

Research Article

Assessment of the Relation between Helicobacter pylori Infection and Insulin Resistance

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Abstract

Objective: The association of H pylori infection with insulin resistance has been reported. The present study was performed to assess the role H. pylori infection in the development of insulin resistance.

Patients and Methods: Our study included 100 healthy subjects with or without gastric manifestations not hypertensive or diabetic, neither had renal, hepatic or cardiac diseases with normal BMI. Selected subjects were divided into 2 groups according to whether they were serum H. pylori IgG positive or negative. Group (I): consists of 50 subjects who were seronegative. Group (II) consists of 50 subjects who were seropositive. Both groups were subjected to the following: medical history and clinical examinations with special emphasis to measurements of BMI, blood pressure. Anti H. pylori IgG antibodies were detected in the serum using ELISA methods confirmed by detection of H. pylori antigen in the stool. The index of insulin resistance was calculated on the basis of fasting serum glucose and insulin according to homeostasis model assessment (HOMA) method; $HOMA-IR = \text{fasting serum insulin } (\mu\text{U/ml}) \times \text{fasting serum glucose (mg/dL)} / 405$.

Results: The following items were significantly higher in group II when compared to group I; FBS, serum insulin, HOMA-IR, total cholesterol, LDL-cholesterol and serum levels of H. pylori IgG ($p < 0.01$ for all), while serum levels of HDL-cholesterol was significantly lower in group II when compared to group I ($p < 0.01$). On the other hand there were no significant differences between two groups as regards age, sex, Arterial blood pressure, liver function tests, renal function tests and BMI. Serum levels of H. Pylori IgG were correlated with serum levels of insulin ($r = 0.713$, $p < 0.01$), HOMA-IR ($r = 0.624$, $p < 0.017$) and fasting blood sugar ($r = 0.0628$, $p < 0.01$).

Conclusions: There is a potential association between H. pylori infection and IR; further studies are needed to strengthen this association and to clarify whether there is a causative link between them.

Keywords: Helicobacter pylori infection; Insulin; H pylori; Diabetic, Gastric manifestations

Introduction

Helicobacter pylorus is a gram-negative, spiral-shaped pathogenic bacterium that specifically colonizes in the gastric epithelium and causes chronic gastritis, peptic ulcer disease, and/or gastric malignancies.

Peptic ulcer disease is now approached as an infectious dis-

ease, in which elimination of the causative agent cures the condition. The role of H. pylori infection in gastric cancers is increasingly recognized, and its role in other diseases of the upper gastrointestinal tract is being evaluated.

It defined Insulin Resistance as inhibition of insulin stimulation of several metabolic pathways including glucose transport, glycogen synthesis and anti-lipolysis, and it is of considerable clinical relevance because it is patho-physiologically linked to several serious medical problems including type 2 diabetes, hypertension,

atherogenic dyslipidemia, abnormalities of blood coagulation and fibrinolysis and non-alcoholic fatty liver disease.

The association of H pylori infection with insulin resistance has been reported. Although it is a controversial subject, some recent studies showed the role of H. pylori in non-gastric pathologies such as coronary artery disease, insulin resistance, and some autoimmune diseases, although there is some controversy about this role [1].

Investigating the impact of H. pylori infection as a risk factor for insulin resistance might support and help understand its effect on coronary artery diseases and atherosclerosis as well. Although there are a few studies on this issue, the pathophysiology of this relationship is not fully understood. Several studies showed that insulin resistance might develop in the presence of inflammation. Another mechanism described for insulin resistance is alterations in counter-regulatory hormones. H. pylori might be responsible for changes in counter-regulatory hormones [2].

The present study was performed to assess the role H. pylori infection in the development of insulin resistance.

Patients and methods

Our study was a case-control (non-randomized) conducted in Bab -El Sharia University Hospital -Al Azhar University (in the period between 1/3/2015 and 1/9/2015) on 100 persons who were healthy with or without gastric manifestations not hypertensive or diabetic, neither had renal, hepatic or cardiac diseases with normal BMI. Patients who were treated previously by H. pylori eradication therapy at any time of their lives or who had Proton Pump Inhibitors (PPIs) or H2 -Blockers, in previous 6 months and patients who were taking corticosteroids, diuretics or contraceptive pills were excluded from the study.

