

Functional bowel disorders and associated risk factors in hemodialysis patients in Turkey

Edip Gökalp Gök¹, Ayça İnci², Melahat Çoban², Dilek Aslan Kutsal³, Seyhun Kürşat⁴

¹Department of Rheumatology, Akdeniz University School of Medicine, Antalya, Turkey

²Department of Nephrology, Antalya Training and Researh Hospital, Antalya, Turkey

³Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Center, İstanbul, Turkey

⁴Department of Nephrology, Celal Bayar University School of Medicine, Manisa, Turkey

ABSTRACT

Background/Aims: Functional bowel disorders (FBDs) impair the quality of life in patients with end-stage renal disease (ESRD). The aim of our study was to determine the prevalence and distribution of the subtypes of FBDs in hemodialysis (HD) patients.

Materials and Methods: This prospective, cross-sectional study included 80 patients who received HD for more than 3 months (patient group) and 80 healthy controls (control group). FBDs were diagnosed according to the Rome II diagnostic criteria by excluding organic pathologies.

Results: Forty-six (57.5%) patients were males, and their average age was 62.13 ± 12.92 (23–90) years. The mean duration of dialysis was 57.48 ± 59.23 (3–312) months, and the mean Kt/V (K: dialyzer clearance of urea, t: dialysis time, V: volume of distrubition of urea) value was 1.53 ± 0.31 . The rate of FBDs was significantly higher in the patient group than in the control group (p=0.01). In total, 7.5% of the patients had irritable bowel syndrome, 3.8% had functional bloating, and 16.3% had functional constipation. FBDs were significantly higher in women (p=0.004). While there was no statistically significant difference between patients with and those without FBDs in terms of the presence of additional diseases, smoking, alcohol use, educational level, marital status, and residential areas (p>0.05), serum phosphorus (P) levels were significantly higher in the patients with FBDs (p=0.03).

Conclusion: FBDs and their functional constipation subtype are more common in HD patients than in the healthy population in Turkey. FBDs are most frequently observed in females and housewives with high serum P levels.

Keywords: Functional bowel disorders, end stage renal disease, irritable bowel syndrome, functional constipation

INTRODUCTION

Gastrointestinal symptoms (GISs) in patients with endstage renal disease (ESRD) show changes depending on uremia, the treatment model, changes in diet, and drugs used (1) and are also seen in 77–79% of these patients (2). GISs show differences depending on the stage of chronic kidney disease (CKD) and type of renal replacement therapy. In a study conducted in hemodialysis (HD) patients, nausea (74%) was the most frequently reported GIS; further, vomiting, constipation, and diarrhea were found at rates of 68%, 59%, and 25%, respectively (3). For diagnosis of Functional bowel disorders (FBDs) ; first alarm symptoms were excluded to suggest any organic disorders and then FBDs were diagnosed by the Manning or Rome criteria. First, they were defined using the Manning criteria (4). The Manning criteria were then developed as the Rome criteria. The Rome I, Rome II, and Rome III (2006) diagnostic criteria for FBDs were published (5).

In according to the symptoms which exist on its own, FBDs are divided into five subgroups: irritable bowel syndrome (IBS), functional bloating, functional con-

 Address for Correspondence:
 Ayça İnci
 E-mail: aycainci2004@hotmail.com

 Received:
 August 15, 2016
 Accepted: December 8, 2016

 © Copyright 2017 by The Turkish Society of Gastroenterology • Available online at www.turkjgastroenterol.org • DOI: 10.5152/tjg.2016.0415

12

stipation, functional diarrhea and unspecified (6). The prevalence of IBS varies according to the definition criteria in normal populations and ranges between 3.7% and 25% according to the Rome II criteria (7). In Turkey, this rate has been reported to be 21% in the normal population and 44% in HD patients (8). Functional constipation occurs in up to 27% of the normal population (9). To the best of our knowledge, no study has compared functional constipation in a normal population with that in HD patients in Turkey.

It is known that the GISs are more common in patients with diabetes mellitus (DM) than in a healthy population (10). However, in a study, there was no significant difference between patients with uremia with and those without DM in terms of the prevalence of GISs. Therefore, this suggests that the presence of DM does not cause GISs in this patient group (11). In a study by Shakil et al. (12), there was a significant relationship between the presence of DM and the increased incidence of constipation in patients with uremia.

In HD patients, there are few studies to evaluate the prevalence of FBDs and their subtypes and associated factors. The aim of our study was to determine the prevalence of FBDs and their subtypes and FBD-related risk factors in HD patients.

