Comparison of Uremic Patients with Non-Uremic Controls Regarding Gastroscopic Findings and Helicobacter Pylori Positivity

Üremik Hastaların Nonüremik Kontrollerle Gastroskopik Bulgular ve Helicobacter Pylori Pozitifliği Açısından Karşılaştırılması

ABSTRACT

OBJECTIVE: We aimed to investigate the relationship between gastroscopic findings and Helicobacter pylori (H. pylori) in uremic patients; and to compare them with the normal population.

MATERIAL and METHODS: Sixty two patients who had dyspeptic symptoms and who had a gastroscopic examination were included. These patients were grouped as hemodialysis group (n=29); peritoneal dialysis group (n=12), predialysis group (n=29) and the control group (n=29).

RESULTS: On pathological examinations of biopsies obtained for all participants of the study; 20 patients had gastritis, two had duodenitis, 14 had H. pylori positivity and one had malignancy in the hemodialysis group. Of the 12 peritoneal dialysis patients; 11 had gastritis, three had duodenitis and seven had H. pylori positivity. Twenty eight of the 29 predialysis patients had gastritis, two had duodenitis, 22 had H. pylori positivity. Of the 29 control subjects; 27 had gastritis, seven had duodenitis and 19 had H. pylori positivity. There was no difference between groups regarding gastroscopic and histopathological findings. The use of proton pump inhibitors did not affect these findings.

CONCLUSION: In spite of the differences in gastric mucosal physiology in uremia; the rate of H. pylori infection and gastroscopic findings are not different in uremic and nonuremic population.

KEY WORDS: Uremia, Gastroscopy, H. pylori

ÖZ

AMAÇ: Üremik hastalarda gastroskopik bulgular ile Helicobacter pylori (H. pylori) pozitifliği arasındaki ilişkiyi incelemeyi; ve bu hastaları normal popülasyonla karşılaştırmayı amaçladık.

GEREÇ ve YÖNTEMLER: Dispeptik semptomları olan ve gastroskopik muayenesi yapılmış olan 62 hasta dahil edildi. Hastalar hemodiyaliz grubu (n=29); periton diyalizi grubu (n=12), prediyaliz grubu (n=29) ve kontrol grubu (n=29) olarak gruplandırıldı.

BULGULAR: Çalışmanın tüm katılımcılarından alınan biyopsi örneklerinin patolojik incelemesinde hemodiyaliz grubunda 20 hastada gastrit, iki hastada duodenit, 14 hastada H. Pylori pozitifliği ve bir hastada malignite mevcuttu. On iki periton diyalizi hastasının 11'inde gastrit, üçünde duodenit ve yedisinde H. pylori pozitifliği vardı. 29 prediyaliz dönemdeki hastanın 28'inde gastrit, ikisinde duodenit, 22'sinde H. pylori pozitifliği vardı. Kontrol grubundaki 29 kişiden 27'sinde gastrit, yedisinde duodenit ve 19'unda H. pylori pozitifliği bulundu. Gruplar arasında gastroskopik ve histopatolojik bulgular açısından fark yoktu. Proton pompa inhibitörü kullanımının bu bulgular üzerine etkisi yoktu.

SONUÇ: Üremide mide mukoza fizyolojisindeki değişikliklere rağmen, H. pylori enfeksiyon oranı ile gastroskopik bulgular üremik ve nonüremik popülasyonda farklı değildir.

ANAHTAR SÖZCÜKLER: Üremi, Gastroskopi, H. pylori

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Received : 17.12.2012
Accepted : 23.02.2013

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INTRODUCTION

Chronic renal failure (CRF) is a public health problem in both our country and the world. Many factors play a role in the etiology of CRF. Diabetic nephropathy and hypertensive nephrosclerosis are the most frequent causes of CRF in Turkey according to the registry reports of the Turkish Society of Nephrology (1). Uremia affects the gastrointestinal system as well as all systems in the body.

