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Association Between Anxiety and Depression With Dialysis Adequacy in Patients on Maintenance Hemodialysis

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Abstract

Background: Depression and anxiety are common among hemodialysis patients and affect their treatment outcomes. Dialysis adequacy also affects the hemodialysis patients' survival rates.
Objectives: This study aimed to evaluate the correlation between anxiety and depression with dialysis adequacy.
Patients and Methods: In this cross-sectional study, 127 hemodialysis patients (73 males, 57.5%) with the mean age of 55.7 ± 17.5 were enrolled. Demographic and recent laboratory data were collected using self-administered questionnaires and by reviewing medical records. Dialysis adequacy measures including the Kt/V and urea reduction rate (URR) were calculated using standard formulas. The Hospital Anxiety and Depression Scale (HADS) was used to diagnose depression and anxiety. Independent sample t-test and Chi-square test were used to compare the values in different groups. Pearson correlations and linear regression were used to analyze the data using SPSS version 21.
Results: The prevalence rates of depression and anxiety (HADS score $\geq$ 8) were 31.5% and 41.7%, respectively. The prevalence of both conditions was significantly higher in women than in men ($P < 0.05$). The mean values of Kt/V and URR were not different in patients with and without depression or anxiety. The anxiety scores were correlated with age ($P = 0.007$, $r = -0.24$) and parathyroid hormone ($P = 0.04$, $r = -0.19$). Younger age and lower parathyroid hormone were the only factors that predicted higher scores of anxiety in linear regression. The Kt/V or URR were not significantly correlated with depression and anxiety scores.
Conclusions: Depression and anxiety are common among hemodialysis patients. There are no statistically significant correlation between depression and anxiety and dialysis adequacy.

Keywords: Anxiety, Depression, Dialysis Adequacy, Hemodialysis

1. Background

While maintenance hemodialysis (MHD) serves as the main therapy for patients with end-stage renal disease (ESRD), it is also associated with a high prevalence of psychological problems (1). Previous studies showed that the prevalence rates of depression and anxiety among MHD patients range from 19.3% to 60.5%, and 27% to 52%, respectively (2-5). Since depression and anxiety are correlated with decreased quality of life, higher rates of hospitalization (6, 7), non-adherence to medical treatment (8, 9), and morbidity and mortality (10, 11) in MHD patients, finding and targeting modifiable risk factors can help to reduce these conditions. Studies in MHD patients suggest that different demographic and laboratory factors may be associated with depression. These include gender (12), age (13), comorbidities (13), physical activity (12), unemployment (12, 14), blood cortisol levels (15), inflammatory markers (13, 16, 17), albumin (13, 17), cholesterol, and hemoglobin (16). Dialysis adequacy is another factor that has recently attracted more attention to its effects on depression (18). The urea reduction rate (URR) and Kt/V are the most common methods for measuring dialysis adequacy. Different studies show that a Kt/v of 1.2 and a URR of more than 65% may improve prognosis in MHD patients (19). Most studies have examined the relationships between dialysis adequacy and patients' quality of life (20) and mortality (21), but there is very little research on the relationship between dialysis adequacy and depression or anxiety (13, 22), although it is presumed that by improving Kt/v and clinical symptoms of

the patients, their psychological conditions can improve (23). With attention to the aforementioned data, and also considering that studies conducted in different cities of Iran reported that most patients do not receive adequate dialysis, studies on the relationship between psychological problems and dialysis adequacy are of a high priority to provide better psychological services for these patients.

2. Objectives

This study aimed to determine the prevalence of depression and anxiety and their potential associations with dialysis adequacy in patients undergoing MHD in three dialysis centers of Shahid Beheshti University of Medical Sciences in Tehran.

3. Patients and Methods

3.1. Study Subjects

A purposive sampling method was used to select the eligible participants for this study and the census method was used to survey all the hemodialysis patients based on inclusion and exclusion criteria. A total of 147 ESRD patients on MHD in three different hemodialysis units in Tehran (Taleghani, Imam Hussein, and Labbafinejad hospitals) were enrolled in this cross-sectional study. The inclusion criteria were: age $\geq$ 18 years, hemodialysis duration of at least three months, three times a week for four hours each time, and willingness to participate in the study. Exclusion criteria were history of psychiatric disorders prior to MHD, history of recent hospitalization, history of bereavement in the past six months, physical or mental disability, and consciousness disturbances. Ten patients were excluded due to hemodialysis duration less than three months, two were excluded because of age < 18 years and three were excluded due to physical and mental disabilities or consciousness disturbances. Five patients refused to participate in the study. Thus, we obtained demographic data (age, sex, marital status, educational level and employment status) of 127 patients using standard questionnaires. The vascular access for all of the patients was arteriovenous fistula. All of the participants were receiving hemodialysis by Fresenius dialysis machine.

