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The Relationship Between Ghrelin Levels and the Presence of Helicobacter Pylori in the Gastric Mucosa in Uremic Patients

Üremik Hastalarda Grelin Düzeyleri ile Mide Mukozasında Helicobacter Pylori Varlığı Arasındaki İlişki

ABSTRACT

OBJECTIVE: Helicobacter pylori (H. pylori) infection is an important risk factor for chronic gastritis and peptic ulcer. Ghrelin is mostly secreted by gastric mucosa. The aim of the study is to examine the relationship between H. Pylori and ghrelin levels in uremic patients.

MATERIAL and METHODS: A total of 91 patients [control group (CG, n=29), hemodialysis group (HD, no=21), peritoneal dialysis group(PD, no=12), predialysis group(PreG, n=29)] were involved. Patients using drugs active on H. pylori and/or gastric acidity were excluded. Besides demographic and biochemical parameters, patients were examined endoscopically; and H. Pylori was searched histopathologically.

RESULTS: H. pylori was found to be positive in 62 patients (68.1%). Those patients were not different from H. pylori negative group regarding demographic and biochemical parameters. H. pylori positivity was statistically similar in patient groups. Ghrelin levels of uremic groups (HD, PD and PreG) were significantly higher than that of CG (4.22±1.00ng/ml vs. 2.81±0.37ng/ml, p<0.001). Ghrelin level was higher in the predialysis group compared with the HD group (4.49±1.18ng/ml vs. 3.81±0.98ng/ml, p=0.040). Ghrelin levels of H. pylori positive and negative patients were not different (3.83±1.2ng/ml vs. 3.65±1.0ng/ml, p=0.50).

CONCLUSION: Ghrelin levels are elevated in uremia, but there is no relationship between ghrelin level and H. pylori positivity in uremic patients.

KEY WORDS: Helicobacter pylori, Ghrelin, Uremia

ÖZ

AMAÇ: Helicobacter pylori (H. pylori) enfeksiyonu kronik gastrit ve peptik ülser için önemli bir risk faktörüdür. Grelin en çok mide mukozasından salınır. Çalışmanın amacı, üremik hastalarda H. Pylori ile grelin düzeyleri arasındaki ilişkiyi incelemektir.

GEREÇ ve YÖNTEMLER: Toplam 91 hasta [kontrol grubu (CG, n=29), hemodiyaliz grubu (HD, no=21), periton diyalizi grubu (PD, no=12), prediyaliz grubu (PreG, n=29)] dahil edildi. H. pylori ve/veya gastrik asidite üzerine etkili ilaç kullanan hastalar dışlandı. Demografik ve biyokimyasal veriler yanında, hastalar endoskopik olarak muayene edildiler ve H. pylori varlığı histopatolojik olarak arandı.

BULGULAR: H. pylori 62 hastada (%68.1) pozitif saptandı. Bu hastalar demografik ve biyokimyasal parametreler açısından H. pylori negatif gruptan farklı değildiler. H. pylori pozitifliği hasta gruplarında istatistiksel olarak benzerdi. Grelin düzeyleri üremik gruplarda (HD, PD ve PreG) kontrol grubundan anlamlı derecede yüksekti (4,22±1,00ng/ml ve 2,80±0,37ng/ml, p<0,001). Grelin düzeyleri prediyaliz grupta HD grubuna kıyasla daha yüksek bulundu (4,49±1,18 ng/ml ve 3,81±0,98 ng/ml, p=0,040). Grelin düzeyleri H. pylori pozitif ve negatif hastalarda farklı değildi (3,83±1,2 ng/ml ve 3,65±1,0ng/ml, p=0,50).

SONUÇ: Grelin düzeyleri üremide yüksektir, fakat grelin düzeyleri ile H. pylori pozitifliği arasında ilişki yoktur.

