# EFFECTS OF HELICOBACTER PYLORI INFECTIONS ON GHRELIN AND LEPTIN LEVELS

AYSE KEFELI[*], ABDULLAH OZGUR YENIOVA[**], SEBAHAT BASYIGIT[***], METIN UZMAN[**], ZELIHA ASILTURK[****], YUSUF TANRIKULU[*****], YASAR NAZLIGÜL[****]

[*]Karatay University, Faculty of Medicine, Gastroenterology Department, Konya, Turkey - [**]Kecioren Trainning and Research Hospital, Gastroenterology Department, Ankara, Turkey - [***]Artvin State Hospital, Gastroenterology Department, Artvin, Turkey - [****]Kecioren Training Hospital, Gastroenterology Department, Ankara, Turkey - [*****]Karatay University, Faculty of Medicine, General Surgery, Konya, Turkey

***ABSTRACT***

***Introduction****: Helicobacter pylori (H. pylori) infection is common throughout the world. Ghrelin and leptin peptides play a crucial role in the homeostasis of the human body. Previously, some studies showed that H. pylori colonization had been associated with circulating leptin and ghrelin levels, but the certain relationship is still uncertain. The goal of this study is to determine the effects of H. pylori infection on serum ghrelin and leptin levels and how these relates to body weight changes before and after H. pylori eradication.*

***Materials and methods****: This study prospectively enrolled 129 dyspeptic patients who had received an endoscopy. A fasting blood sample was obtained from each patient for total ghrelin and leptin analysis. The body mass index (BMI) of each patient was also calculated.*

***Results****: Ninety-four patients tested positive and 35 patients tested negative for H. Pylori. There was no significant difference in the serum leptin and ghrelin levels and BMI between those with or without H. pylori infection. While serum ghrelin concentration was significantly decreased after eradication (8.97 ± 0.61ng/ml, 6.96 ± 0.41ng/ml, p = 0.005, respectively), serum leptin concentration and BMI did not change (6.13 ± 0.86, 5.70 ± 1.1, p = 0.79, 23.43 ± 0.26, 23.16 ± 0.24, p = 0.07, respectively).*

***Conclusion****: However, no difference was detected in serum ghrelin and leptin levels between H. pylori infected patients and controls, ghrelin levels were decreased with H. pylori eradication, and these differences were correlated with differences in BMI. In conclusion, H.pylori might be play a role on body weight change.*

***Keywords****: Ghrelin, Leptin, Helicobacter Pylori (H. Pylori), Cag A, Body Mass Index (BMI).*

*DOI: 10.19193/0393-6384_2016_5_139*

***Received*** *April 30, 2016;* ***Accepted*** *July 02, 2016*

## Introduction

The healthy regulation of energy homeostasis in humans depends on centrally-acting hormones such as ghrelin and leptin[(1)]. Leptin is the peptide product of the obese (ob) gene expressed chiefly by adipocytes and endocrine P cells in the gastric epithelium[(2)]. Serum leptin levels reflect body fat stores and help maintain a stable body weight by suppressing food intake and increasing energy metabolism[(1)].

Ghrelin is a peptide hormone, which is primarily produced by the X/A cells in the gastric oxyntic mucosa[(3)]. Ghrelin stimulates food intake, decreases energy expenditure, and promotes weight gain[(4)]. In contrast to leptin, serum ghrelin levels are inversely related to adipose tissue mass and may help maintain energy homeostasis when nutrients are scarce[(5)]. Unfortunately, regulation of gastric ghrelin secretion is poorly understood.

Helicobacter pylori (H. pylori) infection is the major etiologic agent for chronic active gastritis, and

it also plays a crucial role in gastric and duodenal ulcers, as well as in gastric cancer. The H. pylori-induced inflammatory response affects many gastric cell types, including those responsible for leptin and ghrelin production[6]. The elimination of H. pylori by antimicrobial therapy has been reported to increase food intake and increase weight which suggests that H. pylori could play a role in the regulation of leptin and ghrelin expression. Also, body mass index (BMI) has been reported to increase or decrease following H. pylori eradication[7,8]. In previous studies, H. pylori colonization has been associated with circulating leptin and ghrelin levels, but the relationship between the H. pylori status and their levels is still uncertain[7,9-20].