3.2. Diagnosing Depression and Anxiety

Hospital Anxiety and Depression Scale (HADS) was administered to measure depression and anxiety. The hospital anxiety and depression scale is a 14-item self-administered measure for screening the presence and severity of depression and anxiety symptoms in patients in the week prior to administration of the questionnaire. The time needed to answer it is less than 5 minutes and the target population are people over sixteen years of age.

The hospital anxiety and depression scale has a 7-item subscale for depression (HADS-D) and a 7-item subscale for anxiety (HADS-A). Somatic symptoms are eliminated from both subscales to decrease the false positive results. Thus, HADS is a useful scale for diagnosing depression and anxiety symptoms in outpatients of a general hospital (24). The Iranian version of the HADS is translated and validated with Chronbach's alpha coefficients of 0.86 and 0.78 for HADS-D and HADS-A subscales, respectively (25).

Every item of the scale is scored between zero to three. Thus, subscales of HADS are scored from zero to twenty one. For each subscale, scores between zero and seven are normal, eight to ten are mild, eleven to fourteen are moderate and fifteen to twenty one are severe. A score of eight was considered as the cut-off score for each subscale (26).

3.3. Measurements

Clinical data including medications, comorbidities and the patients' latest laboratory results (complete blood count, biochemical profile, urea and creatinin before and after hemodialysis) performed during the last month were obtained from patients' medical records. Comorbidity was defined as presence of at least one of the following diseases: diabetes mellitus, hypertension, congestive heart failure, coronary artery disease, chronic lung disease, malignancy and autoimmune disorders.

The following biochemical parameters were checked using the HITACHI 717 automatic analyzer device (RXT Technicon system, Japan): Fasting blood glucose (FBS), blood urea nitrogen (BUN), creatinin (Cr), sodium (Na), potassium (K), calcium (Ca), phosphorus (P), alkaline phosphatase (Alkp), cholesterol (Chol), triglyceride (TG), liver enzymes (AST, ALT), iron (Fe), total iron binding capacity (TIBC), and albumin (Alb). Intact parathyroid hormone (iPTH) and ferritin were measured using the ELISA method. Hemoglobin and hematocrit were measured using the automatic blood analyzer with Sysmex system (Sysmex Co, Kobe, Japan).

3.4. Dialysis Adequacy

To assess the adequacy of hemodialysis, URR (27) and Kt/v (28) were calculated by the following formulas:

$$\text{Urinary Reduction Ratio} = 100 \times \left[1 - \left(\frac{\text{Urea After Hemodialysis}}{\text{Urea Before Hemodialysis}}\right)\right] \quad (1)$$

$$\frac{\text{Kt}}{V} = -\ln\left(R - 0.008t\right) + \left(4 - 3.5R\right) \times \frac{\Delta\text{BW}}{\text{BW}} \quad (2)$$

In which, K stands for the dialyzer clearance the rate at which blood passes through the dialyzer expressed in milliliters per minute (mL/min), t stands for time, V is the volume of water a patient's body contains, R is BUN post/BUN pre and BW is body weight.

3.5. Statistical Analysis

Continuous data were tested with the Kolmogorov-Smirnov test for normality and if necessary, logarithmic transformations were used for analysis. Continuous variables were expressed as mean (standard deviation) and categorical values were expressed in percentages. The differences between the two groups were analyzed using independent sample t-test, and chi-square analysis was used for categorical data. Pearson correlations were used to determine the possible correlation between various variables and dependent variables. The linear regression model was also used to assess the ability of different variables in predicting the anxiety and depression scores. Statistical significance was defined as $P < 0.05$. All analyses were performed using the statistical package for the social sciences, version 21.0 for windows (SPSS Inc., Chicago, USA). This study conforms to the provisions of the declaration of Helsinki and was approved by the ethical committee of Shahid Beheshti University of Medical Sciences. Informed consent was obtained from all the subjects.

