Comparison of Gastrointestinal Symptoms between Patients Undergoing Hemodialysis and Healthy Population

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Received: 14 Oct. 2021
Accepted: 10 May 2022
Published: 30 Jul. 2022

Abstract

Background:
Patients with end-stage renal disease (ESRD) complain of many gastrointestinal (GI) problems. The goal of the current study was to compare the prevalence of GI disorders in a relatively large group of patients with ESRD with healthy participants.

Methods:
In a matched case-control study, 597 patients undergoing hemodialysis and 740 healthy participants were investigated. All subjects were asked to complete Rome III questionnaire, including five modules to evaluate GI disorders. The Hospital Anxiety and Depression questionnaire, as well as the 12-general health questionnaire for psychological disorders assessment, were used.

Results:
Our results showed that in patients undergoing hemodialysis, the prevalence of irritable bowel syndrome (IBS) (OR = 1.75), gastroesophageal reflux disease (GERD) (OR = 1.55), and dyspepsia (OR = 3.39) was significantly higher than in healthy control participants, while no significant difference was found in terms of constipation (OR = 0.88). The association remained significant for dyspepsia and IBS even after controlling for psychological disorders as important potential confounding variables. On the other hand, adjustment for psychological disorders led to an insignificant association between hemodialysis and GERD. Surprisingly a significant relationship was observed between constipation and hemodialysis after adjustment for mentioned psychological factors.

Conclusion:
Our results showed that there was a significant relationship between hemodialysis and some GI complaints such as IBS, dyspepsia, GERD, and bloating. Psychological disorders only influence GERD prevalence in patients undergoing hemodialysis.

Keywords:
Hemodialysis, FGIDs, ESRD, Psychological disorders

Please cite this paper as:
Mortazavi M, Adibi P, Hassanzadeh Keshteli A, Feizi A, JameShorani M, Soodavi M, et al. Comparison of gastrointestinal symptoms between patients undergoing hemodialysis and healthy population. *Middle East J Dig Dis* 2022;14(3):310-316. doi: 10.34172/mejdd.2022.288.

Introduction

Gastrointestinal (GI) symptoms are prevalent in patients with end-stage renal disease (ESRD).[1,2] GI symptoms in such patients are related to gastric hypomotility, decreased albumin level, increased drug intake, uremia, and nutritional changes.[3-6] ESRD is also associated with a high prevalence of psychological disorders such as anxiety and depression.[7,8]

The effect of psychological symptoms on functional gastrointestinal disorders (FGDIs) has been proven in the general population.[9-11] Few studies have reported that a higher prevalence of GI disorders in patients with ESRD is related to impaired psychological disorders.[12,13] The aim of our study is to evaluate the prevalence of GI complaints considering the role of psychological disorders in patients with ESRD in a matched case-control study.

Materials and Methods

Study Design

This was an age and sex-matched case-control study that was done in 28 hemodialysis clinics in Isfahan province, Iran.

Participants

Patients with ESRD who had received chronic hemodialysis for more than 1 month participated in our study. Questionnaires were completed by 597 of 973 participating patients. Accordingly, 740 healthy people who had entered in SEPAHAN study were matched by sex and age with participating patients.[14] Patients with severe psychological disturbances or those who were received emergency hemodialysis excluded from the study.

Methods

Before questionnaire distribution, educational workshops were held for staff in 18 hemodialysis clinics that cooperated with us in questionnaire fulfillment. All questionnaires were distributed in hemodialysis clinics by Isfahan University of Medical Sciences (IUMS) deputy of treatment and filled by patients under the supervision of researchers and clinics' staff. Then completed questionnaires were given back to the IUMS deputy of treatment by hemodialysis clinics.

