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Original Article

Assessment of Sleep disturbance in Renal Transplant Recipients and Associated Risk Factors

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ABSTRACT. Sleep disturbances are highly prevalent in ESRD patients. In this study we sought to evaluate the associations of poor sleep with several genetic, laboratory, treatment and demographic factors in renal allograft recipients using a validated sleep quality questionnaire. A cross-sectional study was conducted on renal transplant patients over 18 years of age with stable current stable graft function. All patients completed PSQI and Ifudu questionnaires for assessment of sleep quality and morbidity measures. Kolmogorov-Smirnov test was used for evaluation of distributions besides Student's t-test, and Fisher's exact test for analyses. Mean total PSQI score for the whole patients was 6.5 ± 2.6. Overall 26 (67%) of patients were diagnosed as "poor sleepers" (PSQI total score ≥ 5) and the reminding 13 (33%) were "good sleepers". Compared to "good sleepers", "poor sleepers" significantly had higher serum phosphate levels and ESRD duration (P= 0.05). Hematological disorders were more seen in "poor sleepers" and musculoskeletal disorders had a significant worsening impact on PSQI total score (β= 0.28, P= 0.05). In conclusion our study showed that sleep disturbance is common in renal transplant patients is surprisingly common, and ESRD duration prior to transplant was significantly associate with sleep quality. Future studies with larger sample sizes are necessary for confirming our results.

Introduction

Disorders of sleeping and wakefulness are among the most prevalent complaints in patients with ESRD.[1,2]

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Numerous studies have reported that sleep disturbances are associated with development of several mental and physical health dilemmas both in the general population and among ESRD patients.[3,4]

Despite large number of surveys studying sleep disturbances in patients undergoing chronic dialysis; few studies addressed the kidney transplant recipients. In this study we aimed to evaluate the associations of sleep disturbance in renal allograft recipients using a validated

Table 1. Demographic characteristics of the study patients

Categorical variables	N (%)	Continuous variables	Mean ± SD
Male gender	28 (72)	Age (yr)	41 ± 13
Married	30 (77)	Age at transplantation (yr)	33 ± 15
Educational level		Overall ESRD duration (mo)	38 ± 50
College	9 (23)	Early post transplant laboratory measures	
Diploma	14 (36)	FBS (mg/dL)	133 ± 71
High school	8 (21)	BUN (mg/dL)	36 ± 22
Primary	6 (15)	Creatinine at discharge (mg/dL)	1.4 ± 0.9
Illiterate	2 (5)	Triglyceride (mg/dL)	149 ±98
Living in cities	34 (87)	Na (meq/L)	128 ± 37
Economic condition		K (meq/L)	4.8 ± 0.8
Rich	5 (13)	Ca (mg/dL)	8.7 ± 1.1
Intermediate	2 (5)	Phosphate (mg/dL)	5.5 ± 2.6
Low	16 (41)	Hgb (g/dL)	9.2 ± 1.5
Poor	16 (41)	Cyclosporine trough level (µg/L)	242 ± 104
Cause of ESRD		Cyclosporine morning dosage (mg)	148 ± 34
Hypertension	13 (33)	Cyclosporine night dosage (mg)	146 ± 40
Glomerulonephritis	5 (13)		
Diabetes mellitus	6 (15)		
Unknown	14 (39)		
Living donor	37 (95)		
Rejection EPISODE history	12 (31)		
Preemptive transplantation	5 (13)		
Having caregiver	22 (56)		
Anemia (hgb < 10 g/dL)	16 (41)		
Systolic hypertension (> 140 mmHg)	14 (36)		
Diastolic hypertension (> 90 mmHg)	9 (23)		
Cellcept® based immunosuppression	31 (80)		

sleep quality questionnaire.

Materials and Methods

A cross-sectional study was conducted in stable renal transplant patients attending an outpatient nephrology clinic after obtaining informed consent. 39 patients agreed to participate in the study. The following inclusion criteria were used: over 18 years of age, current stable graft function, and competence to give informed consent. Patients with an elevated serum creatinine level or any concomitant acute disease were excluded from analysis. We extracted all available demographic data, medical history, laboratory test results, and treatment strategies, from our local data registry and outpatient clinic records.