4. Results

A Total number of 127 patients including 73 males (57.5%) were studied. The mean age of the studied population was 55.7 (17.5) years and the mean dialysis duration was 80.9 (85.4) months. Cut-off scores of $\geq$ 8 in HADS-D and HADS-A were used for diagnosing depression and anxiety, respectively. The mean HADS-D score in patients with and without symptoms of depression were 11.3 (3.1) and 3.2 (2.1), respectively; and the mean HADS-A score in patients with and without symptoms of anxiety were 12.0 (3.6) and 3.0 (2.1), respectively.

Prevalence of depression and anxiety in the studied population were 31.5% (n = 40) and 41.7% (n = 53), respectively. Basic characteristics of subjects with and without depression or anxiety are compared in Tables 1 and 2. The prevalence of depression and anxiety were not significantly different in different subgroups regarding marital status, educational level and presence or absence of comorbidities. However, the prevalence rates of depression and anxiety were significantly higher in women compared to men ($P < 0.05$). The prevalence of anxiety, but not depression, was also different in age subgroups.

Table 3 shows the mean age, dialysis duration and laboratory characteristics of the patients according to HADS subscales. The mean age of the patients with symptoms of anxiety was significantly lower than the patient without it (50.3 ± 15.2 versus 59.6 ± 18.0, $P = 0.003$). Among laboratory variables, the mean iPTH levels in patients with anxiety were lower than the normal group ($P < 0.05$). There were no significant differences in mean Kt/V and URR between patients with symptoms of depression or anxiety compared to the normal group.

Upon analysis of correlations, there was no significant correlation between depression score and independent variables. Anxiety score was correlated with age ($r = -0.24$, $P = 0.007$) and parathyroid hormone levels ($r = -0.19$, $P = 0.04$). Hemoglobin, Iron, TIBC, ferritin and albumin were not significantly correlated with depression or anxiety. There were also no significant correlations between Kt/V and URR with depression and anxiety scores (Table 4). Younger age and lower iPTH levels were the only factors that predicted higher scores of anxiety. However, none of the factors assessed in this study significantly predicted

Table 1. Basic Characteristics of the Patients Classified According to the Hospital Anxiety and Depression Scale Depression Subscale[a]

Variable	HADS-D < 8, %	HADS-D ≥ 8, %
Gender		
Male	75.7	24.3
Female	58.5	41.5
Age, y		
20 - 34	85.7	14.3
35 - 49	70.4	29.6
50 - 64	56.2	43.8
≥ 65	68.1	31.9
Marital status		
Single	68.8	31.2
Married	65.2	34.8
Educational level		
Illiterate	54.5	45.5
Minimally literate	64.3	35.7
Diploma	67.6	32.4
University	94.4	5.6
Comorbidity[b]		
Yes	66.7	33.3
No	72.2	27.8

Abbreviation: HADS-D, hospital anxiety and depression scale-depression subscale.
[a] P value < 0.05.
[b] Comorbidity includes diabetes mellitus, hypertension, congestive heart failure, coronary artery disease, chronic lung diseases, malignancies and autoimmune disorders.

Table 2. Basic Characteristics of the Patients Classified According to the Hospital Anxiety and Depression Scale Anxiety Subscale[a]

Variable	HADS-D < 8, %	HADS-D ≥ 8, %
Gender		
Male	67.6	32.4
Female	45.3	54.7
Age, y		
20 - 34	57.1	42.9
35 - 49	40.7	59.3
50 - 64	43.8	56.2
≥ 65	78.7	21.3
Marital status		
Single	53.1	46.9
Married	59.1	40.9
Educational level		
Illiterate	45.5	54.5
Minimally literate	58.9	41.1
Diploma	55.9	44.1
University	77.8	22.2
Comorbidity[b]		
Yes	60.9	39.1
No	55.6	44.4

Abbreviation: HADS-D, hospital anxiety and depression scale-depression subscale.
[a] P value < 0.05.
[b] Comorbidity includes diabetes mellitus, hypertension, congestive heart failure, coronary artery disease, chronic lung diseases, malignancies and autoimmune disorders.

the depression scores (Table 5).