Data collection was done using self-administered questionnaires. The modified Rome III questionnaire was used to assess GI disorders.[14] The questionnaire comprises five modules, including irritable bowel syndrome (IBS), gastroesophageal reflux disease (GERD), dyspepsia, bloating, and constipation. The content and face validity of the main questionnaire in its different subscales were established by the opinion of a relevant panel of experts. A pilot study was also conducted on 100 participants to evaluate the internal consistency using Cronbach's alpha. The minimum acceptable Cronbach's alpha level of 0.7 was exceeded by all sections of the main questionnaire. The face and content validity of the main questionnaire was also found to be satisfactory.[15]

To investigate both anxiety and depression in participants, the Hospital Anxiety and Depression Scale questionnaire was used. Each subscale contains seven questions which are scored on a 4-point scale; thus, the total score in each subscale ranges from 0 to 21. Scores of 11 or higher indicated a case of depression or anxiety. It was previously validated in an Iranian population with Cronbach's alpha coefficient of 0.78 and 0.86 for anxiety and depression subscales, respectively.[16]

To evaluate psychological distress, 12-item General Health Questionnaire (12-GHQ) with good reliability for the Iranian population ($\alpha = 0.87$) was applied.[17] In this questionnaire, each item provides a four-point rating scale as follows: less than usual, no more than usual, rather more than usual, or much more than usual. We calculated the distress scores of participants by using the bimodal scoring method (0-0-1-1), higher scores indicate an elevated level of distress, and the maximum score could be 12. In the present study, participants who got scores of ≥ 4 were considered to have psychological distress.

Statistical Analysis

Quantitative data were expressed as mean $\pm$ SD, while qualitative data were represented by frequency (percentages). FGIDs symptoms and psychological disorders, including anxiety, depression, and psychological distress, between the case and control groups were compared by Chi-square test. The prevalence of sex and age-stratified analysis of FGIDs disorders was compared between the case and control groups. We also compared the prevalence of FGIDs between the case and control groups in terms of having specific psychological disorders or not. Multiple logistic regression was used to determine the relationship between FGID disorders and hemodialysis in different models, including the crude adjusted model, for controlling the confounding effects of psychological disorders (Model 1). All statistical analyses were done using Statistical Package for Social

Sciences (SPSS, Inc., Chicago IL, USA; version 15).

Results

The mean ages of the case and control groups were 55.98±16.43 and 49.16±3.5, respectively ($P>0.05$). The distribution of women was: 38.6% in the control vs 40.3% in the case groups ($P>0.1$).

Comparison of the Prevalence of GI and Psychological Disorders between the Patients Who Undergone Hemodialysis and the Control Group

The comparison of the prevalence of GI disorders between the case and control groups has been shown in Table 1. The prevalence of IBS (OR=1.75), GERD (OR=1.55), and dyspepsia (OR=3.39) in patients undergoing hemodialysis was significantly higher than in the healthy subjects ($P<0.05$). In contrast, the prevalence of bloating in the case group was significantly lower than the control group (OR=0.74, $P<0.05$). The prevalence of constipation was also lower in the case group when compared with the controls (OR: 0.88, $P>0.05$). As shown in Table 1, the prevalence of all psychological symptoms was significantly higher in the case than in the control groups ($P<0.05$).

Stratified Analysis of Comparison of GI Disorders between Patients Undergoing Hemodialysis and Control Participants by Sex and Age

Sex and age-stratified analysis for comparing GI complaints between patients and controls have been summarized in Table 2. The results of stratified analysis by sex showed that the prevalence IBS and dyspepsia were significantly higher in the case than the

Table 1. Prevalence of GIs and psychological disorders in case vs. control group

	Subjects' number (%)		Odds Ratio (95% CI)
Variables	**Case**	**Control**	
IBS	192 (32.2)	262 (21.2)	1.75 (1.41-2.19) *
GERD	226 (37.9)	90 (28.1)	1.55 (1.16-2.09) *
Dyspepsia	234 (39.2)	197 (16)	3.39 (2.71-4.24) *
Bloating	87 (14.6)	231 (18.7)	0.74 (0.56-0.96) *
Constipation	123 (20.6)	280 (22.7)	0.88 (0.69-1.12)
Psychological distress	290 (49.5)	266 (22.1)	3.44 (2.79-4.26) *
Anxiety	96 (16.3)	70 (5.8)	3.15 (2.28-4.37) *
Depression	191 (32.5)	127 (10.6)	4.08 (3.17-5.25) *

