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Original Article

The relationship of depression levels and arterial stiffness in hemodialysis patients

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Abstract

Aim: The most common psychiatric disorder in hemodialysis (HD) patients is depression and is associated with morbidity and mortality. The relationship between depression and arterial stiffness in this patient group is a new field of study and data are limited. The aim of this study is to examine depression, arterial stiffness and other potentially relevant laboratory parameters in HD patients.
Materials and Methods: The study included 58 chronic renal failure patients who underwent hemodialysis for at least 3 months, and the Beck Depression Inventory (BDI) was applied to the participants by the researcher. Pulse Wave Velocity (PWV) figures of the patients were measured on the day the inventory was applied, and laboratory results were obtained within the same month.
Results: Depressive symptoms were determined in 27.6% of the patients, and the severity of depression was 25.9% moderate, 5.2% severe. When patients with and without depressive symptoms were compared, PWV (9.3 ± 1.9 vs. 7.8 ± 2.5, P = 0.04) and phosphorus (5.4 ± 1.5 vs. 4.4 ± 1.1 p = 0.008) levels were significantly higher in the depressive group, while calcium (8.3 ± 0.9mg / dL vs.8.8 ± 0.5mg / dL p = 0.018) levels were significantly lower. Phosphorus level (odds ratio [OR] 2.163; 95% CI 1.174--3.982; p = 0.013) and PWV (OR 1.403; 95% CI 1.018--1.932; p = 0.038) were found as independent predictors for depression in multivariate analysis.
Conclusion: One of the serious problems affecting the quality of life in HD patients is depression. In our study, it has been shown that there is an irrelevant relationship between depression and arterial stiffness and phosphorus levels in HD patients.

Keywords: Arterial stiffness; calcium; depression; hemodialysis; phosphorus

INTRODUCTION

Since chronic kidney disease (CRD) and hemodialysis (HD) treatment which can develop correspondingly cause physical, mental and social problems, mental disorders are frequently encountered in HD patients (1). Despite the prolongation of life expectancy in these patients thanks to hemodialysis treatment, a decrease in psychosocial adjustment is observed. Sticking to a device to survive and the feeling that their lives are not under their control is the most important problem of dialysis patients. While dissonance is common in patients with end-stage renal disease, psychopathology is mostly shaped around depression (2). It has been asserted that depression is one of the most common psychological diseases in HD patients, and in studies conducted with HD patients, 20-30% of this patient group suffers from depression (3-5).

There are many studies showing that depression is more common in patients undergoing hemodialysis treatment due to chronic renal impairment compared to normal healthy individuals (6,7). Depression symptoms in hemodialysis patients are characterized with lasting depressive temperament, suicidal thoughts, inability to concentrate, decreased self-esteem, and hopelessness (8). Depression is stated to be a major cause of fatigue in hemodialysis patients (9).

Arterial aging is defined as age-related degeneration and tissue stiffness in layers of the great arteries (10). Hypotheses predicting genomic instability as a factor in vascular aging often focus on the primary role of DNA damage caused by oxidative stress (11). These changes cause the aorta to lose its elasticity and thus increase the pulse pressure (12). Pulse wave velocity (PWV) is often considered to be the gold standard technique that gives hope for continuous non-invasive measurements (13). Studies on the relationship between depression and PWV are limited and conflicting. Depressive symptoms have been shown to be associated with high PWV in the geriatric patient group (14). While a relationship between high arterial aging and the presence of depression was

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reported (15) in the Rotterdam study, no relationship was found between arterial aging and depression in the Netherlands Study of Depression and Anxiety (NESDA) study with a mean age of 47 years (16).

Atherosclerosis is known to be a risk factor for depression in later life, and depressive symptoms themselves are associated with subsequent cardiovascular disease (17,18). In the vascular depression hypothesis, it has been suggested that structural changes in the brain due to atherosclerosis play an important role in the development of depression in elderly patients (19). We wanted to evaluate whether atherosclerosis is effective in depression among the hemodialysis population where atherosclerosis is prevalent.

