Peptic Ulcer in a Group of Iraqi Diabetic Patients

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Abstract:

Background: Both acute and chronic hyperglycemia can lead to specific gastrointestinal (GI) complication.***H.pylori*** infection is well established cause of dyspepsia, although all the three factors; lifestyle, digestive fluids, and ***H.pylori*** infections may play a role in ulcer development.

Objective:-This study attempts to determine the role of some factors like lifestyle, duration of dyspeptic symptoms, state of diabetic control and ***H.pylori*** infection in diabetic patients.

Methods:-The study was carried in the endoscopy unit of Al-Yarmook Teaching hospital. The total blood samples of 178 subjects with 80 antral biopsies obtained from four groups; 30 diabetic with peptic ulcer (P.U) as patients group and control groups involving 54 non diabetic with no peptic ulcer, 50 non diabetic with peptic ulcer and 44 diabetic with no peptic ulcer. All participants answered a special questionnaire, and every gastric biopsy specimen was subjected to cultural, histology, rapid urease test for ***H.pylori*** diagnosis in addition to blood samples for enzyme- linked immunesorbent assay (ELISA) as a serologic study and to estimate plasma glucose level.

Results: Some dietary factors such as spicy foods 60% and smoking 54% had more influence on the incidence of ***H.pylori*** infection with peptic ulcer disease (PUD). Some dyspeptic symptoms (nausea/ vomiting 93.3%, loss of weight 80%, hematemesis /N-melaena 67%) are seen more in diabetic with P.U.D(patients group) when compared with the other control groups. ELISA test for diagnosis of ***H.pylori*** infection revealed that there is no significant difference (P>0.05) to the incidence of ***H.pylori*** infection in diabetes either with PU 40% or with no PU 59%. The ***H.pylori*** infection was positive in diabetic with P.U (patients group) 73.3% who have dyspeptic symptoms <1year, when compared with (control group) non diabetic with P.U 34% (P<0.01).

Conclusion: Some dietary factors and smoking increased the incidence of P.U.D. Poor glycemic control was not associated with significant increase in the incidence of P.U.D. Duration of dyspeptic symptoms < 1 years with positive result for ***H.pylori*** infection was higher in diabetic patients with P.U.D

Keyword: ***H.pylori***, peptic ulcer, diabetes mellitus.

Introduction:

For almost a century ,doctors believed that lifestyle factors such as ,diet, smoking, alcohol and/or coffee consumption ,stress and non steroidal anti inflammatory drugs (NSAIDs) may cause ulcers [1,2].Later they found that ***Helicobacter pylori*** was a major cause of peptic ulcer diseases (P.U.Ds)and recommended that infected individuals with ulcer should be treated to eradicate the organisms[3,4].

In diabetes mellitus the incidence of ***H.pylori*** is increased, [5]and the role of bacterial infection in diabetic dyspepsia is mainly related to blood glucose concentration [6].Indeed hyperglycemia may induce the infection of ***H***. ***pylori***,& may get reactivated and produce symptoms of dyspepsia in diabetes [7,8].

In general ,development of any disease depends on strains virulence, host genetic susceptibility and environmental factors [9,10].Serology is an important method to determine colonization status and can be used for diagnosis as screening procedure, or to follow the efficacy of eradication[11], ELISA is one of the serological techniques, which has been used to demonstrate a correlation between the titer or level of re-activities and the presence of ***H***.***pylori*** in gastric antrum[12], recently ,for research and epidemiological studies of ***H***. ***pylori*** infection the polymerase chain reaction (PCR) and Urea breath test(UBT) represent the methods of choice for screening patients before upper gastrointestinal endoscopy [13].

Aims of the study:

1-Determination of the role of lifestyle practices and the family history on the incidence of peptic ulcer associated with diabetes mellitus.

2-Estimation of the frequency of different dyspeptic symptoms in diagnosis of peptic ulcer disease with ***H. pylori*** infection among diabetic or non diabetic patients.

3-Studying the frequency of ***H***. ***pylori*** infection in diabetic patients and the duration of dyspeptic symptoms.

Patients, Materials & Methods:

●**Questionnaire**:-

All the participants answered a special questionnaire regarding:-

Age, sex, marital state ,occupation, duration of D.M.,treatment of D.M, duration of P.U symptoms ,treatment of P.U, family history (D.M &P.U), the

lifestyle and any antimicrobial therapies received during the previous months.

