ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

Kocaeli Med J 2024; 13 (1): 6-14, doi: 10.5505/ktd.2024.02328

Böbrek Nakli Hastalarında Uyku Kalitesi ve Nokturi

Sleep Quality and Nocturia in Renal Transplant Patients

Bülent Kaya[1], Saime Paydas[1], Mehmet Gökhan Gök[2], Burak Mete[3], Tolga Kuzu[1], Mustafa Balal[1]

[1] Çukurova Üniversitesi Tıp Fakültesi, Nefroloji Bilim Dalı, Adana, Türkiye.

[2] Çukurova Üniversitesi Tıp Fakültesi, İç Hastalıkları Ana Bilim Dalı, Adana, Türkiye.

[3] Çukurova Üniversitesi Tıp Fakültesi, Halk Sağlığı Ana Bilim Dalı, Adana, Türkiye.

ÖZ

Giriş: Kronik böbrek hastalarında uyku bozuklukları yaygındır. Bununla birlikte, böbrek nakli alıcılarında uyku kalitesi hakkındaki bilgiler sınırlıdır. Alt üriner sistem disfonksiyonu, böbrek nakli sonrası uyku bozukluklarına neden olabilir. Çalışmamızda böbrek nakli alıcılarında nokturi, yaşam kalitesi ve uyku kalitesi arasındaki ilişkiyi değerlendirdik.

Yöntem: Çalışmamıza 18 yaş üstü 99 böbrek nakli alıcısı dahil edilmiştir. Hastaların nakil süresi > 6 ay ve serum kreatininin değeri <2 mg/dl idi. Kan örnekleri ve 24 saatlik idrar örnekleri ile birlikte eş zamanlı olarak biyokimyasal ölçümler, Pittsburg Uyku Kalitesi İndeksi ve SF-36 kısa form sağlık anketleri yapıldı. 71 erkek hastaya Uluslararası Prostat Semptom Skoru (IPSS) uygulandı.

Bulgular: Doksan dokuz böbrek nakli hastasının ortalama yaşı 40.36 ± 10.3 yıl ve nakil süresi 85.5 ± 59.7 ay idi. Nakil öncesi ve nakil sonrası uyku sürelerinin ortalaması sırasıyla 7.72 ± 1.77 ve 7.55 ± 1.37 saat idi. Böbrek nakilli hastaların % 85.9'unda nokturi saptandı. Nokturili hastalarda IPSS daha yüksek, serum potasyum ve idrar dansitesi daha düşüktü. Nokturi ile uyku kalitesi arasında ilişki saptanmadı. Uyku kalitesi kötü olan böbrek nakli alıcıları daha düşük SF-36 skoruna, daha yüksek kan üre nitrojenine sahipti ve nakil sonrası geçen süre daha kısa (< 5 yıl) idi.

Sonuç: Böbrek nakli alıcılarımızda uyku bozuklukları ve nokturi sıklığı yüksekti. Nakil süresi 5 yıldan fazla olan hastalarda yaşam kalitesi ve uyku kalitesi daha iyiydi. Sonuç olarak uyku kalitesi nokturiden bağımsızdı ve yaşam kalitesi ile ilgiliydi.

Anahtar Kelimeler: nokturi, uyku kalitesi, yaşam kalitesi, böbrek nakli

ABSTRACT

Objective: Sleep disorders are common in chronic kidney patients. However, knowledge about sleep quality in kidney transplant recipients (KTrs) is limited. Lower urinary tract dysfunction can also be caused by sleep disorders after renal transplantation. We evaluated the relationship between nocturia, quality of life, and sleep quality in KTrs..

Method: In our study, 99 KTrs >18 years were included. KTrs had a post-transplant period >6 months and serum creatinine <2 mg/dl. Simultaneously biochemical measurements on blood samples and 24-hour urine samples and Pittsburg Sleep Quality Index and SF-36 short-form health questionnaires were performed. The International Prostate Symptom Score (IPSS) was applied to 71 male patients.

Results: The mean age and duration of transplantation 99 KTrs were 40.36 ± 10.3 years and 85.5 ± 59.7 months, respectively. The mean of pretransplant and posttransplant sleep duration was 7.72 ± 1.77 and 7.55 ± 1.37 hours, respectively. Nocturia was present in 85.9% of the KTrs. In patients with nocturia, IPSS was higher, and serum potassium and urinary density were lower. There was no relationship between nocturia and sleep quality. KTrs with poor sleep quality had lower SF-36 score, posttransplant duration <5 years, and higher blood urea nitrogenous.

Conclusion: In our KTrs, the frequencies of sleep disorders and nocturia were high. Quality of life and sleep quality were better in patients with a transplant period of more than five years. In conclusion, sleep quality was independent of nocturia and related to quality of life.

