Research Article

Endoscopic Evaluation and *Helicobacter Pylori* Prevalence in Dyspeptic Patients with Chronic Kidney Disease

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Abstract: Objective: Dyspepsia is a common symptom in chronic kidney disease (CKD) as well as in the normal population and may develop due to functional or organic causes. In the literature, there are different results about dyspepsia symptoms, upper gastrointestinal tract lesions and Hp prevalence in CKD. In this study, endoscopic findings and the prevalence of Helicobacter Pylori (Hp) in dyspeptic chronic kidney patients were investigated and compared with the normal population.

Materials & Methods: 67 patients with dyspeptic CKD (52 hemodialysis, 6 continuous ambulatory peritoneal dialysis, 9 predialysis) and 63 age and gender-matched control groups were included in our study. Gastrointestinal symptom scoring, upper endoscopic examination, histopathological examination of gastric antrum and corpus biopsies taken during this period, and rapid urease test (RUT) for Hp were performed on all cases included in the study.

Results: Gastrointestinal symptom scores were not different between the CKD and control groups (6.2±2.5 vs 7.7±3.6) ($p>0.05$). Although the prevalence of Hp in the CKD group (44.8%) was lower than the control group (54%) according to gastric biopsy findings, there was no difference between them ($p>0.05$). In the endoscopic examination, duodenal ulcer was more common in the control group and duodenitis in the CKD group, and the difference between them was significant ($p<0.05$). When compared with histopathological evaluation, the sensitivity (78% vs. 79%) and specificity (95% vs. 93%) of the urease test were similar in the CKD and control groups in both groups.

Conclusion: Gastrointestinal symptom score and Hp prevalence in chronic kidney disease were similar to the control group. No correlation was found between Hp and gastrointestinal symptom score. In the endoscopic examination, duodenal ulcer was more common in the control group and duodenitis was more common in the CKD group.

Keywords: Dyspepsia, Endoscopy, Chronic renal failure, Helicobacter Pylori, Ulcer, Abdomen.

INTRODUCTION

Dyspepsia refers to chronic or recurrent pain or discomfort in the upper abdomen. The feeling of discomfort is subjective, and may include various symptoms such as premature satiety or upper abdominal fullness [1]. Dyspepsia can be stratified as organic dyspepsia, unspecified dyspepsia and functional dyspepsia. Functional dyspepsia may be defined as the type of dyspepsia where an organic cause cannot be detected as a result of investigations including endoscopy [2].

Although many factors including bacteria are blamed in the pathogenesis of dyspepsia, the most talked about is Helicobacter Pylori (Hp) [3]. Hp is a microorganism identified in 1980s which has been associated with peptic ulcer, atrophic gastritis, gastric cancer and MALTOMA. Relevant acute infection may cause transient nausea, vomiting and dyspeptic symptoms. In many studies based on large populations, Hp was found more frequently in the gastric mucosa of individuals with dyspepsia than in healthy individuals [4]. The role of Hp eradication in symptom control in functional dyspepsia is controversial, but it has also been reported in the literature that Hp eradication is beneficial [5].

Although majority of the population has dyspepsia experience, only half are investigated medically [6]. The severity and frequency of symptoms, fear of underlying disease, low social status, older age, anxiety, psychological stress, inadequate psychosocial support are factors which affect referral to a physician [7].

Symptoms of upper gastrointestinal system are common in chronic kidney disease (CKD). Loss of appetite, hiccups, nausea and vomiting, epigastric pain and retrosternal burning are common complaints [8]. Esophagitis, gastritis, duodenitis, and mucosal erosions are commonly seen in CKD and these gastro duodenal lesions do not corelate with symptoms. In the literature, there exist contradictory results concerning the dyspepsia symptoms, upper gastrointestinal lesions, and Hp prevalence in patients with dyspeptic CKD [9, 10].

The aim of this study is to evaluate endoscopic findings, Hp prevalence and histopathological findings in patients with dyspeptic CKD and to compare the results with dyspeptic patients with normal population.

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doi.org/10.21089/njhs.74.0144

MATERIALS AND METHODS

After obtaining the approval of the Medical Ethics Board of Ondokuz Mayis University, our Medical Faculty (ethical approval number 2006-83), we performed a prospective study at the endoscopy unit of Ondokuz Mayis University over 11 months period. In a total of 130 volunteers, 67 patients with CKD and 63 patients without CKD requiring endoscopy due to dyspepsia were included in the study. Those who had previously received Hp eradication therapy, antibiotics in the last month for any reason, H2-receptor blockers or proton pump inhibitor within the last 10 days were excluded.