ANAHTAR SÖZCÜKLER: Helicobacter pylori, Grelin, Üremi

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INTRODUCTION

Uremia affects the upper gastrointestinal system (GIS) as well as the other systems. Nausea, epigastric burning and pain are frequent symptoms in patients with chronic renal failure (CRF). Although, CRF has been suggested to increase the risk for peptic ulcer disease since many years, some studies have found no significant difference in peptic ulcer disease incidence among CRF patients when compared to the normal population (1, 2). *Helicobacter pylori* (*H. pylori*) infection, as one of the most common worldwide infections, is a main factor for chronic gastritis and peptic ulcer disease and it is also a risk factor for gastric cancer. The increased urea in CRF patients may predispose to colonization of *H. pylori* in the stomach (3). Conflicting results have been obtained related to prevalence of *H. pylori* in dialysis patients. Increased prevalence of *H. pylori* was detected in all CRF patients (4, 5). On the other hand, peptic ulcer recurrence after *H. pylori* eradication was shown to be higher in end-stage renal disease than non-uremic patients (6).

Ghrelin is a recently defined hormone that is mainly secreted from gastric mucosa and it stimulates appetite and the release of growth hormone (7, 8). Recently, serum ghrelin level was found to be 2.8 times more in those with CRF than non-uremic individuals (9). This increased ghrelin level was attributed to impaired renal function in breaking down and eliminating the ghrelin hormone. Increased ghrelin levels were also detected in hemodialysis (HD) and peritoneal dialysis (PD) patients (10).

There are several studies reporting the relationship between plasma ghrelin levels and *H. pylori* infection in non-uremic population, but it is still controversial. Some of them reported that plasma ghrelin levels increased or decreased after the eradication of *H. pylori* (11-14). There are also studies reporting that *H. pylori* infection has no effect on plasma ghrelin levels (15). There is no study investigating the relationship of plasma ghrelin levels and *H. pylori* in uremic population. Hence, our study aimed to investigate the prevalence of *H. pylori* in uremic patients and the correlation between the presence of *H. pylori* and ghrelin levels in different patient groups with uremia and compared with the normal population.

SUBJECTS and METHOD

All the participants were sequentially selected among the patients who were referred to our endoscopy unit between March 2009 and May 2010. Uremic patients were selected and divided into three groups:

Hemodialysis group (HD group): Patients on chronic hemodialysis program thrice a week for more than three months.

Peritoneal dialysis group (PD group): Patients on chronic peritoneal dialysis program for more than three months.

Predialysis group (PreG): Patients with stage 3-4 CRF.

These patients were compared with the control group (CG) involving patients with gastric symptoms and normal renal function (estimated glomerular filtration rate more than 90 ml/min and proteinuria less than 300 mg/day).

The study was started after gaining approval from local ethical committee; and informed consent was taken from all participants. Patients who did not give informed consent; patients aging less than 18 years, those who had been using drugs effective on gastric acidity (H2 receptor blockers, proton pump inhibitors, anti-acids, steroids, non-steroidal anti-inflammatory drugs) within the last months; patients with active gastrointestinal bleeding, history of GIS operation, previously diagnosed chronic GIS disease like inflammatory bowel diseases; those who received *H. pylori* eradication treatment within the last two years; patients with advanced cardiac, hepatic, pulmonary or malignant disease, any systemic infection within the last two weeks and pregnant patients were excluded from the study.

Demographic and clinical data of patients including age, gender, primary kidney disease, comorbid conditions, medications received within the last three months, past medical history and symptoms of upper GIS disease were recorded for each patient. In each patient the endoscopic and histopathological diagnoses (esophagitis, gastritis, duodenitis, ulcer, histopathological positivity for *H. pylori*) were obtained. Besides, blood samples were obtained after 12 hours of fasting in the morning of the endoscopic examination for determination of blood glucose, urea, creatinine, phosphorus, calcium, parathyroid hormone, albumin, white blood cell (WBC), hemoglobin, hematocrit, iron, total iron-binding capacity (TIBC), ferritin, C-reactive protein (CRP) and ghrelin levels. Ghrelin level was measured using Enzyme-Linked Immunosorbent Assay (ELISA).