●**Study groups**:-

178 patients involved in this study were submitted to upper gastrointestinal endoscopies in the gastrointestinal endoscopy unit at AL-Yarmook Teaching hospital. The criteria for inclusion used in this study were endoscopy with provisional diagnosis of P.U.D in diabetic and non-diabetic patients with dyspepsia. Patients included in this study were subdivided into four groups according to the above mentioned criteria as follows:-

a-Diabetic with peptic ulcer:-thirty patients (**12** females&**18** males).

b-Diabetic with no peptic ulcer:-forty four patients (**24** females&**20** males).

c-Non diabetic with peptic ulcer:-fifty patients (**15** females&**35** males).

d-Non diabetic with no peptic ulcer:-fifty four patients (**31** females&**23** males).

●**Biopsy samples:-**

Three biopsies were taken from the antrum of every P.U patients whether diabetic or not [14]. One of the three biopsy specimens was tested by rapid urease test; remaining specimens were used for histological analysis and bacteriological culture for ***H.pylori*** diagnosis [15].

●**Blood sample**:-

ELISA method was carried out according to the manufacturer company instructions (BioRAD-72778), for determination of human serum IgG antibodies against ***H.pylori*** [2], In addition Glucose Enzymatic Colorimetric method was used to measure the level of glucose in all sera of study groups by applying the kit instruction manual of the SYRBIO-Company-France.

●**Statistical analysis**:-

Chi-squared test was used (P value≤0.05 was considered significant) also fisher exact test for small sample size was done in this study [16, 17].

Results:

178 subjects who where considered eligible for the study were interviewed and history was obtained using the questionnaire prepared for this purpose. Table -1-shows the significant association of two factors, these factors are diet habit 60% (P<0.05) and smoking 54% (P<0.01) with the incidence of P.U.D in patients whether diabetic or non diabetic. Otherwise, the other factors in table-1- shows statistically a non-significant difference on the incidence of infections (D.M; P.U) when comparing all the control groups with patients group (diabetic with peptic ulcer) P>0.05.

Table-1-Effect the lifestyle factors on the incidence of P.U &D.M in different study groups (y=yes; n=no)

Lifestyles		**Non diabetic non P.U (54)**	**Non diabetic with P.U (50)**	**Diabetic non P.U (44)**	**Diabetic with P.U (30)**
Smoking/ Alcohol	**y**	8 (15%)	27(**54%**)	14(32%)	12(40%)
	n	46*	23	30	18
Coffee/Tea	**y**	38(70.4%)	43(86%)	39(89%)	26(86.7%)
	n	16	7	5	4
Apple vinegar	**y**	11(20.4%)	9(18%)	12(27.3%)	6(20%)
	n	43	41	32	24
Diet habit with eating spicy food	**y**	20(37%)	27(54%)	20(45.5%)	18(**60%**)
	n	34 *	23	24	12
Family history D.M/P.U	**y**	29(54%)	25(50%)	27(61.4%)	18(60%)
	n	25	25	17	12

***P<0.05**

Fasting blood glucose is used to assess level of glycemic control according to the data in **table-2-**178 subjects were divided into three groups according to the SYRBIO-Company instruction, these with excellent F.B.G(<6.6mmol/L)but not less than(4.5mmol/L),those with acceptable F.B.G(<6.6-10mmol/L) and those with poor glycemic control more than (10mmol/L).However, **table-2-** reveals no significant difference in the positive results of ELISA test with diagnosis ***H. pylori*** infection in diabetic patients plasma with P.U.D either in patients group (diabetic with peptic ulcer) 40% and control group(diabetic non P.U) 59%, as well no significant difference between males and females.

Table -2- Comparison of blood glucose level in different study groups

F.B.G(mmol/L)	Non diabetic non P.U	Non diabetic with P.U	Diabetic non P.U	Diabetic with P.U
4.5-6.6	54(100%)	50(100%)	2(4.5%)	2(7%)
6.6-10	-	-	16(36.4%)	16(53.3%)
>10	-	-	26(**59%**)	12(**40%**)
Total	54	50	44	30

The symptoms of ulcer disease are variable, so **,table-3-**shows the different dyspeptic symptoms associated with the diagnosis of P.U.D with/without D.M. **Table- 3-** reveals the significantly higher predominate of (nausea/vomiting 93.3%, loss of weight 80% and hematemesis/N-melaena 67%) symptoms in patients group(diabetic with peptic ulcer) when compared with all control groups (P<0.01). Moreover, a non-significant difference in the (borborgums 53.3% and acidity 67%) symptoms (P>0.05) were detected in patients group (diabetic with peptic ulcer) when compared with all control groups.