Keywords: nocturia, sleep quality, life quality, kidney transplantation

Gönderim Tarihi: 01.06.2021 **Kabul Tarihi:** 24.04.2024

Correspondence: Uzm. Dr. Bülent Kaya, Çukurova Üniversitesi Tıp Fakültesi, Nefroloji Bilim Dalı, Adana, Türkiye. **E-mail:** bulentkaya32@gmail.com

Atıf/ Cite as: Kaya B, Paydas S, Gok MG, Mete B, Kuzu T. Balal M. Sleep Quality and Nocturia in Renal Transplant Patients.
Kocaeli Med J 2024; 13(1): 6-14, doi: 10.5505/ktd.2024.02328

INTRODUCTION

In patients with end-stage kidney disease (ESRD), sleep-related problems, including insomnia, periodic limb movements during sleep, restless leg syndrome, and obstructive sleep apnea, are frequent (1, 2). Although renal transplantation (RTX) offers a better quality of life than hemodialysis (HD), sleep problems frequently continue in kidney transplant recipients (KTrs) (3, 4). The prevalence of poor sleep quality in KTrs ranges from 30% to 62%(5, 6). Comorbidities such as immunosuppressive drugs, obesity, loss of allografts, cardiovascular diseases, and malignancy contribute to the risk of sleep disorders(7). However, there is limited knowledge about sleep disorders in KTrs, and most of this information is based on studies in patients with the general population or chronic kidney disease (CKD). Sleep disorders, which have a detrimental effect on the general population and CKD patients, may have similar or worse impacts in KTrs (7).

Detrusor muscle hyperactivity, urinary dysfunction, decreased bladder capacity, and bladder compliance is widespread in dialysis patients but increases as the longer dialysis duration (8). After successful RTX, adaptation occurs in the urinary storage and discharge functions in the lower urinary system (LUT) and typically occurs within the first six months (9). However, some patients have long-term LUT dysfunction and symptoms that can affect the quality of life (10). In addition, these patients are advised to drink plenty of water to maintain kidney function, which may further exacerbate LUT symptoms. One of the symptoms of LUT dysfunction in KTrs is nocturia. It has been reported that nocturia adversely affects the quality of life in patients receiving successful RTX (11). Therefore, focusing on LUT dysfunction and symptoms after successful RTX is essential for a better quality of life. We think that nocturia may cause disturbances in sleep and quality of life in KTrs. Therefore, in this study, we aimed to evaluate the relationship between nocturia and sleep and quality of life in KTrs.

MATERIALS AND METHODS

In our study, clinical and laboratory findings of 130 patients older than 18 years old who underwent RTX between 2010-2019 were evaluated cross-sectionally. The inclusion criteria were a post-transplant period of at least 6 months, a serum creatinine value below 2 mg/dl, the absence of acute rejection, and stable renal function for at least 3 months. Exclusion criteria were diagnosis of diabetes mellitus (DM), diagnosis of obstructive sleep apnea, use of diuretics, use of medication or surgery for benign prostatic hypertrophy (BPH), urinary tract and other infections, use of urinary catheters, and lack of written consent for the study. A total of 99 patients, 71 of whom were male, were included in our study.

Demographic data of patients including age, gender, body mass index, comorbid diseases, etiology of renal failure, transplant duration, donor type, renal replacement type and duration before transplantation, and the drugs used were recorded.

Definition of Measurements and Parameters

The sleep quality of patients was determined according to the PSQI (12). According to PSQI, sleep quality assessment consisted of 7 topics including subjective sleep quality, sleep time, habitual sleep efficacy, sleep disturbance-affecting conditions, use of sleeping drugs/substances and daytime dysfunction/sleepiness, and 19 questions, which can be answered by the individual, in which the various factors related to sleep quality were evaluated in the previous month. Each item in the scale is scored between 0 and 3, and the total score ranges from 0 to 21. Overall PSQI score indicates good sleep quality between 0-4 and decreased sleep quality between 5-21(12).

IPSS was used to evaluate patients' LUT symptoms(13). There are seven questions about patient symptoms in IPSS, and it results in a score between 0-35. It is classified as 'mild' with an IPSS score of 0-7, 'moderate' between 8-19, and 'severe' obstruction between 20-35.

The quality of life was evaluated with the SF-36 quality of life scale(14). In this questionnaire, patients were asked questions consisting of eight essential topics (physical functionality, role restrictions due to physical problems, physical pain, general health perception, vitality, social functionality, role restrictions due to emotional problems, perceived mental health). The score of each topic ranged from 0-100. A score of close to 100 indicates a better quality of life, whereas a lower score indicates a worse quality of life.

The number of urination and urine volume were recorded as day-time and night-time. A physical exam was performed. Patients were asked sleep duration and the mean day-time/night-time urination in the last month before transplantation and post-transplant period. Nocturia was defined as two or more urination during the night (15).