All the endoscopic procedures were performed by the same endoscopist. Oral intake of patients was stopped at least 8-10 hours before the procedure. Local oropharyngeal anesthesia was performed using Xylocaine pump spray 10% before the procedure. Midazolam 1-5 mg IV was administered as a sedative when needed. The endoscopic examination procedure of upper GIS was performed by video endoscopy. At least four gastric biopsies, two from the antrum and two from the corpus were obtained. The obtained biopsy samples were fixed and embedded in paraffin; and were evaluated histopathologically in the pathology department of the same hospital.

Statistical analysis: Statistical analysis was performed using SPSS (Statistical Package for Social Sciences) for Windows 16.0 package program. Numerical data were expressed as mean±standard deviation (SD). In the comparison of two groups, Student t-test or Mann Whitney U test was used when appropriate. Chi-square test and Fisher's exact test were used for categorical variables. In the comparison of more than two groups, ANOVA or Kruskal Wallis-H variance analysis was used. The correlation analysis between quantitative parameters

was performed using Pearson and Spearman's (rho) correlation test for parameters with normal and abnormal distribution, respectively. p<0.05 was accepted as statistically significant. Multivariate linear regression analysis model was applied with "backward" method.

RESULTS

The study involved 91 (48 male, 43 female, mean age: 54±15 years) patients. There were 29 patients in the CG and predialysis group, 21 patients in the HD and 12 patients in the PD group. The baseline demographic characteristics of the groups and laboratory results are presented in Table I and Table II, respectively. The groups were well matched for primary kidney disease (p=0.553). The number of diabetic patients in HD, PD and predialysis groups were eight, two and ten, respectively (p=0.390). Consistent with these findings, blood glucose levels were higher in the HD and predialysis groups compared with the CG.

The symptoms necessitating endoscopic examination were epigastric pain in 36 (39.6%), epigastric burning in 30 (33%), retrosternal burning in 2 (2.2%), dyspepsia in 9 (9.9%), nausea in 2 (2.2%), chronic diarrhea in 2 (2.2%) and other symptoms in 10 (11%) patients. There was no difference between the groups in terms of symptomatology or existence of *H. pylori*.

The gastroscopic findings of the groups and the pathological evaluation of the biopsies obtained during gastroscopy are presented in Table III. 62 (68.1%) of the patients had *H. pylori* positivity histopathologically, while the remaining 29 (31.9%) were negative. *H. pylori* positivity rate was 65% in the control group, 67% in the HD group, 58% in the PD group and 76% in the predialysis group. There was no statistically significant difference between the groups regarding this subject. *H. pylori* positive group was not different from negative group in terms of age, gender, serum urea, creatinin, albumin, calcium, phosphorus, parathyroid hormone, iron, TIBC, ferritin, hemoglobin, hematocrit and ghrelin levels. The entire *H. pylori* positive group had histopathologically proven gastritis whereas gastritis was prominent in 24 (83%) patients in the *H. pylori* negative group (p=0.001). Only presence of loose cardia was significantly higher in the *H. pylori* positive group than the negative one [11 (18%) patients vs. 1 (3%) patient, respectively]. Other histopathological and gastroscopic findings were similar between *H. pylori* positive and negative patients. *H. pylori* existence rate also did not differ statistically between the uremic groups (HD, PD and predialysis groups) and CG (Table III).

Mean serum ghrelin level was lower in CG than all other groups (Table II) (p<0.001). In addition, ghrelin level in HD group was lower than predialysis group (p=0.040). Serum ghrelin levels was not different in patients with or without *H. pylori* positivity (3.83±1.2 vs. 3.65±1.0 ng/ml, p=0.50). This was true for all groups when analyzed separately. Serum ghrelin level of the uremic groups was significantly higher than control group (2.81±0.37ng/ml vs. 4.22±1.00ng/ml, p<0.001).

The parameters found to be related with serum ghrelin levels in univariate analyses were as follows: CRP (r=0.20, p=0.05), phosphorus (r=0.341, p=0.001), glucose (r=0.241, p=0.21), creatinine (r=0.403, p<0.0001), urea (r=0.403, p<0.0001), age (r=0.189, p=0.073), and parathyroid hormone (r=0.380, p<0.0001). When these parameters together with age, gender, group, *H. pylori* positivity and being uremic were analyzed by linear regression analysis; only the patients group (B=0.335, Beta=0.372, p=0.009) and being uremic (B=0.703, Beta=0.295, p=0.036) were found to be related to the serum ghrelin level.