5. Discussion

This study aimed to determine the prevalence of depression and anxiety among MHD patients and also to determine the association between these two conditions with dialysis adequacy. We found that depression and anxiety are highly prevalent among MHD patients with the prevalence rates of 31.5% and 41.7%, respectively. Prevalence of both conditions was significantly higher in women. We found no significant association between Kt/V and URR with depression and anxiety. Previous studies reported a prevalence of 19.3% to 60.5% for depression (2, 3) and a prevalence of 27% to 52% for anxiety (4, 5) in MHD patients. The prevalence of depression and anxiety in our study were similar to those in Cukor et al. (29) study with a prevalence of 29% and 45.7% for depression and anxiety, respectively. Studies conducted in Iran reported a prevalence of 50% to 91% for depression and 20% to 60% for anxiety. For example, Sanavi and Afshar (22) showed that the prevalence of depression in MHD patients was 70% using the Beck depression inventory. These differences can be due to the use of various anxiety and depression scales in different studies, variations in sample sizes, locations of the study, patients' socioeconomic status, and ethnic differences.

In our study, the prevalence of both conditions was significantly higher in women, which is in concordance with some other studies. Several studies suggest that the difference between women and men may be due to their greater concerns about future and their obligations to obtain different social roles such as being a mother or a wife, and having a job simultaneously, which may lead to increased anxiety in women. Furthermore, female MHD patients may not get enough emotional and financial support.

Dialysis adequacy has been considered to affect survival in MHD patients (30-33). On the other hand, it is suggested that the presence of psychiatric disorders increases the morbidity and mortality in MHD patients (10, 11). Several studies suggest that dialysis adequacy may be inversely associated with the prevalence of depression and anxiety. For example, Hung et al. (13) in a study on 146 MHD patients revealed a weak association (r = 0.2) between depression and Kt/V. Klaric and Klaric (18) also reported an association between depression and dialysis adequacy in patients treated with peritoneal dialysis but not in MHD patients. They suggest these findings could be due to the uniform distribution of Kt/V in MHD patients. Montinaro et al. (26) found no differences in Kt/v means between depressed and anxious patients with the normal group. Similar to this study, we found no association between dialysis adequacy with depression or anxiety. Different studies use different indices and methods for calculating dialysis adequacy and this can be an obstacle in comparing the studies. On the other hand, strong and plausible evidence regarding the relationship between dialysis adequacy and psychological problems are lacking. Depression and anxiety are chronic conditions and since dialysis adequacy indices may vary in different periods of time, they may not represent the adequacy of dialysis simultaneously with patients' mood.

Anxiety scores were inversely associated with patients' age. This may be in part due to a lower ability of the youth to cope with chronic diseases. Younger patients consider dialysis a more significant impairment in comparison with their older counterparts since this condition puts limitations on their active and dynamic life (34). There were no differences in the depression and anxiety prevalence rates between subgroups divided by marital status, educational level, dialysis duration, and comorbidities.

Chronic renal failure and dialysis are associated with

Table 3. Age, Dialysis Duration and Laboratory Characteristics of the Patients According to HADS Subscales[a,b]

Variable	Depression		Anxiety	
	HADS-D < 8	HADS-D ≥ 8	HADS-A < 8	HADS-A ≥ 8
Age, y	54.6 (18.8)	58.1 (14.1)	59.6 (18.0)	50.3 (15.2)
Dialysis duration, mon	78.4 (84.6)	87.2 (88.4)	84.5 (86.5)	75.5 (84.5)
Hemoglobin, g/dL	10.8 (1.6)	10.8 (1.8)	10.7 (1.6)	10.8 (1.7)
Iron, μg/dL	65.2 (89.5)	52.4 (25.0)	55.8 (30.4)	69.3 (114.2)
TIBC, ng/dL	249.4 (75.8)	235.9 (63.7)	250.7 (79.5)	237.1 (59.8)
Ferritin, ng/mL	421.7 (365.5)	521.3 (477.3)	414.7 (338.4)	508.3 (471.5)
Albumin, g/dL	4.1 (0.4)	4.1 (0.4)	4.0 (0.4)	4.0 (0.5)
iPTH, pg/mL	432.8 (476.0)	273.7 (242.6)	444.0 (499.2)	292.0 (251.5)
Kt/V	1.37 (0.3)	1.40 (0.3)	1.34 (0.3)	1.42 (0.3)
URR	0.67 (0.1)	0.68 (0.1)	0.67 (0.1)	0.69 (0.1)

Abbreviations: HADS-A, hospital anxiety and depression scale-anxiety subscale; HADS-D, hospital anxiety and depression scale depression subscale; iPTH, intact parathyroid hormone; TIBC, total iron binding capacity; URR, urea reduction ratio.
[a] Data are expressed as mean (SD).
[b] P value < 0.05 for depression subscale.