In the blood sample taken in the morning after 12 hours of fasting; glucose, blood urea nitrogen, creatinine, uric acid, total protein, albumin, AST, ALT, sodium, potassium, calcium, phosphorus, complete blood count, C reactive protein, sedimentation, TSH, ferritin, HbA1C, PTH were measured. A spot urine examination was also performed.

Statistical analysis

IBM SPSS V22.0 (Armonk, NY, USA) software was used for statistical analysis. The consistency of continuous variables to normal distribution was tested with the Shapiro-Wilks test. Descriptive statistics of continuous variables were expressed as mean ± SD or median (min-max). Categorical variables were compared using chi-square analysis. The differences between the independent groups in continuous variables were examined using the Student t-test and the Mann Whitney U test. The presence of correlation between the groups was determined by the Spearman correlation test. $P < 0.05$ was accepted for statistical significance.

RESULTS

The mean age of 99 (71 male) KTrs was 40.36 ± 10.3 (20-64) years and the post-transplantation duration was 85.5 ± 59.7 months. The number of patients >50 age was 79 (79.8%). The demographic, clinical, and laboratory features of the patients are shown in table 1.

CKD etiologies of patients; 40 (40.4%) unknown, 20 (20.2%) chronic glomerulonephritis, 19 (19.2%) hypertension, 5 (5.1%) polycystic kidney disease, 2 (2%) nephrolithiasis and 13 (13.1%) other causes. The number of patients using cigarettes and alcohol was 30 (30.3%) and 2 (2%), respectively.

Table 1: Clinical, Laboratory, and Demographic Features of the Patients (N=99)			
Parameters	**n (%) or mean+SD (min-max)**	**Parameters**	**n (%) or mean + SD (min-max)**
Age, year	40.4±10.3 (20-64)	Glucose, mg/dL	92.4±12.2 (70-121)
Male/Female	71(%71.7) / 28(%28.3)	eGFR, ml/min/1.73m2	75.4±22.1 (36.3-129)
BMI, kg/m^2	25.77±4.11 (17.4-38.5)	Creatinine, mg/dL	1.19±0.34 (0.59-1.99)
Donor type, cadaveric / living	15 (%15.2) / 84 (%84.8)	Albumin, g/dL	4.17±0.44 (3-5)
HD duration, month	32.1±42.9, 12(1-180)	Na, mmol/L	140.3±2.4 (132-144)
PD duration, month	41.5±34.8, 41.5(6-120)	K, mmol/L	4.02±0.43 (3-5)
Post TX duration, month	85.5±59.7 (7-358)	Ca, mg/dL	9.71±0.76 (6-11)
HT	54(%54.5)	WBC,$10^3/\mu L$	8263±2234 (3300-15500)
CAD	4(%4)	Hgb,g/dL	14.02±2.02 (9-18)
Daily urine volume, ml/day	3.085±1270 (1000-7000)	Hct, %	41.3±5.9 (27-52)
Pre-TX night sleep time, hour	7.72±1.77 (3-12)	CRP,mg/dL	0.54±1.11 (0-7)
Post-TX night sleep time, hour	7.55±1.37 (3-11)	ESR, mm/h	20.75±15.1 (2-59)
Post-TX day-time urination count	6.29±1.95 (2-10)	Ferritin, ng/ml	154±211 (5-954)
Post-TX night-time urination count	2.43±1.03 (0-6)	HbA1C, %	5.4±0.5 (4-6.2)
Nocturia	85 (%85,9)	TSH, mIU/L	1.8±0.9 (1-5)
SBP, mmHg	125.8±11.5 (100-150)	Urinary density	1010 ±4.89 (1002-1023)
DBP, mmHg	78.7±8.5 (60-100)	Serum osmolality, mOsm/kg H2O	293±4.9 (274-299)
SF-36 score	552±144 (112-782)	IPSS (n=70)	5.3±4.2 (0-21)
Physical functionality	78.7±18.6 (10-100)	IPSS(n=70) mild moderate	 55 (%78.6) 15 (%21.4)
Role restrictions due to physical problems	65.6±35.5 (0-100)	PSQI good (0-4) poor (5-21)	4.9±2.9 (1-12) 50 (%50.5) 49 (%49.5)
Role restrictions due to emotional problems	64.2±39.1 (0-100)		
Energy/vitality	65.1±20.4(10-100)		
Perceived mental health	65.6±18.1 (8-100)		
Sosyal functionality	76.6±26.8 (0-100)		
Physical Pain	78.8±24.1(0-100)		
General health perception	57.2±21.4 (5-100)		

HD: Hemodialysis, PD: Peritoneal Dialysis, HT: Hypertension, CAD: Coronary Artery Disease, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, TX: Transplantation, ESR: Erythrocyte sedimentation rate, PSQI: Pittsburg Sleep Quality Index, IPSS: International Prostate Symptom Score, eGFR: Estimated Glomerular Filtration Rate.