Table I: The demographic characteristics of the groups.

	CG (n=29)	HD group (n=21)	PD group (n=12)	Predialysis group (n=29)	P
Age (years)	48±13	57±11	51±13	59±17	0.036[a]
Gender (male/female)	16/13	15/6	3/9	14/15	NS
Diabetes mellitus		8	2	10	
Hypertensive nephrosclerosis		6	3	9	
ADPKD		2	0	1	NS
Chronic glomerulonephritis		2	2	2	
Chronic pyelonephritis		-	2	2	
Others		3	3	5	

ADPKD: Autosomal dominant polycystic kidney disease.
a: CG-Predialysis group (p=0.039)

Table II: Laboratory findings.

	CG (n=29)	HD group (n=21)	PD group (n=12)	Predialysis group (n=29)	p
Urea (mg/dl)	27.2±13.6	110.6±40.2	91.7±36.1	83.7±47.3	<0.001[a, b, c]
Creatinine (mg/dl)	0.83±0.15	6.21±1.67	7.06±2.40	2.60±1.47	<0.001[a, b, c]
Glucose (mg/dl)	95±17	138±72	120±50	135±73	0.006[a] 0.01[b]
Albumin (g/dl)	4.4±0.7	3.8±0.6	3.6±0.4	3.7±0.7	0.01[a, b, c]
Calcium (mg/dl)	9.2±0.5	8.6±0.9	9.3±1.1	9.2±0.6	NS
Phosphorus(mg/dl)	3.4±0.8	4.9±1.6	4.2±1.0	4.4±1.1	NS
PTH (pg/ml)	48±20	374±283	384±330	161±107	<0.001[b, c], 0.001[d] 0.005[e]
WBC (/mm3)	8648±1943	7365±2614	7408±1751	8058±2916	NS
Hemoglobin (g/dl)	11.9±2.3	11.1±2.7	10.7±1.8	10.6±1.9	NS
Hematocrit (%)	36±7	33±8)	33±6	32±5	NS
Iron (mc/dl)	66±57	77±47	71±45	48±30	NS
TIBC (mcg/dl)	311±79	229±65	214±40	254±83	0.022[a] 0.01[b, c]
Ferritin (ng/ml)	92±183	632±549	369±230	219±422	NS
CRP (mg/L)	13.7±23.1	21.2±31.3	13.5±17.9	24.2±30.6	NS
Ghrelin (ng/ml)	2.81±0.37	3.81±0.98	4.31±0.62	4.49±1.18	<0.001[a, b, c] 0.040[d]

a: Control group versus predialysis group; **b:** Control group versus hemodialysis group; **c:** Control group vs. peritoneal dialysis group; **d:** Predialysis group vs. hemodialysis group; **e:** Predialysis group vs. peritoneal dialysis group

Table III: Distribution of gastroscopic and histopathological findings.

	CG (n=29)	HD group (n=21)	PD group (n=12)	Predialysis group (n=29)	p
Gastroscopic findings					
Esophagitis	3 (%10.3)	3 (%14.3)	2 (%16.7)	4 (%13.8)	0.947
Gastritis	29 (%100)	19 (%90.5)	12 (%100)	29 (%100)	0.111
Duodenitis	10 (%34.5)	12 (%57.1)	6 (%50)	7 (%24.1)	0.089
Ulcer	6 (%20.7)	3 (%14.3)	1 (%8.3)	2 (%6.9)	0.435
Loose cardia	1 (%3.5)	5 (%23.8)	1 (%8.3)	5 (%17.3)	0.129
GOR*	2 (%6.9)	3 (%14.3)	2 (%16.7)	3 (%10.3)	0.767
Histopathological findings					
Gastritis	27 (%93.1)	20 (%95.2)	11 (%91.7)	28 (%95.6)	0.907
Duodenitis	7 (%24.1)	2 (%9.5)	3 (%25.0)	2 (%6.9)	0.185
Malignancy	0 (%0.0)	1 (%4.8)	0 (%0.0)	0 (%0.0)	0.396
H. pylori	19 (%65.6)	14 (%66.7)	7 (%58.3)	22 (%75.9)	0.692