Creatinine clearance was above 90 mL/min according to the Cockcroft-Gault formula in the control group. Creatinine clearance of the patients in the predialysis group was 10-60 mL/min according to the Cockcroft-Gault formula. Hemodialysis patients were on a regular bicarbonate hemodialysis schedule of 3 days a week. Continuous Ambulatory Peritoneal Dialysis (CAPD) patients were undergoing peritoneal dialysis 4 times daily.

Written informed consent were obtained from all patients before participation in the study. All patients were scored for responses to questions on the gastrointestinal symptom rating scale (GSRS) in order to rate the symptoms of dyspepsia [11]. Patients were asked to rate their symptoms of epigastric pain, heartburn, acid regurgitation, sucking sensations in the epigastrium, nausea and vomiting, borborygmus, abdominal distention, bloating and eructation from 0 to 3 (0=None, 1=Short duration, 2=Long duration, 3=Continuous) [12].

Esophagogastroduodenoscopy was performed using a video endoscope (Evis Exera CV-160, serial number: 7415754, Olympus, Japan) following at least 8 hours of fasting. Two punch biopsies were taken from both antrum and corpus for histopathological examination and rapid urease test. For histopathological examination, samples were evaluated according to the Sydney classification.

The commercial test named HelicheckR (Salubris A.Ş. Akgüvercin Sok. No:9 Maltepe 34841 Istanbul, European Union Harmonization Standard: EN980:2003, EN375:2001, 24.04.2004) was used for the Hp "rapid urease test". Biopsy samples were placed in the test solution and incubated at 37 °C for 2 hours. At the end of this period, those with color changes consistent with the control test were deemed as positive.

STATISTICAL ANALYSIS

SPSS 13.0 for Windows package program (Customer ID: 361835) was used for the statistical evaluation. After checking the findings in terms of suitability for normal distribution with Kolmogorov-Smirnov test, Student's t-test was used for the inter-group comparison of features with normal distribution Mann Whitney U test was used for features with non-normal distribution. The x2 analysis and Fisher's exact test were utilized for categorical data. Results are presented with standard deviation. Values with $p<0.05$ were considered statistically significant.

RESULTS

A total of 130 patients were enrolled in the study. There were 67 patients in the CKD group and 63 in the control group. The number of CKD patients undergoing hemodialysis, CAPD and predialysis treatment were 52 (77.6%), 6 (9%), 9 (13.4%), respectively. There was no difference between CKD and control group in terms of gender and age. The duration of CKD and renal replacement therapy and etiology of CKD and are shown in Table **1** and Table **2**, respectively.

In accordance with findings of stomach biopsy, Hp prevalence in CRF group (44,8%) was lower compared to control group (54%), however, there was no statistical difference between them ($p>0.05$). There was no difference between CKD and control groups in terms of gastrointestinal symptom score ($p>0.05$). It was also noted that Hp did not affect the score ($p>0.05$) (Table **3**). There was no relevance between Hp prevalence and average age CRF and renal replacement treatment period ($p>0.05$).

Endoscopic findings of the CKD and control groups did not reveal any statistically significant difference in terms of gastric ulcer, erosive gastritis, erythematous gastritis, esophagitis and hiatal hernia frequency ($p>0.05$). Duodenitis was found in 33 (49.3%) patients in the CKD group and in 11 (17.5%) in the control group ($p <0.001$). There was a statistical difference between the control group and the hemodialysis patients regarding duodenal ulcer ($p<0.05$). Duodenitis rate was highest in the hemodialysis patients and lowest in the control group, and there was a statistical difference between these two groups (Table **4**).

Endoscopic findings of the CKD and control groups were compared in terms of Hp. There was a significant relationship between Hp and duodenal ulcer in the CKD group ($p <0.05$). In the CKD group, erosive gastritis was greater among Hp-negative subjects compared to Hp-positive subjects ($p<0.05$). A significant relationship was observed between duodenal ulcer and Hp in the control group ($p <0.05$). There was no relationship between other endoscopic findings and Hp in the control group (Table **5**).

There was no statistically significant difference between the CKD and control groups regarding histopathological diagnosis ($p>0.05$). Chronic gastritis was the most observed histopathological diagnosis. Chronic gastritis was detected in 96.7% of Hp-positive patients in the CKD group and in 100% of Hp-positive patients in the control group. Chronic gastritis was found in 69% of Hp-negative patients in the CKD group, and Hp was associated with chronic gastritis ($p <0.05$) (Table **6**).

