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Original Article

Quality of sleep in kidney transplant recipients: Any relationship with quality of life?

Rukiye Ozer[1], Necmi Eren[2], Metin Ergul[2], Sibel Gokcay Bek[2], Erkan Dervisoglu[2]

[1]Department of Internal Medicine, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey
[2]Department of Nephrology, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey

Abstract

Aim: The aim of this study is to evaluate the relationship between quality of sleep (QoS) and demographic, clinical, and psychosocial factors in kidney transplant recipients.

Materials and Methods: We examined sixty-four kidney transplant recipients (26 female, 38 male). Clinical, demographic, and biochemical parameters were analyzed. The QoS was evaluated using Pittsburgh Sleep Quality Index (PSQI), health-related quality of life (HRQoL) with SF-36 Health Survey and depressive symptoms with Beck's Depression Inventory (BDI).

Results: A comparison of good and poor QoS (PSQI ≤ 5, PSQI > 5, respectively) groups showed a significant difference only in BDI scores ($p < 0.001$). There was no statistically significant difference regarding urea, creatinine, ferritin, albumin, and other laboratory parameters. Thirty-six of the 46 patients (80%) in the good QoS group were married, while 10 of 19 patients (52%) in the poor QoS group were single. Married individuals had significantly better QoS ($p=0.026$). A comparison of the domains of the HRQoL survey showed significantly better "physical function" in those with good QoS than those with poor QoS (51 ± 6 and 47 ± 8, respectively; $p < 0.017$).

Conclusion: Patients with poor QoS had worse HRQoL. Routine screening of depressive symptoms, which may be manageable is required for improving QoS and HRQoL in these patients.

Keywords: Depression; kidney transplantation; quality of life; quality of sleep

INTRODUCTION

Sleep disorders has been well established in Chronic Kidney Disease (CKD) patients (1). The prevalence of sleep disorders vary between 30% and 80% among CKD, dialysis, and kidney transplant patients (2). In DOPPS study, 49% of the 11,351 participants who have poor quality of sleep (QoS) had a 16% increased likelihood of death (3). In our recent study we have found that fifty-five of the 112 patients (49%) have a good QoS and also found an independent relationship between BDI scores and poor QoS in peritoneal dialysis patients (4).

Although some improvement in sleep-related problems may be observed following successful kidney transplantation, sleep disorders may persist (5). Anxiety, comorbid disorders, depression, immunosuppressive therapy, and stress are found to be responsible for the worse QoS in this group of patients (6). In general, QoS is believed to improve after kidney transplantation. Although better QoS was found among kidney transplant patients, the QoS was still lower in comparison with the normal population (6). It was found a positive relationship with QoS and health related quality of life (HRQoL) in kidney transplant and dialysis patients (7,8), and improvement of QoS has been found to positively impact the life quality (6,8). The objective of this study is to be evaluated QoS in renal transplant patients and to determine the factors affecting it.

MATERIALS and METHODS

We performed a cross-sectional study and examined eligible kidney transplant patients who underwent kidney transplantation at the Medical Faculty of Kocaeli University. Inclusion criteria were: age ≥ 18 years, stable graft function, three months or more post renal transplantation and having willingness for participation. Patients with active psychiatric disorders, drug or alcohol abuse, malignancy and active infection were excluded. Information on demographic characteristics (age, marital status etc.) and as well as on donor characteristics were obtained with face-to-face interviews with patients and were recorded in the sociodemographic information

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Corresponding Author: Necmi Eren, Department of Nephrology, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey
E-mail: necmieren.kou@gmail.com

form. The patients were evaluated with Pittsburg Sleep Quality Index (PSQI), Short Form (SF)-36 Health Survey and Beck's Depression Inventory (BDI). Also information collected on the time since transplantation, comorbid diseases (Hypertension (HT), Diabetes Mellitus (DM), cerebrovascular and ischemic heart disease (IHD)), etiology of the end-stage renal disease (ESRD), current immunosuppressive therapy. Also, C-reactive protein (CRP), ferritin, hemoglobin (Hb), urea, creatinine, eGFR (calculated with CKD-EPI equation), calcium, phosphorus, albumin (Alb), serum triglyceride (TG), total cholesterol, high density and low density lipoprotein cholesterol (HDL and LDL cholesterol, respectively) and body mass index (BMI) were checked at the last follow up. The study was evaluated and accepted by the Ethics Committee, Medical Faculty of Kocaeli University (date: 13 Oct 2015, No: KOÜ İAEK 2015/304).

