

The Impact of *Helicobacter Pylori* Infection, Malnutrition and Insulin Resistance on Type 2 Diabetic Patients Outcome in the Gaza Strip

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Abstract

Background: In recent few years, a significant association has been reported between cardiovascular diseases, dyslipidemia, even diabetes and *Helicobacter pylori* infection. However, there are conflicting reports, and lack of data from in the Middle East and especially Gaza Strip should prompt local studies for establishing the relationship between *H. pylori* and such chronic diseases. Thus, we hypothesized that among Medical services Clinics in the Gaza Strip if type 2 diabetes mellitus, *H. pylori* infection may be associated, then the metabolic control of disease is reduce and a new strategy in prevention and treatment will changed.

This study is the pioneer study, in the Medical services Clinics in the Gaza Strip.

Methodology: A cross-Sectional Study was conducted in the Medical Services Clinics in Gaza Strip; we enrolled 129 patients affected by type 2 diabetes mellitus. We evaluated the relationship between glycosylated hemoglobin (HbA_{1c}) levels, C-Peptide, and *H. Pylori* (IgG-stool) in-patient from Medical services Clinics in the Gaza Strip. Data was collected through hematologica information and structured interview questionnaire.

Results: Highly significant percentage of *H. pylori* (70%) among the DM patients including in the study, But not indicate any significant association between gender and *H. Pylori* status. A significant difference between the means of weight for persons with positive and negative *H. pylori* status. No significant difference was assigned by using t-test between the means of those who suffer from stomach problems and those who are not for three chemical variables FBS, C- peptide and HbA_{1c}. A significant correlation between vegetables and C- peptide, Legumes and C- peptide.

Conclusion: The present study suggests that there is a significant association between *Helicobacter pylori* infection and type 2 diabetes mellitus. *Helicobacter pylori* infection was significantly higher in diabetic obese patients than non-diabetic patients.

Keywords: Type2 diabetes mellitus (T2DM); *Helicobacter pylori* (*H. pylori*); Insulin Resistance (IR); Malnutrition

Introduction

Acid peptic disorders are common in patients with or without diabetes. *Helicobacter pylori* (*H. pylori*) is responsible for most of the duodenal ulcers and many gastric ulcers in normal population. *H. pylori* negatively affect the protective mucous coating of the stomach and duodenum and allow gastric acid to get through to the sensitive lining beneath. Both, acid and the bacteria irritate the gastric lining and cause a sore or ulcer [1].

Helicobacter pylori is a common bacterium and approximately 50 percent of the world's population has been estimated to be infected. Adequate nutritional status, especially frequent consumption of fruits and vegetables and of vitamin C, appears to protect against infection with *H. pylori*. In contrast, food prepared under less than ideal conditions or exposed to contaminated water or soil may increase the

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risk. Overall, inadequate sanitation practices, low social class, and crowded or high-density living conditions seem to be related to a higher prevalence of *H. pylori* infection.

The presence of *H. pylori* and diabetes mellitus (DM) is one of the main causes of gastrointestinal diseases. Additionally, the presence of *H. pylori* in DM cases plays an important role in the development of gastrointestinal diseases. In particular, the worsening of glycemic and metabolic control increases the incidence of *H. pylori* infections and complaints of dyspepsia. A significant relationship between dyslipidemia and *H. pylori* has been reported [2].

Subjects and methods

A Cross-Sectional Study was done randomly selected on 129 Diabetic patients with Type 2, from the Medical Services Patients in the Gaza Strip. All patients provided written informed consent to participate. An inclusion criterion is patients with type 2 diabetic patients, male & female, with BMI less than 30, while exclusion criteria are:

1. Type 1 diabetics
2. Obese diabetics with BMI more than 30
3. Hypertension diabetics
4. Hyperlipidemia diabetics
5. Polycystic ovary syndrome patients
6. Strong family history of diabetes
7. Pregnant women
8. Patients with other hormonal diseases

Demographics (age, gender, and duration of disease) of the patients were documented. Height, weight, and waist circumference were measured and BMI was calculated as weight/height² (kg/m²). Biochemical investigation including hemoglobin A1C, C-peptide, FBS and *H. Pylori* IgG-stool. Dietary assessment it involves estimating food intake. This is achieved by retrospective interview techniques and recording of intake.

Approval of the local ethics committee was obtained for the study.