All patients completed two self-administered questionnaires for assessment of sleep quality and morbidity measures. Baseline assessment was determined using the Pittsburg Sleep Quality Index (PSQI; 7 items; total score, 0 to 21; higher score indicating worse sleep quality).[5,6] Patients were then divided into two groups based on the PSQI score: group I (poor sleepers, PSQI score ≥ 5) and group II (good sleepers, PSQI score < 5). Patients were also assessed for medical comorbidities (Ifudu comorbidity index; 42 items; total score range, 0 to 42; higher scores indicating more medical comorbidities).

For statistical analysis, we used SPSS v.13.0. Kolmogorov-Smirnov test was used for evaluation of distributions. We used Student's t-test, and Fisher's exact test for comparing the demographic, laboratory, and clinical variables as well as the scores of comorbidity measures between the two groups. Univariate and multivariate linear regression models were employed for assessing independent correlates of PS-QI total score.

Table 2. Frequencies of abnormality in the sub categories of sleep quality (PSQI) and comorbidity (Ifudu) questionnaires among the study patients

PSQI sub categories	N (%)	Comorbidity sub categories	N (%)
Perceived sleep quality	22 (56)	Ischemic heart disease	4 (10)
Sleep latency	25 (64)	Non-ischemic heart diseases	24 (62)
Sleep duration	20 (51)	Respiratory disorders	3 (8)
Habitual sleep efficiency	3 (7)	Autonomic neuropathy	6 (15)
Sleep disturbances	3 (7)	Other neurological disorders	10 (26)
Use of sleeping medication	2 (5)	Musculoskeletal disease	6 (15)
Daytime dysfunction over the last month	29 (74)	Infection	3 (8)
		Liver, pancreas &/or biliary disease	10 (26)
		Hematological disorders	11 (28)
		Low back pain, spine &/or joint disorders	13 (33)
		Limb amputation	2 (5)
		Mental or emotional illness	6 (15)
		Genitourinary disorders	9 (23)

Results

Demographic characteristics of the study population as well as their clinical and laboratory data are presented in table 1. Mean total PSQI score for the whole patients was 6.5 ± 2.6. Overall 26(67%) of patients were diagnosed as "poor sleepers" (PSQI total score ≥ 5) and the remaining 13 (33%) were "good sleepers". Table 2 shows frequencies of disorders in each PSQI & comorbidity (Ifudu) sub-categories. Mean scores for sub-scores of PSQI were as follow: subjective sleep quality: 1.0 ± 0.8, sleep latency: 1.2 ± 0.9, sleep duration: 1.3 ± 1.3, habitual sleep efficiency: (no case), sleep disturbances: 3.0 ± 1.4, use of sleeping medication: 3.0 ± 0.2, and daytime dysfunction over the last month: 2.0 ± 1.4.

We evaluated the difference of all variables listed in table 1 between "good sleepers" and "poor sleeper". We found that "poor sleepers" significantly had higher phosphate levels (6.1 ± 2.6 vs. 4.0 ± 1.6, respectively; *P*= 0.05) and ESRD duration (48 ± 58 vs. 20 ± 18 months, respectively; *P*= 0.05) compared to "good sleepers". Considering categories for sleep quality, the only comorbidity index which is more seen among "poor sleepers" is hematological disorders (*P*= 0.03). We also assessed the potential impact of all the mentioned variables (table 1) and comorbidity sub-indices on the PSQI total score using univariate linear regression analysis. Only comorbidity indices: ischemic heart disease, musculoskeletal and hematological disorders and limb amputation represented significant relations (table 3). Multivariable linear regression model revealed only musculoskeletal disorders as the independent comorbidity sub-index affecting PSQI score (*P*= 0.05, β= 0.29).