Table 4. Correlations Between Depression and Anxiety Scores and Different Variables (Pearson Correlation)

Variable	Depression		Anxiety	
	r	P Value	r	P Value
Age, y	0.17	0.06	-0.24	0.007
Dialysis duration, mon	0.03	0.7	0.05	0.5
Hemoglobin	0.05	0.5	0.00	0.9
Iron	-0.06	0.4	0.18	0.4
TIBC	-0.04	0.6	-0.16	0.07
Ferritin	0.04	0.6	0.04	0.6
Albumin	-0.04	0.6	0.02	0.8
iPTH	-0.12	0.2	-0.19	0.04
Kt/V	0.02	0.8	0.16	0.08
URR	-0.01	0.9	0.09	0.3

Abbreviations: iPTH, intact parathyroid hormone; TIBC, Total iron binding capacity; URR, urea reduction ratio.

chronic inflammation (35-37). Some studies suggest that serum hemoglobin (18, 38, 39), albumin (17, 39, 40) and cortisol (15) levels are associated with depression. We found no association between hemoglobin, iron, ferritin and albumin levels with depression or anxiety in our study. Anxiety was inversely associated with intact parathyroid hormone (iPTH) levels in our study. Part of these differences could be due to differences in patients' metabolism, body structure, nutritional and environmental conditions, activities and severity of depression or anxiety.

This study has several limitations. First, we used a single value of Kt/v and URR instead of using a mean value during a period of time. Second, we were not able to run a structured clinical interview to diagnose depression or anxiety disorders and also we used the HADS questionnaire instead, which has been validated for Iranian outpatients. Third, although previous studies suggest that inflammatory biomarkers such as C-reactive protein (CRP) and interleukin-6 (IL-6) may be involved in developing depression symptoms, we did not have information on these biomarkers. Last but not least, we were not able to stratify the patients based on individual comorbidities due to

Table 5. Linear Regression Model of Different Variables for Prediction of Anxiety and Depression Scores

Variable	Depression			Anxiety		
	B[a]	95% CI	P Value	B[a]	95% CI	P Value
Age, y	0.18	-0.01 - 0.11	0.08	-0.29	-0.16 - -0.03	0.004
Dialysis duration, mon	-0.03	-0.01 - 0.01	0.7	-0.13	-0.20 - 0.01	0.2
Hemoglobin	0.05	-0.44 - 0.73	0.6	-0.05	-0.81 - 0.49	0.6
Iron	-0.09	-0.02 - 0.01	0.4	0.09	-0.01 - 0.02	0.3
Albumin	-0.03	-1.92 - 2.56	0.8	-0.03	-2.83 - 2.18	0.8
iPTH	-0.15	-0.01 - 0.00	0.1	-0.20	-0.01 - 0.00	0.04
Kt/V	0.14	-1.40 - 5.78	0.2	0.20	-0.08 - 7.95	0.06

Abbreviations: CI, confidence interval; iPTH, intact parathyroid hormone.
[a]Standardized coefficient for the constant.

small number of patients in most comorbidity subgroups; hence, we were unable to assess the role of the comorbidities separately in this study. The strengths of our study include using a single method for calculating Kt/V and URR for all of the patients, and also a decent sample size compared to other similar studies. Moreover, the study population was recruited from three major hospitals in three different regions in Tehran and may serve as a good representative of MHD patients living in Tehran.

5.1. Conclusion

In conclusion, we found no significant association between dialysis adequacy and depression or anxiety. We suggest that depression and anxiety are common in hemodialysis patients and to improve services to these patients, physicians and personnel should be informed and educated about these conditions.

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Footnotes

Authors' Contribution: Afshan Najafi, collected the data, participated in interpreting the clinical data and statistical analysis and drafted the manuscript. Sorena Keihani, performed the statistical analysis and helped to draft the manuscript. Nazila Bagheri, re-evaluated the clinical data and revised the manuscript. Atefeh Ghanbari Jolfaei, participated in revising the article for intellectual content. Azadeh Mazaheri Meybodi, conceived and designed the evaluation, interpreted All authors read and approved the final manuscript.

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