*Gastroesophageal reflux

DISCUSSION

H. pylori infection is a main factor for chronic gastritis and peptic ulcer disease and also a risk factor for gastric cancer. The increased urea in CRF patients may predispose to colonization of *H. pylori* in the stomach (3). We aimed to investigate the previously unexamined relation between *H. pylori* and ghrelin in uremic patients. The groups were well matched for demographic parameters and primary kidney disease. The only difference among these parameters was between the control group and predialysis group regarding age. It is known that H. pylori positivity increases with age. However, the prevalence of H. pylori was similar in these mentioned groups, so this difference can be ignored. In our study, the gold standard of H. pylori determination which is the histopathological evaluation was preferred in demonstrating gastric mucosa lesions due to H. pylori (16,17). *H. pylori* positivity was detected histopathologically in 68% of the patients. Serum ghrelin level has been found higher in dialysis and predialysis groups than the control group (Table I), confirming previous similar studies comparing patients with HD and PD with non-uremic control group (10). Serum ghrelin level of *H. pylori* positive patients was nearly equal to the ones without *H. pylori* (3.83±1.2ng/ml vs. 3.65±1.0ng/ml, p=0.50). This similarity was present in each of the four groups.

Likewise, ghrelin level was similar in patients with or without histopathologically proven gastritis. These results are different from the studies demonstrating decreased ghrelin levels in *H. pylori* positive patients. No correlation was detected between *H. pylori* and serum ghrelin level in another study conducted in non-uremic population (15). Similarly, in the study of Osawa et al. studying the effect of *H. pylori* eradication on plasma ghrelin level in 134 non-uremic population, plasma ghrelin concentration increased in 50 patients whereas decreased in 84 patients after *H. pylori* eradication (18).

The studies conducted on the relationship between *H. pylori* and ghrelin levels yielded some confusing results. There are different studies in non-uremic population showing the potential relationship between *H. pylori* and gastric ghrelin (19). Some studies have found that ghrelin level decreased in the presence of *H. pylori* (13, 14). Additionally, in the aforementioned study of Osawa et al, it has been showed that expression of preproghrelin mRNA (which shows gastric ghrelin synthesis directly) increased following *H. pylori* eradication but serum ghrelin level decreased (18). However, there are also some studies indicating that this relation may be related with only atrophic gastritis. Furthermore, it has been found that *H. pylori* eradication decreased serum ghrelin levels in prepubertal children (20). Moreover, it has been considered that increased ghrelin may be associated with weight gain observed following *H. pylori* eradication (21).

It has been found that ghrelin plays a gastroprotective role and it shows this effect via prostaglandins (22). Ghrelin and *H. pylori* affect gastric mucosa contrarily in non-dialysis population. For example, ghrelin protects gastric mucosa from deterioration of ischemia/reperfusion by inhibiting the activation of nuclear factor-kappa B whereas *H. pylori* causes mucosal inflammation by the same factor (23). Additionally, ghrelin administered through central or peripheral circulation, increases the gastric movements, rate of gastric emptying and acidic secretion in rats and/or mice and ghrelin secretion is decreased by 70% following gastrectomy (24). Serum ghrelin level has been investigated in the studies conducted with respect to different GIS diseases and it has been found remarkably lower in the patients with chronic gastritis (25). The most common reason of the gastric inflammation in non-uremic population is *H. pylori* infection. *H. pylori* leads to gastric mucosal toxicity and consequently deteriorated gastric mucosa by converting ammonia to urea through the activity of urease (26). Since urea concentration in gastric mucosa is higher in CRF patients, effects of *H. pylori* may be expected to be changed in this patient group. As a matter of fact, it has been found in a study conducted by Aydemir et al that *H. pylori* increased the apoptosis of the gastric epithelial cell and this effect is more remarkable in uremic patients (27).