*P value<0.05

Table 2. Prevalence of functional gastrointestinal disorders in case and control group in a stratified analysis based on sex and age group

	Male	**Female**	**<30**	**30-40**	**40-50**	**>50**
	Case/control %	**Case/control %**	**Case/control %**	**Case/control %**	**Case/control %**	**Case/control %**
IBS	26.3-18*	40.3-23.8*	45.5-20.9*	29.3-22.8	31.6-18.6	32.9-21.5*
OR (95%CI)	1.17-2.24	1.57-2.95	1.62-6.11	0.76-2.56	1.15-3.55	1.2-2.65
GERD	32.3-28.1	45. 8-24.8	45.5-18. 2*	37.9-29.3	24.1-30.3	38.4-29.5#
OR (95%CI)	0.87-1.69	1.65-4.21	1.42-9.88	0.74-2.92	0.36-1.44	0.89-2.46
Dyspepsia	37.1-12.7*	42. 4-18.6*	38.6-12.3*	32.8-19.6*	27.8-12.8*	43.8-16.6*
OR (95%CI)	2.92-5.68	2.33-4.44	2.2-9.1	1.1-3.61	1.43-4.83	2.59-5.93
Bloating	16.6-20.9#	11.4-17*	11.4-22. 8	19-14.3	19-23	13-17. 9#
OR (95%CI)	0.53-1.06	0.4-0.98	0.16-1.15	0.69-2.84	0.41-1.47	0.42-1.09
Constipation	24-12.1*	16.1-31.1*	6.8-19.8*	19-26.4	12.7-22.6*	25.1-18.4
OR (95%CI)	1.6-3.27	0.29-0.62	0.08-0.99	0.32-1.29	0.24-1.01	0.97-2.26

*P value<0.05.
#Marginally significant at P value<0.1

control group both in men and women. The prevalence of constipation was significantly higher in the case than in the control group among men ($P<0.05$), while a contrast result was seen among women. As shown in Table 2, the prevalence of bloating was significantly and marginally lower in the case than in the control group, respectively, among women ($P<0.05$) and men ($0.05<P<0.1$). There was no significant difference in the prevalence of GERD between men and women in the case and the control groups ($P>0.05$).

Stratified analysis of GI disorders by age indicated that the prevalence of dyspepsia was significantly higher in hemodialysis patients than in healthy people in all age categories ($P<0.05$). In addition, the prevalence of IBS in the group aged<30 years and>50 years was significantly higher in the case than in the control group. Moreover, there was a significant and marginal difference in the prevalence of GERD between patients undergoing hemodialysis and healthy subjects in the group aged<30 years ($P<0.05$) and>50 years ($0.05<P<0.1$), respectively. Stratified analysis of bloating by age indicated that its prevalence in the group aged>50 years was lower in patients undergoing hemodialysis than in the healthy subjects ($0.05<P<0.1$). Lower prevalence of constipation in the case than in the control group after age adjustment was observed in the group aged<30 and 40-50 years ($P<0.05$).

Stratified Analysis by Psychological Disorders for Comparing GI Disorders between Patients Undergoing Hemodialysis and Control Group

Stratified analysis of GI disorders by psychological signs showed that the prevalences of dyspepsia and IBS were significantly higher in the case than in the control group in subjects with psychological disorders ($P<0.05$, Table 3). The prevalence of GERD was higher in the case than in the control group of anxious subjects (OR=0.93-2.77, $0.05<P<0.1$). On the other hand, the prevalence of bloating and constipation were significantly lower in the case than in the control subjects with distress ($P<0.05$).

Association between Hemodialysis and GI Disorders

The relationship between the prevalence of hemodialysis and GI disorders was assessed by logistic regression. Our findings showed that there was a significant positive relationship (OR>1, P<0.05) between hemodialysis and all GI disorders except for constipation in crude model. After adjustment for psychological disorders, the associations remained significant for IBS and dyspepsia, and a significant relationship was also observed between hemodialysis and constipation ($P<0.05$, Table 4).

