Depression and Quality of Sleep in Maintenance Hemodialysis Patients

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SUMMARY

Introduction Sleep disorders and psychological disturbances are common in end-stage renal disease (ESRD) patients. However, despite their frequency and importance, such conditions often go unnoticed, since all patients do not clearly manifest fully expressed symptoms.

Objective This study aimed to determine the prevalence of depression and poor sleep quality and to examine the association between these disorders and demographic, clinical and treatment-related characteristics of ESRD patients on hemodialysis (HD).

Methods The study included 222 patients (132 men and 90 women), mean age 57.3±11.9 years, from 3 HD centers in Central Serbia, which provided us with biochemical parameters and demographic data. Sleep quality and depression were assessed using the Pittsburgh Sleep Quality Index (PSQI) and Beck Depression Inventory (BDI), respectively.

Results The average BDI was 16.1±11.3. Depressed patients were significantly older (p=0.041), had a significantly lower dialysis adequacy (p=0.027) and a significantly worse quality of sleep (p<0.001), while they did not show significant difference as regarding sex, employment, marital status, comorbidities, dialysis type, dialysis vintage, shift and laboratory parameters. The average PSQI was 7.8±4.5 and 64.2% of patients were poor sleepers. Poor sleepers were significantly older (p=0.002), they were more often females (p=0.027) and had a significantly higher BDI (p<0.001), while other investigated variables were not correlated with sleep quality. A statistically significant positive correlation was found between BDI and PSQI (r=0.604; p<0.001).

Conclusion Depression and poor sleep quality are frequent and interrelated among HD patients.

Keywords: depression; quality of sleep; dialysis; hemodialysis

INTRODUCTION

Patients on hemodialysis (HD) are thought to be highly susceptible to emotional problems because of the chronic stress related to disease burden, dietary restrictions, functional limitations, associated chronic illnesses, adverse effects of medications, changes in self-perception and fear of death.

Depression is generally accepted to be the commonest psychological problem encountered in patients with end-stage renal disease (ESRD) [1]. Among HD patients it is associated with lower quality of life, lower adherence to treatment regimens, more co-morbid conditions, more functional impairments and higher mortality rate [2, 3]. It possibly affects medical outcomes in these patients through modification of immunologic and stress responses, impact on nutritional status, and/or reduction of compliance with prescribed dialysis and medical regimens [4]. Although prevalent, depression is still often unrecognized since there is a strong overlap between uremic and depressive symptoms.

Sleep is important for overall physical and mental well-being. Manifestations of sleep disturbances can include irregularity in sleeping habits, difficulty falling asleep, early morning awakening and frequent awakening at night, sleep apnea, periodic limb movement during sleep and restless legs syndrome. The etiology of sleep disorders in dialysis patients is not completely understood, but it is known to be multi-factorial. Duration of dialysis therapy, high levels of urea and/or creatinine, pain, disability, malnutrition, muscle cramps, peripheral neuropathy and somatic complaints such as pruritus and bone pain, all common in ESRD patients, were found to contribute to the development of sleep disturbances [5]. The prevalence of sleep problems, on the other hand, is associated with impaired quality of life and higher mortality in patients with ESRD [6].

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Despite their frequency and importance, depressive and sleep disorders often go unnoticed, since not all patients clearly manifest the symptoms. Particularly in ESRD patients' the symptoms of depression may be similar to those that occur with kidney failure or uremia per se, therefore the diagnosis and treatment of depression is often delayed because the symptoms are disguised by/or attributed to uremia. Some studies suggest that depressive disorder and poor sleep quality are independent predictors of health-related quality of life, morbidity and mortality [3, 7, 8]. Still, the complex nature of the individual relationships involving poor sleep quality and depression with quality of life, morbidity and mortality of HD patients is yet to be thoroughly investigated.

OBJECTIVE

In this study we sought to determine the prevalence of depression and poor sleep quality and to examine the association between these disorders and demographic, clinical and treatment-related characteristics of ESRD patients on HD.

METHODS

Patients from 3 dialysis centers in Central Serbia (Novi Pazar, Kruševac and Smederevska Palanka), undergoing HD for at least 3 months, in stable condition and with grossly normal cognition, were invited to participate in this cross-sectional study. A total of 222 patients gave their informed consent and filled in standardized questionnaires (see below). We also recorded patients' demographic data and biochemical parameters within one month of their interview. The study protocol was reviewed and approved by the Ethical Committee, School of Medicine, University of Belgrade.