H.pylori is a small (0.5-3μm), curved, spiral, flagellated Gram-negative bacteria that reproduce in microaerophilic media at 37°C. Most of them produce cytokines that are related clinically with inflammation (2). The natural reservoir of *H. pylori* is human. Transmission is by either fecal-oral or oral-oral route. *H. pylori* colonization rate is highly related with age and the geographic region. Gender has no effect on this rate. Half of the adults are colonized with these bacteria in developed countries, while this number reaches 80-90% in developing countries. *H. pylori* infection plays important roles in the pathogenesis of gastritis, duodenal ulcer, stomach ulcer, gastroesophageal reflux disease, Malt lymphoma, gastric atrophy and gastric cancer (3, 4). Both invasive tests requiring endoscopy such as rapid urease test, histological examination, culture, PCR test and phase contrast microscopic examination of gastric tissue; and noninvasive tests such as serology, 13C and 14C urea breath tests, *H. pylori* stool antigen test (HpSA) may be used for identification of *H. pylori* infection (5).

Gastrointestinal problems are quite frequent in patients with CRF. They present with nausea, epigastric burn and pain, and dyspepsia. Elevated urea levels in these patients may promote colonization of *H. pylori* in the gastric mucosa. There are variable results in the literature about the prevalence of *H. pylori* in the dialysis population. Although it has been thought for many years that CKD is associated with increased risk of peptic ulcer; some studies failed to reveal a statistically significant difference from the normal population. Peptic ulcers due to *H. pylori* infection play an important role in the pathogenesis of upper gastrointestinal bleeding which is among the leading causes of mortality in patients with CKD. It is recommended to treat *H. pylori* when detected in patients with CKD according to the risk stratification.

Herein, we aimed to study the relationship between gastroscopic findings and *H. pylori* colonization in patients with CKD.

PATIENTS and METHODS

Of the patients followed up in our nephrology outpatient unit between 2009 and 2010, those who had upper gastrointestinal endoscopic examination were selected for the study. Patients who gave informed consent were divided into three patient groups: Hemodialysis (HD) group (patients on the HD program for more than three months), peritoneal dialysis (PD) group (patients on chronic PD program for more than three months) and predialysis group (patients with stage-4 CKD). These groups were compared with the control group consisting of individuals with estimated glomerular filtration rate more than 90 ml/min and proteinuria less than 300 mg/day.

Patients were selected from those whose indications for endoscopic examination were determined by physicians other than the investigators. The use of drugs that potentially affect gastric acidity (proton pump inhibitors, H2 receptor blockers, anti-acids, steroids, nonsteroidal anti-inflammatory drugs) was not regarded as an exclusion criterion.

The primary kidney diseases, symptoms related with upper gastrointestinal system and the drugs that patients had used within the last three months were recorded.

Blood samples were obtained from each patient for analysis of glucose, urea, phosphorus, calcium, creatinine, parathyroid hormone, iron, total iron binding capacity (TIBC), ferritin, aspartate transaminase (AST), alanine transaminase (ALT), hemoglobin, hematocrit, platelet count and C-reactive protein (CRP) levels after 12 hours of fasting. These samples were taken from HD patients at the day after the last HD session of the week.

Endoscopic examination was performed with a video endoscope following a fasting period of at least 6-8 hours. The oropharyngeal mucosa was anesthetized with 10% Xylocaine spray before the procedure. Intravenous midazolam (1-5 mg) was used as sedative as needed. At least four biopsy samples were obtained from each patient, two from the antrum and two from the corpus of the stomach. The biopsy specimens were examined histopathologically in the pathology department of the same hospital.

Statistical analyses were conducted with the SPSS (Statistical Package for Social Sciences) for Windows 17.0 standard version package program. Numeric values were expressed as mean ± standard deviation (SD). The paired student t-test or Mann-Whitney U test were used for intergroup comparisons. Correlation analyses were performed by Pearson and Spearman's rho correlation tests for numeric and nonnumeric parameters, respectively. For the comparison of groups with normal distribution, the Student t-test or ANOVA were used. In case of abnormal distribution, Kruskal Wallis-H variant analysis was used for comparison of more than two groups. P values less than 0.05 were regarded as statistically significant.