Table 2. Comparison of Clinical and Laboratory Features of Patients with and Without Nocturia in Renal Transplant Recipients (N=99)

Parameters	Nocturia (+) (n=85)	Nocturia (-) (n=14)	P
Age, year	40.26±10.3	41±10.3	0.804[1]
Age <50 / ≥50	67/18	12/2	0.729[4]
BMI	25.4±4.14	27.7±3.4	0.060[1]
Male/female	58/27	13/1	0.105[4]
SF-36 score	549±148	568±120	0.767[2]
PSQI	4.98±3.1	4.4±1.9	0.891[2]
IPSS	5.8±4.4	3.08±2.4	0.011[2]
HT, yes/no	49/36	5/9	0.127[3]
CAD, yes/no	4/81	0/14	1.000[4]
Preemptive/ dialysis	15/70	1/13	0.456[4]
Day-time urine count	6.36±1.80	5.86±2.71	0.295[2]
Night-time urine count	2.65±0.93	1.14±0.53	<0.001[2]
Daily urine volume, L	3171±1273	2559±1156	0.111[2]
HD duration, month	35.27±45.2	12.9±9.6	0.226[2]
PD duration, month	43.1±34.9	36.3±41.3	0.782[1]
RTX duration, month	87.4±62.5	73.6±38.1	0.714[2]
Sleep time before RTX, hour	7.67±1.74	8.0±1.96	0.910[2]
Sleep time after RTX, hour	7.56±1.37	7.43±1.39	0.405[2]
SBP, mmHg	126±11.5	124.6±10.9	0.827[2]
DBP, mmHg	78.5±8.8	79.3±8.3	0.739[2]
Serum C0 tacrolimus,ng/mL	5.41±1.98	4.92±2.01	0.445[2]
Serum C2 cyclosporin,ng/mL	412±243	478±210	0.217[1]
Glucose, mg/dL	90.8±12.2	95.5±11.2	0.121[2]
Creatinine, mg/dL	1.19±0.34	1.20±0.32	0.710[2]
Albumin, g/dL	4.19±0.45	4.07±0.26	0.319[2]
Na, mmol/L	140.4±2.5	139.9±1.5	0.289[2]
K, mmol/L	3.98±0.42	4.28±0.47	0.017[2]
Ca, mg/dL	9.72±0.78	9.64±0.63	0.287[2]
WBC, $10^3/\mu L$	8388±2176	7507±2511	0.124[2]
Hgb, g/dL	13.96±2.08	14.36±1.65	0.670[2]
CRP, mg/L	0.48±1.1	0.86±1.3	0.262[2]
HbA1C, %	5.39±0.56	5.53±0.79	0.182[2]
TSH, mIU/L	1.89±1.01	1.57±0.65	0.360[2]
Serum osmolality, mosm/kg	293±6.1	292±3.5	0.475[2]
Urinary density	1010.2±4.7	1013.1±5.2	0.068[2]

1Student T-test, 2Mann-Whitney U test, 3 Chi-Square test, 4Fisher-exact test
HT: Hypertension, HD: Hemodialysis, PD: Peritoneal Dialysis, CAD: Coronary Artery Disease, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, CRP: C-reactive protein, RTX: Renal Transplantation, PSQI: Pittsburg Sleep Quality Index, IPSS: International Prostate Symptom Score.

Immunosuppressive drugs were methylprednisolone (95, 96%), tacrolimus (82, 82.8%), cyclosporin (16, 16.2%), mycophenolate (67, 67.7%), everolimus (8, 8.1%), azothiopurine (14, 14.1%). The mean serum level of tacrolimus (C0) and cyclosporin (C2) were 5.33 ± 1.98 (2-10) ng/ml and 416.5 ± 234.2 (66-767) ng/ml, respectively. Antihypertensive drugs were beta blocker 35 (35.4%), angiotensin converting enzyme inhibitor/angiotensin receptor blockers (ACEI/ARB) 22 (22.2%), alpha blocker 10 (10.1%), calcium channel blocker 46 (46.5%).

Nocturia was detected in 85.9% (85) of the KTrs. According to the median age below 40 years old and above, the frequencies of nocturia were 86%(43/50) and 85.7%(42/49) in respectively, and there was no statistical difference (p=0.620).

PSQI and SF-36 questionnaires were applied to all KTrs, and the IPSS questionnaire was answered by 71 male KTrs.

Clinical and laboratory characteristics of patients with and without nocturia are shown in table 2. There was significant differences for IPSS score (p=0.011), night urine count (p<0.001), and serum potassium level (p=0.017) between KTrs with/out nocturia. However, PSQI scores were similar in these two groups (p=0.891).