Questionnaires

PSQI: QoS was evaluated using PSQI, that includes seven parts (scored from 0 to 3): (i) sleep duration (SD); (ii) sleep latency (SL); (iii) subjective sleep quality (SSQ); (iv) sleep disturbances (SD); (v) sleep efficiency (SE); (vi) daytime dysfunction; and (vii) use of hypnotic sedatives. The validation studies were conducted by Agargun et al. (9). Patinets with PSQI score of > 5 are accepted to have poor QoS (10).

BDI: Depressive symptoms were evaluated with BDI (21-section tool) designed to evaluate the characteristics symptoms of depression. Each section is scored in a 4-point Likert scale, where a score of 0 shows the absence of the problem, while a score of 3 reflects severe problem. Therefore the total score range is between 0 and 63. Hisli et al., performed the validation studies of BDI in Turkish populations (11). Patients with a score of ≥ 17 were classified as having depression.

HRQoL: The SF-36 form is non-disease specific questionnaires that measure the QoL. This is a self-evaluated tool with 36 items that evaluates eight sections (rated between 0 and 100: lowest to highest QoL): mental health (MH), vitality (V), social functioning (SF), bodily pain (BP), physical functions (PF), general health perceptions (GHP), limitation of role functions-physical, role limitations emotional. Koçyiğit et al., conducted the validation studies of SF-36 in Turkish populations (12).

Statistical Analysis

Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. Median value was used where normal distribution is absent. The significance of the difference between groups was evaluated using the t-test for variables with normal distribution, and Mann Whitney U test for variables without normal distribution. Chi-square test was used for the comparison of categorical variables. Multiple logistic regression analysis was performed to determine the independent predictors of the QoS. The relationship between PSQI and clinical, biochemical, and HRQoL measures was analyzed with Spearman's correlation test. A p value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 20 (SPSS, Inc., Chicago, IL, USA).

RESULTS

Sixty-four patients (26 female, 38 male; age: 40.8 ± 10.8 years), of whom 54 received living donor and 10 received kidney transplantation from deceased donor, were evaluated. The demographic, ESRD etiology, clinical and laboratory data of transplant patients are shown in Table 1. Overall, 45 patients (70%) had good QoS, and 19 (30%) had poor QoS.

Table 1. Demographic, Clinical and Laboratory Features of kidney transplant recipients

Variable	n=64
Age (year)	40.8±10.8
Gender (F/M)	26/38
Time since transplantation (month)	57.5±47.8
Donor (living/deceased)	54/10
BMI (kg/m^2)	25.5±4.1
Current immunosuppressive therapy (%)	
Tacrolimus + Mikofenolat Mofetil + Steroid	44 (69%)
Cyclosporine regimens	10 (15%)
Other regimens	10 (15%)
ESRD etiology (%)	
Hypertensive nephropathy	19 (29.7%)
Primary Glomerulonephritis	13 (20.3%)
PKD	1 (1.6%)
Nephrolithiasis	6 (9.4%)
VUR	4 (6.3%)
Unknown	17 (26.6%)
Comorbid conditions	
Ischemic heart disease	1 (1.6%)
Cerebrovascular disease	3 (4.7%)
Hypertension	33 (51.6%)
Diabetes Mellitus	9 (14.1%)
Laboratory Features	
Urea (mg/dl)	39.2±19.1
Creatinine (mg/dl)	1.3±0.8
Serum Albumin (g/dl)	4.3±0.4
eGFR (ml/dk/1,73 m^2)	64.5 (54-80.75)
Proteinuria (mg/gün)	542±938