RESULTS

Sixty two patients (mean age: 54.1±15.0 years) and 29 nonuremic subjects were included in the study. The male/female ratio and the mean age of the HD group (n=21) were 15/6 and 57.4±11.3 years respectively. Twelve PD patients (three male and nine female) were included with a mean age of 51.3±13.8 years. The corresponding data were 14/15 and 59.0±17.2 years

Table I: Gastrointestinal symptoms of the study groups.

	HD group (n=21)	PD group (n=12)	Predialysis group (n=29)	Control group (n=29)
Epigastric pain	11 (%52.3)	3 (%25.0)	17 (%58.6)	20 (%68.9)
Epigastric burn	10 (%47.6)	3 (%25.0)	16 (%55.2)	19 (%65.5)
Retrosternal burn	5 (%23.8)	2 (%16.7)	6 (%20.6)	9 (%31.0)
Dyspepsia	7 (%33.3)	2 (%16.7)	4 (%13.8)	5 (%17.2)
Nausea	2 (%9.5)	0 (%0)	5 (%17.2)	5 (%17.2)
Chronic diarrhea	0 (%0)	1 (%8.3)	0 (%0)	1 (%3.1)
Asymptomatic	1 (%4.8)	4 (%33.3)	2 (%6.9)	1 (%3.1)

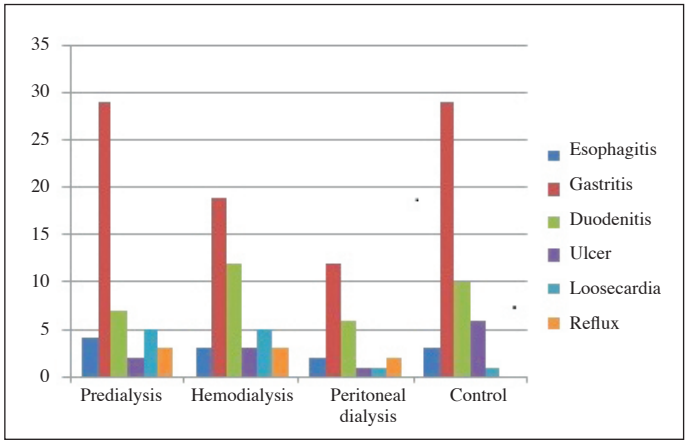

Figure 1: *Endoscopic findings of the groups.*

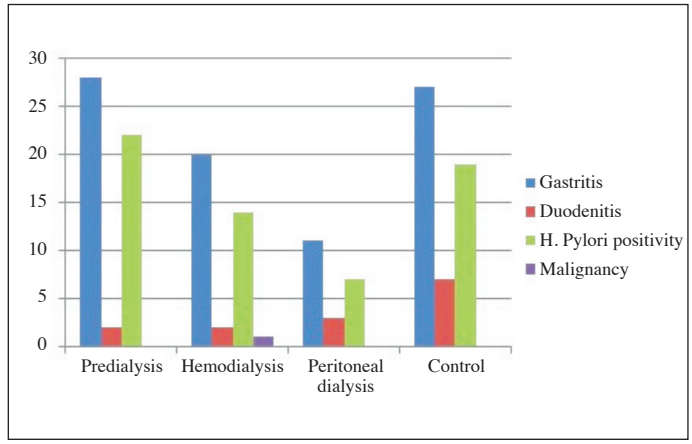

Figure 2: *Pathological findings of the groups.*

in the predialysis group (n=29); and 16/13 and 48.6±13.7 years in the control group.

The primary kidney diseases of the 62 uremic patients were diabetic nephropathy (n=20; 22%), nephrosclerosis (n=18; 19.8%), chronic glomerulonephritis (n=6; 6.6%), chronic pyelonephritis (n=4; 4.4%) and autosomal dominant polycystic kidney disease (n=3; 3.3%). The primary cause was unknown in 11 patients (12.1%).

