Helicobacter Pylori Infection and Metabolic Parameters: Is There an Association in Elderly Population?

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ABSTRACT

Background: The association between *Helicobacter pylori* (HP), as one of the most prevalent infections, and serum glucose level was inconsistent with previous studies. Moreover, there are contradictory reports about the relationship between HP infection and lipid profile. The purpose of this study was to determine the relationship between HP infection with glycemic and lipid profiles in elderly people.

Methods: This cross-sectional study was conducted on 1,300 subjects over 60 years in Amirkola Health and Ageing Project. After using a standard questionnaire, the venous sampling was done to determine FBS, triglyceride (TG), cholesterol, low density lipoprotein (LDL), high-density lipoprotein (HDL) and IgG anti-HP after a 12-h overnight fast. The information about the individuals was analyzed using SPSS-17. The $P < 0.05$ was considered statistically significant.

Results: The prevalence of HP infection in diabetic and nondiabetic subjects was 77.5% and 75.7%, respectively, which had no statistically significant difference. Also, there was no significant difference between the serum lipid level including TG, LDL and HDL cholesterol with levels of anti-HP antibodies. The rate of HP infection in patients with hypertension was 75% and 78.3% in healthy patients, in which the difference was not statistically significant. In terms of body mass index (BMI), the prevalence of infection in the group with normal BMI was 77.3% and for the overweight and obese elderly population, it was 74.7%, and 77.5%, respectively ($P = 0.445$).

Conclusions: The findings revealed that in a large population of elderly in the northern part of Iran, HP infection is not associated with BMI, serum glucose and lipid profile as well as blood pressure.

Keywords: Body mass index and hypertension, diabetes mellitus, glucose level, *Helicobacter pylori,* lipid profile, triglyceride and cholesterol

Original Article

INTRODUCTION

Since the discovery of gram-negative bacilli *Helicobacter pylori* (HP) by "Varan" and "Marshall" in 1984, a world-wide

distribution of this bacterium has been shown.[1] It is estimated that about half of the world's population is infected, and its prevalence is highly variable in developing countries and lower in developed countries;[2] in a study in northern part of Iran, the number of infected males and females has been reported 68.7%, and 73.7%, respectively.[3]

The infection in acute condition induces a polymorphonuclear cell infiltration in the gastric mucosa in which if the infection is not efficiently cleaned, a chronic infiltration of mononuclear cells can be replaced. Being replaced by mononuclear cells can cause the local production of proinflammatory cytokines that are responsible for the remote tissues and organic system complications of this bacteria.[4]

Besides gastric involvement, HP can also cause extra digestive problems. Although the present information has not still completely proven the relationship between HP with these complications, but it cannot be ruled out.[5] These complications include endocrine disorders, such as diabetes mellitus, osteoporosis, hyperparathyroidism, obesity, autoimmune thyroid disease, and hyperlipidemia.[6]

The relationship between HP and diabetes mellitus was first reported in 1989.[7] It is possible that immunosuppression in diabetes mellitus can increase the risk of HP infection and perhaps justifies various reports based on the prevalence of HP infection in patients with diabetes.[8,9] However, the results of a number of studies showed no association between HP infection and diabetes,[1,7,9-12] and in a study conducted by Zelenková *et al*., the serological prevalence of HP infection was reported less in diabetic patients than in healthy subjects.[13] The results of the relationship between HP infection and dyslipidemia are described in both high levels of low-density lipoprotein (LDL) cholesterol and low, high-density lipoprotein (HDL). It can be justified that chronic infection with HP can lead lipid profile toward atherogenic by activating proinflammatory cytokines like tumor necrosis factor-α, interferon-α, interleukin (IL)-6, IL-1. These cytokines affect fat metabolism in several ways, such as activating lipoprotein lipase in adipose tissue, stimulating hepatic synthesis of fatty acids and affecting lipolysis.[14]

There are different results in terms of the relationship between HP infection and obesity. Some studies stated that HP infection in overweight individuals does not increase and thus being seronegative is not associated with body mass index (BMI).[15-17] Other researchers hypothesized that the absence of HP infection in childhood is associated with an increased risk of morbid obesity, an inverse association between HP infection and obesity has been described;[18] and finally, some studies found this infection associated with increased BMI due to the decreasing effect of HP on gastric movements.[19]

Given the high prevalence of HP infection in Mazandaran Province (78%),[3] the study of the relationship between this infection and glucose and lipid markers in this region seems logical. Hence, this study aimed to investigate the blood glucose level, lipid, blood pressure and BMI in patients with HP infection compared with healthy subjects.

METHODS

This cross-sectional study was conducted on a total number of 1,616 elderly subjects initially enrolled in Amirkola Health and Ageing Project.[20] Subjects with the previous history of anti-HP therapy, recent use of antibiotics or antisecretory drugs were excluded and finally 1300 subjects were studied.

A questionnaire that includes the demographic, pharmaceutical history, previous medical history, height, weight was filled out by one of the health center staff.