Statistical Analysis

SPSS 18.0 package program was used for statistical analysis of data. The data were summarized in percentage, mean \pm SD, and median values. The statistical relationships between nutritional habits, malnutrition, blood analysis and variables were assessed using the tests: chi-square, t-test, Pearson correlation, one way ANOVA, Kurshall Wallis test, and Fisher's Exact test. P-values were calculated for the ordinal level measures (P<0.05). The results were assessed with hazard ratio and in a 95% confidence interval.

Results

Chemical measurements of participants

The summary statistics of the chemical measurements of participants, namely FBS, C- Peptide and HbA1c are given in Table 1

Variable	Mean	Std. Deviation	Normal range
FBS	142.95	47.47	70-110 mg/dl
C - peptide	1.89	1.23	0.5 – 3.2 ng/ml
HbA1c	6.79	1.21	4 – 6 mmol/dl

Table 1: Chemical measurements of participants.

The frequency and percentage of *H. pylori* are given in Table 2, and around 70.5% of the sample found has positive *H. pylori*.

<i>H. pylori</i>	No. (%)
Positive	91 (70.5%)
Negative	38 (29.5%)
Total	129 (100.0%)

Table 2: Distribution of *H. Pylori*.

Deviation of three Chemical variables FBS, C-peptide and HbA1c according to the gender gives in table 3, associated with the mean difference. In order to assess any significant difference between the means of the chemical variables with respect to the age T-test is conducted as given in Table 3. It is found there is no significant difference between the means of chemical variables due to the gender.

chemical variable	Gender	N	Mean	Std. Deviation	Mean difference	t-value	p-value
FBS	Male	65	144.55	52.21	3.23	0.385	0.701
	Female	64	141.33	42.47			
C peptide	Male	65	1.84	1.32	-0.083	-0.384	0.702
	Female	64	1.93	1.13			
HbA1c	Male	65	6.79	1.24	0.014	0.066	0.947
	Female	64	6.78	1.19			

Table 3: Student t-test of the biochemical variables according to the gender.

Anthropometric measurements of participants

The summary statistics of the anthropometric measurements of participants, namely weight, height, BMI and Waist circumference are given in Table 4.

Variable	Mean	Std. Deviation
Weight (kg)	83.24	10.52
Height (cm)	176.83	53.21
BMI (kg/cm ²)	27.87	2.24
Waist circumference(cm)	90.43	15.02

Table 4: Anthropometric measurements of participants.

Table 5 gives the summary statistics of the anthropometric variables according to the *H. pylori* status. Results in Table 6 shows that there is significant difference between the means of weight for persons with positive and negative *H. pylori* status. The mean weight for positive *H. pylori* is higher than the mean weight of the negative group. Consequently, the mean of BMI of positive groups is significantly higher than the mean BMI for the negative group.

Anthropometric variables	H. Pylori	N	Mean	Std. Deviation	Mean difference	t-value	p-value
Weight	Positive	91	84.87	9.77	5.54	2.802	0.006*
	Negative	38	79.33	11.33			
Height	Positive	91	179.76	62.99	9.95	0.968	0.335
	Negative	38	169.82	8.54			
BMI	Positive	91	28.14	2.21	.910	2.130	0.035*
	Negative	38	27.23	2.22			
Waist circumference	Positive	91	90.75	14.39	1.06	0.365	0.716
	Negative	38	89.68	16.59			

Table 5: Student t-test of the Anthropometric variables according to the H. pylori status.

Stomach pain and stomach ulcer

There are 81 (62.8%) of the sample are suffering from stomach pain or stomach ulcer, no significant difference was assigned by using t-test between the means of those who suffer from stomach problems and those who are not for three chemical variables FBS, C- peptide and HbA1c as given in Table 6.

Are you suffering from stomach pain or stomach ulcer?	N	FBS		C - peptide		HbA _{1c}	
		Mean	SD	Mean	SD	Mean	SD
Yes	81	144.98	46.74	2.00	1.32	6.89	1.21
No	48	139.54	48.98	1.70	1.04	6.62	1.20
Total	129	142.95	47.47	1.23	0.11	6.79	1.21
t- value		0.627		1.328		1.234	
P-value		0.532		0.187		0.219	

Table 6: T -test for the chemical variables based on their stomach status.

Taking any drugs in the past few days

A total of 93 (72.1%) of the sample have taken at least a drug the previous day of the interview. Among those who have taking a drug following percentages are recorded for a list of drugs as shown in Table 7.