MATERIALS AND METHODS

This cross-sectional study included 80 patients who were older than 18 years, without alarm symptoms, who were diagnosed with CKD by taking the history and conducting physical examinations and clinical and laboratory tests, and received HD for more than 3 months (patient group) among 120 patients in our Nephrology Clinic. These patients were compared with 80 healthy controls with similar age and gender (control group). The study was conducted between March 2015 and January 2016. All patients underwent polysulfone and bicarbonate dialysis for 4 h three times a week. The blood flow rate and dialysate flow rate were set at 250-300 mL/min and 500 mL/min, respectively. People who had cognitive or cognitive dysfunction (memory loss, dementia, difficulty in understanding the guestion), acute or active infection in the last 3 months, a major surgical intervention in the last 6 months, and another known active disease history and those who were unwilling to participate were excluded.

The causes of CKD, the mean duration of HD, habits, additional diseases, and tests [hemoglobin (Hgb), albumin, calcium, phosphorus (P), and parathyroid hormone] performed at recent visits of the patients were recorded. The Kt/V value, which is used as an indicator of dialysis adequacy, was calculated from the equation described by Daugirdas (13). In the definition of Kt/V, K is the dialyzer clearance of urea at a given blood flow rate (ml/min), t is the dialysis time in minutes, and V is the volume of distribution of urea (I). The Kt/V value should be between 1.2 and 1.4 in patients without DM and above 1.4 in patients with DM for adequate dialysis treatment (14). The present study was

approved by the Ethics Committee of Training and Research Hospital, and signed consent forms were received from the patient and control groups.

Functional bowel disorders were diagnosed according to the Rome II diagnostic criteria by excluding organic pathologies. Drossmann edited Rome II criteria in the book named "Functional Gastrointestinal Disorders" (15). The Rome II diagnostic criteria were validated and previously used in Turkish patients by Kasap et al. (16) (Table 1). A questionnaire was used to determine the prevalence and distribution of the subtypes of FBDs in the patient and control groups (ANNEX-1).

(ANNEX-1): These were questions used for IBS, functional bloating, functional constipation, functional diarrhea, and unspecified FBDs. In the evaluation of the questionnaire, it was decided that (1) was never or rarely, (2) was sometimes, (3) was often, (4) was almost, and (5) was always. Then the following questions were asked:

A1: Did you have pain or discomfort around your stomach or belly in the last 1 year? A2: Did you have pain or discomfort around your stomach or belly in the last 3 months? A3: Did your pain or discomfort during the last 3 months change according to your complaints in the last 1 year? A4: Was pain or discomfort around your stomach or belly constantly since the last 1 year? A5: How old were you when this pain or discomfort began? A6: Mark the location of your pain or discomfort around your stomach or belly in the illustration (You can select more than one area). A7: If you have pain in more than one area, the pain in which area annoys you most? A8: Did the pain or discomfort around your stomach or belly since the last 1 year affect your daily life? A9: How bad was your pain or discomfort around your stomach or belly in the last 1 year? A10: Was there reduction in or relief from pain or discomfort around your stomach or belly on defecation in the last 1 year? A11: Did you defecate more frequently in the last 1 year since your pain

Table 1. Rome II criteria

1. The presence of abdominal discomfort or pain that is relieved with defecation and/or associated with a change in frequency of stools and/or associated with a change in the form (appearance) of stools.

2. The presence of two or more of the following symptoms:

- Abnormal stool frequency
- Abnormal stool form (lumpy/hard/loose/watery)

• Abnormal stool passage (straining/urgency/feeling of incomplete evacuation)

- Passage of mucus
- Bloating or feeling of abdominal distension

3. The symptoms described above to maintain during 3 months or longer or occur in intervals over a 12-month period.

4. The presence of symptoms not associated with other gastrointestinal disorders.

or discomfort around your stomach or belly started? A12: Did you defecate less frequently in the last 1 year since your pain or discomfort around your stomach or belly started? A13: Did you have loose stools in the last 1 year since your pain or discomfort around your stomach or belly started? A14: Did you have hard stools in the last 1 year since your pain or discomfort around your stomach or belly started? A15: Did your pain or discomfort reduce with burping in the last 1 year? A16: Did you have pain or discomfort after meals in the last 1 year? A17: Did your pain or discomfort wake you from your sleep in the last 1 year? A18: Did your pain or discomfort spread to your back or shoulder in the last 1 year? A19: Did your pain or discomfort last longer than 20 min in the last 1 year?

Those who selected the 3rd, 4th, and 5th options in the question on A1 and at least two of the questions on A10, A11, A12, A13, and A14 were considered to have IBS.