BMI: body mass index; PKD: Polycystic Kidney Disease; VUR: Vesicoureteral reflux; eGFR: estimated Glomerular filtration rate

Table 2. Comparison of Laboratory and Demographic Features Between Good and Poor Sleepers

Variables	Good Sleepers PSQI≤5 (n=45)	Poor Sleepers PSQI>5 (n=19)	P value
PSQI score	2.7±1.3	7.3±1.9	**<0.001**
BDI score	4±3	10±8	**<0.009**
Age (years)	42.5±10.2	36.7±11.5	0.068
Time since transplantation (months)	45±33	19±30	0.547
Diabetes Mellitus, n (%)	6 (13)	3 (15)	0.796
Ischemic heart disease, n (%)	1 (2)	0 (0)	0.513
Hypertension, n (%)	24 (53)	9 (47.4)	0.663
Cerebrovascular disease, n (%)	3 (6)	0 (0)	0.249
Married patients, n (%)	36 (80)	10 (52)	**0.026**
BMI (kg/m^2)	26±4	19±3	0.115
Urea (mg/dl)	45±33	19±30	0.489
Creatinine (mg/dl)	1.4±1	1.1±0.5	0.308
CRP (mg/dl)	0.5±0.6	0.2±0.1	0.056
eGFR (ml/dk/1.73 m^2)	62±24	65±32	0.691
Albumin (g/dl)	4.3±0.4	4.3±0.3	0.785
Calcium (mg/dl)	10.3±0.7	9±0.6	0.338
Ferritin (ng/ml)	281±329	356±426	0.453
Total cholesterol (mg/dl)	191±53	192±55	0.916
Triglycerides (mg/dl)	174±83	150±59	0.253
LDL (mg/dl)	125±36	116±32	0.314
HDL (mg/dl)	49±16	50±15	0.828
Phosphorus (mg/dl)	4.4±7	3.2±0.5	0.439
ALP (U/L)	92±46	88±41	0.763
Hemoglobin (g/dl)	13.2±2	13.3±2	0.908

PSQI: Pittsburg Sleep Quality Index; BDI: Beck's Depression Inventory; BMI: Body mass index; CRP: C-reactive protein; eGFR: estimated Glomerular filtration rate; LDL: low density lipoprotein; HDL: high density lipoprotein; ALP: alkaline phosphatase

Table 3. Comparison of the Components of the Health Related Quality of Life Scale Between Good and Poor Sleepers

Variables	Good Sleepers PSQI≤5 (n=45)	Poor Sleepers PSQI>5 (n=19)	P value
Quality of life components			
Physical function	51±6	47±8	**0.017**
Physical Role Difficulty	52±8	49±11	0.216
Pain	55±9	52±8	0.237
General health	50±8	48±8	0.492
Vitality	54±8	49±11	0.094
Social function	46±10	43±11	0.192
Emotional Role Difficulty	49±10	44±12	0.059
Mental Health	46±9	46±8	0.840
BDI score	4±3	10±8	**<0.001**

BDI: Beck's Depression Inventory

PSQI score in patients with good or poor QoS was 2.7 ± 1.3 and 7.3 ± 1.9, respectively (p < 0.001). There were no significant differences between patients with or without good QoS in terms of comorbidities such as DM, HT, cerebrovascular disease and ischemic heart disease (p > 0.05). Additionally, no significant differences with regard to age, time since transplantation, BMI, urea, creatinine, eGFR, albumin, and Hb were found between those with good or poor QoS (p > 0.05) (Table 2).

A comparison of married or single patients showed that 36 of the 45 patients (80%) in the good QoS group were married, while 10 of the 19 patients (52%) with poor QoS were single.

Comparison of the sub-domains of the HRQoL questionnaire showed significantly lower PF among those with poor QoS (p=0.017), without any meaningful differences in other domains. BDI scores in patients with poor or good QoS were 10 ± 8 and 4 ± 3, respectively (p < 0.001) (Table 3).

