The Association between *Helicobacter Pylori* Infection and Insulin Resistance

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ABSTRACT

Introduction: *Helicobacter pylori* are associated with severe gastrointestinal pathologies. Moreover, it is associated with other conditions such as atherosclerosis, insulin resistance, diabetes mellitus and some autoimmune diseases. The purpose of this study is to search the relation between *Helicobacter pylori* infection and Insulin Resistance. **Methods:** Ninety patients complaining of dyspepsia was selected from Gastroenterology, Hepatology and Infectious Diseases Department, Benha University Hospital. The patients were divided into two groups with matching age, sex and the basic laboratory investigations results. Group (A) patients were *Helicobacter pylori*-positive. Group (B) patients were *Helicobacter pylori* negative based on endoscopic findings and confirmed by histopathological diagnosis and exclusion of other causes of dyspepsia. Insulin resistance was compared between the two groups. **Results:** In the present study, there was statistically significant association between *Helicobacter pylori* positive patients (51/90; 56.7%) and insulin resistance (IR) compared to *Helicobacter pylori* negative patients (39/90; 43.3%) (P value <0.001). The mean value of IR was 3.6 ± 0.58, 2.2 ± 0.36 respectively for *Helicobacter pylori* positive and *Helicobacter pylori* negative patients. There was no statistical significant difference between *Helicobacter pylori* positive and *Helicobacter Pylori* negative patients as regard to other investigations (P value >0.05). **Conclusion:** Insulin resistance has a role in the chronicity of H. pylori infection and the reduction of IR will lead to a better response of therapy in these patients.

KEY WORDS: *Helicobacter pylori,* insulin resistance.

INTRODUCTION

Helicobacter pylori (H. pylori) is a gram negative, noninvasive, non spore forming, spiral shaped bacteria. *H. Pylori* infection is one of the most prevalent chronic infections worldwide.[1] *H. pylori* infection increases insulin resistance (IR) since it causes a chronic inflammation and affects gastrointestinal hormones function in insulin regulation.[2] The prevalence of IR syndrome, and its component is rapidly increasing worldwide as a consequence of the ongoing obesity epidemic that significantly increases with age.[3] IR syndrome is included in degenerative conditions that have an increasingly high impact on aged population and their association with *H. pylori* infection, which affect more than half of the world population has only been addressed.[4] However, a published data has described the association between *H. pylori* infection, IR and metabolic syndrome.[5] A systemic review by nine studies, including 2120 patients confirmed the eradication of *H. Pylori* and its role in decreasing IR.[6]

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MATERIALS AND METHODS

The study was conducted on 90 patients with dyspeptic complaints attending the Department of Hepatology, Gastroenterology and Infectious Diseases at Benha University Hospital. All the patients presented with dyspeptic complaints such as epigastric pain, heartburn, nausea and vomiting. Exclusion Criteria include; diabetes mellitus, pregnancy, intake of proton pump inhibitors in the last two weeks, renal failure and recent gastrointestinal tract surgery.

All the patients were subjected to the following: Thorough history taking, including non-steroidal anti-inflammatory drug (NSAID) intake, history of smoking and medical examinations, including body mass index (BMI). Relevant laboratory investigations were done; complete blood count (CBC), liver profile, kidney function test as well as fasting serum insulin and insulin resistant by homeostasis model assessment of insulin resistant (HOMA –IR).[7]

HOMA –IR=(fasting serum insulin μm/ml multiplied by fasting plasma glucose (mg/dl). Venous blood was taken under complete aseptic conditions and the instructions of the manufacturer of the insulin assay was observed. Insulin was estimated using Enzyme Immunoassay Kit which is a solid phase enzyme linked immunosorbant assay (ELISA).[7]

Pelvi-Abdominal Ultrasonography:
Abdominal ultrasound was done (with patients fasted for 6 hours) for evaluation of liver (including size, echo pattern and portal vein), spleen, gall bladder and kidneys (including presence of stones). (LOGICLG) with a convex probe (3.75MHX) was used. Upper

gastrointestinal endoscope was done after getting patient's consent. The procedures included complete evaluation of the esophagus, stomach and duodenum. Two antral biopsy samples were taken under complete aseptic conditions. The biopsies were preserved in a sterile container using diluted formalin solution.

Histopathological examination of the antral biopsies:
Routinely processed Formalin-fixed paraffin embedded gastric antral tissues were used in this study.