In this study, hypertension was defined based on blood pressure measurement using "Omron" pressure gauge M3 Intelligence Model, in a resting and standing position with the standard procedure. The diagnosis of hypertension was made according to systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or history of hypertension and the use of antihypertensive medications.[4]

Weight was measured by "Seca" digital scale with the accuracy of 0.1 kg and with light clothes; and height was measured by stadiometer with an error of 0.5 cm; and BMI was calculated by dividing weight (kilograms) to the square of height (meters). After calculating BMI, the patients were divided into three groups: Nonoverweight (BMI < 25), overweight (BMI: 25-30) and obese (BMI > 30).[9] After a 12-h overnight fast,

15 cc of blood was collected from the antecubital vein for triglycerides (TGs), total cholesterol, HDL, LDL, and blood glucose in order to measure the anti-HP antibody titer, and poured into the tubes containing ethylenediaminetetraacetic acid to obtain centrifuged plasma. Diagnosis of HP was made by measuring IgG antibody titers against HP using ELISA method by kits "Patan Elm" made in Iran. IgG concentration samples ≤20 ur/ml were considered negative and >20 ur/ml positive.

Diabetic individuals include those under the treatment with antidiabetic drugs and with fasting plasma glucose ≥126 mg based on the American Diabetes Association (ADA) standards[4] defined as diabetic patients who referred to the Endocrinology Department of Ayatollah Rouhani and Shahid Beheshti Hospitals.

Furthermore, the LDL level was calculated using Friedewald formula. Total cholesterol above 200 mg/dl, TGs above 200 mg/dl, LDL >160 mg/dl were high and HDL < 40 in men and 50 in women was considered low.[4]

The research protocol was approved by the Ethical Committee of Babol University of Medical Sciences and all subjects were requested to fill out the voluntary informed consent before the study.

Data were analyzed using SPSS software version 17 (Chicago, IL, USA) using Pearson correlation coefficient, Chi-square and ANOVA test. Also, $P \leq 0.05$ was defined as the level of significance.

RESULTS

In this study 1,300 subjects with an average age of 69.23 ± 7.31 were enrolled, of which 759 persons (58.4%) were males, and 541 (41.6%) were females.

Among the subjects, 305 patients (30.4%) were diabetics and 808 patients (62.2%) hypertensive.

According to BMI, 440 patients (33.8%) were normal, 549 patients (42.2%) overweight and 311 (23.9%) obese.

In terms of HP infection, 991 patients (76.2%) were positive for the antibody and the average of age in HP positive subjects was significantly higher than the seronegative group (70.2 ± 7.8 vs. 68.9 ± 7.2).

The prevalence of *H. pylori* infection in the diabetic and nondiabetic group was 303 patients (77.5%) and 688 patients (75.7%), respectively; this difference was not statistically significant [Table 1].

Table 1: Frequency of HP infection in different groups of elderly people based on gender, diabetes, hypertension and BMI

Variable	HP positive (%)	HP negative (%)	*P*
Gender			
Male	594 (78.3)	165 (21.7)	0.42
Female	397 (73.4)	144 (26.6)	
Diabetes			
Yes	303 (77.5)	88 (22.5)	0.523
No	688 (75.7)	221 (24/3)	
Hypertension			
Yes	606 (75)	202 (25)	0.202
No	385 (78.3)	107 (21.7)	
BMI			
<25	340 (77.3)	100 (22.7)	0.445
25-29.9	410 (74.7)	139 (25.3)	
≥30	241 (77.5)	70 (22.5)	

HP=*Helicobacter pylori*, BMI=Body mass index

The prevalence of HP infection in the healthy and hypertensive groups was 385 patients (78.3%) and 606 patients (75%), respectively, in which this difference was not significant. Also, the mean value of systolic and diastolic blood pressure was almost the same in two groups based on HP infection.

The prevalence of this infection in patients with normal BMI was 77.3% and in the overweight and obese elderly was 74.7% and 77.5%, respectively, wherein the difference was not statistically significant.

The rate of HP infection in elderly men and women was 78.3%, and 73.4%, respectively, which was not statistically significant. Blood lipids, including TGs, cholesterol, HDL and LDL in patients with HP positive and negative was similar [Figure 1], and there was no relationship between the antibody levels and the different amounts of lipids [Figure 2].

DISCUSSION

The results from various studies indicate that the prevalence of HP infection rises with age, but the rate in both genders (male and female) is seen almost the same which has also been found in the present study. In this survey, 77.5% of the diabetic group and 75.7% of nondiabetic groups were HP-positive which was not statistically significant. In other words, the prevalence of HP infection in the elderly with diabetes was not higher than the