The patients were administered two questionnaires: Beck Depression Inventory (BDI), second version, for the level of depression [9] and Pittsburgh Sleep Quality Index (PSQI) to assess the quality of sleep [10].

The BDI is the most widely used tool for self-assessment of the level of depression for the purposes of clinical research. This questionnaire consists of 21 questions, each of which features 4 response options for the previous 2 weeks. A higher score for this questionnaire indicates a greater level of depression. Patients who had a BDI score ≥14 were considered to have depressive symptoms [11]. The second version of BDI used in this research allows reliable testing of patients over 65 years of age. The BDI has been used in several studies of patients with ESRD and has been shown to correlate highly with diagnostic criteria of depression, quality of life, functional status, severity of illness and mortality over time [12]. It had been previously validated in the population of HD patients in Serbia [11].

PSQI assesses the quality of sleep during the previous 1-month period and comprised 19 self-rated questions that yielded information relating to 7 specific patient components, such as subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleep-inducing medication, and level of daytime dysfunction. Each component was scored according to a scale from 0-3, and the overall questionnaire yielded a global PSQI score between 0-21, where a higher final score indicated a lower quality of sleep.

The original English versions of these two questionnaires were translated to Serbian by a licensed translator for the purpose of this investigation.

Venous blood samples for laboratory analyses were drawn before and immediately after the first dialysis session of the week. Hemoglobin (HGB) was determined with the cyanmethemoglobin method (reference range for HD patients 110-112 g/dl) [13] on the Cell Dyn 1700 counter. Hematocrit (HCT) was calculated from the equation HCT = (MCV × erythrocyte count)/10. Serum iron (Fe^{2+}) and total iron binding capacity (TIBC) were determined with an Opton spectrophotometer. Transferrin saturation index was calculated from the equation TSAT = (Fe^{2+}/TIBC) ×100% (TSAT – transferin saturation; TIBC – total iron-binding capacity) (normal range 20-40%) [13]. Serum ferritin was determined by immunochemistry MEIA technique, on (reference range 400–600 ng/mL*)* [13]. Serum urea was measured by urease glutamate dehydrogenase method. The Alcyon machine (Abbot) was used to measure serum calcium by photometry (reference range 2.3-2.7 mmol/L), serum phosphates by photometric UV method (normal range 0.8-1.5 mmol/L) and serum albumin by spectrophotometry staining with bromcresol green (lower threshold for HD patients is 40 g/l). Intact parathyroid hormone (iPTH) was determined on autogenous counter, by immunoradiometric assay ELSA-PTH (CIS, France), the recommended range for HD patients is 150-300 pg/mL [13]. Eventual laboratory errors were minimized by an internal control system. Dialysis dose was assessed based on a single pool Kt/V, calculated by using the Daugirdas's formula [14].

All values recorded were presented as mean ± standard deviation. The parameters of interest were analyzed using unpaired Students t-test, Mann-Whitney test, chi-square test, ANOVA, Kruskal-Wallis test. The Pearson correlation coefficient was used to examine association between BDI and PSQI. All statistical calculations were performed with the Statistical Package for Social Sciences (SPSS version 19.0; SPSS Inc., Chicago, Illinois, USA) for Windows operating system (Microsoft Corp., Redmond, Washington, USA). A p value less than 0.05 was considered significant.

RESULTS

Demographic and dialysis-related characteristics of the study population are presented in Table 1. Men comprised 59.5% of the study population. The mean age was 57.3±11.9 years. Most patients (72.1%) were married, and only 4 (1.8%) were actively employed. HD was performed on a thrice weekly basis using machinery with controlled ultrafiltration, with bicarbonate based dialysate and

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polysulfone high and low flux dialysers. One third of patients (69; 31.1%) were on low-flux biacarbonate dialysis, 114 (51.3%) on high-flux bicarbonate dialysis and 39 (17.6%) were on hemodialfiltration (HDF). The average dialysis vintage was 61.4±60.3 months (range 3–324 months). Exactly 50% of patients were dialyzed in the morning shift. Twenty-eight patients (12.6%) had diabetes, 13 (5.9%) were hepatitis C positive and 9 (4.1%) were hepatitis B positive.

