Association between *Helicobacter pylori* and Serum Leptin in Iranian Dyspeptic Patients

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ABSTRACT

BACKGROUND

To investigate any possible relationship between serum leptin level and *H. pylori* infection in dyspeptic Iranian adults.

METHODS

A total of 153 dyspeptic patients referring to Firoozgar hospital for esophagogastroduodenoscopy were enrolled in the study. Serum leptin level was measured before endoscopy, after overnight fasting. Two biopsy specimens were taken from antrum for each patient during endoscopy: one to detect *H. pylori* infection by Rapid Urease Test (RUT) and the other evaluated by an expert pathologist, blind to the RUT results and patients. Serum leptin level was compared between *H.pylori*-positive negative groups.

RESULTS

A total of 153 dyspeptic patients with the mean age of 43.2±14.3 years were evaluated. The overall prevalence of *H.pylori* infection was 49.6%. *H.pylori* infection was significantly associated with serum leptin level ($p<0.001$). In addition, we found a significant relationship between serum leptin level and gender ($p<0.02$). Furthermore, serum leptin level was correlated with age (r=0.17, $p=0.0031$). However, the *H.pylori*-positive group was older in comparison to the *H.pylori* negative group (45.65±13.9 vs. 40.7±14.13, $p=0.035$). The two groups were not significantly different in terms of gender, height, weight or BMI.

CONCLUSION

H.pylori infection may influence leptin production. Advanced age might expose the individual to *H.pylori* infection and consequently influence the leptin level.

KEYWORDS

Helicobacter pylori; Leptin; Dyspeptic

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INTRODUCTION

Helicobacter pylori (*H.pylori*: HP) is a Gram-negative microaerophilic bacillus[1] which colonizes the human stomach[2] and is respon-

sible for chronic gastritis, atrophic gastritis, peptic ulcer disease, gastric mucosal associated lymphoid tissue lymphoma and gastric adenocarcinoma.[1-4] Therefore, *H. pylori* infection is considered as class I carcinogen by World Health Organization. Furthermore, it is reportedly related to dyspepsia[5,6] Although not a fatal disease, dyspepsia often affects the patients' function and quality of life quality.[7] The incidence of *H. pylori* infection is related to socio-economic and sanitary conditions,[8] therefore, the infection is expected to be more prevalent in developing countries.[9] In Iran, *H. pylori* infection is endemic With previous studies suggesting a prevalence rate as high as 30% in some provinces, compared to only 30% in developed countries.[10,11]

Leptin, a product of Ob gene, is secreted primarily from adipose tissue cells,[12,13] but it has recently been found in gastric mucosa, as well.[13,14] Leptin exerts its effects mainly via leptin receptors which have recently been demonstrated to possess immune and inflammatory functions.[9] Serum leptin level rises with eating and the influence of gastric leptin signals satiety to hypothalamic center, providing a feedback response.[13-16] In this way, leptin regulates food intake and body weight.[2,14,16]

Several studies indicate *H.pylori* infection to be associated with serum and gastric leptin levels.[15-19] Recent studies suggest that the interaction of human immune system with *H.pylori* infection depends on the presence of leptin receptors on T lymphocytes in gastric lamina properia.[9] Eradication of *H.pylori* infection has been shown to alter serum and gastric leptin levels.[8,16] Studies by Pacifio et al.[16] and Chaung et al.[17] demonstrated decreased gastric leptin level with gastric epithelial injuries caused by *H.pylori* infection, while other reports indicate a high[5] or unchanged.[15,18,19] serum leptin levels in association with *H. pylori* infection.

Considering the high prevalence of *H.pylori* in Iran, this study is designed to assess possible associations between serum leptin level and *H.pylori* infection in dyspeptic adults using high accuracy diagnostic methods.

MATERIALS AND METHODS

This cross-sectional study was conducted between March 2009 and November 2010 in Firoozgar General Hospital. One hundred and fifty three dyspeptic adults referring to the gastroenterology clinic of Firoozgar Hospital were enrolled in the study. A diagnosis of dyspepsia was made based on ROME II criteria and normal endoscopic findings. The criteria for performing UGEI on dyspeptic patients were age above 55 year, presence of iron deficiency anemia or occult blood in stool, persisting symptoms of dyspepsia after standard treatment, or family history of cancer. All of them have indication for Upper Gastro-Esophageal Endoscopy (UGIE).

The exclusion criteria were history of coagulopathy, malignancies, gastrointestinal surgery, major underlying diseases, gastric or esophageal varices, or treatment with steroid, immunosuppressive, antibiotic or antacid (H_2 blocker or proton pump inhibitor) during the preceding month. Also, patients with recent weight change were excluded from the study.

The height and body weight were measured with a digital calibrated scale. Body Mass Index (BMI) was calculated as weight divided by height squared (Kg/m^2). Trained staff interviewed the patients to complete a detailed questionnaire including demographic data, gastrointestinal symptoms (heart burn, bloating, early satiety, abdominal pain or discomfort), personal and familial history of peptic ulcer disease or cancers.