Twenty seven patients (29.7%) were using proton pump inhibitors. The drugs effective on gastric acidity, directly or indirectly through the prostaglandin system, used by the patients were as follows: Acetylsalicylic acid (n=19; 20.9%), phosphorus binders (n=4; 4.4%), H_2 receptor blockers (n=2; 2.2%) and antiacids (n=1; 1.1%).

The gastrointestinal symptoms in the study groups are presented in Table I. Groups were similar regarding these symptoms; although asymptomatic patients were relatively more frequent and epigastric pain and burn were more common in the PD group; dyspepsia was more common in the HD group; and nausea was more common in the predialysis and the control groups.

The laboratory findings of the groups are presented in Table II.

The study groups were not statistically significantly different (p=0.908) regarding gastroscopic and histopathological findings as presented in Table III, Figure I, Table IV and Figure II. There was no statistically significant relationship between the use of proton pump inhibitors and the gastroscopic and histopathological findings.

DISCUSSION

The prevalence of *H. pylori* infection has been reported by many studies to be similar in both uremic and nonuremic subjects. *H. pylori* positivity was reported as 29-36% in a study that involved 76 HD patients, 202 transplanted patients and 247 control subjects: and the rate was similar in the three groups (6). These findings are consistent with our study with similar prevalence rates in the groups (Table IV). There are conflicting

Table II: Laboratory data of the groups.

	Control group (Mean±SD)	HD group (Mean±SD)	PD group (Mean±SD)	Predialysis group (Mean±SD)	P
Glucose (mg/dl)	96±17	140±74	120±50	136±74	NS
Urea (mg/dl)	26±13	110±41	91±36	85±47	<0.001**
Creatinin (mg/dl)	0.8±0.15	6.1±1.66	7.1±2.41	2.6±1.49	<0.001
Total protein (g/dl)	6.73±0.76	7.05±0.75	6.37±0.67	7.26±1.5	NS
Albumin (g/dl)	3.64±0.71	3.77±0.63	3.55±0.40	3.74±0.6	NS
AST (U/L)	23.2±24.0	20.2±17.4	17.3±8.7	22.4±15	NS
ALT (U/L)	20.9±15.4	19.6±14.3	20.8±15.1	18.8±15	NS
Calcium (mg/dl)	9.3±0.5	8.6±0.9	9.3±1.1	9.2±0.6	0.012**
Phosphorus (mg/dl)	3.4±0.79	4.5±1.52	4.2±0.97	4.42±1.1	0.002**
PTH (pg/ml)	48.05±21.12	376±291	384±330	159±108	<0.001**
CRP (mg/dl)	14.4±23.8	21.1±32.1	13.6±17.9	24.5±31.1	NS
Hemoglobin (g/dl)	11.9±2.3	11.1±2.8	10.7±1.8	10.6±1.8	NS
Hematocrit (%)	36.4±6.9	33.5±8.6	32.7±5.7	32.5±5.2	NS
Platelet (x10^3/ml)	262±78	203±83	258±56	275±99	NS
WBC (/ml)	6692±1542	7418±2671	7408±1751	8050±2959	NS
Iron (μg/dl)	69.4±59.1	78.8±48.1	71.3±45.3	47.6±30	NS
TDBK (μg/dl)	314±77	229±66	214±40	253±84	NS
Ferritin (ng/ml)	90±188	634±563	368±230	224±428	<0.001**

**Control group vs. predialysis group **Control group vs. other groups*

ALT: Alanine transaminase; **AST:** Aspartate transaminase; **PTH:** Parathyroid hormone; **CRP:** C-reactive protein; **WBC:** White blood cells; **TIBC:** Total iron binding capacity

Table III: Gastroscopic findings of the groups.