B1: Did you get your meal before it was finished due to early satiety in the last 1 year? B2: Did you feel dyspepsia after eating around your stomach or belly in the last 1 year? B3: Did you have nausea in the last 1 year (you want to vomit but could not)? B4: Did you have non-drug-induced or involuntarily vomiting in the last 1 year? B5: Did you vomit 3 days a week in any three months of the last 1 year? B6: Did you retch in the last 1 year? B7: Did you feel bloating, tightness, or fullness in your abdomen in the last 1 year?

Those who selected the 3^{rd} , 4^{th} , and 5^{th} options in the question on B7 and had no IBS were considered to have functional bloating.

D1: Did you have problems with your bowel in the last 1 year? D2: Did you have problems with your bowel in the last 3 months? D3: Did you have less than three bowel movements per day in the last 1 year? D4: Did you have less than three bowel movements per week in the last 1 year? D5: Did you have hard or lumpy stools in the last 1 year? D6: Did you have loose or watery stools in the last 1 year? D7: Did you feel incomplete evacuation in the last 1 year? D8: Did you need to strain during bowel movement in the last 1 year? D9: Did you experience an urgent need to go to the toilet in the last 1 year? D10: Did you see mucus in your stools in the last 1 year? D11: Did you feel an obstacle in your anus during bowel movements in the last 1 year? D12: Did you try to defecate by adding a pressure in or around the anus with your finger in the last 1 year?

Those who selected the 3^{rd} , 4^{th} , and 5^{th} options in at least two of the questions on D4, D5, D7, D8, D11, and D12 and the 1^{st} option in the question on D6 and who had no IBS were considered to have functional constipation.

Those who selected the 5th option in the question on D6 and the 1st option in the question on A1 were considered to have functional diarrhea.

Those who had bowel complaints but who were not diagnosed with any FBDs were considered to have unspecified FBDs.

Statistical Analysis

Statistical data were obtained using Statistical Package for the Social Sciences, version 20.0. Results were expressed as mean±standard deviation. Dependent variables were the presence of FBDs and their subgroups, and independent variables were age, gender, occupation, marital status, education level, the presence of comorbid disease, drug use, smoking, alcohol use, and tests performed at patients' recent visits. Chisquare and independent sample t-tests were used. Values were expressed as mean±standard deviation. P<0.05 with a 95% confidence interval was considered to be statistically significant.

RESULTS

This study included 80 patients who were followed by the Nephrology Clinic, and these were compared with 80 controls. Of the 80 patients, 46 (57.5%) were males and 34 (42.5%) were females. Of the 80 controls, 43 (53.8%) were males and 37 (46.3%) were females. The average age of the patients was 62.13±12.92 years, and the average age of the controls was 60.45±9.85 years. Twenty-six (32.5%) patients had DM, and 37 (46.2%) had hypertension and/or coronary artery disease. The mean duration of dialysis was 57.48±59.23 (3-312) months, and the mean Kt/V value was 1.53±0.31. While 51 (63.7%) patients lived in rural areas and 29 (36.3%) lived in urban areas, the corresponding rates were 50 (62.5%) and 30 (37.5%) in the controls. While 13 (16.2%) patients and 30 (37.5%) controls were uneducated, 12 (15%) patients and 10 (12.5%) controls knew only to read/write. While 43 (53.8%) and 8 (10%) patients completed primary school and high school, respectively, 26 (32.5%) and 14 (17.5%) controls completed primary school and high school, respectively. Only the patient group had people with a university degree, and there were a total of 4 (5%). Among the patients, 30 (37.5%) were housewives, 3 (3.8%) were workers, 26 (32.5%) were farmers, 11 (13.7%) were officers, and 10 (12.5%) were in other professions; among the controls, 36 (45%) were housewives, 13 (16.2%) were workers, 19 (23.8%) were farmers, and 12 (15%) were officers. While 58 (72.5%) were married, 2 (2.5%) were single and 20 (25%) were widowed among the patients, 69 (86.2%) were married, 2 (2.5%) were single, and 9 (11.3%) were widowed among the controls. The clinical and biochemical characteristics and demographic data are summarized in Tables 2 and 3.

The Rome II criteria were used to determine the prevalence of FBDs in the patient and control groups. FBDs were found in 22 (27.5%) patients and 10 (12.5%) controls, and this difference was statistically significant (p=0.01) (Table 4).

Functional bowel disorders were found in 32 individuals. In total, 68.7% and 31.3% of those with FBDs were respectively formed by the patients and healthy controls.

According to symptoms that exist on their own, FBDs are divided into four subgroups: IBS, functional bloating, functional constipation, and functional diarrhea. Among the patients, 7.5% had IBS, 3.8% had functional bloating, 16.3% had functional constipation. Among the controls, 2.5% had IBS, 8.8% had functional bloating, and 1.3% had functional constipation. Functional constipation was significantly higher in the patient group than in the control group (p=0.001). Functional diarrhea was not observed in either group (Table 5).