Correlation analyses showed weak positive correlation between PSQI and BDI scores and weak negative correlation between PSQI and PF score (r=0.331, p=0.007 and r= - 0.264, p=0.035, respectively). In the multiple logistic regression analysis, only BDI scores emerged as an independent predictor of the poor QoS in transplant patients (Table 4).

Table 4. Multiple Logistic Regression Analysis. Results Regarding Poor Sleep Quality (PSQI> 5)

	Odds ratio	95% Reliability	β coefficient	p value
Gender	0.63	0.107-3.726	-0.462	0.61
Hemoglobin	1.203	0.739-1.958	0.185	0.458
Ferritin	0.999	0.997-1.002	-0.001	0.662
Calcium	0.557	0.178-1.746	-0.585	0.557
eGFR	1.022	0.988-1.056	0.021	0.209
Serum Albumin	1.4	0.2-9.787	0.336	0.735
Proteinuria	1.331	1-1.002	0.001	0.171
BMI	0.843	0.682-1.041	-0.171	0.113
Time since transplantation	0.996	0.978-1.015	-0.004	0.701
Donor	0.202	0.024-1.726	-1.598	0.144
BDI	1.306	1.087-1.586	0.267	**0.004**

eGFR: Estimated Glomerular filtration rate; BMI: Body mass index; BDI: Beck's Depression Inventory

DISCUSSION

In this cross-sectional observational study, the prevalence of poor QoS in a cohort of 64 kidney transplant patients was found to be 30%. Patients with poor or good QoS did not differ significantly in terms of age and gender; clinical parameters (BMI and time since transplantation); markers of nutritional status such as serum albumin, total cholesterol; as well as inflammatory parameters such as ferritin and CRP (Table 2). Married patients had significantly better QoS than unmarried participant. Also, those with poor QoS had significantly higher BDI and lower PF scores.

Previous studies showed an association between higher BMI and poor QoS and shorter sleep duration (13). However, in our study BMI was not correlated with global PSQI scores.

In healthy populations, sleep disorders are 1.5 to 2 times higher among female subjects, while this difference is somewhat attenuated in CKD patients (3,14,15). In a longitudinal study conducted by Brekke et al., they did not find a significant difference between female and male kidney transplant recipients in terms of QoS (16). Similarly no difference was found in QoS between female and male subjects in our study.

Sleep disorders are also more common in the elderly, partially thought to be related with increasing prevalence of comorbid conditions with ageing (17,18). However, in the current study, no significant age differences between poor and good sleep quality groups was found.

Comorbid conditions are known to adversely affect the sleep and life quality (19). In a previous study by Sayin et al. comparing kidney transplant recipients with subjects receiving other types of renal replacement treatments, transplant recipients were found to have lower incidence of comorbid conditions (19). In our study HT (52%) was the most common comorbid condition among our patients, followed by DM (14%), and ischemic heart disease (2%). Similar to the study by Mucsi et al., who could not find significantly difference between poor and good sleep quality groups with regard to comorbid disease (20), we also did not find such differences between the two groups.

As malnutrition marker, albumin is an important indicator of the QoL in ESRD patients. There is a well-known

relationship between malnutrition and worse HRQoL (21). In our study, however, poor and good sleep quality groups had similar serum albumin levels, in line with Mucsi et al.'s report. (20).

Until now, controversial results have been obtained in studies of CKD patients evaluating the relationship between QoS and inflammation (22-24). Despite some studies suggesting a possible association between inflammation and poor QoS, others have not confirmed these findings. One study in hemodialysis (HD) patients found higher hsCRP levels, in subjects with poor QoS (22). On the other side, in kidney transplant recipients with poor QoS, no differences in inflammatory markers were reported (25). Inflammatory markers such as CRP or ferritin were similar in our patients with poor or good QoS.