Drug	yes		No	
	n	(%)	n	(%)
Insulin, Glucophage, or Amaryl	93	100	0	0
Ratidine, Omeprazole	29	31.18	64	68.82
Antacids	33	35.48	60	64.52
Baby Aspirin	32	34.41	61	65.59
Folic acid	77	82.80	16	17.20
Multivitamins	44	47.31	49	52.69
Antibiotics	36	38.71	57	61.29
NSAID (Diclofen, ibrorofen, etc.)	38	40.86	55	59.14
Dietary Supplement & herbs	59	63.44	34	36.56

Table 7: Drug history of the participants.

Food frequency

Results in Table 8 show that in general there are insignificant correlation between food groups and Chemical variables, but there are significant correlation between vegetables and C- peptide, Legumes and C- peptide. A significant correlation is detected between vegetables, hot drink and HbA_{1c}.

Food Groups	Chemical Variables					
	FBS		C- peptide		HbA _{1c}	
	Pearson Correlation	p-value	Pearson Correlation	p-value	Pearson Correlation	p-value
Grains, starches	.062	.488	.272	.002*	.101	.256
Fruit	.040	.650	.085	.337	.047	.597
Vegetables	.048	.592	.174	.049*	.189	.032*
Proteins	.081	.362	.081	.360	.151	.089
Legumes	.107	.226	.246	.005*	.148	.094
Nuts	-.022	.800	.095	.285	-.146	.098
Desert	-.050	.576	.102	.252	.105	.239
Cold drinks	.123	.166	-.044	.621	.239	.006*
Hot drinks	.013	.883	.046	.602	.059	.505
Fried Food	-.091	.305	.098	.272	-.079	.376
Fast food	-.030	.733	.063	.478	.052	.559
Spices	.148	.095	.132	.135	.052	.562
Pickles	.019	.831	.081	.359	-.049	.584
Honey	-.140	.113	-.066-	.456	.040	.649

*Significant correlation at 0.05 level of significance.

Table 8: Correlation between the food groups and Chemical variables.

Discussion

Socioeconomic description of the study sample

This result disagreed by Yu Chen results (2011) which evaluate the relationship between *H. pylori* and HbA_{1c} levels in type 2 DM patients with higher BMI (more than 30), and their findings indicate a role of *H. pylori* in impaired glucose tolerance in adults that may be potentiated by higher BMI level [3].

In this context there is no clear data regarding the relationship between *H. Pylori* and type 2 diabetic patients whom have BMI < 30.

Distribution of *H. Pylori*

The results of this study showed a highly significant percentage of *H. pylori* (70.5%) among the diabetic patients including in the study, this result is consistent with some literature and inconsistent with others.

The results are supported by the study of Bener (2007) his results found that *Helicobacter pylori* infection was significantly higher in diabetic patients than non-diabetic subjects [4].

This result inconsistent with many researchers as Yu Chen and Martin J. Blaser study (2011), that study reported no difference between type 2 DM patients and non-diabetics with regard to the prevalence of both *H. pylori* infection [3].

Correlation between gender and chemical variables

The current study revealed no significant association between the means of chemical variables (FBS, C- peptide, and HbA1c) according to the gender.

No statistically significant difference found between the socioeconomic variables according to the gender. This does not indicate any significant association between gender and *H. pylori* status.

One possibility is that the pathophysiological mechanisms in diabetes mellitus development differ between men and women, with men more susceptible to leptin produced in the adipose tissue, while in women the protective effects of ghrelin produced in the stomach. At least, this respect In multivariate linear regression, higher levels of leptin were associated with insulin resistance among men, but not among women. Among women, insulin resistance was associated with lower adiponectin/leptin ratio and ghrelin [5].

Further studies are needed to illuminate possible gender differences in the pathophysiology of insulin resistance, including both samples with newly diagnosed type 2 diabetes mellitus, the metabolic syndrome [5].

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Anthropometric measurements of participants

The current study shows a significant correlation between the anthropometric variables according to the *H. pylori* status, and there is significant difference between the means of weight for persons with positive and negative *H. pylori* status.

Per E. Wändell study in 2012 shows that factor analysis showed that leptin in women was closely related to anthropometric variables, but in men both related to anthropometric and inflammatory variables. Gender differences could indicate different pathophysiologic mechanisms of insulin resistance and type 2 DM among men and women, where leptin possibly could be a better marker among men, and ghrelin among women [5].