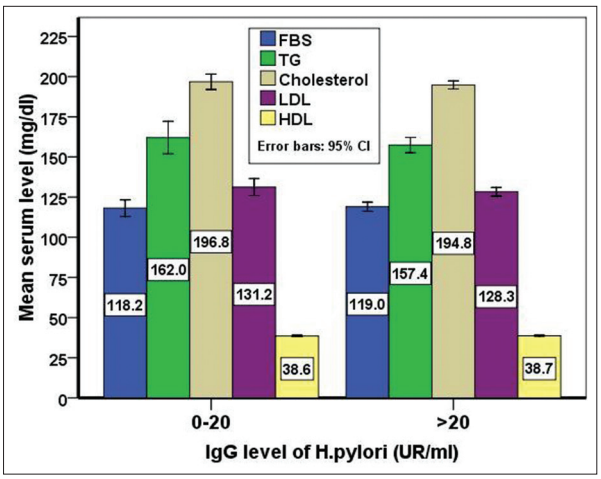

Figure 1: Mean blood glucose and lipid levels in elderly subjects with *Helicobacter pylori* infection (IgG>20) and healthy (IgG<20)

nondiabetics. Thus diabetes is not a risk factor for HP infection.

These findings were confirmed by the results of other studies that there is no relationship between HP infection and diabetes.[1,7,11-12,21] Even in a study conducted by Zelenková *et al*., the prevalence of HP infection in diabetics has been reported less in the normal subjects.[13]

However, some studies have linked diabetics with HP infection and have known diabetes as a predisposing factor to infection with HP[2,22-27] possibly because the chemical changes of gastric mucosa and immune suppression have been reported in these patients due to reduced gastric movement and its peristaltic activity. The large sample size of the subjects in the present cross-sectional study in comparison with the relatively small samples in case studies can be the reason of the different results. Although Gunji *et al*., in a cross-sectional study in Japan on 7,394 patients with HP infection clearly associated it with metabolic syndrome.[25]

In terms of lipid parameter in the present study, the serum level of blood lipids, including TGs, cholesterol, HDL and LDL was similar in patients with HP positive and negative, and there was no relationship between the antibody levels and different amounts of lipids which was the same with the results of other studies.[28,29] However, contradictory findings were reported in some studies.[30-32] In the study of Hack-Lyoung *et al*., HP infection was associated with the higher levels of LDL, but they did not report any relation with TGs and HDL.[31] While in Hoffmeister *et al*.'s study, a significant relationship between HP infection with reduced levels of HDL, cholesterol/HDL, reducing ApoA1 and increasing ApoB was observed.[32]

In Satoh *et al*.'s study, HP infection in Japanese patients was significantly associated with increased HDL and decreased LDL.[30]

In terms of HP infection and obesity, there are also different results; the present study showed no relationship between HP infection and obesity.

The study of Kyriazanos *et al*. also expressed no relationship between the prevalence of HP infection in patients with overweight and being seropositive BMI is not associated with HP infection.[15-17] Even in a study, an inverse association between HP infection and obesity has been reported.[18] However, some studies found a relationship between this infection and increased BMI regarding the effect of HP on decreasing the gastric movements.[19]

There are also different results in terms of the relationship between HP infection and hypertension. No relationship between these two categories was found in Harvey *et al*.'s study;[33] although Migneco *et al*. observed a relationship between HP infection and hypertension, with the eradication of the infection, the high blood pressure (especially diastolic blood pressure) improved. This study may explain the relationship in a way that following the release of vasoactive substances from the primary site of infection, a cascade of cytokines is activated and may damage the endothelium and causes hypertension.[34]

Although some data showed that virulent strains of HP, such as cytotoxin-associated gene ($CagA^+$) are associated with many extra-digestive manifestations such as type 2 diabetes mellitus and its complications due to an immune-mediated injury at the level of the endothelium caused by a systemic immune response to the infection, we did not deal with this issue in our study.[34]

The association of metabolic parameters and HP is still controversial with emphasis on the possible linkage between them. However, the high prevalence of both might explain the coincidence and further studies are needed to elucidate whether any causative link exists.

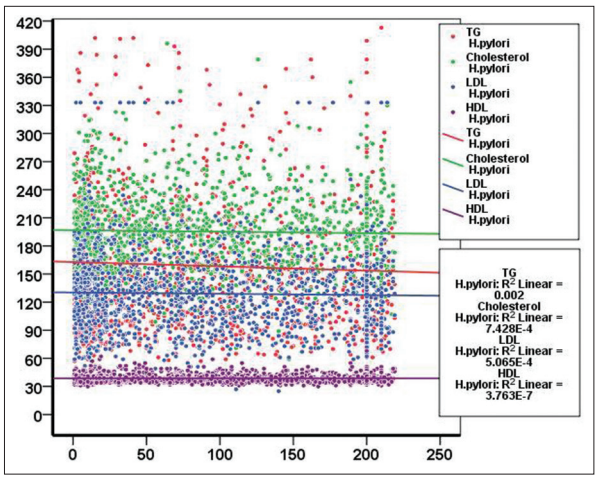

Figure 2: Distribution of *Helicobacter pylori* antibody levels in terms of the different levels of triglyceride, cholesterol, low density lipoprotein and high density lipoprotein in the elderly subjects

CONCLUSIONS

The findings revealed that in a large population of elderly in northern part of Iran, HP infection is not associated with BMI, serum glucose and lipid profile as well as blood pressure even after adjustment for other risk factors.

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