Rapid urease testing and histopathological examination revealed that Hp positivity was higher in the control group compared to the CKD group (p>0.05). The rate of positive rapid urease tests was lower than the Hp positivity in histopathological tests in both groups. When the hemodialysis, CAPD, predialysis and control subjects were compared in terms of Hp, no Hp was found in the CAPD group. There was a statistical difference between the predialysis and CAPD patients regarding Hp infection in histopathological evaluation (p<0.05). There was no difference between the hemodialysis, CAPD, predialysis and control subjects in terms of urease test positivity (p >0.05) (Table **7**). Hp positivity was not associated with CKD and hemodialysis duration (p >0.05).

Table 1. Duration of the Chronic Kidney Disease (CKD) and Renal Replacement Therapy.

Patient Group (n)	CKD duration (month)	Renal Replacement Therapy Duration (month)
Hemodialysis (52)	81.4 ± 54.8	42.5 ± 35.2
CAPD (6)	74.3 ± 36	59.6 ± 38.8
Predialysis (9)	27.3 ± 27.3	-

CAPD: Continuous Ambulatory Peritoneal Dialysis.

Table 2. Etiology of Chronic Kidney Disease.

Disease	% (n)
Diabetes Mellitus	6 (4)
Hypertension	22.4 (15)
Glomerulonephritis	23.9 (16)
Polycystic Kidney Disease	4.5 (3)
Other	17.9 (12)
Unknown	25.4 (17)

Table 3. Gastrointestinal Symptom Score in Hp-Positive and Hp-Negative Patients in the Chronic Kidney Disease (CKD) Group and the Control Group.

Gastrointestinal Symptom Score	CKD (n:67)	Control (n:63)	p value
Hp (+)	5.6±2.3	7.9±3.9	p>0.05
Hp (-)	6.7± 2.6	7.4±3.2	p>0.05
Total	6.2±2.5	7.7±3.6	p>0.05

Table 4. Endoscopic Findings of the Chronic Kidney Disease (CKD) and Control Groups .

	CKD					
Endoscopic Finding	**Hemodialysis (n:52) % (n)**	**CAPD (n:6) % (n)**	**Predialysis (n:9) % (n)**	**Total (n:67) % (n)**	**Control (n:63) % (n)**	**p value**
Gastric Ulcer	5.8 (3)	0	11.1 (1)	6 (4)	3.2 (2)	>0.05
Duodenal Ulcer	**3.8 (2)a**	**0**	**22.2 (2)**	**6 (4)b**	**19 (12)ab**	**<0.05**
Erosive Gastritis	34.6 (18)	50 (3)	0	31.3 (21)	20.6 (13)	>0.05
Erythematous gastritis	59.6 (31)	50 (3)	88.9 (8)	62.7 (42)	77.8 (49)	>0.05
Esophagitis	26.9 (14)	0	22.2 (2)	23.9 (16)	11.1 (7)	>0.05
Duodenitis	**55.8 (29)a**	**33.3 (2)**	**22.2 (2)**	**49.3 (33)b**	**17.5 (11)ab**	**<0.001**
Hiatal Hernia	13.5 (7)	12.5 (1)	11.1 (1)	13.4 (9)	11.1 (7)	>0.05
Other	5.8 (3)	0	11.1 (1)	6 (4)	9.5 (6)	>0.05

CAPD: Continuous Ambulatory Peritoneal Dialysis.

[a]Statistical significance between the hemodialysis group and the control group, p<0.05.

[b]Statistical significance between the total CKD group and the control group, p<0.05.

Table 5. Endoscopic Findings of the Chronic Kidney Disease (CKD) and Control Groups .

Endoscopic Finding	CKD (n:67)			Control (n:63)		
	Hp(+) (n:30) % (n)	Hp(-) (n:37) % (n)	p value	Hp(+) (n:34) % (n)	Hp(-) (n:29) % (n)	p value
Gastric Ulcer	3.3 (1)	8.1 (3)	>0.05	2.9 (1)	3.4 (1)	>0.05
Duodenal Ulcer	**13.3 (4)**	**0**	**<0.05**	**29.4 (10)**	**6.9 (2)**	**<0.05**
Erosive Gastritis	16.7 (5)	43.2 (16)	<0.05	23.5 (8)	17.2 (2)	>0.05
Erythematous gastritis	52.4 (22)	47.6 (20)	>0.05	76.5 (26)	79.3 (23)	>0.05
Esophagitis	30 (9)	18.9 (7)	>0.05	5.9 (2)	17.2 (5)	>0.05
Duodenitis	46.7 (14)	51.4 (19)	>0.05	17.6 (6)	17.2 (5)	>0.05
Hiatal Hernia	6.7 (2)	18.9 (7)	>0.05	5.9 (2)	17.2 (5)	>0.05
Other	10 (3)	2.7 (1)	>0.05	11.3 (4)	6.9 (2)	>0.05

Table 6. Histopathological Diagnoses in Hp-Positive and Hp-Negative Patients in the Chronic Kidney Disease (CKD) Group and the Control Group.