Variables correlated with nocturia are shown in table 3. Sleep quality was reduced in 49 (49.5%) of the KTrs, according to PSQI. (Table 4). Factors related with poor sleep quality were age >50 year (p=0.040), lower SF-36 score (p<0.001) (Figure 1) and higher BUN level (p=0.038).

Comparing to < 60 months in KTrs with post-transplant duration longer than 60 months, both life quality and scores for sleep quality were better (p=0.020, p=0.025) (Table 5) (Figures 2 and 3). Nocturia was not different for the post-transplant duration (p=0.478)

Table 3. Variables Correlated with Nocturia in Renal Transplant Recipients (n=99)

Parameters	rho/p
Gender	-0.190/0.059
Potassium	-0.241/0.016
Urine density	-0.184/0.068
Serum osmolality	0.072/0.478
SF36	-0.012/0.905
PSQI	0.014/0.892
IPSS	0.307/0.010
Nighttime urination count	0.557/<0.001
Daily urine volume	0.161/0.112
Posttransplantation duration	0.037/0.716
HD duration	0.146/0.229
PD duration	0.073/0.812
Sleep time before RTX	0.011/0.911
Sleep time after RTX	0.084/0.408

Spearman correlation test
RTX: Renal Transplantation, HD: Hemodialysis,
PD: Peritoneal Dialysis, PSQI: Pittsburg Sleep Quality Index,
IPSS: International Prostate Symptom Score.

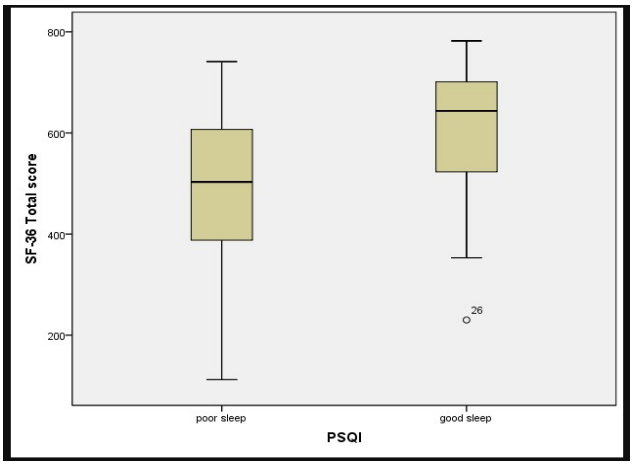

Figure 1. Patients with lower SF-36 scores had worse sleep quality (p <0.001)

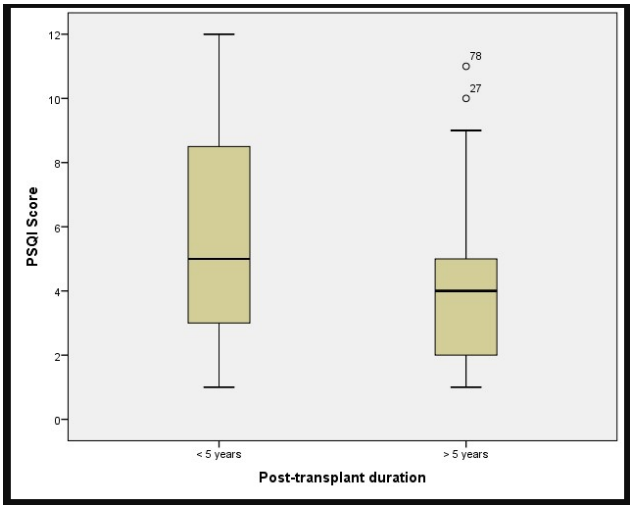

Figure 2. Kidney transplant patients with a post-transplant period longer than 5 years had better sleep quality (p=0.025).

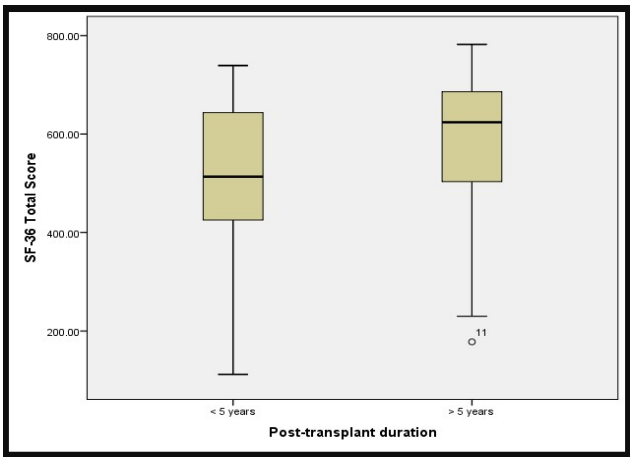

Figure 3. The SF-36 score was higher in kidney transplant patients with a post-transplant period longer than 5 years (p=0.020).