Three four micron thick serial sections mounted on grease free slides were subjected to H & E (haematoxylin and eosin) stain for histopathological examination to show the degree and activity of gastritis, presence of dysplasia or metaplasia. Giemsa stain was done for identification of *H. pylori* organism. All specimens were investigated by one histopathologist who was blinded to the results of HOMA -IR. Patients were divided into two groups according to the presence of H. pylori infection:

Group A: *H. pylori* positive patients
Group B: *H. pylori* negative patients

All patients were informed about the study protocol and written consent was obtained from them.

Statistical analysis:
This study is an observational (cohort, case control and cross- sectional study). The collected data were tabulated and analyzed using SPPS (Statistical Package for Social Science) Program version 17 software. The data were parametric or non-parametric, categorical or quantitative. The statistical analysis was done accordingly.[8]

Statistical tests:
Descriptive statistics were presented by mean ± SD for quantitative data and frequencies (no %) for categorical variables data. Analytic statistics were done using chi-square $(X)^2$ tests, and student T test. The accepted level of significance in this study was $p < 0.05$.

RESULTS

In the present study the patients with *H. pylori* positive was 56.7% and patients with *H. pylori* negative was 43.3%. There was statistical significant association between the groups as regard to IR (3.68±0.58ng/ml), (2.23±0.37ng/ml) respectively, p value <0.001 (Table I).The other parameters and investigations between the groups were of no statistical significant. (p value >0.005 (Table I, II).

Table I. The sex distribution, symptoms and the results of investigations between the 2 groups

	Group (B)		Group(A)		Total		X^2	p
	No.	%	No.	%	No.	%		
Female	22	56.4%	25	49.0%	47	52.2%	0.5	>0.05
Male	17	43.6%	26	51.0%	43	47.8%		

Symptoms of the patients		Group (B) (n=39)		Group(A) (n=51)		Total		X^2	p
		No.	%	No.	%	No	%		
Nausea	No	31	79.5%	44	86.3%	75	83.3%	0.3	>0.05
	Yes	8	20.5%	7	13.7%	15	16.7%		
Vomiting	No	19	48.7%	24	47.1%	43	47.8%	0.1	>0.05
	Yes	20	51.3%	27	52.9%	47	52.2%		
Hiccup	No	29	74.4%	39	76.5%	68	75.6%	0.1	>0.05
	Yes	10	25.6%	12	23.5%	22	24.4%		
Epigastric pain	No	5	12.8%	9	17.6%	14	15.6%	0.4	>0.05
	Yes	34	87.2%	42	82.4%	76	84.4%		
Heartburn	No	28	71.8%	28	54.9%	56	62.2%	2.7	>0.05
	Yes	11	28.2%	23	45.1%	34	37.8%		
Eructation	No	32	82.1%	45	88.2%	77	85.6%	0.7	>0.05
	Yes	7	17.9%	6	11.8%	13	14.4%		

Abdominal US		Group (B) (n=39)		Group(A) (n=51)		Total		X^2	p
		N	%	N	%	N	%		
Liver	Normal	32	82.05%	46	90.2%	78	86.6%	0.7	>0.05
	Bright hepatomegaly	5	12.8%	4	7.8%	9	10%		
	chronic liver diseases	2	5.15%	1	2%	3	3.4%		
Gall bladder	Normal	32	82.1%	43	82.4%	75	83.3%	0.1	>0.05
	Gall bladder stones	7	17.9%	8	15.7%	15	16.7%		
Spleen	Normal	31	79.5%	44	86.3%	75	83.3%	0.7	>0.05
	Enlarged	8	20.5%	7	13.7%	15	16.7%		
Kidneys	Normal	34	87.2%	37	72.5%	71	78.9%	2.8	>0.05
	Renal Stones	5	12.8	14	27.5	19	21.1		

Endoscopic finding		**(B) No**	**Percentage (%)**	**(A) No**	**Percentage (%)**	**total**		**X^2**	
	Normal	32	82.05%	46	90.2%	78	86.6%	0.7	>0.05
Esophagitis	No	28	71.8%	40	78.4%	68	75.6%	0.5	>0.05
	Yes	11	28.2%	11	21.6%	22	24.4%		
Hiatus Hernia	No	30	76.9%	34	66.7%	64	71.1%	1.1	>0.05
	Yes	9	23.1%	17	33.3%	26	28.9%		
Gastritis	No	17	43.6%	18	35.3%	35	38.9%	0.6	>0.05
	Yes	22	56.4%	33	64.7%	55	61.1%		
Duodenitis	No	33	84.6%	35	68.6%	68	75.6%	3.1	>0.05
	Yes	6	15.4%	16	31.4%	22	24.4%		
Duodenal Ulcer	No	37	94.9%	51	100.0%	88	97.8%	2.7	>0.05