Table 3. Stratified analysis of functional gastrointestinal disorders prevalence in case and control group by psychological disorders

	IBS		GERD		Dyspepsia		Bloating		Constipation	
	Case-control %	OR** (95% CI)	Case-control %	OR** (95% CI)	Case-control %	OR** (95% CI)	Case-control %	OR** (95% CI)	Case-control %	OR** (95% CI)
Anxiety	28.5-20.2*	1.57 (1.23-2)	33.3-28#	1.28 (0.93-1.77)	36.6-14*	3.53 (2.75-4.53)	15.4-9.20	0.77 (0.57-1.02)	21.3-22.2	0.95 (0.73-1.23)
Depression	26.5-19.7*	1.47 (1.12-1.92)	30.6-26.8	1.19 (0.84-1.7)	31.6-3.1*	3.05 (2.32-4.03)	16.9-19.2	0.85 (0.63-1.15)	21.2-21.6	0.97 (0.73-1.29)
Psychological distress	41.4-33.1*	1.42 (1.01-2.01)	45.2/40	1.23 (0.76-1.99)	50.3-28.9*	2.48 (1.75-3.53)	10.3/18.8*	0.49 (0.3-0.81)	23.1-33.8*	0.58 (0.4-0.85)

*P value<0.05

#Marginally significant at P value<0.1.

**All odds ratios (95% CI) present the odds of suffering from FGIDs in patients with psychological disorders in comparison to patients without psychological disorders.

Table 4. Association between hemodialysis and functional gastrointestinal disorders

	IBS	GERD	Dyspepsia	Bloating	Constipation
Crude	0.56 (0.45-0.7)*	1.55 (1.16-2.09)*	0.29 (0.23-0.36)*	1.35 (1.03-1.76)*	0.88 (0.69-1.12)
Model1	0.76 (0.6-0.96)*	1.19 (0.86-1.63)	0.41(0.32-0.53)*	1.20 (0.91-1.6)	0.76 (0.59-0.98)*

Model 1: Adjusted for psychological disorders

*P value<0.05

Discussion

GI complaints are frequent in patients with ESRD.[18,19] In addition, these patients experience some psychological disorders such as depression and anxiety.[20,21] The current study was performed to detect the prevalence of GI symptoms in patients undergoing hemodialysis in comparison with healthy controls, considering the effects of psychological disorders.

In the current study, the prevalence of some GI complaints, including dyspepsia, IBS, and GERD, was higher in patients undergoing hemodialysis than in healthy subjects. Cano and colleagues also reported that the prevalence of some GI disorders is higher in patients undergoing hemodialysis than in both public community and non-uremic general medical outpatients. They concluded that the higher prevalence of GI disturbances in patients with ESRD is not related to depression or anxiety.[22] Strid and others did a study to compare the prevalence of GI disorders between patients with chronic renal failure (CRF) (including hemodialysis patients, peritoneal patients, and pre-dialytic patients) and healthy controls. They used Gastrointestinal Symptom Rating Scale (GSRS) to assess GI symptoms. They also reported that the prevalence of GI disorders was higher in patients with CRF than in controls. Findings of the study indicated that GI disorders in patients with CRF was associated with psychological symptoms.[12] As our results assumed, psychological disorders affected the association between GI disorders and hemodialysis. Controlling for psychological disorders led to an insignificant association between GERD, bloating, and hemodialysis showing the confounding role of psychological disorders in the association between GERD, bloating, and hemodialysis. Conversely, psychological disorders did not impact IBS, or dyspepsia-association. IBS and dyspepsia association remained significant after adjustment for psychological disorders. Unexpectedly, adjusting for psychological disorders led to a significant connection between constipation and hemodialysis.

Upper GI tract complications are frequent in patients with CRF.[23] Kawaguchi and colleagues assessed the prevalence of GERD among hemodialysis patients and compared it with the prevalence of GERD in Japan. The findings of the study supposed that the prevalence of GERD among hemodialysis patients had increased; however, they could not find the related risk factors.[24] There was also a higher prevalence of GERD in patients undergoing hemodialysis than in control participants in the present study, but a psychological adjustment in patients with GERD showed that depression and distress were among the risk factors in hemodialysis patients that made them prone to GERD.

