

# Depression in hemodialysis patients: the role of dialysis shift

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**OBJECTIVE:** Depression is the most important neuropsychiatric complication in chronic kidney disease because it reduces quality of life and increases mortality. Evidence demonstrating the association between dialysis shift and depression is lacking; thus, obtaining such evidence was the main objective of this study.

**METHOD:** This cross-sectional study included patients attending a hemodialysis program. Depression was diagnosed using Beck's Depression Inventory. Excessive daytime sleepiness was evaluated using the Epworth Sleepiness Scale.

**RESULTS:** A total of 96 patients were enrolled (55 males, age  $48 \pm 14$  years). Depression and excessive daytime sleepiness were observed in 42.7% and 49% of the patients, respectively. When comparing variables among the three dialysis shifts, there were no differences in age, dialysis vintage, employment status, excessive daytime sleepiness, hemoglobin, phosphorus levels, or albumin levels. Patients in the morning shift were more likely to live in rural areas ( $p < 0.0001$ ), although patients in rural areas did not have a higher prevalence of depression ( $p = 0.30$ ). Patients with depression were more likely to be dialyzed during the morning shift ( $p = 0.008$ ). Independent risk factors for depression were age ( $p < 0.03$ ), lower levels of hemoglobin ( $p < 0.01$ ) and phosphorus ( $p < 0.01$ ), and dialysis during the morning shift ( $p = 0.0009$ ). The hospitalization risk of depressive patients was 4.5 times higher than that of nondepressive patients ( $p < 0.008$ ).

**CONCLUSION:** These data suggest that depression is associated with dialysis shift, higher levels of phosphorus, and lower levels of hemoglobin. The results highlight the need for randomized trials to determine whether this association occurs by chance or whether circadian rhythm disorders may play a role.

**KEYWORDS:** Depression; Dialysis Shift; Hemodialysis.

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## INTRODUCTION

Chronic Kidney Disease (CKD) is a silent disease that is frequently diagnosed in the advanced stages when dialysis and renal transplantation are the only options. The beginning of dialysis treatment causes subtle changes in the life of CKD patients, mainly in the physical and social spheres. For this reason, individuals diagnosed with CKD usually develop neuropsychiatric complications. Depression is the most important of them, due to its high prevalence, reduction in quality of life, and potential to increase mortality (1,2). The

prevalence of depression in CKD patients, even those in the predialysis stages, is higher than that reported for the general population and for individuals with other chronic diseases (1,2). Depressive patients with CKD on hemodialysis have a higher risk of death and hospitalizations compared with those without depressive symptoms (3). Despite the high prevalence (60% in some series) and damaging consequences, depression is still a misdiagnosed disorder because of the superposed symptoms related to uremia (anorexia, fatigue, sleep disorders) and the absence of a systematic psychiatric evaluation (4). Beck's Depression Inventory (BDI) is one of the most widely used tests for assessing the severity of depression in this population and was recently modified for dialysis patients due to the high prevalence of symptoms that can mimic the clinical presentation of depression in this population (5). Unemployment, white race, dialysis vintage, and female sex are recognized factors associated with depression in dialysis patients (6,7). Usually, dialysis units have morning, afternoon, and evening shifts, and patients are

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distributed depending on their own preference. Recent studies have suggested that dialysis shift may have an impact on sleep disorders, quality of life, and mortality (8-10). However, evidence regarding the influence of dialysis shift on the prevalence of depression is scarce (11).

Therefore, we aimed to evaluate the influence of the dialysis shift on depression frequency in a population of patients undergoing hemodialysis. In addition, we assessed the main outcomes related to depression symptoms and management and identified possible biochemical markers of depression in this specific population.

## ■ MATERIALS AND METHODS

This cross-sectional study included patients 18 years of age or older who were attending a hemodialysis program at a tertiary hospital. Patients who had undergone less than six months of dialysis, those with advanced malignancy, and those who were intellectually unable to answer the questionnaires or who refused to participate were excluded. The prevalence of depression symptoms was assessed using Beck's Depression Inventory (BDI), which is a questionnaire that includes 21 queries with graduated answers from 0 to 3 that addresses issues such as sadness, guilt, tiredness, concern with personal appearance, being able to work, sexual interest, and other issues (12). Recently, BDI was validated for CKD patients through a comparison with a structured psychiatric interview using ICD-10 criteria and applied by a trained psychiatrist. Based on this study, the BDI cut-off of 10, which was validated for the general population, was raised to sixteen or higher for CKD patients (5). BDI was also validated in dialysis patients against the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (SCID), and an identical cut-off was found (13). BDI has already been translated, adapted, and validated in Brazilian Portuguese, showing good reliability and validity (14). Excessive daytime sleepiness (EDS) was also evaluated using the Epworth Sleepiness Scale (ESS), and patients with values higher than 9 were considered to have EDS, as described previously (15).