Following an overnight fasting and prior to endoscopy, 10 milliliters of venous blood was obtained from each patient. The samples were centrifuged at 3600 rpm and stored in a -20˚C refrigerator. Subsequently, quantitative measurements of serum leptin were made with double checked ELISA kits for human leptin level (Biovendor, Germany).

Endoscopy was performed by two expert gastroenterologists (Fujinoon 2600) under adequate sedation. During endoscopy, two biopsies were taken from antrum. One specimen was used for *H.pylori* detection using Rapid Urease Test (RUT) and the other was rinsed in normal saline for hematoxylin

and eosin staining. The patients were divided in two groups based on their infection state with *H.pylori* on histologic evaluation.

All statistical analyses were performed using the Statistical Package for Social Sciences, version 16 for Windows™ (SPSS® Inc., Chicago, IL). Continuous variables are presented as mean ± SD. In order to test the differences between parametric and non-parametric variables in the two study groups (*H.pylori*-positive and *H.pylori*-negative), we used independent sample Student's t-test and Mann-Whitney U test. Spearman's correlation coefficient and χ^2 test were performed for quantitative and categorical variables, respectively. P values below 0.05 were considered statistically significant.

The study was approved by the Institutional Review Board of the Tehran University of Medical Sciences and written informed consents were obtained from all patients.

RESULTS

A total of 153 dyspeptic patients, consisting of 67 males and 86 females, were recruited in this study.

The patients were aged 43.2 ± 14.3 years on the average. Other baseline characteristics (age, gender, body mass index) are shown in Table 1. The overall prevalence of *H.pylori* infection was 49.6%. As demonstrated in Table 1, there was no significant difference in gender, height, weight and BMI between the two groups. The *H.pylori*-positive group was older in comparison to the *H.pylori*-negative group (45.65 ± 13.9 vs. 40.7 ± 14.13 years, p=0.035). The *H.pylori* infection status was significantly related to serum leptin level (p<0.001) with a lower median leptin level in *H.pylori*-positive patients. The overall mean level of leptin was 10.39 ng/mL (5.8 ± 1.05 ng/mL for the *H.pylori*-positive and 14.8 ± 1.62 ng/mL for the *H.pylori*-negative). Serum leptin correlates with age (r=0.17, p=0.0031) but not with the BMI (r=0.04, p=0.588). We observed a significant relationship between serum leptin level and male gender (p<0.02). Also, we did not find an association with age, sex and BMI with leptin level in either group.

Table 1: Characteristics of participants

Variables	*H.pylori* Positive	*H.pylori* Negative	*p-value*
Count	77	76	
Age(Years) (mean ± SD)	45.65 ± 13.9	40.7 ± 14.3	0.035
Gender (M:F)	34 : 43	33 : 43	0.927
Height (m)	1.6 ± 9.8	1.6 ± 9.9	0.585
Weight (Kg)	70.4 ± 13.6	69.0 ± 15.7	0.549
BMI (Kg/m²)	25.6 ± 4.1	29.8 ± 4.7	0.700

DISCUSSION

Recent studies have demonstrated that in addition to the adipose tissue, certain other tissues express leptin, including placenta, ovaries, skeletal muscle and stomach. The role of leptin in regulating body weight, hunger and satiety through affecting the release of gastric hormones is well documented.[5,15,18]

In this study, serum leptin level was lower in *H.pylori* positive subjects, which is consistent with some previous reports.[8,19,20] Observed lower leptin levels in *H.pylori*-positive patients and elevated plasma leptin levels after *H.pylori* eradication. Similarly, Roper et al.[2] found a lower leptin level in *H.pylori* positive adult males. There are also studies which indicate no difference in serum leptin level among *H.pylori* infected patients and non-infected individuals.[15,18,19]

BMI is another factor that influences leptin levels. Leptin is a regulating factor of feeding behavior and might be related to anorexia due to chronic inflammation. Also, previous studies have reported increased levels of inflammatory agents in presence of of *H.pylori* infection.[20,21] This finding suggests that leptin levels might rise in presence of *H.pylori* induced gastritis. In this context, gastric leptin may have a role. Nevertheless, serum leptin level does not change significantly after *H.pylori* eradication.[20] It seems that leptin secretion probably has a close relationship with adipose tissue mass. However, we found no correlation between BMI and serum leptin level in *H.pylori* positive patients. The association leptin level and high BMI in *H.pylori*-positive patients is controversial.[2] However, we cannot offer a

clear explanation for this finding. We suggest that it may be related to the limited number of participants and lower BMI as well as higher mean age in the *H.pylori*-positive group. Moreover, we did not verify gastric leptin levels. Furthermore, the mean age of *H.pylori* infected patients was significantly lower compared to others; this finding is similar to other reports. For example, Semnani and Bastos found a close relationship between *H.pylori* infection and age.[22,23] although Roper et al.[12] could not verify these results. These controversies might be due to the differences in baseline leptin level and other factors affecting serum leptin levels.

In conclusion, in the present study we could not find an association between *H.pylori* infection and high serum leptin levels. It might be assumed that *H.pylori* infection may alter gastric leptin levels through inducing injuries on gastric mucosa and consequently leptin producing cells, leading to decline of circulating leptin level.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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