Previous studies have reported that IBS is prevalent among patients undergoing hemodialysis.[1,25] Our results also showed that the prevalence of IBS was higher in patients undergoing hemodialysis than in healthy participants. However, there are no consistent findings of the relationship between psychological factors and IBS in patients with ESRD. After adjustment for psychological disorders in patients undergoing hemodialysis and IBS comparisons remained statistically significant, showing that the higher prevalence of IBS in these patients is not related to any of these psychological disorders. This is in agreement with Cano and others that showed IBS in patients with ESRD was not related to psychological complaints.[22] Conversely Kahvecioglu and co-workers indicated that psychological symptoms' prevalence in patients undergoing hemodialysis and IBS were more than IBS negative patients.[26] Although both mentioned studies used Hospital Anxiety and Depression Scale questionnaire for psychological disorders evaluation, our sample size was larger in comparison with them.

The prevalence of dyspepsia was higher in patients undergoing hemodialysis than in control subjects in the current study. This is in agreement with the findings of previous studies.[22,27] After controlling psychological disorders in patients with dyspepsia, higher prevalence of dyspepsia in hemodialysis patients remained significant statistically. It shows that psychological symptoms do not affect the prevalence of dyspepsia. It is possible that dyspepsia in these patients is caused by slow gastric emptying, failure of the gastric fundus to relax properly, and hypersensitivity to gastric distention, as others suggested.[28,29]

Constipation has been considered a serious problem in patients with ESRD who are on hemodialysis. Some factors are assumed to cause constipation in these patients, including nutritional habits, long-term use of medications, lack of physical activities,

and dehydration[6]. In the current study, constipation was insignificantly lower in patients undergoing hemodialysis than in healthy controls. The finding was in contrast to others.[6,22,30] Adjusting for psychological disorders led to an unexpected significant difference in constipation prevalence between the case and control groups among patients with distress. It means that distress is related to higher prevalence of constipation in healthy controls in comparison with patients undergoing hemodialysis. We suppose that the lower prevalence of constipation in the present study is related to some factors such as higher dietary fiber intake and laxative use in patients with ESRD. Further investigation for assessing the hypothesis is warranted.

Our findings indicated that the prevalence of bloating was significantly lower in the case than in the control group. Previous investigations have not shown a significant difference between the prevalence of bloating between patients undergoing hemodialysis and controls.[13,22] The higher prevalence of bloating in control participants than in patients undergoing hemodialysis are influenced by anxiety and depression unexpectedly. Chong and others reported that the prevalence of bloating was significantly higher in patients with psychosomatic symptoms. They did not compare GI complaints between patients undergoing hemodialysis and controls, considering the role of psychosomatic factors.

To our knowledge, our study is the first one that has reported the effect of age and sex on GI disorders prevalence among patients undergoing hemodialysis in detail. As our results showed, the prevalence of constipation was higher in patients undergoing hemodialysis than control group among men. Prevalence differences in GERD among women and men and bloating in men were not significant. Age differences influenced the difference in all GI complaints between case and control groups except for dyspepsia.

Conclusion

Some GI disorders, including IBS, GERD, and dyspepsia, are prevalent among patients undergoing hemodialysis, but psychological disorders are only related to GERD. Interestingly differences in the prevalence of constipation and bloating are also related to psychological disorders. Further studies are needed to detect factors that affect the prevalence of GI disorders in patients undergoing hemodialysis.

Acknowledgments

We would like to acknowledge the patients for their participation and the staffs of hemodialysis centers. We also thank MS. Donya Sheibani and MS. Homa Saadat, hemodialysis part of treatment deputy experts, Isfahan University of Medical Sciences, for their cooperation.

Ethical Approval

The study was approved by the research ethics committee (project number: 393452), Isfahan University of Medical Sciences, and signed informed consent was obtained from all the participants after explaining the study's purpose.

Conflict of Interest

The authors declare no conflict of interest related to this work.

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