	HD group (n=21)	PD group (n=12)	Predialysis group (n=29)	Control group (n=29)
Esophagitis	3 (14.3%)	2 (16.7%)	4 (13.8%)	3 (10.3%)
Gastritis	19 (90.5%)	12 (100%)	29 (100%)	29 (100%)
Duodenitis	12 (57.1%)	6 (50%)	7 (24.1%)	10 (34.5%)
Ulcer	3 (14.3%)	1 (8.3%)	2 (6.9%)	6 (20.7%)
Loose cardia	5 (23.8%)	1 (8.3%)	5 (17.3%)	1 (3.5%)
Reflux	3 (14.3%)	2 (16.7%)	3 (10.3%)	2 (6.9%)

reports about the prevalence of *H. pylori* in uremia. The authors found the prevalence of duodenal ulcer as 11% among 249 patients in the transplantation waiting list (7). In another study conducted with 75 patients with end-stage renal disease, the rates of peptic ulcer, superficial gastritis, duodenitis and atrophic gastritis were found to be 8% (5% duodenal ulcer, 1% gastric ulcer), 66%, 40% and 15%, respectively (8). Kang et al (9) reported the rates of peptic ulcer and erythematous gastritis as 2% and 51% in 114 HD patients. Besides these results of increased incidence of peptic ulcer in patients with CKD; later studies (8) have found similar rates compared to the general population as in our study (7). With our results presented in Table III; it may

Table IV: Histopathological findings of the groups.

	HD group (n=21)	PD group (n=12)	Predialysis group (n=29)	Control group (n=29)	P
Gastritis	20 (95.2%)	11 (91.7%)	28 (95.6%)	27 (93.1%)	0.90
Duodenitis	2 (9.5%)	3 (25.0%)	2 (6.9%)	7 (24.1%)	0.18
H. pylori positivity	14 (66.7%)	7 (58.3%)	22 (75.9%)	19 (65.6%)	0.69
Malignancy*	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.33

* Adenocarcinoma

be said that rate of peptic ulcer disease is not increased in uremic patients compared with nonuremic subjects.

H. pylori is one of the most frequent infections in the world, with half of the world population having the microorganism (10). The incidence is over 80% in Japan and South America; while it was reported to be positive in 40% of the population in UK and 20% in Scandinavian countries (11). In a study conducted in our country, 76.8% of the asymptomatic subjects aged 18-24 years were found to be *H. pylori* positive (12). The TURHEP (Turkey Helicobacter Pylori Prevalence) study reported the *H. pylori* seroprevalence as 82.7% (13). The prevalence rates in the groups of our study (58-75%) are similar to the TURHEP study. There are other studies showing similar rates of *H. Pylori* prevalence in uremic and nonuremic subjects (14, 15); and one study has reported a lower rate in uremic patients (16). The lower prevalence in uremic patients was explained by more frequent use of broad spectrum antibiotics, and inhibition of the growth of the microorganism due to higher levels of urea nitrogen in gastric secretions. Moreover; high levels of proinflammatory cytokines (IL-1, IL6, IL8 and TNF) were claimed to inhibit growth of the microorganism in the gastric mucosa by way of stimulating migration of inflammatory cells to gastric mucosa and also by way of causing progression of gastric mucosal atrophy and increased gastric pH (16).

The most common reason of gastric inflammation in the nonuremic population is *H. pylori* infection. *H. pylori* causes damage in the gastric mucosa through conversion of ammonium to urea by urease enzyme. The activity of *H. pylori* is expected to be different in uremic patients due to higher levels of urea in the gastric mucosa (17). Aydemir et al (18) showed that *H.pylori* accelerates gastric epithelial cell apoptosis; and this effect is more exaggerated in uremic patients. It has been shown by animal studies that ischemic vascular insult is more prominent in uremic ones (19). As is well known; *H. pylori* infection is related with gastritis, gastric and duodenal ulcer and gastric carcinoma (20). Moreover, there is decrease in gastric acid secretion (hypochlorhydria) in uremic patients; and it is related with increased gastrin levels (9). All these findings lead to the conclusion that gastric mucosal inflammation and its pathogenesis are different in uremic patients.

CONCLUSION

In spite of the differences in gastric mucosal physiology in uremia; the rate of *H. pylori* infection and gastroscopic findings are not different in the uremic and nonuremic populations. Moreover; patients on PD, HD and those with stage-4 CKD are not different regarding the incidence of *H. pylori* infection and gastroscopic findings.

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