In one study involving HD patients, those with good or poor QoS had similar Hb levels. In that same study, a multivariate linear regression analysis identified BDI, dialysis duration, and Hb levels as predictors of PSQI score in subjects with poor QoS (15). Novak et al., however, reported no associations between anemia and QoS in kidney transplant recipients (6). Similarly, in our study we could not demonstrated significant differences in terms of Hb levels between poor and good QoS groups.

Impaired sleep is related with reduced HRQoL not only in the community but also in dialysis patients (26). Sleep is an important component of health and represents a fundamental aspect of both physical and psychological wellbeing. Previously, it has been well established that kidney transplantation may improve the QoL by alleviating some sleep related problems and chronic insomnia (5, 6, 27). Kidney transplantation cannot completely solve sleep problems in CKD patients (28). It has been previously shown that poor QoS is associated with lower educational level, younger age, and more severe depressive symptoms among kidney transplant recipients (29). From these reports, it appears that poor QoS may represent a constituent of depressive symptomatology (29).

In the study by Sabbatini et al. although kidney transplant recipients had better QoS than HD patients, they were still more likely to experience sleep disorders in comparison with individuals who had no chronic disorders (8). In that same study, sleep apnea and RLS persisted in 18% and 37% of the patients, respectively, despite normal kidney functions after kidney transplantation (8). Again, Kauchee et al. found that 62% of the patients who underwent kidney transplantation had poor QoS (30), as compared to 30% in our study.

Kidney transplant recipients are expected to have better QoL as compared to CKD or dialysis patients. In organ transplant patients, HRQoL is an important outcome that can be measured. A successful kidney transplantation should result in a better QoL. It has been proven that patients who underwent kidney transplantation experienced a significant improvement in their QoL as compared to pre-operative period (31,32). However, although restoration of normal kidney functions and health are anticipated outcomes after kidney transplantation, patients may experience a myriad of problems such as a continuous risk of rejection, adaptation to drug therapy with significant side effects, risk of infection, recurrent hospitalization, change in body appearance, and the need for regular monitoring. Mental and behavioral efforts to circumvent these difficulties may have a significant impact on QoS and QoL (33).

LIMITATIONS

There are some limitations in our study, firstly, the information on QoS was obtained through the use of individual questionnaires. Sleep disorders may be more accurately defined using polysomnographic tests. Secondly, anxiety was not investigated, and other psychiatric disorders were not ruled out. Also, comparisons were performed against historical controls and our study did not include a control group. Although BDI is a reliable tool to assess the depressive mood, it is not used for the diagnosis of major depressive disorder. Furthermore, inclusion of patients who underwent successful kidney transplantation only, may also be considered a limitation. The sleep and life quality results reported herein reflect only the study period, and does not allow assessment of changes occurring over time. Patients sleep and life quality were not measured before the transplantation, precluding identification of changes in HRQoL and QoS scores. Also, although patients seem to be properly matched with regard to important sociodemographic characteristics such as age and marital status, this study included only 64 participants, and therefore it may not reflect all transplant patients.

CONCLUSION

HRQoL and QoS are important indicators of treatment outcomes in kidney transplant recipients, in addition to being closely linked with not only with morbidity, but also with mortality. It is important to discover the aspects of life that are most intensely affected by kidney transplantation and to understand the best strategy to monitor HRQoL in each patient.

Previous studies examining the association between sleep disorder and QoL have shown that sleep disorders lead to a significant decline in QoL in almost all patients with chronic disorders. In our analysis, the most pronounced effects were observed on BDI scores with regard to QoS. Similarly, PF, a component of the QoL, has also been shown to be influenced by the sleep quality.

In conclusion, more common use of patient-rated measurement tools for investigational purposes as well as an increased awareness regarding sleep and life quality will increase the responsibility of the health-care providers, identify interventions to improve QoS and QoL, and consequently will improve patient satisfaction and life quality.

Conflict of interest: The authors declare that they have no competing interest.

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Ethical approval: The study protocol was approved by the Ethics Committee, Medical Faculty of Kocaeli University (date: 13 Oct 2015, No: KOÜ İAEK 2015/304).

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