Depression

Signs of depression were found in 109 (49.1%) patients. Among them 41 (18.4% of all the patients) had mild depression (BDI=14–19), 33 (14.9%) had moderate depression (BDI=20–28) and 35 (15.8%) had severe depression (BDI≥29). The average BDI was 16.1±11.3 (range 0–52). Depressed patients were significantly older (p=0.041), while sex, employment, marital status and comorbidities (diabetes and hepatitis) were not significantly correlated with depression (Table 2). Dialysis type, dialysis vintage and shift were not significantly related to the presence of depression, but depressed patients had significantly lower dialysis adequacy (p=0.027). The depressed patients had significantly worse quality of sleep than patients without signs of depression (p<0.001).

Serum hemoglobin, calcium, phosphorus, iPTH and albumin were almost identical in depressed and non-depressed patients. Serum ferritin was higher in depressed patients, while TSAT was higher in non-depressed ones. Results of blood analyses did not significantly correlate with presence of depression (Table 3).

Quality of Sleep

The PSQI ranged from 0-19 (average 7.8±4.5), and 142 patients (64.2%) were poor sleepers. The average sleep latency, representing the length of time that it takes to accomplish the transition from full wakefulness to sleep was 36.86 ± 35.90 minutes (recommended <20 minutes). The average sleep efficiency, representing the ratio of time spent asleep (total sleep time) to the amount of time spent in bed, was 81.73±18.00% (reference range 80-95%). The patients slept 6.87±1.86 hours/night on average (recommended sleep time ≥7 hours). Poor sleepers were significantly older (p=0.002) and they were more often females (p=0.027). Compared with good sleepers, poor sleepers had a significantly higher BDI (p<0.001). Marital status, employment, comorbidities (diabetes and hepatitis), type of dialysis, dialysis vintage, shift and adequacy were not significantly correlated with sleep quality (Table 4).

Poor sleepers had higher hemoglobin, calcium and iPTH than good sleepers, and lower ferritin and TSAT, but the differences were not statistically significant (Table 5).

A statistically significant positive correlation was found between BDI and PSQI (r=0.604; p<0.00; Graph 1).

Table 1. Demographic and dialysis-related characteristics of the study population at the beginning of the investigation

Variables	Values
Age (years)	57.3±11.9
Male/Female	132/90
Married/Not married	160/62
Employed/Unemployed	4/218
Hemoglobin (g/l)	102.6±16.9
Calcium (mmol/l)	2.3±0.2
Phosphorus (mmol/l)	1.6±0.4
iPTH (pg/ml)	225.7±334.6
Ferritin (ng/ml)	309.2±31.8
Albumin (g/l)	35.3±4.9
Kt/V	1.2±0.3

Values are expressed as mean value ± standard deviation, and number of patients.

Table 2. Comparison of demographic data, comorbidity, dialysis-related characteristics and quality of sleep in patients with and without depression

Variables		Patients with depression (BDI≥14)	Patients without depression (BDI<14)	p
Age (years)		59.0±11.0	55.7±12.6	0.041
Sex	Male	63 (57.8%)	69 (61.1%)	0.620
	Female	46 (42.2%)	44 (38.9%)	
Marrital status	Married	82 (75.2%)	78 (69.0%)	0.607
	Unmarried	13 (11.9%)	18 (15.9%)	
	Divorced	3 (2.8%)	6 (5.3%)	
	Widowed	11 (10.1%)	11 (9.7%)	
Employment	Employed	107 (98.2%)	111 (98.2%)	1.000
	Unemployed	2 (1.8%)	2 (1.8%)	
Diabetes	Yes	16 (14.7%)	12 (10.6%)	0.362
	No	93 (85.3%)	101 (89.4%)	
Hepatitis C	Yes	8 (7.3%)	5 (4.4%)	0.355
	No	101 (92.7%)	108 (95.6%)	
Hepatitis B	Yes	4 (3.7%)	5 (4.4%)	1.000
	No	105 (96.3%)	108 (95.6%)	
Type of dialysis	Low flux	44 (40.4%)	40 (35.4%)	0.670
	High flux	52 (47.7%)	56 (49.6%)	
	Hemodiaflitration	13 (11.9%)	17 (15.0%)	
Dialysis vintage (months)		61.3±55.8	61.5±55.8	0.395
Shift	Morning	52 (47.7%)	60 (53.1%)	0.422
	Afternoon	57 (52.3%)	53 (46.9%)	
Adequacy (Kt/V)		1.1±0.2	1.2±0.4	0.027
PSQI		10.1±4.6	5.7±3.3	<0.001

BDI – Beck Depression Inventory; PSQI – Pittsburgh Sleep Quality Index
Values are expressed as mean value ± standard deviation, and number of patients (%).