With positive (seroprevalence: ELISA and gastric biopsies: culture, histopathology and RUT) ***H. pylori*** infection was found to be more prevalent in both groups who have upper digestive tract symptoms with P.U (diabetic with P.U and non diabetic with P.U).

Table-3- Distribution of dyspeptic symptoms in different study groups

Symptoms	Non diabetic non P.U (54)	Non diabetic with P.U (50)	Diabetic non P. (44)	Diabetic with P.U (30)
Epigastric pain	44(82%)	47(94%)*	38(86%)*	20(67%)
Borborgums	44(82%)*	42(78%)*	28(64%)	16(53.3%)
Early satiety	35(65%)	41(76%)*	27(61.4%)	22(74%)
Nausea/Vomiting	30(56%)*	27(54%)*	20(46%)*	28(93.3%)
Hematemesis & Melina	11(20.4%)*	29(58%)	11(25%)	20(67%)
Loss of weight	26(48.1%)*	28(56%)*	27(61.4%)	24(80%)
Acidity	39(72.2%)	36(72%)	33(75%)	20(67%)

(P<0.01)*

Table-4-shows , the highest incidence of P.U symptoms duration <1 year with positive (seroprevalence ELISA and gastric biopsies) of ***H.pylori*** was obtained in patients group (diabetic with peptic ulcer) 73.3% when compared with control group (non diabetic with peptic ulcer) 34% (P<0.01), while the least incidence of P.U symptoms duration >5 years with the positive (seroprevalence ELISA and gastric biopsies) of ***H.pylori*** infection can be found in patients group (diabetic with peptic ulcer) 6.66% ,compared with control group(non diabetic with peptic ulcer) 36%(P<0.01).

Table-4- the duration of P.U symptoms among P.U patients with or without diabetes.

History of P.U Symptoms	Non diabetic with P.U	Diabetic with P.U
<1 year	17 (34%)	22 (73.3%)
1-5 year	15 (30%)	6 (20%)
>5 year	18 (36%)	2 (6.66%)
Total	50	30
P value	P<0.01	

Discussion:

The results study showed that the effect of the lifestyle factors on the incidence of P.U and D.M in different studied groups was similar to that reported by **AL-Baldawi, (2001) and Rosenstock et al., (2003**) who found that smoking is associated with the development, delayed diagnosis and recurrence of P.U as well as resistance to treatment[18,2]; **Fonseca et al., (2002**) reported that diet has also been thought to play a role in P.U.D.Certain foods can cause

dyspepsia ,this is also true for beverages containing alcohol[19]. This can be explained by the effect of prolonged un-neutralized gastric acidity ,altered gastric emptying, decreased proximal duodenal bicarbonate production and cigarette-induced generation of noxious mucosal free radicals[20,1].Our result shows no statistically significant difference in family history of P.U and D.M in all study groups, this work is not agreement with **Powers, (2001) and Peura, (2004**) who suggest the hereditary factors to be more important in the pathogenesis of P.U.D whether in diabetic or not[21,22]. The explanation for this familial aggregation of ulcers is multifactorial exposure to the same environmental factors, showing psychological stresses, food habits and similar risk of exposure to ***H.pylori*** infection in addition to genetic factors [1].Furthermore, the caffeine, oil and acid in coffee irritate the stomach which can cause excess of gastric acidity that leads to a variety of digestive disorders [23].

In general, the transmission of ***H. pylori*** occurs predominantly and perhaps even exclusively within families. So, ***H. pylori*** would represent the first human pathogen recognized to display this remarkably restricted mode of transmission [13, 24].