This table show that there was no statistical significant between the 2 groups, as regard to sex distribution, abdominal US findings and endoscopic findings, value(P >0.05)

Table II. Laboratory findings in the studied groups (CBC,serum albumin and creatinine by Mean and SD

		N	Mean	Std. Deviation	t	p
Hb (gm/dl)	Group (B)	39	11.2333	2.21637	2.2	>0.05
	Group (A)	51	12.0471	1.18665		
WBCS White cell count (c/ mm3)	Group (B)	39	7632.1	2339.91473	0.1	>0.05
	Group(A)	51	7611.0	2164.36951		
Platelets (c/ mm3)	Group(B)	39	293274.4	1.46088.5	0.1	>0.05
	Group(A)	51	291750.9	1.23417.9		
S. creatinine (mg/dl)	Group(B)	39	1.3769	1.75566	1.3	**>0.05**
	Group(A)	51	1.0216	0.18688		
S. albumin (gm/dl)	Group(B)	39	4.2359	0.84992	1.1	>0.05
	Group(A)	51	5.1294	5.31332		

There was no statistical significant difference between group (A),group(B) for the investigations as regard the CBC , Albumin and Creatinine.p value >0.05

Table III. show the age /BMI and IR between the studied groups

Age/BMI	N	Mean Age/BMI	SD. Age/BMI	t	p
Group (B)	39	43.05/25.14	10.58/1.08	1.3/1.8	>0.05
Group(A)	51	40.14/25.56	10.41/1.11	1.3/1.8	>0.05
IR in the studied Groups		Mean.IR	SD .IR	t	p
Group(B)	39	2.2256	.36614	13.7	<0.001
Group(A)	51	3.6804	.58070	13.7	<0.001

There was statistical significant between H. positive and H.P negative as regard to I R (P value <0.001), but no difference as regard to CBC (P value >0.05).

DISCUSSION

Although *H. pylori* seems to be a cause for gastric local inflammation, it can invade and colonize human stomach and directly interact with gastric epithelial cells. Moreover, it is associated with non-gastrointestinal tract conditions such as atherosclerosis, insulin resistance, diabetes mellitus and some autoimmune diseases.[9] The first evidence for the association between chronic *H. pylori* infection and IR was proved by authors whom reported that *H. pylori* increases IR.[2] Degenerative conditions including IR syndrome that have an increasingly high impact on aged population, their association with *H. pylori* infection which affect more than half of the world population has only recently been addressed.[4] There was no statistical significant difference with regard to the sex distribution in both groups, the clinical symptoms of the patients, abdominal ultrasound findings and the findings of endoscope examinations (Table II).[2, 4]

In the present study the patients with *H. pylori* positive was 56.7% (group A) and patients with *H. pylori* negative was 43.3% (group B) based on the histopathological diagnosis. There was no statistical significant difference with regard to the BMI and age between *H. pylori* positive patients and *H. pylori* negative patients (Table III).[10,11] Regarding hepatic echo pattern reported by abdominal ultrasonography, fatty liver was detected in 7.8% of *H. Pylori* positive cases and 12.8% of *H. Pylori* negative cases and that was of no statistical significant (Table I).[4] In the present study there was no statistical significant difference between *H. Pylori* positive and *H. Pylori* negative patients with regard to the CBC (Table II).

HOMA -IR in *H. Pylori* positive cases was 3.7 while it was 2.3 in *H. pylori* negative cases with a high statistical significant difference between the two groups (P value <0.001). This is consistent with other authors (table III).[4,11,12] The explanation for that could be chronic inflammation and alteration in counter –regulatory hormones are deemed responsible for IR pathogenesis. Although the pathogenic link between *H. pylori* infection and IR remains elusive, this infection may influence the pathophysiology of IR.[13] A significant association between increased oxidative stress and IR was studied in *H. Pylori* infection. It has been reported that *H. pylori* infection is associated with increased tissue and systemic oxidative stress that were proposed as the main cause for the development of