We hypothesized that gastric H. pylori colonization affects the physiologic regulation of gut hormones involved in food intake, energy expenditure, and body weight maintenance. The hormones, including ghrelin and leptin affect overall metabolic function, so that decreasing H. pylori in the population may be causally associated with increasing obesity. We determined serum ghrelin and leptin concentrations before and after H. pylori eradication in healthy subjects.

## Materials and methods

### *Patients*

The study subjects were 129 patients referred for an upper gastrointestinal endoscopy procedure from Feb 2011 to Jan 2012. The study was approved by the Kecioren Research Hospital Ethics Committee, Kecioren research Hospital, Ankara, Turkey (Ethics Committee approval no: 147; date: 10/10/2012).

Informed written consent was obtained from all patients after explaining the methods of the study. The exclusion criteria were the following: age < 18 or > 65 years, pregnancy, BMI > 30 kg/m$^2$, diabetes mellitus, celiac disease, irritable bowel disease, history or diagnosis of colorectal disease, systemic infection, thyroid and liver diseases, impairment of kidney function test, use of medications effective against H. pylori during the preceding 3 months, alcohol abuse, drug addiction, chronic corticosteroid or nonsteroidal anti-inflammatory drug use, and prior gastrointestinal surgery.

### *Clinical evaluation and specimen collection*

All patients presented after a 12-hour overnight fast. Before the scheduled endoscopy, a physician conducted a preprocedure evaluation, which included taking a patient history and administering a physical examination. Demographic and clinical informations were collected via a questionnaire administered by trained interviewers at admission into the study. Height and weight were recorded for each participant, and BMI was calculated as weight (kilograms) divided by height (meters squared). Immediately prior to endoscopy and eight weeks after eradication therapy, a 15 ml blood sample was collected, centrifuged, and stored as serum at -800C until examined.

### *Endoscopy*

A complete endoscopic evaluation of the esophagus, stomach, and duodenum up to the second portion was performed with a Video Endoscope (Fujinon EG-450 WR 5 0, Japan). Two biopsies were obtained from the gastric antrum and body for histological examination. The physicians performing the endoscopy were blinded to the H. pylori status of the subjects and used identical techniques in obtaining biopsies from each subject. Biopsies were stained with hematoxylin-eosin for tissue diagnosis and with Giemsa to detect the presence of H. pylori.

### *Histopathological examination*

Corporal and antral biopsies were examined by specialized gastrointestinal pathologists. In case of the histological examination of gastric biopsy specimens proved positive for bacterial cells with characteristic morphological features typical of H. pylori these patients were categorized as H. pylori+. Each sample was evaluated for the presence and grade of chronic gastritis, acute gastritis, and atrophy/intestinal metaplasia in the body and antrum.

### *Serum peptide determination*

• *Cytotoxin-associated gene A (CagA) analysis*

Serum cytotoxin-associated gene A (CagA) was measured with a commercial kit according to the manufacturer's instructions (Japan Institute for the Control of Aging [JaICA®], Shizuoka, Japan).

• *Ghrelin analysis*

Serum samples were assayed for immunoreactive ghrelin concentration using a commercial radioimmunoassay (RIA) (Phoenix Pharmaceuticals, Europe Phoenix GMBH, Karlsruhe, Germany). The lower and upper limits of detection for this assay were 0 and 100 ng/ml, respectively.

• *Leptin analysis*

Serum leptin levels were determined in all

groups using a commercially available RIA (Linco, Inc., St. Charles, MO, USA) with the lower and upper limits of detection for this assay of 0 and 100 ng/ml, respectively.

### *Eradication of H. pylori*

All patients received a quadruple therapy program for 14 days consisting of 300 mg colloidal bismuth subcitrate (equivalent to Bi2 O3 120 mg, two tablets taken orally one hour before breakfast and dinner); tetracycline hydrochloride, 500 mg (qid, one hour after meals and at bedtime, with a glass of water); metronidazole, 500 mg (tid, after meals) and proton pump inhibitor (PPI) (rabeprazole 20 mg, bid, 30 minutes before meals).

Three groups were formed according to CagA status (negative, positive/CagA negative, and positive/CagA positive groups), and serum ghrelin and leptin levels and BMI were compared among these groups before and after treatment.