Table 3. Comparison of laboratory data between the patients with and without depression (mean value ± SD)

Laboratory data	Patients with depression (BDI≥14)	Patients without depression (BDI<14)	p
Hemoglobin (g/l)	102.4±17.8	102.8±16.1	0.884
Calcium (mmol/l)	2.3±0.2	2.3±0.2	0.619
Phosphorus (mmol/l)	1.60±0.4	1.63±0.4	0.617
iPTH (pg/ml)	211.6±320.6	241.5±350.8	0.556
Ferritin (ng/ml)	283.8±249.5	334.6±373.4	0.241
TSAT (%)	28.2±28.8	25.8±14.6	0.430
Albumins (g/l)	34.7±5.0	34.8±4.8	0.080

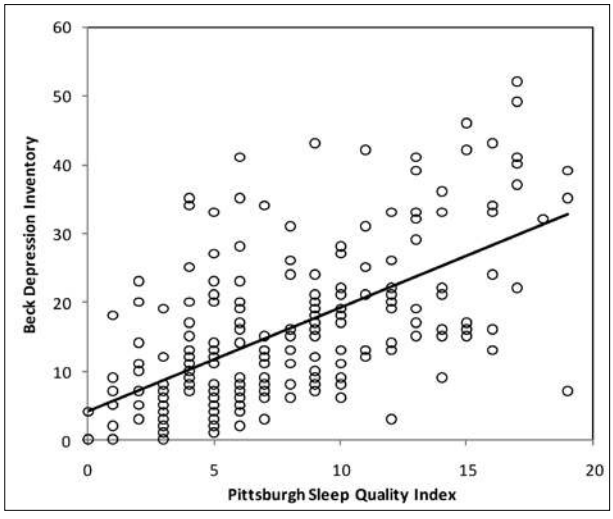
Table 4. Comparison of demographic data, comorbidity, dialysis-related characteristics and depression status in good and poor sleepers

Variables		Good sleepers (PSQI≤5)	Poor sleepers (PSQI>5)	p
Age (years)		53.7±13.8	59.3±10.1	0.002
Sex	Male	54 (69.2%)	76 (53.9%)	0.027
	Female	24 (30.8%)	65 (46.1%)	
Marrital status	Married	50 (64.1%)	109 (77.3%)	0.071
	Unmarried	17 (21.8%)	13 (9.2%)	
	Divorced	3 (3.8%)	5 (3.5%)	
	Widowed	8 (10.3%)	14 (9.9%)	
Employment	Employed	75 (96.2%)	140 (99.3%)	0.130
	Unemployed	3 (3.8%)	1 (0.7%)	
Diabetes	Yes	7 (9.0%)	21 (14.9%)	0.209
	No	71 (91.0%)	120 (85.1%)	
Hepatitis C	Yes	5 (6.4%)	8 (5.7%)	1.000
	No	73 (93.6%)	133 (94.3%)	
Hepatitis B	Yes	4 (5.1%)	4 (2.8%)	0.460
	No	74 (94.9%)	137 (97.2%)	
Type of dialysis	Low flux	27 (34.6%)	55 (39.0%)	0.386
	High flux	37 (47.7%)	70 (49.6%)	
	Hemodiaflitration	14 (17.9%)	16 (11.3%)	
Dialysis vintage (months)		69.8±69.9	56.8±54.5	0.408
Shift	Morning	52 (47.7%)	60 (53.1%)	0.422
	Afternoon	57 (52.3%)	53 (46.9%)	
Adequacy (Kt/V)		1.2±0.2	1.2±0.4	0.114
BDI		10.3±8.0	19.2±11.6	<0.001

Values are expressed as mean value ± standard deviation, and number of patients (%).