IR, B cell dysfunction, impaired glucose tolerance and type 2 diabetes mellitus.[14] However, others reported that decreased somatostatin and increased gastrin hormone levels in patients with *H. pylori* infection may have a role in the development of IR as somatostatin regulates pancreatic insulin secretion and has an inhibitory effect on insulin release.[2,15] Chronic inflammation and production of a large amount of pro-inflammatory and vasoactive substances as cytokines (IL-8, 10, 12) and acute phase proteins as C-reactive protein were found to involve in the pathogenesis of IR.[15] Moreover, other researchers reported that chronic inflammation promotes platelets activation and platelets – leucocyte aggregations, which were involved in IR.[16] Also it is reported that *H. pylori* infection causes chronic atrophic gastritis with concomitant decrease in vitamin B12 and folate concentrations and increases in the homocysteine level, and this may play a role in the pathogenesis of IR.[16]

In contrary others stated that there is no association between *H. pylori* infection and IR.[10,11] The explanations of this difference were due to selection of diabetic and dyslipidemic patients in the study. In addition, the diagnosis of *H. pylori* infection was done by serum H. pylori immunoglobin G antibody concentration and not by histopathological examination of antral biopsies, which is considered as the gold standard diagnostic tool.

CONCLUSION

There was a strong association between *H. pylori* positive and insulin resistant. There was no difference between *H. pylori* positive patients and *H. pylori* negative patients as regard to the symptoms and laboratory investigations. Further studies on a large number of patients to prove the association between *H. pylor*i and IR and to explore the benefit of *H. pylori* eradication in reduction of IR and vice versa.

REFERENCES

1. Cave DR. Transmission and epidemiology of Helicobacter pylori. Am J Med 1996; 100:12-17.
2. Aydemir S, Bayraktaroglu T, Sert M, et al. The effect of Helicobacter pylori on insulin resistance. Dig Dis Sci 2005; 50:2090-3.
3. Razzouk L and Muntner P. Ethnic, gender and age – related differences in patients with the metabolic syndrome. Curr Hypertens Rep 2009; 11:127–32.
4. Gen R, Demir M, Atasseven H. Effect of H-pylori eradication on insulin resistance, serum lipids and low grade inflammation. South Med J 2010;103:190- 6.
5. Eshraghian A, Eshraghian H, Ranjbar Omrani G. Insulin resistance and metabolic syndrome: is Helicobacter pylori criminal? Minerva Gastroenterol Dietol 2011; 57:379-85.
6. Polyzos SA, Kountouras J, Zavos C, Deretzi G. The association between Helicobacter pylori infection and insulin resistance: a systematic review. Helicobacter 2011; 16:79-88.
7. Banerji MA, Faridi N, Atluri R, Chaiken RL, Lebovitz HE. Body composition, visceral fat, leptin, and insulin resistance in Asian Indian men. J Clin Endocrinol Metab 1999; 84:137-44.
8. Knapp RG,Miller MC. Clinical Epidemiology and Biostatistics. Baltimore, Md: Williams & Wilkins; 1992:136.
9. Pellicano R, Fagoonee S, Rizzetto M, Ponzetto A. Helicobacter pylori and coronary heart disease: which directions for future studies? Crit Rev Microbiol 2003; 29:351-9.
10. Gao XY, Kuang HY, Liu XM, et al. Circulating ghrelin/obestatin ratio in subjects with Helicobacter pylori infection. Nutrition 2009; 25:506-11.
11. Ozdem S, Akcam M, Yilmaz A, Artan R. Insulin resistance in children with Helicobacter pylori infection. J Endocrinol Invest 2007; 30:236-40.
12. Gunji T, Matsuhashi N, Sato H, et al. Helicobacter pylori infection significantly increases insulin resistance in the asymptomatic Japanese population. Helicobacter 2009; 14:144-50.
13. Polyzos SA, Kountouras J, Zavos C. Nonalcoholic fatty liver disease: the pathogenic roles of insulin resistance and adipocytokines. Curr Mol Med 2009; 72:299-314.
14. Aslan M, Horoz M, Nazligul Y, et al. Insulin resistance in H pylori infection and its association with oxidative stress. World J Gastroenterol 2006; 12:6865-8.
15. Basso D, Plebani M, Kusters JG. Pathogenesis of Helicobacter pylori infection. Helicobacter 2010; 15:14-20.
16. Hsieh MJ, Chen CC, Lee TH, et al. Metabolic syndrome and homocysteine level as predictors of the severity of coronary artery disease in patients with carotid stenosis. Am J Med Sci 2009;338:447-52.