### Statistical analysis

SPSS (Statistical Package for the Social Sciences) software version 15.0 for Windows (SPSS Inc., Chicago, IL) was used for statistical analysis. Data are expressed as mean ± SD or median depending on the distribution of the values. Continuous variables were compared using a Student's t-test. Distribution of the groups was analyzed using the Kolmogorov-Smirnov (KS) test. Correlations were analyzed using the rank test, with a value of $P \leq 0.005$ considered as significant to allow for an overall 5% Type I error. Categorical variables were compared using the independent t-test and the Mann-Whitney U test for two groups, and the Kruskal-Wallis test for the remaining two groups. P value of less than 0.05 was accepted as statistically significant.

## Results

One hundred and twenty-nine patients (72 [55.8%] female and 57 [44.2%] male) were included in the study. The mean age of the patients was 36.8 ± 10.9 years. The age range was from 18 to 64 years. There was no significant difference with regard to mean age between males and females (Table 1).

BMI values were found to be between 24.9 and 29.9 kg/m$^2$ in 25 patients, between 20 and 24.9 kg/m$^2$ in 100 patients, and less than 20 kg/m$^2$ in 4 patients.

By histopathological examination, H. pylori was positive in 94 patients (73%), while it was negative in 35 patients (27%). Antibodies against CagA were analyzed for 87 positive patients. Of these, 54 were positive for antibodies against CagA while the remaining 33 did not bear CagA strains. Demographic and clinical characters of all groups are shown in Table 1. There was no significant difference between the negative, positive/CagA negative, and positive/CagA positive groups with respect to gender, age, BMI, and cholesterol (Table 1).

| | H.pylori (-) | H.pylori (+) CagA (-) | *H.pylori (+) CagA (+)* | *p* |
|---|---|---|---|---|
| **Mean age, year** | 37.2±12.7 | 35.5±10.2 | 37.8±10.2 | 0.6 |
| **Female/male (n,%)** | 21/14 (17.2/11.5) | 35/19 (28.7/15.6) | 14/19 (11.5/15.6) | 0.1 |
| **Glucose (mg/dl)** | 89±11.5 | 92±15 | 89±12 | 0.44 |
| **Total cholesterol (mg/dl)** | 166.85 | 170.2 | 179.1 | 0.75 |
| **LDL (mg/dl)** | 100.2 | 103.1 | 109.6 | 0.65 |
| **TRG (mg/dl)** | 115.8 | 109.3 | 138.4 | 0.28 |
| **Ghrelin (ng/ml)** | 9.5 ± 0.5 | 8.3 ± 0.5 | 9.2 ±0.8 | 0.53 |
| **Leptin (ng/ml)** | 7.2 ± 1.4 | 6.6 ± 1.24 | 6.3 ± 0.7 | 0.59 |
| **BMI (kg/m2)** | 23.3 ± 0.3 | 23.2±0.1 | 23.2±0.2 | 0.9 |

**Table 1**: Demographic, clinical, and biochemical characters of all groups.
*H.pylori: Helicobacter pylori, LDL: Low density lipoprotein TRG: Triglycerides BMI: Body Mass Index*

Of 94 positive patients, 7 did not come to control, and 8 did not accept eradication therapy. Hence, 79 were given prescription medications for H. pylori eradication. The study flow chart is shown in Figure 1.

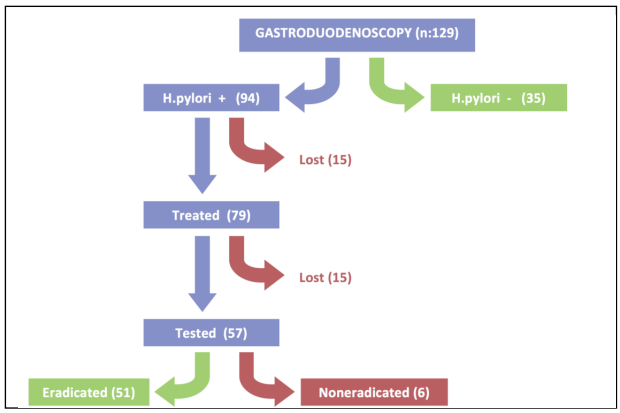


**Fig: 1**: Study flow chart.

The eradication rates were found to be 64.5% (Intent to treat [ ITT ]; n:79) (95% CI 0.53 and 0.75) and 89% (per protocol [ PP ]; n:57) (95% CI 0.81 and 0.97) (Figure 1).