Selected subjects were divided into 2 groups according to whether they were serum H. Pylori IgG positive or negative. Group (I): consists of 50 subjects who were seronegative. Group (II): consists of 50 subjects who were seropositive. Both groups

were subjected to the following: medical history stressing on: age, sex, history suggesting chronic diseases & drug intake, family history of DM and chronic liver, renal or cardiovascular diseases. Clinical examinations with special emphasis to measurements of BMI, blood pressure.

Anti H. pylori IgG antibodies were detected in the serum using ELISA methods (H. pylori is positive when the serum level exceeds 20 U/ml) confirmed by detection of H. pylori antigen in the stool. Fasting insulin was estimated by monoclonal immune radioinertic assay [3]. In addition to measurements of lasting blood sugar, ALT, AST, albumin, serum creatinine, total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides.

The index of insulin resistance was calculated on the basis of fasting serum glucose and insulin according to homeostasis model assessment (HOMA) method; $MOMA-IR = \text{fasting serum insulin (pU/ml)} \times \text{fasting serum glucose (mg/dl)} / 405$ [4].

Statistical analysis: Data were expressed as Mean \pm SD. Differences between groups were tested with tailed-student's t-test for unpaired data. For correlation analysis, Pearson's correlation coefficient was calculated. A value of $P < 0.01$ and a value of $r > 0.05$ were considered significant.

Result

The following items were significantly higher in group II when compared to group I; FBS ($p < 0.01$), serum insulin ($p < 0.01$), HOMA-IR ($p < 0.01$). Total cholesterol ($p < 0.01$), LDL-cholesterol ($p < 0.01$) and serum levels of H.pyloriIgG ($p < 0.01$). While serum levels of HDL-cholesterol was significantly lower in group II when compared to group I ($p < 0.01$). On the other hand there were no significant differences between two groups as regards age, sex, arterial blood pressure, liver function tests, renal function tests, height, weight, and BMI (Table I).

Serum levels of H. pylori IgG were correlated with serum levels of insulin ($r = 0.713$, $p < 0.01$ & Figure 2), HOMA-IR ($r = 0.624$, $p < 0.017$ fig 1) and fasting blood sugar ($r = 0.0628$, $p < 0.01$ & Figure 3).

	Group I (seronegative)	Group II (seropositive)	T value	P value
Age (years)	38.8 \pm 13.7	40.38 \pm 11.6	1.372	0.173 (NS)
Sex (M/F)	24/26	22/28	1.2	0.12(NS)
Body MI. (kg/m ²)	23.1 \pm 1.8	22.4 \pm 2.2	-1.792	0.1 (NS)
Diastolic B.P. mmHg	78.1 \pm 8.2	80 \pm 9.8	1.393	0.167(NS)
Systolic B.P. mmHg	118.7 \pm 11.3	121.1 \pm 8.9	1.821	0.72(NS)
S. Insulin (mIU/mL)	6.42 \pm 1.88	13.06 \pm 4.30	16.533	<0.01(S)
FBG (mg/dl)	92.1 \pm 10.9	101.86 \pm 17.10	6.216	<0.01(S)
HOMA-IR	1.58 \pm 0.768	3.28 \pm 1.329	12.648	<0.01(S)
IIDL-C (mg/dl)	54.2 \pm 5.840	43.96 \pm 7.08	7.794	<0.01(S)
Triglycerides (mg/dl)	123.9 \pm 28.747	149.18 \pm 20.24	4.2	<0.01(S)

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Cholesterol (mg/dl)	150.39 ±19.121	169.82 ± 19.63	5.521	<0.01(S)
ALT (IU/L)	27.4±5.5	29.3±5.1	1.340	0.183(NS)
AST (IU/L)	25.4±2.8	27.8±5.6	1.235	0.178(NS)
S. Creatinine (mg/dl)	0.8±0.2	0.8±0.3	1.092	0.278(NS)
S. Albumin (G/L)	4.4±1.2	4.2±1.1	1.793	0.76(NS)
H. pylori	8.6 ±1.4	94.7±15.4	8.7	<0.01(S)