Functional bowel disorders were significantly higher in women (p=0.004). The mean Kt/V value was 1.61±0.30, and the mean duration of dialysis was 58.73±56.73 months in the patients with FBD; there was no statistically significant difference between the two groups (p=0.9). There was no a statistically significant relationship between the groups with and those without FBDs in terms of the presence of additional diseases and smoking and alcohol use (p>0.05). The serum P level was significantly higher in the group with FBDs (p=0.03). Among the patients with FBDs, 16 (72.7%) lived in urban areas and 6 (27.3%) lived in rural areas. Although FBDs occurred at a higher rate in those living in urban areas, this difference was not statistically significant (p=0.3). Among the patients with FBDs, while 7 (31.8%) did not complete primary school, 15 (68.2%) graduated from primary school or above. The distribution was similar in the patients without FBDs. In terms of occupational distribution, it was observed that in the group with FBDs, the rate of housewives was statistically significantly higher (p=0.003) but that the rate of farmers was statistically significantly less

Table 2. Clinical and biochemical characteristics of the patient and control groups

	Patient group (n=80) Mean±SD (n %)	Control group (n=80) Mean±SD (n %)
Age (years)	62.13±12.92	60.45±9.85
Gender		
Male	46 (57.5%)	43 (53.8%)
Female	34 (42.5%)	37 (46.3%)
Comorbid diseases		
DM	26 (32.5%)	
HT/CAD	37 (46.2%)	
No	17 (21.3%)	
Duration of dialysis (Months	i) 57.48±59.23	
Kt/V	1.53±0.31	
Ca (mg/dL)	9.41±1.07	
P (mg/dL)	5.11±1.22	
PTH (pg/mL)	333.59±204.89	
Hgb (g/dL)	10.19±1.33	

SD: standard deviation; DM: diabetes mellitus; HT: hypertension; CAD: coronary artery disease; Kt/V: K: dialyzer clearance of urea, t: dialysis time, and V volume of urea distribution; Ca: calcium; P: phosphorus; PTH: parathyroid hormone; Hgb: hemoglobin

Gök et al. Functional bowel disorders in hemodialysis patients

(p=0.001). Among the patients with FBDs, 14 (63.6%) were married and 8 (36.4%) were single or widowed. Although the rate of those married was higher, this difference was not statistically significant (p=0.27) (Tables 6 and 7).

When the mean duration of dialysis was divided into subgroups such as $\leq 12,12-60$, and ≥ 60 months and the mean Kt/V

Table 3. Demographic d	ata of the patient and	control groups
------------------------	------------------------	----------------

	Patient group (n=80) Mean±SD (n %)	Control group (n=80) Mean±SD (n %)
Residential area		
Rural	51 (63.7%)	50 (62.5%)
Urban	29 (36.3%)	30 (37.5%)
Educational level	13 (16.2%)	30 (37.5%)
Uneducated	12 (15%)	10 (12.5%)
Only able to read/write Primary school	43 (53.8%)	26 (32.5%)
High school	8 (10%)	14 (17.5%)
University	4 (5%)	0
Occupation		
Housewife	30 (37.5%)	36 (45%)
Worker	3 (3.8%)	13 (16.2%)
Farmer	26 (32%)	19 (23.8%)
Officer	11(13.7%)	12 (15%)
Others	10 (12.5%)	0
Married	58 (72.5%)	69 (86.2%)
Single	2 (2.5%)	2 (2.5%)
Widowed	20 (25%)	9 (11.3%)

 Table 4. The prevalence of FBDs according to the Rome II criteria

	Patient group (n=80)	Control group (n=80)	р		
FBDs according to the Rome II criteria					
Yes	22 (27.5%)	10 (12.5%)	0.01		
No	58 (72.5%)	70 (87.5%)			
Chi-square test FBD: functional bowel disord	der				

 Table 5. The distribution of the subtypes of FBDs according to the Rome

 Il criteria

	Patient group (n=80)	Control group (n=80)	р
Irritable bowel syndrome	6 (7.5%)	2 (2.5%)	0.14
Functional bloating	3 (3.8%)	7 (8.8%)	0.19
Functional constipation	13 (16.3%)	1 (1.3%)	0.001
Functional diarrhea	0	0	