There was no significant difference in mean levels of ghrelin among the negative, positive CagA negative, and positive CagA positive groups (9.516 ± 0.55 ng/ml; 8.396 ± 0.53 ng/ml; 9.240 ± 0.85 ng/ml; p = 0.53, respectively) (Figure 2) (Table 1).

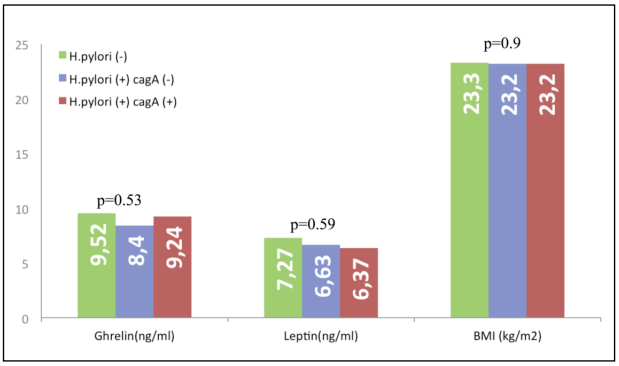


**Fig: 2**: Before and after treatment mean serum ghrelin, leptin and BMI levels.
*BMI: Body Mass Index*
*H.pylori: Helicobacter Pylori*

There was no significant difference in mean levels of leptin among negative, positive CagA negative, and positive CagA positive groups (7.272 ± 1.45ng/ml; 6.631 ± 1.24 ng/ml; 6.369 ± 0.74 ng/ml; p = 0.59, respectively) (Figure 2) (Table 1).

There was no significant difference among negative, positive CagA negative, and positive CagA positive groups with respect to BMI (23.26 ± 0.19 kg/cm2; 23.29 ± 0.32 kg/cm$^2$; 23.30 ± 0.35 kg/cm$^2$; p = 0.9, respectively) (Figure 2) (Table 1).

Patients with a negative urea breath test after eradication therapy were analyzed for serum ghrelin and leptin levels.

While before treatment mean ghrelin levels were 8.97 ± 0.61ng/ml, after treatment mean ghrelin levels were 6.96 ± 0.41ng/ml. After treatment mean ghrelin levels were significantly lower than before treatment levels (p = 0.005). There was no significant difference between the before treatment and after treatment periods with respect to leptin levels (6.1 ± 0.23ng/ml, 5.7 ± 0.42ng/ml, respectively) (p = 0.059) (Figure 3).

There was no significant difference between before treatment and after treatment BMI values (23.43 ± 0.26 kg/cm$^2$, 23.16 ± 0.24 kg/cm2, respectively) (p = 0.07) (Figure 3).

The difference in before treatment and after treatment ghrelin levels was negatively correlated with the difference in before treatment and after treatment BMI values (r = -0.29, p = 0.036), but there was no correlation between the difference in before treatment and after treatment leptin levels and before treatment and after treatment BMI levels (r = 0.019, p = 0.89).

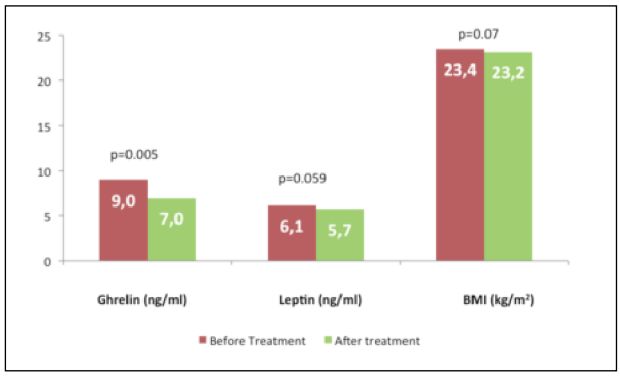


**Fig: 3**: Before and after treatment serum ghrelin, leptin and BMI levels.
*BMI: Body Mass Index*

## Discussion

H. pylori causes chronic inflammation, atrophy, and mucosal changes in the gastric mucosa. That is why the impact of leptin and ghrelin production according to their serum levels in H. pylori infection is an intriguing issue.