MATERIALS and METHODS

For the research, approval was obtained from the Ethics Committee of the Selcuk University Faculty of Medicine with the approval number 2016/166 dated 01.04.2020. The sample of the study consisted of 58 patients aged 18 and over, who received HD treatment with the diagnosis of ESRD in the Hemodialysis Department of Selcuk University Faculty of Medicine and gave consent to participate in the study. Beck Depression Inventory, developed by Beck and adapted into Turkish by Hisli, was used to determine the depression levels of the patients (20,21). PWV (PulseWaveVelocity) figures were measured using Mobil-O-Graph NG (İ.E.M GmbH Stolberg Germany) arteriograph device in the hemodialysis clinic on the day of the inventory. This device enables the determination of all arterial stiffness parameters from the upper extremity, over the brachial artery by the oscillometric method, and gaining the result of the measured arterial stiffness parameters is transferred to the computer program. Measurements were performed through the non-graft arm without fistula in patients with AV fistula or grafts. At the beginning of hemodialysis, the patients were measured after waiting in the supine position for at least 5 minutes at rest. It was noted that the patients did not take stimulants such as cigarettes and coffee for half an hour before the process. Moreover, the routine laboratory data of the patients every month were recorded. After collecting all the data, the patients were divided into two groups as with and without depressive symptoms based on 17 which is the cut-off score of BDI. PWV figures, other clinical and laboratory findings of the groups were compared. In addition, according to the BDI score, 17-29 points were accepted as moderate depression and 30-63 severe depression.

Statistical Analysis

In order to test the normal distribution Kolmogorov–Smirnov test was used. While non-normally distributed continuous variables were expressed as median (interquartile range), continuous variables were expressed as mean±standard deviation. Categorical data were showed in percentages. Due to producing statistical analyses, the Chi-square test was applied for analyzing the categorical variables, the t test was applied for analyzing the continuous variables, and the Mann–Whitney U test was applied for analyzing the non-normally distributed data. Multivariate regression analysis was performed to determine independent predictors of depression development. To give this analysis, variables with a p value of <0.05 in the univariate analysis were included in the multivariate analysis which is called stepwise backward elimination. A p value of <0.05 was appraised to be significant. SPSS 25.0 (IBM Corp., SPSS, NY, USA) program was prefered for the statistical accounts.

RESULTS

A total of 58 HD patients participated in this study, which investigated the relationship of depression with arterial aging and other laboratory parameters in HD patients. The average age of the study population is 59.2 ± 14.7, 53.4% of the patients are male, 31% are diabetic and 69% are hypertensive. Participants were divided into two groups according to the degree of their depressive symptoms, and in the group with depressive symptoms, PWV (9.3 ± 1.9 vs. 7.8 ± 2.5, P = 0.04) and phosphorus (5.4 ± 1.5 vs. 4.4 ± 1.1 p = 0.008) levels were found to be significantly higher.

Table 1. Clinical and laboratory features of depressive compared with non-depressive in hemodialysis CKD patients

Parameters	Depressive (n=16)	Nondepressive (n=42) (n=218)	p
Age (Year)	57.6 ± 13.1	59.7 ± 12.3	0.603
Gender (female / male)	7/9	20 /22	0.792
Hemodialysis vintage (months)	49.6±14.6	47±15.2	0.802
Diabetes Mellitus			0.196
Yes	7 (% 43.8)	11 (% 26.2)	
No	9 (% 56.3)	31 (% 73.8)	
Hypertension			0.196
Yes	9 (%56.3)	31 (% 73.8)	
No	7 (% 43.8)	11 (% 26.2)	
Body mass index (kg/m²)	24.9± 3.5	25.4± 4.6	0.705
Systolic blood pressure (mmHg)	142.3 ± 33.0	130.3±25.9	0.121