Histopathological Diagnosis	CKD (67)			Control (63)		
	Hp(+) (n:30) % (n)	Hp(-) (n:37) % (n)	p value	Hp(+) (n:34) % (n)	Hp(-) (n:29) % (n)	p value
Chronic Gastritis	96.7 (29)	62.2 (23)	<0.05	100 (34)	69 (20)	<0.05
Normal Mucosa	0 (0)	27 (10)	<0.05	0	24.1 (7)	<0.05
Other	3.3 (1)	10.8 (4)	>0.05	0	6.9 (2)	>0.05

Table 7. Hp Prevalence in the Chronic Kidney Disease (CKD) and Control Groups.

Hp Detection Method	CKD					
	Hemodialysis (n:52) % (n)	CAPD (n:6) % (n)	Predialysis (n:9) % (n)	Total (n:67) % (n)	Control (n:63) % (n)	p value
Rapid Urease Test	36.5 (19)	0	55.6 (5)	35.8 (24)	46 (29)	>0.05
Histopathology	46.2 (24)	0a	66.7 (6)a	44.8 (30)	54 (34)	**<0.05**

CAPD: Continuous Ambulatory Peritoneal Dialysis.
a Statistical significance between the CAPD group and the predialysis group, p<0.05.

DISCUSSION

In the present study, GSRS was employed to quantitatively assess dyspepsia symptoms [11]. Similar gastrointestinal symptom scores were found in the CKD group and the control group. Furthermore, Hp positivity and dyspepsia scores were not related.

The pathogenesis of dyspepsia and gastrointestinal lesions in CKD remains unclear. Gastrin levels are known to increase in CKD. The cause of hypergastrinemia is the gastrin-induced decrease in renal clearance and the inadequate negative feedback mechanism against hypergastrinemia [12]. Acid hypersecretion, which results from hypergastrinemia, may be thought to be playing a key role in the development of gastrointestinal lesions; however, gastrin levels in CKD are inversely proportional to gastric acidity. High gastrin levels occur in response to hypochlorhydria rather than the cause of gastro duodenal lesions [13, 14]. A significant decrease is seen in gastrin levels following Hp eradication [15, 16]. Although some studies have demonstrated significant improvement in dyspepsia symptoms with Hp eradication, Hp is not thought to be involved in functional dyspepsia before [17]. In the last 10 years, it is reported that Hp eradication has been shown to be effective in improving dyspeptic symptoms [18, 19]. On the other hand, no relationship was found between Hp and dyspepsia in a limited number of studies performed in CKD [10, 15, 16, 20]. In the present study, no relationship was observed between Hp presence and dyspepsia score. In CKD,

an increase has been observed in gastrointestinal motility and in some mediators such as cholecystokinin, neurotensin, and glucagon. Potential hyperkalemia, hypocalcemia and acidosis in CKD have been associated with dyspepsia [21]. Prolonged gastric emptying time has been reported in CKD. Increased levels of gastrointestinal hormone levels and uremic toxins, acidosis, electrolyte disturbances, and impaired gastric myoelectrical activity may result in prolonged gastric emptying time. These findings have also been associated with dyspeptic symptoms and malnutrition. It has been determined that Hp does not affect gastric emptying time [21, 22]. These factors may cause dyspepsia in CKD through altered acid secretion and gastrointestinal dysmotility.

Offerhaus and colleagues have reported that Hp does not have a role in peptic ulcer predisposition in CKD [23]. Gladziwa and colleagues investigated the prevalence of peptic ulcer in hemodialysis, predialysis and control groups, and they found it to be lower in the hemodialysis group. Peptic ulcer was also associated with Hp in all three groups. In the present study, similar to these findings, duodenal ulcer was less common and associated with Hp in CKD. As is the case in the present study, chronic active gastritis was associated with Hp and was the most common histopathological diagnosis. Ozgur and colleagues found a higher rate of duodenal ulcer in the control group compared to hemodialysis patients (22% vs 6%), similar to the findings of the present study [24]. Duodenitis was more common in the hemodialysis group (38% vs 12%). However, gastritis rate was higher in the control group (19% vs 43%) [25]. In our study, we found no relationship between GSRS and Hp positivity.