Table 1: Shows comparison between two groups as regarded all studied parameters

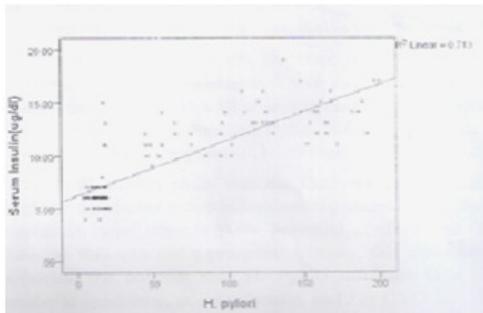


Figure 1: Shows correlation between Anti H. pylori titer and ROMA-IR. There is a highly significant correlation between both parameters ($r=0.624$, $p<0.01$).

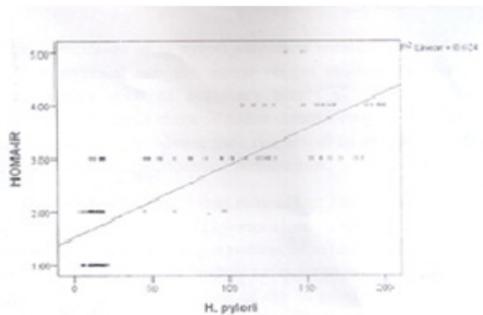


Figure 2: Shows correlation between H. pylori IgG and S. Insulin. There was a highly significant correlation between both parameters ($r=0.713$, p -value <0.01).

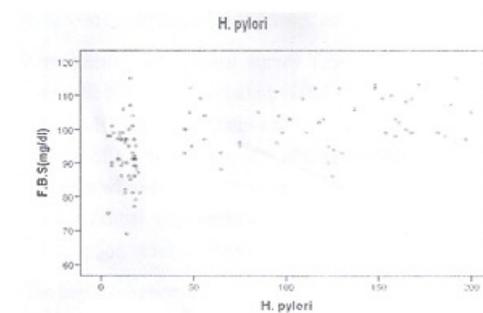


Figure 3: Shows correlation between H. pylori IgG and FBS, there is correlation parameters <0.01). Highly significant between both ($r=0.628$, p -value).

	Group 1 Mean ± SD	Group 2 Mean ± SD	T value	P value
FBS (mg/dl)	92.1 ± 10.9	101.86 ± 17.10	6.216	<0.01
TC (mg/dl)	150.39 ± 19.121	169.82 ± 19.63	5.521	<0.01
TG (mg/dl)	123.9 ± 28.747	149.18 ± 20.24	4.2	<0.01
HDL (mg/dl)	41.56 ± 5.840	47.42 ± 7.08	7.794	<0.01

Table 2: Shows the comparison between the two groups as regards gluco-parameters and lipid profile and by using independent student T test it showed that the difference is highly significant ($p<0.01$).

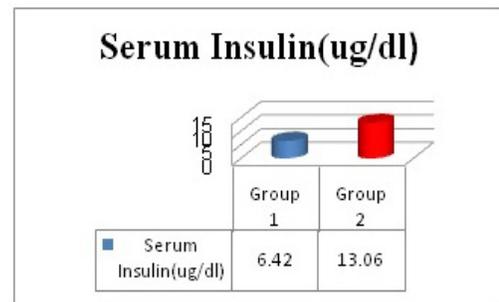


Figure 4: Shows comparison between the two groups as regard S. Insulin. There was a high significant difference between the two groups.

	Group 1 Mean ± SD	Group 2 Mean ± SD	T value	P value
FBS (mg/dl)	92.1 ± 10.9	101.86 ± 17.10	6.216	<0.01
S. Insulin	6.42 ± 1.88	13.06 ± 4.30	16.133	<0.01
HOMA-IR	1.58 ± 0.768	3.28 ± 1.329	12.648	<0.01

Table 3: Shows the relation of H. pylori infection two groups to gluco-parameters and by using independent T test it show that the relation between FBG, S. Insulin, HOMA-IR and H. pylori infection is highly significant ($p<0.01$).