Diastolic blood pressure (mmHg)	85.0±22.3	81.0±17.1	0.468
Pulse wave velocity (m/s)	9.32 ± 1.96	7.8± 2.5	**0.040**
Urea (mg/dl)	132.6±35.4	117.6±30.7	0.115
Creatinine (mg/dl)	6.89±1.4	7.77±2.17	0.139
Uric acid (mg/dl)	5.6 ± 0.8	5.5 ± 1.0	0.747
Calcium (mg/dl)	8.3±0.9	8.8±0.5	**0.018**
Phosphorus (mg/dl)	5.4±1.5	4.4±1.1	**0.008**
Albümin (g/dl)	3.8(2.7-4.4)	3.7 (1.7-4.4)	0.552
Ferritin (ng/ml)	504.6±75.8	481.3 ± 55.1	0.776
Parathormon (pg/ml)	704.6±205.3	442.6±91.3	0.079
Total cholesterol (mg/dl)	180.1±49.2	187.1±48,9	0.630
LDL cholesterol (mg/dl)	106.1 ± 34.8	111.2±40.1	0.657
HDL cholesterol (mg/dl)	48.5±15.6	41.3 ±12.5	0.056
Triglyceride (mg/dl)	162.6 ± 62.4	170.0± 69.4	0.151
Hemoglobin (g/dl)	11.6 ± 1.2	11.2 ± 1.2	0.396
NLR	3.90±1.53	3.51±1.83	0.452
Kt/V	1.48±0.19	1.61±0.34	0.191
URR	72.0±4.7	74.4±6.7	0.207
BDI score	22.5 (17-35)	4.5(0-16)	**<0.001**

CRP: C reactive protein ; BDI: Beck depression inventory; LDL: Low-density lipoprotein; HDL: high-density lipoprotein; NLR: Neutrophil lymphocyte ratio; URR: Urea reductionrRatio . Data are presented as mean±standard deviation or median (minimum- maximum)

Table 2. Univariate and multivariate regression analysis for determinants of depression

	Univariate analysis	
	OR (95% CI)	**P value**
Age (years)	0.990 (0.952-1.030)	0.627
Diabetes mellitus (present vs absent)	0.456 (0.137-1.520)	0.201
Hypertension (present vs absent)	2.192 (0.658-7.304)	0.201
Gender	1.169 (0.367-3.723)	0.792
Dialysis vintage (per 1 month increase)	1.002 (0.986-1.019)	0.798
Systolic blood pressure (per 1 mmHg increase)	1.017 (0.995-1.038)	0.124
Diastolic blood pressure (per 1 mmHg increase)	1.012 (0.980-1.045)	0.461
Pulse wave velocity (per 1 m/s increase)	1.292 (1.003-1.663)	**0.047**
Hemoglobin (per 1 g/dL increase)	1.236 (0.762-2.004)	0.390
Calcium (per 1 mg/dL increase)	0.368 (0.150-0.899)	**0.028**
Phosphorus (per 1 mg/dL increase)	1.810 (1.119-2.928)	**0.016**
Parathormon (per 1 pg/mL increase)	1.001 (1.000-1.002)	0.092
Kt/V	0.244 (0.029-2.030)	0.192
	Multivariate analysis (Nagelkerke R^2 = 0.363)	
	Adjusted OR (95% CI)	**P value**
Pulse wave velocity (per 1 m/s increase)	1.403 (1.018-1.932)	0.038
Phosphorus (per 1 mg/dL increase)	2.163 (1.174-3.982)	0.013

OR: odds ratio

Furthermore, calcium (8.3 ± 0.9mg / dL vs.8.8 ± 0.5mg / dL p = 0.018) levels were found to be significantly lower in the group with depressive symptoms compared to patients without depressive symptoms. The comparison of both groups according to age, gender, PWV and laboratory findings is given in Table 1.

Univariable and multivariable adjusted regression analyses were performed to determine the independent determinants of depression in hemodialysis patients. In univariable logistic regression analysis calcium, phosphorus and PWV and were all found to be associated with presence of depression in hemodialysis patients.

These variables were then used to construct a multivariate model. The results of the multivariable adjusted regression analysis demonstrated that the levels of phosphorus (odds ratio [OR] 2.163; 95% CI 1.174–3.982; p= 0.013) and PWV (OR 1.403; 95% CI 1.018–1.932; p = 0.038) were the independent predictors of depression (Table 2).