FBDs Yes (n=22) No (n=58) р Gender Male 7 (31.8%) 39 (67.2%) Female 15 (68.2%) 19(32.8%) 0.004 DM 7 (31.8%) 19 (32.8%) HT/CAD 8 (36.4%) 29 (50.0%) 0.32 No 7 (31.8%) 10 (17.2%) Duration of dialysis (Months) 58.73±56.73 57.0±60.2 0.90 Kt/V 1.61±0.30 1.50±0.31 0.18 Smoking Yes 7 (31.8%) 21 (36.2%) No 15 (68.2%) 37 (63.8%) 0.71 Alcohol use Yes 1 (4.5%) 4 (6.9%) No 54 (93.1%) 0.69 21 (95.5%) Ca (mg/dL) 9.70±1.26 9.30±0.98 0.14 P (mg/dL) P<3.5 1 (4.5%) 7 (12.1%) 0.31 3.5<P<5.5 10 (45%) 34 (58.6%) 0.21 P>5.5 11 (50.5%) 17 (29.3%) 0.08 PTH (pg/mL) 370.59±246.02 319.56±187.50 0.32 Hgb (g/dL) 10.11±1.45 10.22±1.30 0.75

Chi-square test, Student's t-test

FBDs: functional bowel disorders; DM: diabetes mellitus; HT: hypertension; CAD: coronary artery disease; Kt/V: K: dialyzer clearance of urea, t: dialysis time, and V volume of urea distribution; Ca: calcium; P: phosphorus; PTH: parathyroid hormone; Hgb: hemoglobin

value was divided into subgroups such as \leq 1.4 and >1.4, there was no statistically significant relationship between the subgroups and FBDs (p>0.05) (Table 8).

DISCUSSION

Chronic GISs are frequently seen in patients with CKD (17) and are observed at rates as high as 70% (11). Although FBDs have no mortality risks, they are an important for public health because of the prevalence, negative impact on the quality of life, high cost, and failure of curative treatment (18). There is no biomarker for diagnosing FBDs, and they are diagnosed according to symptomatic criteria. The Rome criteria are most commonly used in diagnosing FBDs (15). In the present study, the Rome II questionnaire (11) was used as it was easy to understand and could be easily answered by the study participants.

The study included 80 patients with ESRD who received HD and 80 controls who met the inclusion criteria. FBDs were found in 22 (27.5%) patients; thus, FBDs were statistically sig-

Table 7. The comparison of demographic data between the patients with and those without FBDs

	FBDs		
	Yes (n=22)	No (n=58)	- p
Residential area			
Rural	16 (72.7%)	35 (60.3%)	
Urban	6 (27.3%)	23 (39.7%)	0.30
Educational Level			
Uneducated or only able to read/write	7 (31.8%)	18(31.0%)	
Primary school or above	15 (68.2%)	40(69.0%)	0.94
Occupation			
Housewife	16 (63.6%)	14 (27.6%)	0.003
Worker	2 (9.1%)	1 (1.7%)	0.12
Farmer	1 (4.5%)	25 (43.1%)	0.001
Officer	2 (9.1%)	8 (13.8%)	0.57
Others	3 (13.6%)	8 (13.8%)	0.98
Marital Status			
Married	14 (63.6%)	44 (75.9%)	
Single/Widowed	8 (36.4%)	14 (24.1%)	0.27
EBDs: functional bowel disorders			

Table 8. The comparison of demographic data between the patients with and those without ${\sf FBDs}$

	FBDs		
-	Yes (n=22)	No (n=58)	p
Duration of dialysis (Months)			
≤12 months	6 (27.3%)	17 (29.3%)	0.85
12–60 months	7 (31.8%)	21 (36.2%)	0.71
≥60 months	9 (40.9%)	20 (34.5%)	0.59
Kt/V			
≤1.4	7 (31.8%)	20 (34.5%)	
>1.4	15 (68.2%)	38 (65.5%)	0.82

FBDs: functional bowel disorders; Kt/V: K: dialyzer clearance of urea, t: dialysis time, and V volume of urea distribution

nificantly increased in the patient group than in the control group (p=0.01). Functional constipation is a common problem in HD patients (19), and its prevalence is known to be 53% (20). In a study in HD patients, chronic constipation was found in 40% of patients and chronic diarrhea was found in 24% of patients (2). In our study, functional bloating was found in 3.8% of the patients and 8.8% of the controls (p=0.19) and functional constipation was found in 16.3% of the patients and 1.3% of the controls (p=0.001). Functional constipation was statistically significantly increased in the patient group than in the control group. Functional diarrhea was not observed in both groups.