Also in uremic animal models, it has been found that gastric mucosal inflammation is different from the non-uremic ones and ischemic vascular deterioration is more remarkable (28). As known, frequency of peptic ulcer does not increase in uremic patients even in decreased gastric acid secretion (hypochlorhydia) present in the uremic patients (29). All of these findings suggest that gastric mucosal inflammation in uremic patients is different from the non-uremic patients and occurs through a different physiopathological mechanism. Toxins or factors different from *H. pylori* may have a role in gastric mucosal inflammation in the uremic patients.

Our study has some limitations. First of all the study is cross-sectional and the sample size is small in PD group and only patients with sufficient symptoms to warrant endoscopy were included.

CONCLUSION

Ghrelin concentration increases in uremic patients. However; high ghrelin levels in uremic population are independent of presence of *H. pylori* in gastric mucosa.

REFERENCES

1. Andriulli A, Malfi B, Recchia S, Ponti V, Triolo G, Segoloni G: Patients with chronic renal failure are not at a risk of developing chronic peptic ulcers. Clin Nephrol 1985; 23(5): 245-248
2. Franzin G, Musola R, Mencarelli R: Morphological changes of the gastroduodenal mucosa in regular dialysis uraemic patients. Histopathology 1982; 6(4): 429-437

3. Khetmat H, Ahmadzad-Asl M, Amini M, Lessan-Pezeshki M, Einollahi B, Pourfarziani V, Naseri MH, Davoudi F: Gastroduodenal lesions and Helicobacter pylori infection in uremic patients and renal transplant recipients. Transplant Proc 2007; 39(4): 1003-1007
4. Nardone G, Rocco A, Fiorillo M, Del Pezzo M, Autiero G, Cuomo R, Sarnelli G, Lambiase A, Budillon G, Cianciaruso B: Gastroduodenal lesions and Helicobacter pylori infection in dyspeptic patients with and without chronic renal failure. Helicobacter 2005; 10(1): 53-58
5. Misra V, Misra SP, Shukla SK, Jaiswal PK, Agarwal R, Tondon S: Endoscopic and histological changes in upper gastrointestinal tract of patients with chronic renal failure. Indian J Pathol Microbiol 2004; 47(2): 170-173
6. Tseng GY, Lin HJ, Fang CT, Yang HB, Tseng GC, Wang PC, Hung TL, Deng YC, Cheng YT, Huang CH: Recurrence of peptic ulcer in uraemic and non-uraemic patients after Helicobacter pylori eradication: A 2-year study. Aliment Pharmacol Ther 2007; 26(6): 925-933
7. Aydın S, Özkan Y, Caylak E, Aydın S: Ghrelin and its biochemical functions: Review. Turkiye Klinikleri J Med Sci 2006; 26(3): 272-283
8. Hosoda H, Kojima M, Kangawa K: Biological, physiological, and pharmacological aspects of ghrelin. J Pharmacol Sci 2006; 100(5): 398-410
9. Yoshimoto A, Mori K, Sugawara A, Mukoyama M, Yahata K, Suganami T, Takaya K, Hosoda H, Kojima M, Kangawa K, Nakao K: Plasma ghrelin and desacyl ghrelin concentrations in renal failure. J Am Soc Nephrol 2002; 13(11): 2748-2752
10. Pérez-Fontán M, Cordido F, Rodríguez-Carmona A, Peteiro J, García-Naveiro R, García-Buela J: Plasma ghrelin levels in patients undergoing haemodialysis and peritoneal dialysis. Nephrol Dial Transplant 2004; 19(8): 2095-2100
11. Nwokolo CU, Freshwater DA, O'Hare P, Randeva HS: Plasma ghrelin following cure of Helicobacter pylori. Gut 2003; 52(5): 637-640