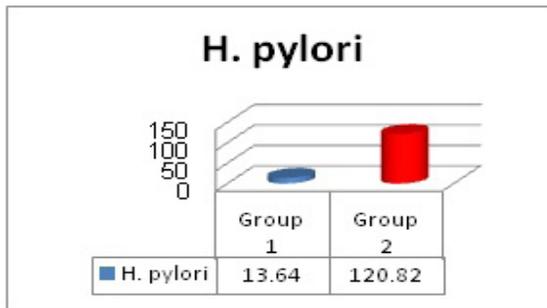


Figure 5: Shows comparison between the two groups as regard serum H.pyloriIgGlevel. There was a high significant difference between the two group- value = -16.201, p - value <0.01.

Discussion

The association of H pylori infection with insulin resistance has been reported. Although it is a controversial subject, some recent studies showed the role of H. pylori in non-gastric pathologies such as coronary artery disease, insulin resistance, and some autoimmune diseases, although there is some controversy about this role [5].

The aim of this study is to investigate the effect of H. pylori infection on insulin resistance (HOMA-IR scores) in asymptomatic population.

In this study all factors that may affect Insulin resistance were eliminated such as old age, sex difference, Obesity, Hypertension, smoking, strong family history of diabetes and hypertension, a trial to get results of effect of H. pylori infection per sec on Insulin resistance. HOMA-IR score was highly associated with H. pylori infection. HOMA-IR in the infected group was greater than that of the non-infected group. On the other hand, H.pylori infected group was significantly associated with increased serum triglycerides, total Cholesterol but with lower HDL-Cholesterol Level, that is in agreement with [6].

To date, a few studies in the literature have described the correlation between H. pylori infection and insulin resistance. Three case-control studies, in accordance with this study, demonstrated that HOMA-IR scores in cases with H. pylori infection was significantly higher than those in cases without H. Pylori infection, suggestive of a potential role of H. pylori infection and increasing insulin resistance [7].

Gunji et al. [8] study was the first report providing the direct evidence that H. Pylori infection significantly and independently increases insulin resistance in a large asymptomatic population, after adjusting for potential confounders of metabolic and lifestyle features. Although this was not a prospective study, this cross-sectional survey of a large population supported the concept that H. Pylori infection is a potential risk factor in developing metabolic

syndrome, atherosclerosis, and/or CVD.

Retrospective longitudinal survey found that eradication of H. Pylori did not improve metabolic parameters including HOMA-IR scores [9]. Thus, the interaction between H. pylori sero status and insulin resistance remains controversial. Most importantly, because of a small sample size of cases enrolled in those previous studies, it has remained uncertain whether the effect of H. pylori on insulin resistance, if present, was independent of other potential confounders, including central adiposity, metabolic parameters, alcohol consumption, smoking status, dietary habits, and physical activity [10].

The key mechanisms of pathologic and physiologic events involved in H. pylori infection is initiation and continuation of inflammatory response in the hosts. H pylori infection facilitates the disturbance of cytokines networks, including TNF-a, IL-I b, IL-6, IL-8 and IFN-v [11]. H pylori infection also causes accumulation of reactive oxygen species through activation of leukocytes and macrophages. Alterations of cytokine profiles, oxidative stress, and subsequent inflammation status are responsible for developing insulin resistance in the hosts [12].

Indeed, chronic inflammation, represented by elevation of C-reactive protein and IL-6, are reported to have a correlation with subsequent onset of type-2 diabetes. Statins, which down-regulate CRP in an LDL-C independent manner, reduced the risk of diabetes and atherosclerosis. In this context, to gain deeper insight into the biologic pathway from H. pylori infection to increasing insulin resistance, it is necessary to explore the details of cytokine kinetics, inflammatory conditions, and oxidative stress between H. pylori-seropositive and sero negative must be considered in interpreting the results of this study. First, evaluation of the H. pylori infection status in this study was based on the detection of H. pylori-specific antibody alone. Although specificity and sensitivity of the ELISA in this study was more than 85%, a minority of false-positive or false-negative subjects might be included in this study subjects [13].

Second, because of cross-sectional design in this study, results do not necessarily imply a causative role of H. pylori for developing insulin resistance in infected hosts. However, it is reported that H. pylori infection is usually acquired early in life. Thus, results imply that H. pylori infection in childhood eventually caused the impairment of insulin sensitivity through life-long course of infected individuals. Further clinical studies in prospective design are required to clarify this interaction [8].