Although Hp prevalence was lower in hemodialysis patients compared to the control subjects in our study for urease test, there was no statistical difference. On the other hand, in dialysis patients, H. pylori prevalence was found to be significantly higher in pathological examination. Huang *et al*. evaluated the effectiveness of urea breath test in hemodialysis and dyspeptic patients with normal renal function in 2000. They found the prevalence of Hp as 47.1% in the hemodialysis group and 60% in the control group, but there was no statistical difference between them [26]. In another study, Hp frequency was found to be lower than the normal population, and our results are consistent with the literature [27]. Uremia, dialysis could have been to increase the risk of lesions in the gastrointestinal tract [28].

In a study conducted by Huang and colleagues evaluating the efficacy of urea breath test, chronic gastritis was found to be the most common endoscopy finding among hemodialysis patients. They associated Hp with gastric ulcer in the hemodialysis group [26]. Nakajima and colleagues found gastric ulcer in 5.9% of dialysis patients while this rate was 11.7% for duodenal ulcer, 25.5% for atrophic gastritis, 21.6% for superficial gastritis, 17.7% for erosive gastritis and 7.8% for verrucous gastritis. Compared to the control group, i.e., the predialysis group, gastric ulcer was not observed in the predialysis group; however, other endoscopic findings were similar. In the said study, Hp prevalence of the hemodialysis group was as low as that observed in the present study [29]. In the endoscopic study by Simunic and colleagues, non-ulcer lesions were found in 47.3% in the hemodialysis group while the rate of duodenal ulcer was 5% and esophagitis 43.6%. The most common histopathological diagnosis was chronic active gastritis. There was no difference between the CKD group and the control group in terms of endoscopic and histopathological findings [30]. In another recent study, it was determined that the most common endoscopic diagnosis was gastritis in hemodialysis patients, and chronic atrophic gastritis was found to be statistically significantly more common in hemodialysis patients [9]. In our study, the most common endoscopic diagnoses in patient subgroups were erythematous gastritis and duodenitis, respectively. We found the rate of duodenal ulcers to be lower in the CKD group compared to the control group, and the frequency of duodenitis to be higher. The higher frequency of Hp in the control group may partially explain the difference in duodenal ulcer rate in this group. Because we found that duodenal ulcers were associated with Hp in both groups. We found no difference between the groups for gastric ulcer, erosive gastritis, erythematous gastritis, esophagitis, and hiatal hernia. We found erosive gastritis higher in the Hp negative CKD group compared to Hp positive. We did not find any relationship between Hp and other endoscopic findings in the CKD and control groups. When CHB subgroups (Hemodialysis, CAPD, predialysis) and control group were compared in terms of endoscopic findings, duodenal ulcer was higher in control group than hemodialysis group. In the hemodialysis group, duodenitis was higher than the control group. We found no difference in endoscopic findings in the CAPD and predialysis groups.

There was no correlation between the duration of CKD or hemodialysis with Hp prevalence. This finding is consistent with some other studies [26, 30]. However, in some studies, Hp prevalence was shown to decrease with increased duration of hemodialysis. Authors suggest that this may be related to the several medications CKD patients receive, including antibiotics, the toxic effect of aluminum-containing phosphorus binders for Hp, and the fact Hp growth may not be possible in the presence serum urea levels above 6 mmol/L [29, 31].

Our study has some limitations. As it is a single-center study, the results cannot be generalized. Our sample size could have been higher.

CONCLUSION

In conclusion, the present study found similar dyspepsia scores in the control group and the CKD group. We suggest that since endoscopy may cause false negative results in

urease test, it would be appropriate to perform histopathological examination.

AUTHORS' CONTRIBUTION

Özgür Ecemiş and Ahmet Bektaş: Design.

Müge Ustaoğlu, Hasan Eruzun, Tülay Bakir and Ahmet Bektaş: Writing, Statistics.

Müge Ustaoğlu, Hasan Eruzun, Özgür Ecemiş: Editing.

Müge Ustaoğlu, Hasan Eruzun, Özgür Ecemiş and Ahmet Bektas: Data Interpretation.

Müge Ustaoğlu, Hasan Eruzun and Özgür Ecemiş: Translate.

Tülay Bakir and Ahmet Baktis: Supervising.

CONFLICT OF INTEREST

Declared none.

ACKNOWLEDGEMENTS

Declared none.

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Received: February 02, 2023 Revised: April 03, 2023 Accepted: April 03, 2023