Although the relationship between FBDs and gender was not fully clarified, it has been reported to be higher in women. The reason for this may be that female steroids reduce the pain threshold by affecting visceral sensitivity or the serotonin synthesis differences in the central nervous system between genders (21). In a study performed in 196 HD patients by Fiderkiewicz et al. (17) IBS was found in 27 (13.8%) patients. This rate was 18% in women and 11% in men, but this difference was not statistically significant. In our study, there were 7 (31.8%) males and 15 (68.2%) females among the patients with FBDs who received HD, and FBDs were significantly higher in women (p=0.004).

In previous studies, it was found that upper GIS-related mortality was more common in the first 2 years of HD and decreased in the following years (22). There are very few studies investigating the lower GISs. In our study, there was a statistically significant relationship between FBDs and the duration of HD.

In a study conducted in the general population by Kasap et al. (16), it was reported that FBDs were statistically significantly less in single people than in married and widowed people and that it was approximately equal in both married and widowed people. In a study performed in Elazig by Celebi et al. (23), there was no a statistically significant relationship between marital status and FBDs. In our study, among the patients with FBDs, 14 (63.6%) were married and 8 (36.4%) were single/widowed. Although married people were found at a higher rate, this difference was not statistically significant. In our study, among the patients with FBDs, while 7 (31.8%) did not complete primary school, 15 (68.2%) graduated from a primary school or above. The distribution was similar in patients without FBDs. Among the patients with FBDs, 16 (72.7%) lived in urban areas and 6 (27.3%) lived in rural areas. Although FBDs were found to be at a higher rate in people who lived in urban areas, this difference was not statistically significant (p=0.3).

In a study by Kasap et al. (16), it has been reported that FBDs were higher in housewives and unemployed people and that IBS was higher in farmers, housewives, and unemployed people. In our study, among the patients with FBDs, 63.6% were housewives, 9.1% were workers, 9.1% were officers, and 4.5% were farmers. In terms of occupational distribution, it was observed that in the group with FBDs, the rate of housewives was statistically significantly higher (p=0.003) but that the rate of farmers was statistically significantly less (p=0.001).

Regardless of glycemic control, GISs are known to be more common in patients with DM than in the normal population (24). In a study performed in patients with CKD, there was no statistically significant difference between those with and those without DM in terms of the prevalence of the symptoms of FBDs (11). In a study conducted in HD patients, there was no statistically significant relationship between IBS and DM (17). In our study, 31.8% of the patients had DM and 36.4% of them had coronary artery disease/hypertension. There was no statistically significant relationship between the presence of additional diseases and FBDs.

In a study by Kasap et al. (16), there was no statistically significantly relationship between smoking and alcohol use and FBDs. In our study, while 31.8% used cigarettes and 4.5% drunk alcohol in the patient group, 36.2% used cigarettes and 6.9% drunk alcohol in the group without FBDs. However, there was no statistically significant difference between the two groups in terms of smoking and alcohol use.

In the literature, till date, there is no study showing the relationship between the development of FBDs and levels of serum P in HD patients. In our study, the serum P level was found to be 5.57 ± 1.51 mg/dL in the group with FBDs and 4.94 ± 1.05 in the group without FBDs; thus, the serum P level was significantly higher in the group with FBDs (p=0.03). The P level was ≤ 3.5 in 4.5% of the group with FBDs and 12.1% of the group without FBDs (p=0.31), 3.5-5.5 in 45% of the group with FBDs and 58.6% of the group without FBDs (p=0.21), and ≥ 5.5 in 50.55%of the group with FBDs and 29.3% of the group without FBDs. Although the P level was ≥ 5.5 in 50.55% of the group with FBDs, this difference was not statistically significant (p=0.08). The relationship between hyperphosphatemia and FBDs may be due the continuous use of calcium- and aluminum-containing phosphate binders in HD patients.

It is known that high Hgb levels in HD patients increase the quality of life. In a study, there was a statistically significant relationship between Hgb levels and the symptoms of IBS in HD patients (17). In our study, there was no statistically significant difference between the group with and that without FBDs in terms of mean Hgb levels.

In a study by Fiderkiewicz et al. (17), there was no statistically significantly relationship between the development of IBS and Kt/V in HD patients. While the mean duration of dialysis was 58.73 ± 56.73 months and the mean Kt/V value was 1.61 ± 0.30 in the group with FBDs, the mean duration of dialysis was 57.0 ± 60.2 months and the mean Kt/V value was 1.50 ± 0.31 in the group without FBDs. However, there was no statistically significant difference between the two groups. When the dialysis time of the patients was divided into subgroups such as ≤ 12 months, 12-60 months, and ≥ 60 months, the duration of dialysis was shown to have no effect on the development of FBDs.