Table 4. Comparison of Patients with Good and Poor Sleep Quality According to PSQI in Renal Transplant Recipients (n=99)

Parameters	PSQI; good sleep quality (n=50)	PSQI; poor sleep quality (n=49)	P
Age, year	42.4±10.9	38.22±9.31	0.040[1]
Age, <50 / ≥50	35/15	44/5	0.014[3]
Female/male	12/38	16/33	0.339[3]
BMI, kg/m2	26.06±4.24	25.47±3.99	0.478[1]
Smoking, yes/no	19/31	11/38	0,092[3]
HT, yes/no	30/20	24/25	0.271[3]
CAD, yes/no	2/48	2/47	0.684[4]
Nocturia, yes/no	44/6	41/8	0.537[3]
SF-36	613±114	490±146	<0.001[2]
IPSS	5.34±4.15	5.25±4.31	0.807[2]
Preemptive/dialysis	9/41	7/42	0.616[3]
Tacrolimus, yes/no	43/7	39/10	0.398[3]
Cyclosporine, yes/no	7/43	9/40	0.555[3]
Steroid, yes/no	49/1	46/3	0.362[4]
Mycophenolate, yes/no	33/17	34/15	0.719[3]
Everolimus, yes/no	5/45	3/46	0.715[4]
Azothiopurine, yes/no	7/43	7/42	0.967[3]
Daytime urine count	6.4±1.97	6.18±1.94	0.584[1]
Night time urination count	2.46±1.07	2.41±0.99	0.793[2]
Daily urine volume, ml	3240±1199	2927±1332	0.078[2]
Post-transplant duration, month	96.1±66.7	74.6±49.8	0.127[2]
Sleep time before transplantation, hour	7.64±1.51	7.80±2.01	0.709[2]
Sleep time after transplantation, hour	7.62±1.19	7.47±1.54	0.416[2]
SBP, mmHg	126.4±11.2	125±11.7	0.571[2]
DBP, mmHg	78.4±8.6	78.8±8.6	0.976[2]
Serum C0 tacrolimus, ng/mL	5.72±2.1	4.89±1.8	0.077[2]
Serum C2 cyclosporine, ng/mL	348±235	468±235	0.345[2]
eGFR, ml/min/1.73m^2	71.8±22.6	78.4±21.7	0.133[1]
Glucose, mg/dL	93.8±12.8	89±11.1	0.064[2]
BUN, mg/dL	16.8±6.8	19.9±9.3	0.038[2]
Creatinine, mg/dL	1.14±0.34	1.24±0.32	0.119[2]
Albumin, g/dL	4.1±0.36	4.24±0.48	0.086[2]
Na, mmol/L	140.7±2.1	139.9±2.6	0.151[2]
K, mmol/L	4.02±0.47	4.03±0.39	0.846[2]
Ca, mg/dL	9.6±0.8	9.8±0.7	0.216[2]
Hgb, g/dL	14.1±1.9	13.8±2.1	0.576[2]
CRP, mg/L	0.56±1.2	0.51±1.1	0.849[2]
ESR, mm/h	21±14	20±16	0.374[2]
HbA1C, %	5.4±0.56	5.4±0.62	0.718[2]
TSH, mIU/L	1.74±0.75	1.96±1.15	0.712[2]
Serum osmolality, mosm/kg	293±4.7	293±6.8	0.540[2]
Urinary density	1011±4.7	1010±5	0.422[1]

[1]Student T-test, [2]Mann-Whitney U test, [3] Chi-Square test, [4]Fisher-exact test

HT: Hypertension, CAD: Coronary Artery Disease, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, CRP: C-reactive protein, ESR: Erythrocyte Sedimentation Rate RTX: Renal Transplantation, PSQI:Pittsburg Sleep Quality Index, IPSS: International Prostate Symptom Score, eGFR: Estimated Glomerular Filtration rate.

Table 5. Comparison of Patients with a Transplant Period of More Than Five Years and Shorter in Renal Transplant Recipients (n=99).

Parameters	Posttransplant duration <60 month (n=44)	Posttransplant duration >60 month (n=55)	p
Nocturia, yes/no	39/5	46/9	0.478[3]
SF-36	517.3±142.7	579.9±139.8	0.020[2]
PSQI	5.75±3.23	4.22±2.49	0.025[2]
IPSS	5.8±4.8	4.9±3.7	0.588[2]
Day-time urination count	6.32±2.05	6.27±1.88	0.991[2]
Night-time urination count	2.36±0.89	2.49±1.13	0.907[2]
Daily urine volume, ml/day	3071±1340	3096±1223	0.816[1]
Posttransplant sleep time hour	7.43±1.54	7.64±1.22	0.612[2]

[1]Student T-test, [2]Mann-Whitney U test, [3] Chi-Square test
PSQI: Pittsburg Sleep Quality Index, IPSS: International Prostate Symptom Score.