DISCUSSION

HD is the most well-known Renal Replacement Therapy (RRT) method used to excrete residuum and fluid that cannot be excreted from the body due to the failure of kidney functions (22). The goal of HD treatment is to increase the life expectancy of individuals and to keep their living standards high, but it may also have negative consequences. Depression is common in HD patients (23). In the light of this information, it becomes important to examine depression and related factors in patients receiving HD treatment.

Some of the characteristic features of arterial aging triggered by a decrease in antioxidative capacity and an increase in oxidative stress (24) are increased vascular calcification and endothelium dysfunction (25). Pulse wave velocity is the non-invasive gold standard method for arterial stiffness measurement. PWV is highly predictive for conditions such as major cardiovascular endpoints, cognitive dysfunction, and dementia (26). This device has already been tested and validated in end-stage renal disease patients receiving HD treatment (27). In a study conducted with 1433 geriatric patients, a positive significant relationship was found with the degree of depression in patients with PWV higher than 12 m / s (28). In a study conducted with 81 hemodialysis patients, a strong positive correlation was found between depression, malnutrition, inflammation and arterial stiffness, and these four factors were determined as risk factors for cardiovascular diseases and all-cause mortality in chronic HD patients (29). On the other hand, in prospective studies, it was found that depression treatment significantly changed arterial stiffness in the geriatric patient group (26,30). In the literature examining the relationship between depression and arterial stiffness in HD patients is limited as far as it is known there is no such a study in the literature in Turkey. In our study, there is a strong positive correlation between depression and arterial stiffness compatible with the current literature.

The mechanism between arterial stiffness and depression has not been fully elucidated. However, some mechanisms were proposed. The vascular depression hypothesis was proposed by Alexopoulos et al in 1997. The 'Vascular Depression' hypothesis suggests that cerebrovascular disease may predispose, accelerate, or perpetuate some geriatric depressive syndromes (31). Van Sloten et al. also revealed the results supporting this with their clinical studies. It has been suggested that arterial stiffness may make way for depression through cerebral microvascular damage (14). Arterial stiffness can cause microvascular damage through increased pulsatile load on the microcirculation. Impaired vasoreactivity can lead to cerebral hypoperfusion and microvascular ischemia. Ischemia can damage the frontal and subcortical structures or their connective pathways involved in mood regulation and thus lead to depression (32, 33).

Although the focus of our study was depression and arterial stiffness in hemodialysis patients, we also evaluated depression and other related factors in this patient group. When we reviewed the literature, in a cross-sectional study with 173 HD patients, depression levels were found to be associated with low blood albumin and high parathyroid hormone levels (34). In a study comparing 110 HD patients and 40 healthy controls, depression was found to be associated with low selenium, hemoglobin, and albumin levels (35). In another cross-sectional study, no relationship was found between depression and any nutritional marker in HD patients (36). In a study conducted with 145 HD patients, depression symptoms were determined in 46% of the patients, and the only biochemical parameter related to depression was associated with serum phosphorus level (37). As it is seen, the findings of studies showing the relationship between nutritional and biochemical parameters and depression in HD patients are contradictory. In our study, a significant relationship was found between low blood calcium and high blood phosphorus and depression level.

The relation between high phosphorus levels and depression has several possible mechanisms. Non-compliance with treatment is common in depressed patients (38). The non-compliance of these patients with phosphorus-lowering therapy may explain the phosphorus-depression relationship. In addition, non-compliance with a phosphorus-poor diet in depressive dialysis patients may also contribute to the hyperphosphatemia-depression relationship (39). Another hypothesis that explains the relationship between hyperphosphatemia and depression is based on the fact that both are associated with endothelial dysfunction. Indeed, endothelial dysfunction is directly related to serum P level (40) and depressed individuals have an abnormal microvascular function (41).

Our study has some limitations. Single-center patients were included in our study. Our number of patients is relatively low.

CONCLUSION

In conclusion, depression, the most common psychiatric disorder in HD patients, is independently associated with arterial stiffness and phosphorus levels measured by PWV. Studies on this subject are limited and contradictory. As far as we know, especially in this patient group are no studies showing the relationship between depression and arterial stiffness in Turkey. We believe that our study will be a guide for more comprehensive studies to be conducted.

Competing interests: The authors declare that they have no competing interest.

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