An additional questionnaire was applied to assess general data (age, gender, scholarship level, marital state, address in urban or rural area, occupation, cause of CKD, comorbidities, antidepressant drugs, number of hospitalizations in the last year) and data related to the dialysis session (time on dialysis, interdialytic weight gain, and single pool Kt/V [which measures dialysis dose]). Laboratory parameters were analyzed, such as hemoglobin, calcium, phosphorus, and albumin. The statistical analysis was performed based on the median values of the last three months. The patients were evaluated according to their dialysis shift: morning, afternoon, or evening.

## Ethics

The study was submitted and approved by a local ethics committee (protocol number 1325), and all subjects provided written informed consent. This study was performed in accordance with the Helsinki Declaration of 1975.

## Statistical analysis

The data are expressed as the mean  $\pm$  standard deviation (SD). For the statistical analysis and data description, patients were stratified according to dialysis shift (morning, afternoon, and evening). Numerical variables were submitted to

the Kolmogorov-Smirnov test and compared using ANOVA with a Bonferroni post-test. The Mann-Whitney test was performed to analyze variables that were not normally distributed. Categorical variables were examined by a Chi-square test. The association between the laboratory data, demographic data, and the presence of depression was evaluated by logistic regression (Enter method). The variables used in the logistic regression model were gender, age, dialysis vintage, unemployment, dialysis shift, hospitalization, rural area, hemoglobin, and phosphorus. The significance level adopted was  $p < 0.05$  with a 95% confidence interval. All statistical analyses were performed using SPSS software (SPSS Inc., Chicago, IL).

## ■ RESULTS

After application of the exclusion criteria, 96 patients were enrolled during the four months of data collection (December 2009 to March 2010). Among these patients, 55 were male, and the mean age was  $48 \pm 14$  years. The main clinical, demographic, and laboratory characteristics are summarized in Table 1. Most of the patients were married (63.5%) and not employed (88.5%). Depression symptoms and EDS were observed in 41 (42.7%) and 47 (49%) patients, respectively. The dose of dialysis, expressed as Kt/V, was adequate for all patients.

There were no differences between individuals in the three dialysis shifts with respect to age, dialysis vintage, employment status, hemoglobin, phosphorus, albumin levels, or EDS (Table 2). Patients in the morning shift lived farther from the dialysis unit ( $p < 0.0001$ ), in a rural area. The prevalence of depression was higher among patients in the morning shift (Table 2).

When comparing patients with and without depression, we found no difference in gender, dialysis vintage, employment status, or address in a rural area. The most important difference in depression prevalence was between individuals in the morning and evening dialysis shifts (Pearson

**Table 1 - Demographic and clinical data (N = 96).**

Variable	Patients (N = 96)
Age, years	48.1 $\pm$ 13.7
Male gender, n (%)	55 (57.3)
Marital status	
Single, n (%)	17 (17.7)
Married, n (%)	61 (63.5)
Divorced, n (%)	10 (10.4)
Widowed, n (%)	8 (8.3)
Employment	
Yes, n (%)	11 (11.5)
No, n (%)	85 (88.5)
Comorbidities	
Hypertension, n (%)	74 (77)
Heart failure, n (%)	18 (18.7)
Diabetes mellitus, n (%)	14 (14.5)
Liver disease, n (%)	06 (6.2)
Lupus erythematosus, n (%)	03 (3.1)
Hypothyroidism, n (%)	02 (2)
Dialysis vintage, years	5.1 $\pm$ 3.7
Interdialytic weight gain, kg	2.4 $\pm$ 0.9
Hemoglobin, g/dl	9.9 $\pm$ 1.6
Phosphorus, mg/dl	5.7 $\pm$ 1.5
Albumin, g/dl	3.9 $\pm$ 0.4
Kt/V	1.2 $\pm$ 0.2

Values are expressed as the mean  $\pm$  SD unless indicated otherwise.



**Table 2 - Variables among dialysis shifts.**

	Morning shift N=39	Afternoon shift N=37	Evening shift N=20	p-value
Age, years	47 ± 14	48 ± 15	50 ± 5.3	0.71
Dialysis vintage, years	5.3 ± 3.1	4.8 ± 3.8	5.5 ± 4.8	0.75
Unemployed, n (%)	35 (89.7)	34 (91.9)	16 (80)	0.38
Hemoglobin, g/dl	9.7 ± 1.8	10.3 ± 1.6	10.1 ± 1.1	0.59
Phosphorus, mg/dl	5.7 ± 1.6	5.6 ± 1.5	5.6 ± 1.3	0.95
Albumin, mg/dl	3.8 ± 0.3	3.9 ± 0.5	3.9 ± 0.5	0.35
EDS, n (%)	18 (46.2)	20 (54.1)	9 (45)	0.73
BDI>16, n (%)	21 (53.8)	16 (43.2)	4 (20)	0.04*
Rural area, n (%)	24 (61.5)	7 (18.9)	0 (0)	0.0001**

Values are expressed as the mean ± SD unless otherwise indicated. EDS, excessive daytime sleepiness; BDI, Beck's Depression Inventory.