Third, insulin resistance was evaluated by HOMA-IR scores alone. Insulin resistance is a cluster of physiologic disorders including cytokine disturbance, subclinical inflammation, reactive oxygen species, and macrophage functions. It is no doubt that the estimation of these cytokine and chemokine profiles would pro-

vide more detailed aspects of insulin resistance [14].

An association between H. Pylori infection and Insulin Resistance seems to be appealing, given that almost half of the world's population is affected by H. Pylori infection, the prevalence of Insulin Resistance is increasing worldwide and, if an association was proved, H. pylori eradication might have therapeutic beneficial effects on Insulin Resistance-related morbidity, including diabetes and NAFLD [14]. Nevertheless, existing evidence remains insufficient either to support a solid association between H. pylori infection and HOMA-IR or to introduce H. pylori eradication for treating IR.

In conclusion, although results of this study and previous studies seem to indicate that: There is a potential association between H. pylori infection and IR, Further studies are needed to strengthen this association and to clarify whether there is a causative link between them. If a causal link between H. pylori infection and IR is confirmed in the future, this may have a major impact on the pathophysiology and management of Insulin Resistance and its sequel as metabolic syndrome, including Type 2 DM, hypertension, dyslipidemia and Non-Alcoholic Fatty Liver Disease.

References

1. Sukanuma M, Yamaguchi K, Ono Y, Matsumoto H, Hayashi T, et al. (2008) TNF-alpha-inducing protein, a carcinogenic factor secreted from H. pylori, enters gastric cancer cells. *Int J Cancer* 123: 117-122.
2. Hidekazu S, Francesco FG, Toshihiro N and Antonio G (2011) Intra-gastric Manifestations of Helicobacter pylori Infection *Helicobacter* 161: 65-69.
3. Aydemir S, Bayraktaroglu T, Sert M, Sokmen C, Atmaca H, et al. (2005) The effect of Helicobacter pylori on insulin resistance. *Dig Dis Sci* 50: 2090-2093.
4. Marschner I, Bottermann P, Erhardt F, Linke R, Löffler G, et al. (1974) Group experiments on the radioimmunological insulin determination. *HormMetab Res* 6: 293-296.
5. Matthews DR, HoskerJP, Rudenski AS, Turner RC. (1985): Homeostasis model assessment: insulin resistance and beta cell function from fasting plasma glucose and insulin concentration in man. *Diabetologia*; 28: 412-429.
6. Gunji T, Matsidiashi N, Sato H, Fujiabayashi K, Okumura M, Sasabc N, et al. (2009): Helicobacter pylori infection significantly increases insulin resistance in the asymptomatic Japanese population. *Helicobacter* 14:144-50.
7. Aydemir S, Bayraktaroglu T, Sert M, Sokmen C, Atmaca H, et al. (2005) The effect of Helicobacter pylori on insulin resistance. *Dig Dis Sci* 50: 2090-2093.
8. Park SH, Jeon WK, Kim SH, Kim HJ, Park DI, et al. (2005) Helicobacter pylori eradication has no effect on metabolic and inflammatory parameters. *J Natl Med Assoc* 97: 508-513.
9. Sukanuma M, Yamaguchi K, Ono Y, Matsumoto H, Hayashi T, et al. (2008) TNF-alpha-inducing protein, a carcinogenic factor secreted from H. pylori, enters gastric cancer cells. *Int J Cancer* 123: 117-122.
10. Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, et al. (2004) Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med* 350: 2362-2374.
11. Abadi AT, Taghvaei T, Mobarez AM, Carpenter BM, Merrell DS (2011) Frequency of antibiotic resistance in Helicobacter pylori strains isolated from the northern population of Iran. *J Microbiol* 49: 987-993.
12. Aydemir S, Bayraktaroglu T, Sert M, Sokmen C, Atmaca H, et al. (2005) The effect of Helicobacter pylori on insulin resistance. *Dig Dis Sci* 50: 2090-2093.
13. Polyzos SA, Kountouras J, Zavos C, Deretzi G (2011) The potential adverse role of leptin resistance in nonalcoholic fatty liver disease: a hypothesis based on critical review of the literature. *J ClinGastroenterol* 45: 50-54.
14. Sebastian S and Pierre M (2011): Helicobacter pylori Infection" *N Engl J Med* 363:1175-1186.