Several studies which have detected lower circulating ghrelin levels in H. pylori infections have been found in the literature[10,13,15,21-32]. It was thought that the main reason for the decrease in ghrelin levels was gastric atrophy. Two studies which used pepsinogen as a marker of atrophy found a correlation between pepsinogen and the ghrelin level[15,17]. The site of gastric involvement in H. pylori infections is similar to the localization of ghrelin secreting/producing cells. This might be the reason for the decreased ghrelin level in infections, but there are many another things which can cause gastritis. For example, Checchive et al. have compared the serum ghrelin levels between patients with and without autoimmune gastritis and found lower ghrelin levels in patients with autoimmune gastritis than in the controls, which is similar to some studies conducted on H. pylori infected patients[33].

This difference existed even after H. pylori positive subjects were excluded. Therefore, this study gives rise to the idea that there is not a significant effect of H. pylori bacteria on serum ghrelin level. Similarly, in our study, there was no significant difference in ghrelin levels between positive and negative groups. Furthermore, Checchi at al. have pointed out there was a strong negative correlation between gastric mucosal damage and serum ghrelin levels, and they emphasized that serum ghrelin levels might be a specific and sensitive marker to determine gas-

tric mucosal damage, whether positive or not. It is a fact that measurement of the serum ghrelin level is an easier method to employ than the measurement of the pepsinogen 1/pepsinogen 2 ratio for determining gastric atrophy[34].

While many researchers have shown that there was no relationship between H. pylori infection and serum ghrelin levels, 10 other studies showed that the ghrelin level was lower in H. pylori infected people[10,12,17,35,36-41]. One hundred and twenty-nine female and male patients were included in our study, and serum ghrelin levels were found to be unchanged by H. pylori infection.

In this study, we measured serum ghrelin levels 8 weeks after the end of therapy. The mean serum ghrelin level was decreased. In a study conducted by Nwokolo et al., one of the first studies in this field, conducted on 10 patients, an increase in serum ghrelin levels was detected after H. pylori eradication. Accordingly, it was believed to have increased production of gastric mucosal ghrelin which caused weight gain after H. pylori eradication[8,18]. We encountered different results regarding the changes in serum ghrelin levels after H. pylori eradication than were found in previous studies[8,15,24,42,43]. While some have detected an increase in serum ghrelin levels after H. pylori eradication, others have observed no change in the serum ghrelin level after H. pylori eradication[17,22,23,32,44].

The largest study in this field was performed by Osawa et al., and they showed a significant decrease in serum ghrelin levels after H. pylori eradication[45]. While the after treatment measurements were performed in the 3rd and 4th months after the end of therapy in the mentioned study, Pacifico et al. had the longest follow-up time by measuring serum ghrelin levels 12 months after H. pylori eradication, and they showed a significant decrease in serum ghrelin levels after eradication[36].

Alterations in serum ghrelin level after H. pylori eradication treatment can be related to the type of the H. pylori bacteria. Isomoto et al. detected an association between the H. pylori type and alterations in gastric mucosal ghrelin level.27,41 They found lower serum ghrelin levels in Type 1 H. pylori infection, which express strong virulence factors such as CagA and VacA, than in Type 2 H. pylori infections. In contrast, in our study, when comparing the CagA positive and negative groups, there was no significant difference noted in serum ghrelin levels before and after H. pylori eradication treatment between groups.

It is widely known that weight gain after H. pylori eradication is a fact[46,47]. However, there have been claims of increases in serum ghrelin levels after H. pylori eradication, but this has not yet been proven. A review of the literature presents varying and conflicting results. Only Osawa et al. have investigated BMI in follow-up after H. pylori eradication. They found that serum ghrelin levels decreased after H. pylori eradication and have been correlated inversely with gain weight, similar to the findings of our study.