Chi-Square = 6.20; CI 0.06-0.75; *p* = 0.015). There was no difference between morning and afternoon dialysis shifts (Pearson Chi-Square = 0.85; CI 0.26-1.61; *p* = 0.37). The difference between afternoon and evening shifts was marginally significant (Pearson Chi-Square = 3.07; CI 0.09-1.17; *p* = 0.09).

Using the logistic regression model, elderly patients had a higher risk of depression, as shown in Table 3. Lower levels of hemoglobin and phosphorus were significantly associated with depression symptoms. Depressive patients had a hospitalization risk that was 4.5 times higher than that of nondepressive patients (IC 1.48-14.01; *p* < 0.008). Other variables used in the logistic regression (gender, dialysis vintage, unemployment, and address in a rural area) were not associated with depression. Only 19 (19.8%) patients were being administered the appropriate drug treatment for depression.

## DISCUSSION

Based on our data, we have shown that the prevalence of depression symptoms was 42.7%. We found that depression was associated with dialysis during the morning shift, older age, lower hemoglobin and phosphate, and a high risk of hospitalization. The significance of the observed high frequency of depression becomes more evident if we compare it with the prevalence of 5% in the general adult population (16).

In a recent analysis, it was demonstrated that CKD patients on dialysis had a higher risk of depression than predialysis patients, with a frequency of depressive symptoms of 34.5%

for the dialysis group *vs.* 13.3% for the predialysis group (17). Previous studies have demonstrated a high variability (from 20 to 65%) in the prevalence of depression in dialysis patients (1,4,6,17,18). This disparity could be the result of different diagnostic tools or a distinct BDI cut-off. The BDI is one of the most widely used tests for assessing the severity of depression. In the general population, the diagnosis of depression is based on receiving 10 points on the BDI. In patients with CKD, due to the presence of symptoms that can mimic the clinical presentation of depression (fatigue, anorexia, sleep disorders), the cut-off is higher; patients who score 16 or more points are considered to be depressed, with a sensitivity and specificity of 92 and 80%, respectively (5). In our study, we adopted the criteria mentioned above; hence, our prevalence was similar to the previous analysis with the same methodology (17,19). Recently, Lossman et al. compared BDI and the Hospital Anxiety and Depression Scale (HADS) in patients with CKD and depressive symptoms diagnosed by the Mini International Neuropsychiatric Interview (MINI) (20). Both the HADS and BDI were considered valid screening instruments for the diagnosis of depression in dialysis patients, with no significant difference between the scales. Therefore, in the last several years, BDI has been utilized by several authors for the measurement of depressive symptoms in CKD patients (21-23).

Consistent with previous findings, depressed patients had lower levels of hemoglobin (23,24). Due to the similarity between anemia and depressive symptoms, this is likely to be only a random association.

In our study, we found a strong correlation between low levels of phosphorus and depression. In fact, low phosphorus

**Table 3 - Independent risk factors for depression (logistic regression).**

	Depressed (n = 41)	Non-depressed (n = 55)	RR (IC)*	p-value
Age, years	50.5 ± 14	46.3 ± 13.4	1.05 (1.00-1.10)	0.03
Gender				
Male, n (%)	19 (34.5)	36 (65.5)	0.41 (0.13-1.30)	0.13
Female, n (%)	22 (53.7)	19 (46.3)		
Dialysis vintage, years	5.0 ± 3.7	5.3 ± 3.7	1.00 (0.99-1.01)	0.38
Unemployment, n (%)	38 (92)	43 (78)	0.42 (0.07-2.46)	0.33
Dialysis shift				
Morning, n (%)	21 (21.9)	18 (18.8)	7.9 (1.66-37.59)	0.009
Afternoon, n (%)	16 (16.7)	21 (21.9)	4.07 (0.90-18.41)	0.068
Evening, n (%)	4 (4.2)	16 (16.7)	§	§
Hospitalizations, n (%)	28 (68.3)	25 (45.5)	4.55 (1.48-14.01)	0.008
Rural area, n (%)	15 (36.6)	16 (29.2)	2.0 (0.53-7.51)	0.30
Hemoglobin, g/dl	9.4 ± 1.4	10.3 ± 1.6	0.60 (0.40-0.88)	0.010
Phosphorus, mg/dl	5.2 ± 1.3	6.1 ± 1.6	0.50 (0.29-0.85)	0.011

Values are expressed as the mean ± SD unless otherwise indicated. \* Relative risk (95% confidence interval). § Used as a reference on regression.



was an independent factor associated with depression. Moreover, depressive patients also presented a tendency to have lower albumin levels, which was associated with an increased risk of depression. These findings suggest that, at least in the present study, low levels of phosphorus might be the result of the poor nutritional status of depressed patients, as previously demonstrated by others (25,26). However, it must be stressed that this relationship was not clarified in the present study because an additional assessment of nutritional status was not performed.