DISCUSSION

Nocturia occurs when the amount of urine at night is more than the functional capacity of the bladder. It disturbs the individual's night's sleep and can make you tired during the day. It can cause difficulty in concentration and daily activities. It can also affect the social life of the person by reducing his energy during the day. Also, getting out of bed to urinate in the dark at night can cause a fall risk, especially in the elderly (16). In general population-based studies, nocturia has been reported to be significantly associated with comorbid diseases such as hypertension, diabetes mellitus, hyperlipidemia, and cerebral stroke (17). Nocturia is also associated with an increased risk of mortality (18, 19).

We found nocturia in a significant proportion (85.9%) of our 99 KTrx. In various population-based studies, the frequency of nocturia has been reported to be 11-43.9% between the ages of 20-40 and 68.9-93% over the age of 70 (20). In a small number of studies, the frequency of nocturia in KTrs was reported as 37-93% (21-23). Nocturia frequency increases with increasing age (24). A decrease in glomerular filtration rate, increased risk of hypertension and cardiovascular disease, physiological changes in the lower urinary system, and BPH in men can explain the appearance of nocturia in older ages (25-27). In our study, we did not find a relationship between nocturia and age, which may be due to the relatively young age of our patients (mean age 40.5 ± 10.2) and the absence of patients with BPH.

We did not find any relationship between pre-transplant and post-transplant duration and nocturia. As the HD duration increases, the amount of urine decreases gradually and becomes oligoanuric. Bladder inactivity and, therefore, atrophic changes develop over time in the bladder wall. On the other hand, bladder atrophy and bladder dysfunction may be less common in peritoneal dialysis patients since it preserves residual urine. Adaptation of the bladder occurs within six months after successful renal transplantation (28). Therefore, the relationship of nocturia with renal replacement type is expected in the first six months.

Of our patients mean duration after transplantation was 30 months. Therefore, we can say that our patients are in the period of full adaptation of the bladder.

Our KTrs with nocturia had lower serum potassium levels comparing to without nocturia. Hypokalaemia impairs the kidney's ability to concentrate maximum urine and is associated with mild polyuria. Hypokalaemia causes defective activation of renal adenylate cyclase and renal tubular water reabsorption induced by anti-diuretic hormone (29). In investigating etiological causes in a KTrs with nocturia, hypokalemia should not be forgotten.

Nocturia, which negatively affects night sleep, can increase daytime fatigue and negatively affect the quality of life. Studies in the general population reported that nocturia is associated with decreased quality of life (30, 31). In the KTrs with and without nocturia, we evaluated sleep quality and life quality with PSQI, IPSS, and SF36 questionnaires. IPSS scores were only different for nocturia. As reported by Zermann et al. (21), nocturia did not affect sleep and quality of life in our KTrs.

Sleep quality was impaired in 49.5% of our KTrs, but there was no relation with nocturia. The quality of life of patients with sleep disorders was also reduced. Interestingly the quality of life and sleep quality in patients with a post-transplant period of more than five years were better. This may be related to the normalization of life with the transplanted kidney and adaptation to normal living conditions (32). Sleep quality of patients who were followed up for five years after RTX was reported in 46% improvement and 21% deterioration compared to the pretransplant period (33). It has been reported that sleep quality in solid organ transplant patients does not improve until 3 years after transplantation (34). The post-transplant period is longer than four years; more sleep difficulties were reported than the first four years (35). In other words, there is uncertainty between sleep quality and kidney transplantation. In another study, the quality of life improved in KTrs; however, it was reported that this benefit was not seen in sleep quality (36). Problems such as insufficient dialysis

and uremic symptoms (hypervolemia, itching, neuropathy), depression, sleep apnea syndrome, restless leg syndrome in patients with ESRD can lead to sleep disorders(37). Improvement in sleep quality is expected with the regression of these problems after RTX. Evaluation of sleep quality in our patients was performed cross-sectionally after RTX; however, when the last month's quality of night sleep before RTX was also asked, no significant difference was found for sleep disorders.

Comparing older age, younger KTrs had poor sleep quality. Quality of life in patients with sleep disorders was also reduced. In the literature, depression, and anxiety have been reported more frequently in KTrs(38, 39).

It has also been reported that KTrs with poor sleep quality were more depressed (33). In addition, other factors that negatively affect quality of life in KTrs include comorbid diseases, concerns about graft function, sexual dysfunction, and immunosuppressive drugs (40).

We did not find any relation between immunosuppressive drugs, serum calcineurin level, and both nocturia and sleep quality. Insomnia is among the side effects reported in the use of tacrolimus therapy (41, 42). The relationship between the cumulative dose of tacrolimus and insomnia has also been reported in lung transplant recipients (43). However, there are few studies about the relationship between sleep disturbance and the use of calcineurin inhibitors in the literature.