It is well-known that H. pylori infections can cause a decrease in appetite. For this reason, the impact of this infection on serum leptin levels, which are accepted as a satiety hormone and have a regulatory role on food intake, has been intriguing. There are conflicting results about serum leptin levels, H. pylori infection, and its eradication. Two studies showed that serum leptin levels were lower in H. pylori infected patients than in the control group[35,36]. Several others showed no change in serum leptin levels[12,15,48]. There are conflicting data on the effects of H. pylori eradication on serum leptin levels, too[21,48]. Similar to our study, results from Kebapcilar's Turkish study and two Japanese studies showed no change in serum leptin levels after H. pylori eradication[7,49,50]. This study showed that there was no difference in serum leptin level between positive and negative patients and that H. pylori eradication did not affect serum leptin levels.

In conclusion, although there is an opinion that H. pylori induced infection can cause alterations in serum ghrelin levels depending on the gastric mucosal damage and alterations in serum leptin levels depending on the systemic inflammatory effect, there has been conflicting data which either support or refute this thesis. In our study, however, no difference was detected in serum ghrelin and leptin levels between H. pylori infected patients and controls, ghrelin levels were decreased with H. pylori eradication, and these differences were correlated with differences in BMI. In order to obtain accurate information about this issue, further larger scale studies with longer follow-up times are needed.