The association between depression and dialysis shift has not been fully explored in CKD patients. Recently, it has been determined that patients in the morning dialysis shift present a higher incidence of depressive symptoms (11). In the present study, we observed that the risk of depression was strikingly increased in patients who attended the morning dialysis shift compared with those who attended the evening shift. This noticeable advantage of the evening shift has already been demonstrated for EDS and mortality (9,10). Taken together, our findings are similar and show a lower risk of depression among individuals attending the evening shift; notably, there was no difference in age, time on dialysis, or employment status among the three dialysis shifts. It must be noted that in our dialysis unit, patients who received treatment during the morning shift needed to wake up rather early because most of them lived far from the hospital (rural area); thus, it took them a long time to arrive at the dialysis center. Furthermore, if these patients waited too long for their dialysis session, they would not arrive at their houses until the end of the day. In contrast, most of the patients attending the evening shift lived nearby and usually did not spend much time traveling home from the dialysis clinic. Based on this information, it is tempting to speculate that sleep deprivation may influence the higher incidence of depression observed in those attending the morning shift. However, we found no differences in EDS between dialysis shifts. It is noteworthy that the subjective sleep measurement using the Epworth Scale did not rule out the presence of sleep disturbances (27). Relatedly, Unruh et al. demonstrated that the polysomnography sleep time did not correlate with the self-reported sleep time in dialysis patients (28). This result can explain the lack of association between sleepiness assessed by the Epworth Scale and the morning shift in our data.

It can be argued that living in a rural area, rather than the morning shift itself, could be associated with depression. However, in multiple regression analysis, rural area was not an independent risk factor for depression. Moreover, the influence of the distance to the dialysis center on variables such as quality of life and depression has been recently studied, and distance was not found to have an effect (29).

Despite the high prevalence of depression observed in our study, less than 20% of depressive patients were receiving appropriate treatment with antidepressants or alternative therapies, and most of them were not undergoing periodic psychiatric monitoring or psychotherapy. Alternative treatments, such as cognitive-behavioral therapy and exercise programs, have recently been demonstrated to have a positive impact on the management of depression (30,31); however, these treatments were not prescribed. Only a minority of CKD patients with depression are appropriately treated, especially those who require pharmacologic therapy (32,33). The main reason for this lack of treatment may be the absence of controlled trials studying the safety of

antidepressants in this particular population (32,34). However, serotonin selective reuptake inhibitors have been used in ESRD patients without any adverse effects requiring cessation (35).

This study has several strengths. First, to our knowledge, this is the first study assessing the influence of dialysis shift on depression as the main objective. Second, we used a well-validated tool—the BDI—to assess the depression symptoms. Third, all patients were examined by the same observer, diminishing the bias in collecting data. This study also has several limitations. The design of the study did not allow us to make conclusions based on follow-up or cause-effect. We could not clarify the association between low phosphorus and depression, and we were only able to make an assumption that depression is influenced by nutritional parameters. The patients were not examined by a psychiatrist to confirm the clinical diagnosis of depression. Finally, despite making adjustments to account for differences among the three dialysis shifts with respect to the address of the patients (rural or urban area), we could not guarantee that the beta error was completely eliminated.

In summary, depression is highly prevalent and most likely misdiagnosed among many CKD patients requiring dialysis. Despite the high prevalence rates, only a few patients were being properly treated for depression. The hospitalization risk in CKD patients increases markedly with the presence of depression. The most important factors associated with depression were dialysis shift and lower levels of phosphorus and hemoglobin. The association between depression and dialysis in the morning shift highlights the need for further studies to clarify this relationship. Sleep deprivation is thus far the most plausible explanation for our findings.

## ■ AUTHOR CONTRIBUTIONS

Teles F conceived the study, performed the data analysis, and participated in the manuscript writing. Azevedo V performed all of the data collection. Elias RM participated in the manuscript writing and review. Miranda CT and Miranda MP participated in the manuscript writing and statistical analysis. Teixeira MC participated in the manuscript writing and review. All authors read and approved the final manuscript.

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