In studies performed in HD patients, it has been reported that IBS was more common in the general population and was seen at rates between 11% and 44% (2). Although it is not fully understood, genetic factors, changes in bowel motility, visceral hypersensitivity, psychosocial factors, changes in the function of the central nervous system to stimulation, and changes in the serotonergic system play a role in its pathogenesis (25).

The prevalence of IBS varies depending on the diagnostic criteria used, sex, age, and race. In a study conducted in the United Kingdom, it was reported that the prevalence of IBS was higher in dialysis patients than in those without renal insufficiency and randomly selected groups; this could be caused by uremia or uremia treatment (11). In studies that investigated the prevalence of IBS in HD patients using the Rome II criteria, its prevalence was reported to be 11% in Australia (2), 11.5% in all European countries (26), and 21% in England (11). In a study conducted in Turkey, the prevalence of IBS was reported to be higher in chronic dialysis patients than in the normal population (8). In our study, among the HD patients, 7.5% had IBS, 3.8% had functional bloating, and 16.3% had functional constipation. The prevalence of IBS was similar to that in the community, and there was no statistically significant difference between the patient and control groups.

Constipation is a common problem in patients with uremia due to causes such as the use of antacids containing aluminum, dehydration, and physical activity (27). In our study, the prevalence of functional constipation was found to be higher in HD patients than in the controls. The reasons for this situation may be an intake of foods containing low fiber, vitamin C, and potassium (28); the use of excess ion-exchange resin (1); and prolonged total colonic transit time (19).

Our study has several limitations. Firstly, this study was performed with a small number of patients in a single center. Further studies should be conducted with a greater number of patients in many centers. Secondly, additional symptoms that are not present in the Rome criteria should also be questioned due to the high comorbidity in HD patients (17). Thirdly, the psychological status and the use of laxatives, which could affect GISs, were not evaluated. Fourthly, the relationship between the mean dialysis duration of the patients and the presence of FBDs was investigated, but the results were not compared by following the patients for a long time. Fifthly, the Rome III criteria that are known to give more meaningful and accurate results were not used in the present study, and this may have influenced the results.

Consequently, FBDs and the subgroup of functional constipation are more common in HD patients than in the healthy population. While the educational level and residential area do not have an effect on the development of FBDs, it is frequently observed in females and housewives.

While the mean duration of dialysis and the Kt/V value (one of the dialysis adequacy parameters) do not have an effect on the development of FBDs, high serum P levels have an effect, regardless of the serum calcium levels. The cause of this may be the use of phosphate binders or aluminum-containing drugs in this patient group. Thus, effective dialysis reducing the serum P levels may be useful in the suppression of the symptoms of FBDs.

Further studies are needed to investigate the role of hyperphosphatemia on the development of FBDs in HD patients worldwide due to the lack of studies conducted on this subject. Moreover, further long-term studies are needed to investigate the pathophysiology, etiology and risk factors of GISs in HD patients and the effect of these symptoms on the quality of life of patients.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Celal Bayar University School of Medicine.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – E.G.G.; Design – E.G.G., A.İ.; Supervision – M.Ç., D.A.K., S.K.; Resources – E.G.G., A.İ.; Materials – E.G.G., A.İ.; Data Collection and/or Processing – E.G.G., A.İ.; Analysis and/or Interpretation – E.G.G., A.İ., M.Ç., D.A.K., S.K.; Literature Search – E.G.G., A.İ.; Writing Manuscript – E.G.G., M.Ç.; Critical Review – E.G.G., A.İ., M.Ç., D.A.K., S.K.; Other – E.G.G., A.İ.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

- 1. Yasuda G, Shibata K, Takizawa T, et al. Prevalence of constipation in continuous ambulatory peritoneal dialysis patients and comparison with hemodialysis patients. Am J Kidney Dis 2002; 39: 1292-9. [CrossRef]
- Hammer J, Oesterreicher C, Hammer K, Koch U, Traindl O, Kovarik J. Chronic gastrointestinal symptoms in hemodialysis patients. Wien Klin Wochenschr 1998; 110: 287-91.
- Abu Farsakh NA, Roweily D, Rababaa E, Butchoun R. Brief report:Evaluation of the upper gastrointestinal tract in uraemic patients undergoing haemodialysis. Nephrol Dial Transplant 1996; 11: 847-50. [CrossRef]
- 4. Manning AP, Thompson WG, Heaton KW, Morris AF. Towards positive diagnosis of the irritable bowel. Br Med J 1978; 2: 653-4. [CrossRef]
- Drossman DA. The functional gastrointestinal disorders and the Rome III process. Gastroenterology 2006; 130: 1377-90. [CrossRef]
- 6. The American Gastroenterological Association Institute. J Gastro 2005; 11: 61.
- Kang JY. Systematic review: The influence of geography and ethnicity in irritable bowel syndrome. Aliment Pharmacol Ther 2005; 21: 663-76. [CrossRef]
- 8. Kahvecioglu S, Akdag I, Kiyici M, et al. High prevalence of irritable bowel syndrome and upper gastrointestinal symptoms in patients with chronic renal failure. J Nephrol 2005; 18: 61-6.
- Pare P, Ferrazzi S, Thompson WG, Irvine EJ, Rance L. An epidemiological survey of constipation in Canada: definitions, rates, demographics and predictors of health care. Am J Gastroenterol 2001; 96: 3131-7. [CrossRef]
- Bytzer P, Talley NJ, Leemon M, Young LJ, Jones MP, Horowitz M. Prevalence of gastrointestinal symptoms associated with diabetes mellitus: A population-based survey of 15,000 adults. Arch Intern Med 2001; 161: 1989-96. [CrossRef]