## References


1) Cummings DE, Overduin J. *Gastrointestinal regulation of food intake*. J Clin Invest 2007; 117: *13-23*.
2) Bado A, Levasseur S, Attoub S, et al. *The stomach is a source of leptin*. Nature 1998; 394: *790-793*.
3) Kojima M, Hosoda H, Date Y, Nakazato M, Matsuo H, Kangawa K. *Ghrelin is a growth-hormone-releasing acylated peptide from stomach*. Nature 1999; 402: *656-660*.
4) Nakazato M, Murakami N, Date Y, et al. *A role for ghrelin in the central regulation of feeding*. Nature 2001; 409: *194-198*.
5) Tschop M, Weyer C, Tataranni PA, Devanarayan V, Ravussin E, Heiman ML. *Circulating ghrelin levels are decreased in human obesity*. Diabetes 2001; 50: *707-709*.
6) Blaser MJ, Atherton JC. *Helicobacter pylori persistence: biology and disease*. J Clin Invest 2004; 113: *321-333*.
7) Azuma T, Suto H, Ito Yet al. *Gastric leptin and Helicobacter pylori infection*. Gut 2001; 49: *324-329*.
8) Nwokolo CU, Freshwater DA, O'Hare P, Randeva HS. *Plasma ghrelin following cure of Helicobacter pylori*. Gut 2003; 52: *637-640*.
9) Cho I, Blaser MJ, Francois F, et al. *Helicobacter pyloriand overweight status in the United States: data from the Third National Health and Nutrition Examination Survey*. Am J Epidemiol 2005; 162: *579-584*.
10) Salles N, Menard A, Georges A, et al. *Effects of Helicobacter pylori infection on gut appetite peptide (leptin, ghrelin) expression in elderly inpatients*. J Gerontol A BiolSci Med Sci 2006; 61: *1144-1150*.
11) Konturek PC, Czesnikiewicz-Guzik M, Bielanski W, Konturek SJ. *Involvement of Helicobacter pylori infection in neuro-hormonal control of food intake*. J Physiol Pharmacol 2006; 57: *67-81*.
12) Jun DW, Lee OY, Lee YY, Choi HS, Kim TH, Yoon BC. *Correlation between gastrointestinal symptoms and gastric leptin and ghrelin expression in patients with gastritis*. Dig Dis Sci 2007; 52: *2866-2872*.
13) Shiotani A, Miyanishi T, Uedo N, Iishi H. *H. pylori infection is associated with reduced circulating ghrelin levels independent of body mass index*. Helicobacter. 2005; 10: *373-378*.
14) Gokcel A, Gumurdulu Y, Kayaselcuk F, et al. *Helicobacter pylorihas no effect on plasma ghrelin levels*. Eur J Endocrinol 2003; 148: *423-426*.
15) Isomoto H, Nakazato M, Ueno H, et al. *Low plasma ghrelin levels in patients with Helicobacter pylori-associated gastritis*. Am J Med 2004; 117: *429-432*.
16) Osawa H, Nakazato M, Date Y, et al. *Impaired production of gastric ghrelin in chronic gastritis associated with Helicobacter pylori*. J Clin Endocrinol Metab 2005; 90: *10-16*.
17) Cindoruk M, Yetkin I, Deger SM, Karakan T, Kan E, Unal S. *Influence of H. pylorion plasma ghrelin in patients without atrophic gastritis*. World J Gastroenterol 2007; 13: *1595-1598*.
18) Tatsuguchi A, Miyake K, Gudis K, et al. *Effect of Helicobacter pylori infection on ghrelin expression in human gastric mucosa*. Am J Gastroenterol 2004; 99: *2121-2127*.
19) HaqqAM, Farooqi IS, O'Rahilly S, et al. *Serum ghrelin levels are inversely correlated with body mass index, age, and insulin concentrations in normal children and are markedly increased in Prader-Willi syndrome*. J Clin Endocrinol Metab 2003; 88: *174-178*.
20) Asakawa A, Inui A, Kaya T. *Ghrelin is an appetite-stimulatory signal from stomach with structural resemblance to motilin*. Gastroenterol2001; 120: *337- 345*.
21) Konturek P.C., Czesnikiewicz G.M., Brzozowskı T. *Neuro-hormonal control of food intake; Basic mechanısms and clinical implications*. J Physiol and Pharmacol 2005; 56(6): *5-25*.
22) Kawashima J, Ohno S, Sakurada T, et al. *Circulating acylated ghrelin level decreases in accordance with the extent of atrophic gastritis*. J of Gastroenterol 2009; 44(10): *1046-1054*.
23) Plonka M, Konturek PC, Bielanski W. *Relationship between ghrelin and Helicobacter pylori infection in Polish adult shepherds and their children*. Aliment Pharmacol Ther 2006; 24: *160-168*.
24) Isomoto H, Ueno H, Saenko VA, et al. *Impact of Helicobacter pylori infection on gastric and plasma ghrelin dynamics in humans*. Am J Gastroenterol 2005; 100(8): *1711-1720*.
25) Plonka M, Bielanski W, Konturek SJ, et al. *Helicobacter pylori infection and serum gastrin, ghrelin and leptin in children of Polish shepherds*. Dig Liver Dis 2006; 38(2): *91-97*.
26) Chuang CH, Sheu BS, Yang, et al. *Gender difference of circulating ghrelin and leptin concentrations in chronic Helicobacter pylori infection*. Helicobacter 2009; 14(1): *54-60*.
27) Isomoto H, Nishi Y, Ohnita K, et al. The relationship between plasma and gastric ghrelin levels and strain diversity in helicobacter pylori virulence. Am J Gastroenterol2005;100(6):1425-1427.
28) Alonso N, Granada ML, Salinas I, et al. Plasma ghrelin concentrations in type 1 diabetic patients with autoimmune atrophic gastritis. Eur J Endocrinol 2007; 157(6):763-769.
29) Salles N, Menard A, Georges A, et al. *Effects of Helicobacter pylori infection on gut appetite peptide (leptin, ghrelin) expression in elderly inpatients*. J of Gerontol A Biol Sci Med Sci 2006; 61(11): *1144-1150*.
30) D'Onghia V, Leoncini R, Carli R, et al. *Circulating gastrin and ghrelin levels in patients with colorectal cancer: correlation with tumour stage, Helicobacter pylori infection and BMI*. Biomed Pharmacother 2007; 61(2-3): *137-141*.
31) Nishi Y, Isomoto H, Uotani S, et al. *Enhanced production of leptin in gastric fundic mucosa with helicobacter pylori*. World J Gastroenterol 2005; 11(5); *695-699*.
32) Czesnikiewicz-Guzik M, Loster B, Bielanski W, et al. *Implications of oral Helicobacter pylori for the outcome of its gastric eradication therapy*. J Clin Gastroenterol 2007; 41(2): *145-151*.
33) Checchi S, Montanaro A, Pasqui L, et al. *Serum ghrelin as a marker of atrophic body gastritis in patients with parietal cell antibodies*. J ClinEndocrinol Metab 2007; 92(11): *4346-4351*.
34) Osawa H. *Ghrelin and helicobacter pylori infection*. World J Gastroenterol 2008; 14(41): *6327-6333*.
35) Roper J, Francois F, Shue PL, et al. *Leptin and ghrelin in relation to H.pylori status in adult males*. J Clin