Discussion

The prevalence of poor sleep in the present study was 67%. This finding represents a relatively higher prevalence of sleep disturbance

Table 3. Linear regression evaluating impact of various comorbidity measures with PSQI total score in the study patients

Comorbidity measures	Univariate		Multivariate	
	β	*P*	β	*P*
Ischemic heart disease	0.43	0.007	0.20	0.248
Musculoskeletal disease	0.34	0.032	0.29	0.05
Hematological disorders	0.47	0.003	0.32	0.08
Limb amputation	0.36	0.024	0.09	0.652
Comorbidity total score	0.40	0.013	-	-

among renal transplant patients compared to study by Sabbatini et al[3] where 52% prevalence of sleep disturbance was reported. On the other hand, our finding seems quite comparable with sleep-wake complaints in dialysis patients reported in previous studies.[7-10]

At least two other recent studies have evaluated this issue.[11,12] Molnar et al[11] reported high risk for sleep apnea in the kidney transplanted population that was approximately equivalent to patients undergoing dialysis. Beecroft et al[12] in their survey found that sleep apnea improves just in a minority of patients following successful kidney transplantation; however, specific determinants of improvement were not identified in their survey.

Several factors including anemia, advanced age, sex, and hormone imbalance may contribute to sleep disorders in CRF patients.[13] A number of previous studies have reported that male gender, use of specific medications, comorbidity, and impaired kidney function are associated with high risk for sleep apnea in this patient population.[11] In our study, no association between sleep quality and age, sex, immunosuppression type, presence of diabetes mellitus, and serum creatinine level was identified. However, although total comorbidity score showed a significant relationship with total PSQI score (table 3), only musculoskeletal disorders represented an independent risk factor for higher PSQI scores and therefore worse sleep quality. On the other hand, regarding quality of sleep categories, "poor sleepers" were more likely to have hematological disorders compared to "good sleepers".

Iliesco et al[2] in their study on hemodialysis patients found that anemia is a risk factor for poor sleeping. In the present study, we did not detect any association between hemoglobin levels and quality of sleep in renal transplant patients. Disturbance in immune function;[15] metabolic changes,[15] low serum PTH levels[16] are known risk factors for poor sleep, however, infection rate and metabolic profile was not different. We did not measure the PTH levels however; we found that elevated serum phosphate values in renal transplant patients are significantly common in "poor sleepers". Socioeconomic level and education level are established risk factors for health related quality of life in ESRD patients.[2] However, we did not find any data on the potential association between these factors and quality of sleep in renal patients. In this study, we did not detect any impact for the abovementioned factors as well as area of residence, gender and marital status on the sleep quality in our kidney transplant population. Other assessed risk factors including cause of renal failure, history of rejection episodes, rehospitalization due to infection, type of transplantation, having family caregiver, immunosuppression type, and age also did not affect sleep quality in this study.

In this study, ESRD duration presented as a significant risk factor for poor sleeping in renal recipients. Iliescu et al[2] in their study on hemodialysis patients found no impact for the duration of ESRD on the patients' sleep quality. However, corroborating to our finding, Sabbatini et al[16] found that being over one year and less than eight year on dialysis (ESRD duration) is a significant risk for poor sleeping. We also found no association between sleep quality and human leukocyte antigen haplotypes expression.

The low quality of sleep observed in transplant patients with a functioning allograft obviously shows that the poor quality of sleep in renal patients has some extra factors other than renal dysfunction. Polysomnographic evaluations and surveys with larger study population for a more precisely uncovering the associations of specific sleep components seem necessary.

For a more precise interpretation of this study's results, we should acknowledge and consider its limitations. Our study had a limited population size. Moreover, its exclusion and inclusion criteria may result in some types of selection bias and also make it difficult to compare it with other reports. Laboratory measures were essentially not determined at the time of study and we used the last post-transplant available data for this purpose.

In conclusion, our study shows that sleep quality in renal transplanted patients is surprisingly poor, and associated with duration of ESRD

phosphate levels. The PSQI questionnaire seems an easy and feasible tool to investigate the quality of sleep in renal transplant patients. Future studies with larger sample sizes are necessary for confirming our findings.

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