 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 (Fedorchenko and Martynuk, 2018).

Helicobacter pylori infection prevalence study in relation to age it was found to be greater in 5th and 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? Patients aged <24 years of sero prevalence of Helicobacter pylori among IDDM patients prominently greater than controls and corresponding rate among IDDM aged >24 years was prominently lower than control (Güvener et al., 2017).

Infection acquisition of an early age particularly in the developing countries has been observed. In fact in most under developed countries there was an endemic of Helicobacter pylori goes unimpeded and most adults are infected. The rate of prevalence was found to be increased with all age groups until 60-70 years. On the other hand the factual relation of Helicobacter pylori infection to age remains indecisive in this research, 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 greater positivity, both in Diabetics (75%) and non-diabetics (42.8%). This apparently suggests a male predilection for Helicobacter pylori infection (Fedorchenko and Martynuk, 2018).

A greater Helicobacter pylori infection prevalence was established in diabetic women than in control women (80% vs 37.37%, p<0.01), while there was no difference between found in males. Thus in all probability the infection has no gender preference, and the same is supported by similar findings (Fedorchenko and Martynuk, 2018).

According to this research the Helicobacter pylori infection prevalence among diabetes elevated as per the disease duration, reaching hundred percent with duration exceeding 10 years. The mean value of diabetes in diabetics as per Helicobacter pylori was 7.85±3.93 and in diabetics deprived of 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 (Fedorchenko and Martynuk, 2018).

CONCLUSION:
According to this study the comparisons of different issues in diabetes mellitus patients with and deprived of Helicobacter pylori were done. Although the complication number of each type i.e. neuropathy, nephropathy, retinopathy and cardiovascular were proportionally greater is patients of diabetes with Helicobacter pylori than among those of diabetes deprived of Helicobacter pylori yet the difference was not found to be significant in any of these. CAD was more prevalent in diabetic patients with than deprived of 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. 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. Therefore no association has been found between frequency of the infection and duration of diabetes.

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