Table 5. Comparison of laboratory data in good and poor sleepers (mean value ± SD)

Laboratory data	Good sleepers (PSQI≤5)	Poor sleepers (PSQI>5)	p
Hemoglobin (g/l)	102.2±17.5	103.1±16.7	0.725
Calcium (mmol/l)	2.2±0.2	2.3±0.2	0.117
Phosphorus (mmol/l)	1.6±0.4	1.6±0.4	0.589
iPTH (pg/ml)	168.8±173.6	257.6±392.7	0.887
Ferritin (ng/ml)	322.4±335.2	302.1±312.4	0.661
TSAT (%)	29.4±25.8	25.6±21.0	0.250
Albumins (g/l)	35.5±4.8	35.2±5.0	0.760



Graph 1. Correlation between Beck Depression Inventory and Pittsburgh Sleep Quality Index (r=0.604; p<0.001)

DISCUSSION

Dialysis patients face the burdens of long-term illness, numerous treatment or disease-related stressors, the challenge of life-long behavior change, emotional distress and loss of personal control [2]. Depression is considered the most frequent psychological issue among HD patients. Its prevalence varies widely across studies, which may, in part, be a reflection of different diagnostic tools used [15]. Most recent studies, however, used the BDI to assess the prevalence of depressive symptoms in HD population [3, 11, 16, 17, 18]. In this study we used the second version of BDI, which allows reliable testing of patients over 65 years. The cut-off value of 14 points defining the presence of depression was adopted based on previous studies which used the same version of BDI [11, 17, 19]. The prevalence of depression of 49.1% found in our study was within the 26% to 72.38% range of prevalence reported by other authors, even though most previous studies included patients under 65 years and a rather smaller number of patients, usually less than 100 [3, 11, 16-20]. Similarly, the prevalence of moderate to severe depression in our study is comparable with the 13.3% to 48.9% prevalence range in HD patients in previous studies [11, 16, 21]. The average BDI of 16.1 in our HD population is also within the range detected in previous studies [3, 16, 17, 19].

In general population depression is usually associated with older age, as was noted in our study population [3]. However, other studies on HD patients failed to depict such correlation, possibly because they included mostly younger population, as previously mentioned [2, 3, 11, 16-20]. Similar to our results, previous studies did not report significant correlation between dialysis adequacy and depression [3, 22]. On the other hand, dialysis type and vintage were not significantly associated with depression in our study population, while other investigations reported conflicting results on this subject [2, 16, 17]. Lower BDI and lower prevalence of depression were associated with HDF treatment in previous studies [23]. Lack of significant difference in our study group might be due to the fact that a rather small number of patients were receiving HDF, as determined by the National Health Fund standards. Some prospective studies suggested that higher prevalence of depression is present in HD patients following the start of dialysis, but the cross-sectional design of our study and the inclusion criterion of at least 3 months dialysis vintage preclude such conclusion in our study [24]. It is possible that patients eventually accept and adapt to the treatment regime, thus lowering the prominence of depressive symptoms.

In some previous studies depression in HD patients was associated with low levels of hemoglobin and albumin [25, 26]. Lack of correlation between laboratory parameters of anemia and depression in our study may be due to better therapeutic correction of anemia in our study group.

Sleep complaints and their etiology in HD patients have received increasing attention over the last years. Several studies suggest a potential link between sleep deprivation, poor sleep quality and sleep disorders, and increased mor-

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tality [6]. Consistent with the results of several previous studies, our survey confirmed high prevalence of sleep disorders among maintenance HD patients [6, 16, 27, 28]. A wide variety of potential factors probably contribute to high prevalence of sleep problems in HD patients, including biological, lifestyle and/or psychological factors. There is a discrepancy among studies examining sleep in the elderly indicating a controversy as to the nature of sleep problems associated with aging even in the healthy population. Considerable evidence demonstrates that age is associated with significant changes in numerous objective sleep parameters, as well as subjective sleep quality determined by the PSQI [29, 30]. Furthermore, some authors found that women reported more insomnia across all age groups [31]. Finally, there are conflicting results in the literature regarding the role of gender and age in sleep diseases in ESRD patients. Significant correlation between older age and female gender with poorer sleep quality in our study population is consistent with data published by several other authors [27, 32].