Endocrinol Metab 2008;93(6): *2350-2357*.
36) Pacifico L, Anania C, Osborn JF, et al. *Long-term effects of Helicobacter pylori eradication on circulating ghrelin and leptin concentrations and body composition in prepubertal children*. Eur J Endocrinol 2008; 158(3): *323-332*.
37) de Martel C, Haggerty TD, Corley DA, Vogelman JH, Orentreich N, Parsonnet J. *Serum ghrelin levels and risk of subsequent adenocarcinoma of the esophagus*. Am J Gastroenterol 2007; 102(6): *1166-1172*.
38) Shak JR, Roper J, Perez-Perez GI, et al. *The effect of laparoscopic gastric banding surgery on plasma levels of appetite-control, insulinotropic, and digestive hormones*. Obes Surg 2008; 18(9): *1089-1096*.
39) Uzzan B, Catheline JM, Lagorce C, et al. *Expression of ghrelin in fundus is increased after gastric banding in morbidly obese patients*. Obes Surg 2007; 17(9): *1159-1164*.
40) An JY, Choi MG, Noh JH, Sohn TS, Jin DK, Kim S. *Clinical significance of ghrelin concentration of plasma and tumor tissue in patients with gastric cancer*. J Surg Res 2007: 143(2): *344-349*.
41) Nweneka CV, Prentice AM. *Helicobacter pylori infection and circulating ghrelin levels-a systematic review*. BMC Gastroenterol 2011; 11: *7-25*.
42) Choe YH, Lee JH, Lee HJ, et al. *Ghrelin Levels in Gastric Mucosa before and after Eradication of Helicobacter pylori*. Gut Liver 2007; 1(2): *132-137*.
43) Lee ES, Yoon YS, et al. *Eradication of Helicobacter pylori increases ghrelin mRNA expression in the gastric mucosa*. J Korean Med Sci 2010; 25(2): *265-271*.
44) Jang EJ, Park SW, Park JS, et al. *The influence of the eradication of Helicobacter pylori on gastric ghrelin, appetite, and body mass index in patients with peptic ulcer disease*. J Gastroenterol Hepatol 2008; 23(2): *278-285*.
45) Osawa H, Kita H, Ohnishi H, et al. *Changes in plasma ghrelin levels, gastric ghrelin production, and body weight after Helicobacter pylori cure*. J Gastroenterol 2006, 41(10): *954-961*.
46) Cummings DE, Weigle DS, Frayo RS, et al.. *Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery*. N Engl J Med 2002; 346: *1623-630*.
47) Leidy HJ, Gardner JK, Frye BR, et al. *Circulating ghrelin is sensitive to changes in body weight during a diet and exercise program in normal-weight young women*. J Clin Endocrinol Metab 2004; 89: *2659-2664*.
48) Francois F, Roper J, Joseph N, et al. The effect of H.pylori eradication on meal associated changes in plasma ghrelin and leptin. BMC Gastroenterol 2011; 11: *37*.
49) Kebapcilar L, Sari I, Renkal AH, et al. *The influence of Helicobacter pylori eradication on leptin, soluble CD40 ligand, oxidative stress and body composition in patients with peptic ulcer disease*. Intern Med 2009; 48(24): *2055-2059*.
50) Considine RV, Sinha MK, Heiman ML, et al. *Serum immunoreactive-leptin concentrations in normal weight and obese humans*. N Engl J Med 1996; 334: *292-295*.

*Author Contributions: A. Kefeli designed the study, performed the research, and wrote the paper. A. O. Yeniova, S. Basyigit, and M. Uzman performed the endoscopies. Z. Asilturk and Y. Tanrikulu analyzed the data. A. O. Yeniova and Y. Nazlıgul revised the research.*

*Ethics Committee Approval: This study was approved by Kecioren Research Hospital Ethics Committee at Kecioren Research Hospital, Ankara, Turkey (Ethics Committee approval no: 147; date: 10/10/2012).*

*All procedures performed in this study involving human participants were done in accordance with the ethical standards of the institutional and/or national research committee, the Declaration of Helsinki (1964) and its later amendments, or with comparable ethical standards.*

*Corresponding author*
AYSE KEFELI, MD
Karatay University, Faculty of Medicine, Gastroenterology Department, Konya
*(Turkey)*