- 11. Cano AE, Neil AK, Kang JY, et al. Gastrointestinal symptoms in patients with end-Stage renal disease undergoing treatment by hemodialysis or peritoneal Dialysis. Am J Gastroenterol 2007; 102: 1990-7. [CrossRef]
- 12. Shakil A, Church RJ, Rao SS. Gastrointestinal complications of diabetes. Am Fam Physician 2008; 77: 1697-702.
- 13. Daugirdas JT. Second generation logarithmic estimates of singlepool variable volume Kt/V: An analysis of error. J Am Soc Nephrol 1993; 4: 1205-13.
- 14. Daurgidas JT. Chronic hemodialysis prescription: A urea kinetic approach. Handbook of dialysis'de. Eds.Daurgidas JT, Ings TS (2nd ed). Boston Little, Brown and Company, 1994: 92-120.
- 15. Drossman DA, Corazziari E, Delvaux M, et al. Rome, The functional gastrointestinal disorders. McLean, VA: Degnon Associates, 2000.
- 16. Kasap E, Bor S. The prevalence of functional bowel disease. Current Gastroenterology 2006; 10: 165-8.
- 17. Fiderkiewicz B, Rosołowska AR, Myśliwiec M, et al. Factors associated with irritable bowel syndrome symptoms in hemodialysis patients. World J Gastroenterol 2011; 17: 1976-81. [CrossRef]
- Maxwell PR, Mendall MA. Irritable Bowel Syndrome. Lancet 1997; 350: 1691-5. [CrossRef]
- 19. Wu MJ, Chang CS, Cheng CH, et al. Colonic transit time in longterm dialysis patients. Am J Kidney Dis 2004; 44: 322-7. [CrossRef]
- 20. Murtagh FE, Addington-Hall J, Higginson IJ. The prevalence of symptoms in end-stage renal disease: a systematic review. Adv Chronic Kidney Dis 2007; 14: 82-99. [CrossRef]

- Nishizawa S, Benkelfat C, Young SN, et al. Differences between males and females in rates of serotonin synthesis in human brain. Proc Natl Acad Sci USA 1997; 94: 5308-13. [CrossRef]
- 22. Chachati A, Goodon JP. Effect of haemodialysis on upper gastrointestinal tract pathology in patients with chronic failure. Nephrol Dial Transplant 1987; 1: 233.
- 23. Çelebi S, Acik Y, Deveci SE, et al. Epidemiological features of irritable bowel syndrome in a Turkish urban society. J Gastroenterol Hepatol 2004; 19: 738-43. [CrossRef]
- 24. Quan C, Talley NJ, Jones MP, Howell S, Horowitz M. Gastrointestinal symptoms and glycemic control in diabetes mellitus: a longitudinal population study. Eur J Gastroenterol Hepatol 2008; 20: 888-97. [CrossRef]
- 25. Locke GR, Zinsmeister AR, Talley NJ, Fett SL, Melton LJ. Familial association in adults with functional gastrointestinal disorders. Mayo Clin Proc 2000; 75: 907-12. [CrossRef]
- 26. Hungin AP, Whorwell PJ, Tack J, Mearin F. The prevalence, patterns and impact of irritable bowel syndrome: an international survey of 40,000 subjects. Aliment Pharmacol Ther 2003; 17: 643-50. [CrossRef]
- 27. Kang JY. The gastrointestinal tract in uremia. Dig Dis Sci 1993; 38: 257-68. [CrossRef]
- 28. Kalantar-Zadeh K, Kopple JD, Deepak S, D Blok , Blok G. Food intake characteristics of hemodialysis patients as obtained by food frequency questionnaire. J Ren Nutr 2002; 12: 17-31. [CrossRef]