12. Tatsuguchi A, Miyake K, Gudis K, Futagami S, Tsukui T, Wada K, Kishida T, Fukuda Y, Sugisaki Y, Sakamoto C:Effect of Helicobacter pylori infection on ghrelin expression in human gastric mucosa. Am J Gastroenterol 2004; 99(11): 2121-2127
13. Shiotani A, Miyanishi T, Uedo N, Iishi H: Helicobacter pylori infection is associated with reduced circulating ghrelin levels independent of body mass index. Helicobacter 2005; 10(5): 373–378
14. Osawa H, Nakazato M, Date Y, Kita H, Ohnishi H, Ueno H, Shiiya T, Satoh K, Ishino Y, Sugano K: Impaired production of gastric ghrelin in chronic gastritis associated with Helicobacter pylori. J Clin Endocrinol Metab 2005; 90(1): 10-16
15. Gokcel A, Gumurdulu Y, Kayaselcuk F, Serin E, Ozer B, Ozsahin AK, Guvener N: Helicobacter pylori has no effect on plasma ghrelin levels. Eur J Endocrinol 2003; 148(4): 423-426
16. De Korwin JD: Advantages and limitations of diagnostic methods for H. Pylori infection. Gastroenterol Clin Biol 2003; 27: 380-390
17. Aksoy DY, Aybar M, Ozaslan E, Kav T, Engin D, Ercis S, Altinok G, Hascelik G, Uzunalimoglu B, Arslan S: Evaluation of the Helicobacter pylori stool antigen test (HpSA) for the detection of Helicobacter pylori infection and comparison with other methods. Hepatogastroenterology 2003; 50(52): 1047-1049
18. Osawa H, Kita H, Ohnishi H, Nakazato M, Date Y, Bowlus CL, Ishino Y, Watanabe E, Shiiya T, Ueno H, Hoshino H, Satoh K, Sugano K: Changes in plasma ghrelin levels, gastric ghrelin production, and body weight after Helicobacter pylori cure. J Gastroenterol 2006; 41(10): 954-961
19. 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(10): 2866-2872
20. Pacifico L, Anania C, Osborn JF, Ferrara E, Schiavo E, Bonamico M, Chiesa C: 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
21. Osawa H: Ghrelin and Helicobacter pylori infection. World J Gastroenterol 2008; 14(41): 6327-6333
22. Locatelli V, Bresciani E, Bulgarelli I, Rapetti D, Torsello A, Rindi G, Sibilia V, Netti C: Ghrelin in gastroenteric pathophysiology. J Endocrinol Invest 2005; 28(9): 843-848
23. Konturek PC, Brzozowski T, Walter B, Burnat G, Hess T, Hahn EG, Konturek SJ: Ghrelin-induced gastroprotection against ischemia-reperfusion injury involves an activation of sensory afferent nerves and hyperemia mediated by nitric oxide. Eur J Pharmacol 2006; 536(1-2): 171-181
24. Langer FB, Reza Hoda MA, Bohdjalian A, Felberbauer FX, Zacherl J, Wenzl E, Schindler K, Luger A, Ludvik B, Prager G: Sleeve gastrectomy and gastric banding: Effects on plasma ghrelin levels. Obes Surg 2005; 15(7): 1024-1029
25. Isomoto H, Ueno H, Nishi Y, Yasutake T, Tanaka K, Kawano N, Ohnita K, Mizuta Y, Inoue K, Nakazato M, Kohno S: Circulating ghrelin levels in patients with various upper gastrointestinal diseases. Dig Dis Sci 2005; 50(5): 833-838
26. Moss SF, Calam J, Agarwal B, Wang S, Holt PR: Induction of gastric epithelial apoptosis by Helicobacter pylori. Gut 1996; 38(4): 498-501
27. Aydemir S, Ozdemir BH, Gur G, Dogan I, Yilmaz U, Boyacioglu S: Effects of Helicobacter pylori infection on gastric epithelial cell kinetics in patients with chronic renal failure. World J Gastroenterol 2005; 11(45): 7183-7187
28. Cheville NF: Uremic gastropathy in the dog. Vet Pathol 1979; 16(3): 292-309
29. Kang JY, Wu AY, Sutherland IH, Vathsala A: Prevalence of peptic ulcer in patients undergoing maintenance hemodialysis. Dig Dis Sci 1988; 33(7): 774-778