No significant difference in positive results (seroprevalence: ELISA) of ***H.pylori*** infection with P.U.D and hyperglycemia in diabetic patients with or without P.U and no significant difference between males and females. This is in accordance with **Everhart, (2000) and Candelli et al., (2003)** who suggest that the plenty antibiotics taken by diabetics used for treatment such as genitourinary tract infections specially females are more likely to have ***H.pylori*** infection eradication[25,26], but it contradicts the data reported by **Quatrini et al., (2001**)who found that ***H.pylori*** infection was significantly associated with F.B.G concentration among women and to explain these results, they found that women who had higher basal and meal stimulated serum gastrin concentration than men, so, gastrin can inhibit glucose absorption in the small intestine, and amplifies glucose stimulated insulin release then leads to lower F.B.G concentrations in population[8]. Abu-Farsak, (2001) and Rosenstock et al.,(2003) attributed the sex difference to the presence of more risk factors in men specially smoking which is associated with the development of delayed healing and recurrence of P.U, as well as, resistance to treatment, in addition to the physiological stresses[1,2].Moreover, poor glycemic control in diabetes and chronic dyspepsia has been attributed to gastric emptying and the absorption of delay, causing mismatch between the onset of insulin action and the absorption of carbohydrate[27],in addition the dietary habits and increased prevalence of obesity, as well as, the patients and family education for self management [28], hence ,the control of blood glucose substantially decreased the risk of many D.M complications[29].

The symptoms of P.U.D are variable, our findings which were not very much different from that reported by **Block et al., (2002) and Sargyn et al., (2003)**[30,31], but it contradicts the data reported by **Bakka et al., (2002) and Candelli et al., (2003)**,who suggested that a wide variety of gastrointestinal (GI) symptoms have been reported to occur in adults with diabetes or non diabetic [32,26], so, the mechanism for development of P.U symptoms, include acid-induced activation of chemical receptors in the duodenum, enhanced duodenal sensitivity to bile acids, and pepsin or altered gastroduodenal motility, and most likely the autonomic neuropathy or acute hyperglycemia have been implicated in the pathogenesis[20,27].

Two groups who have upper digestive tract symptoms with P.U(diabetic with P.U as patients group and non diabetic with P.U as control group) with positive (seroprevalence:ELISA and gastric biopsies:culture,histopathology and RUT) of ***H.pylori*** infection was found to be more prevalent in both groups, but this work doesn't agree with **Xia et al., (2001);Jones et al., (2002**) who reported that ***H.pylori*** infection is not associated with specific symptoms profile in diabetic or non diabetic [33,34].

Many of dyspeptic symptoms may be present in two control groups who don't have an ulcer(diabetic non P.U and non diabetic non P.U), this is in accordance with **McCarthy et al., (1995) and Peura, (2004**)who found that many patients infected with ***H.pylori*** have recurrent abdominal symptoms, non ulcer dyspepsia (NUD)without ulcer diseases[35,22].

H. pylori infection was positive in diabetic with PU(patients group) who have dyspeptic symptoms <1 year 73.3%, these results resemble that reported by **Jaskowski et al., (1997); De-Luis et al., (1998); Arslan et al., (2000)** and **Quatrini et al., (2001**) who found that the association between ***H. pylori*** infection, glycemic status and duration of diabetes with upper GI symptoms in diabetic subjects[36,37,6,8], but it doesn't agree with **Kaufman, (1997**)who showed no significant difference has been found between the frequency of the ***H. pylori*** infection and types of D.M or its duration[38].

However, symptoms of diabetes mask the symptoms of gastrointestinal tract unless this infection is so sever [21], the other complications of diabetes, the duration of disorder and poor glycemic control seem to be associated with more sever GI problems [39.40].Many of GI complications of diabetes seem to be related to dysfunction of neurons

supplying the gastric nervous system, this may lead to abnormalities in gastric motility, sensation, secretion and so on [29, 40, 28].

Conclusions:

1-Some of the lifestyle factors may play a significance role on the incidence of P.U and D.M. specifically the diet habit ($P<0.05$) and smoking ($P<0.01$).

2-Nausea, vomiting, loss of weight and hematemesis /N-malaena symptoms may be significantly present in diabetics with P.U group ($P<0.01$) while, borborgums and acidity symptoms may be not.

3- The duration of P.U symptoms (<1 year) with positive result for ***H.pylori*** infection with P.U.D significantly higher in diabetic patients ($P<0.01$).

4-There is no effect of poor glycemic control to the incidence of ***H.pylori*** infection with P.U.D in diabetic or non diabetic patients ($P>0.05$).

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