That result agreed with Perdichizzi G., *et al.* [6] findings, which found a higher prevalence of *H. pylori* infection in type 2 DM obese patients.

Similar to other study conducted by Yu Chen [3], found that there was a synergistic interaction between *H. pylori* and higher body mass index (BMI).

Diabetes history

This study identifies significant differences between the means of the C- peptide, HbA1c categories, and FBS categories.

There is a significant difference between mean of C- peptide for the category 1-5 and more than 10 years. While for the HbA1c there are significant differences between the mean of more than 10 categories.

This result similar to Robert P study (2012), the findings show there may be a link between *H. pylori* bacteria and type 2 diabetes mellitus in adults, and found that the presence of *H. pylori* bacteria was consistently associated with elevated levels of glycosylated hemoglobin (HbA1c) [7].

In addition Yu Chen., *et al.* study (2011), in their studies indicated that there was no association between *H. pylori* with seropositivity HbA1c levels and history of self-reported diabetes mellitus. The current study result is inconsistent with their results [3].

Stomach pain and stomach ulcer

The study results showed that more than a half of the samples (62.8%) are suffering from stomach pain or stomach ulcer, no significant difference between the means of those who suffer from stomach problems and those who are not for three chemical variables FBS, C-peptide and HbA1c, the result shows that there is insignificant association between the *H. pylori* and stomach problems.

The study results agreed with Woodward M study (2000), that study reported no difference between type 2 DM patients and non-diabetics with regard to the prevalence of both *H. pylori* infection related with gastro duodenal disorders [8].

Another study by Xia, *et al.* (2001), also similar with current study results, *H. pylori* infection appears not to be associated with diabetes mellitus or upper GI symptoms in diabetes mellitus [9].

Taking any drugs in the past few days

There is lack of data regarding the correlation between drugs and the influence of *H. pylori*. This item needs deep investigation, our study showed a high rate of taken drugs in the past few days, more than half of the samples (72.1%) have taken at least a drug in the previous day of the interview.

Food frequency

Dietary habits and the nutritional status of Palestinian type 2 diabetic patients, eating behaviours characterized by missing meals (particularly breakfast or dinner), snacking, consumption of fast foods, unconventional meals, consumption of soft drinks, and dieting [10].

Dietary habits

The results of this study highlight Grains, starches, bran and mixed bread, fruit and vegetables, desserts, animal fat, fried food, olive oil, fish, vegetables, fruits, proteins, legumes, nuts, cold drinks, soda beverages and hot drinks, tea, coffee, and nuts which are considered as the main dietary factors that may be associated positively or negatively with type 2 DM.

The present study results show that half of the food groups means are significantly less than one, namely, Grains, starches, Nuts, Desert, cold drinks, hot drinks, fast food, Pickles and Honey, where the others are significantly more than one.

In general the current study shows that there are insignificant correlations between food groups and chemical variables, but there are significant correlations between vegetables and C-peptide, legumes and C-peptide. And there is a statistically significant correlation detected between vegetables, hot drink and HbA1c.

Conclusion & Recommendation

In the present study, *H. pylori* infection, insulin resistance and malnutrition in type 2 DM patients, were done for all subjects.

- a. An adequate lifestyle, socioeconomic factors, and some biochemical alterations could play an important role in the etiology of type 2 DM patients.
- b. This study demonstrates the strong relationship between *H. pylori* infection as a risk factor for insulin resistance, more than 70.5% of the samples found to have positive *H. pylori*.
- c. Greater attention of the eradication of *H. pylori* has been shown to play important roles in the etiology of other chronic diseases.
- d. We can conclude that there is insignificant association between the *H. pylori* and diabetes mellitus history (the duration of diabetes). *H. pylori* infection is not associated with duration of diabetes.
- e. The study exhibited a positive significant difference between the means of weight for persons with positive and negative *H. pylori* status. Consequently, the mean of BMI of positive groups is significantly higher than the mean BMI for the negative group.
- f. The results suggest that data seem to indicate a potential association between *H. pylori* infection, malnutrition and IR, further studies are needed to strengthen this association and to clarify whether there is a causative link between them.
- g. Serum *H. pylori* should be integrated into routinely para-clinical investigations in all patients with type 2 DM.

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