Some previous studies reported worse sleep quality to be associated with longer time on dialysis, morning shift and lower Kt/V, but we did not find significant correlations between the type of dialysis, dialysis vintage, dialysis adequacy and shift, and sleep quality in our study population [27, 28]. Time on dialysis may be associated with progressive appearance of symptoms and concurrent diseases commonly associated with chronic HD treatment, thus indirectly influencing the quality of sleep. However, in our study population such correlation was not observed. Lack of association between dialyzing in the morning shift and sleep problems in our study population may be due to the fact that we strive to and in most cases achieve to fulfill our patients wishes on the shift in which they dialyze, thus adjusting dialysis shift with their individual biorhythm.

Sabbatini et al. [28] demonstrated a relationship between high iPTH and sleep disorders, which might be related to pruritus and bone pain. Furthermore, previous studies found that poor sleepers had lower hemoglobin [33]. We did not find such correlations between sleep quality and hemoglobin, PTH, calcium, phosphorus and iron stores levels, identically to other authors' findings [16]. This is probably due to the fact that the patients in our study population had iPTH levels within the recommended range and almost identical hemoglobin levels in good and poor sleepers groups.

Consistent to findings of other authors, poor sleep quality and depression were found to be significantly correlated in our study population [16, 33, 34].

There are clearly some limitations to our survey. Although we took into consideration several psychosocial dimensions, including marital status and employment, we omitted some psychosocial factors, such as participants' economic status, level of education, levels of religious and spiritual activity, family support and some other emotional stresses such as the level of anxiety, worry and fear. Furthermore, although the PSQI contains some questions with respect to restless legs syndrome and sleep apnea, those factors are not scored and are not informative enough for a definitive diagnosis. We did not perform other objective sleep measurements such as polysomnography to prove our observations, but the correlations between the PSQI and polysomnography have been reported to be significant in certain domains [35]. The severity and co-morbidity in HD patients may be an independent risk factor for depression and sleep disorders. In this study we only assessed the relationship between viral hepatitis and diabetes with depression and sleep quality. A more thorough investigation of correlation between dialysis related symptom burden, depression and quality of sleep in our study population is currently being conducted.

CONCLUSION

Maintenance HD is associated with a high prevalence of depression and sleep disturbance. Understanding the degree to which depression and sleep disturbance affects this large and growing population may help facilitate the implementation of symptom-alleviating therapies to improve psychological and overall well-being, quality of life, and consequently, reduce morbidity and mortality risk in this population, and their treatment costs. Our results, thus, advocate for incorporating a routine assessment and, if necessary, treatment of depression and sleep disorders into the standard care provided to HD patients.

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Депресија и квалитет сна код болесника на хемодијализи

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КРАТАК САДРЖАЈ

Увод Поремећаји спавања и психичког статуса се често јављају код болесника с терминалном инсуфицијенцијом бубрега. Упркос учесталости и значају, ова стања се ретко благовремено дијагностикују и лече, јер се симптоми не испољавају увек у пуном обиму.

Циљ рада Циљ истраживања био је да се код болесника на хемодијализи процени преваленција депресије и лошег квалитета спавања, као и повезаност између ових поремећаја и демографских, клиничких и одлика у вези с начином лечења.

Методе рада Истраживањем су обухваћена 222 болесника (132 мушкарца и 90 жена, старости од 57,3±11,9 година) из три центра за хемодијализу у централној Србији. Квалитет спавања је процењен Питсбуршким индексом квалитета спавања (*PSQI*), постојање депресије Бековим индексом депресије (*BDI*), а демографски и подаци о лабораторијским анализама узети су из историја болести.

Резултати Просечна вредност *BDI* била је 16,1±11,3. Болесници са депресијом су били статистички значајно старији (p=0,041), имали лошију адекватност дијализе (p=0,027) и лошији квалитет спавања (p<0.001), али нису се значајно разликовали по полу, радном и брачном статусу, постојању коморбидитета, врсти, смени и трајању дијализе, нити вредностима лабораторијских параметара у односу на болеснике без знакова депресије. Просечна вредност *PSQI* била је 7,8±4,5, а 64,2% болесника су имала лош квалитет спавања. Болесници с лошим квалитетом спавања су статистички значајно чешће били женског пола (p=0,027), старији (p=0,002) и са вишим вредностима *BDI* (p<0,001). Доказана је статистички значајна позитивна корелација између *BDI* и *PSQI* (r=0,604; p<0,001).

Закључак Депресија и лош квалитет спавања су чести и међусобно повезани код болесника на хемодијализи.

Кључне речи: депресија; квалитет спавања; дијализа; хемодијализа

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