Our study is cross-sectional and prospective studies are needed to evaluate the effect of kidney transplants on sleep disorders. In addition, other limitations of our research include a small number of patients, the absence of urodynamic studies showing bladder dysfunction, the amount of fluid consumed by patients, and the determination of urine counts based on the patient's memory.

As a result, nocturia was detected in a significant number of patients. We did not find any relationship between nocturia and sleep disorders. The quality of life of patients with sleep disorders was also reduced. Quality of life and sleep quality were better in patients with a transplant period of more than five years. We can say that the quality of sleep is independent of nocturia and is related to the quality of life.

Ethics Committee Approval: Ethics committee approval was obtained with decision number 29 of the ethics committee of Çukurova University Faculty of Medicine, session number 111, dated May 21, 2021. All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Author contributions: All authors contributed to the manuscript.

(I) Concept: B.K., S.P., M.B., (II) Design: B.K., S.P., M.B., (III) Supervision: B.K., S.P., M B., (IV) Resources: B.K., S P., M B., T K., MG G., (V) Materials: B.K., S.P., M.B., (VI) Data collection and/or processing: B.K., S.P., M.B., T.K. M.G.G., (VII) Analysis and/or interpretation: B.M., B.K., S.P., (VIII) Literature search: B.K., (IX) Writing masnuscript: B.K., (X) Critical Review: B.K., S .P.

Conflict of Interest: None declared

Funding: None declared

Informed Consent: We confirm that each participant provided informed consent before participating in the study.

Acknowledgements: We appreciate all study participants.

REFERENCES

1. Cengic B, Resic H, Spasovski G, Avdic E, Alajbegovic A. Quality of sleep in patients undergoing hemodialysis. Int Urol Nephrol. 2012;44(2):557-567.
2. Shafi ST, Shafi T. A comparison of quality of sleep between patients with chronic kidney disease not on hemodialysis and end-stage renal disease on hemodialysis in a developing country. Ren Fail. 2017;39(1):623-628.
3. Sabbatini M, Crispo A, Pisani A, Gallo R, Cianciaruso B, Fuiano G, et al. Sleep quality in renal transplant patients: a never investigated problem. Nephrol Dial Transplant. 2005;20(1):194-198.
4. Silva DS, Andrade Edos S, Elias RM, David-Neto E, Nahas WC, Castro MC, et al. The perception of sleep quality in kidney transplant patients during the first year of transplantation. Clinics (Sao Paulo). 2012;67(12):1365-1371.
5. Reilly-Spong M, Park T, Gross CR. Poor sleep in organ transplant recipients: self-reports and actigraphy. Clin Transplant. 2013;27(6):901-913.
6. Kachuee H, Ameli J, Taheri S, Assari S, Riahipour F, Khedmat H, et al. Sleep quality and its correlates in renal transplant patients. Transplant Proc. 2007;39(4):1095-1097.
7. Parajuli S, Tiwari R, Clark DF, Mandelbrot DA, Djamali A, Casey K. Sleep disorders: Serious threats among kidney transplant recipients. Transplant Rev (Orlando). 2019;33(1):9-16.
8. Chen JL, Lee MC, Kuo HC. Reduction of cystometric bladder capacity and bladder compliance with time in patients with end-stage renal disease. J Formos Med Assoc. 2012;111(4):209-213.
9. Silva DM, Prudente AC, Mazzali M, Borges CF, D'Ancona C. Bladder function evaluation before renal transplantation in nonurologic disease: is it necessary? Urology. 2014;83(2):406-410.
10. Tsaur I, Jones J, Melamed RJ, Blaheta RA, Gossmann J, Bentas W. Postoperative voiding dysfunction in older male renal transplant recipients. Transplant Proc. 2009;41(5):1615-1618.
11. Mitsui T, Shimoda N, Morita K, Tanaka H, Moriya K, Nonomura K. Lower urinary tract symptoms and their impact on quality of life after successful renal transplantation. Int J Urol. 2009;16(4):388-392.
12. Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193-213.
13. D'Silva KA, Dahm P, Wong CL. Does this man with lower urinary tract symptoms have bladder outlet obstruction?: The Rational Clinical Examination: a systematic review. JAMA. 2014;312(5):535-542.
14. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med

Care. 1992;30(6):473-483.

15. Weiss JP, Blaivas JG, Bliwise DL, Dmochowski RR, Dubeau CE, Lowe FC, et al. The evaluation and treatment of nocturia: a consensus statement. BJU Int. 2011;108(1):6-21.

16. Kim SY, Bang W, Kim MS, Park B, Kim JH, Choi HG. Nocturia Is Associated with Slipping and Falling. PLoS One. 2017;12(1):e0169690.

17. Kim SY, Bang W, Kim MS, Park B, Kim JH, Choi HG. Analysis of the Prevalence and Factors Associated with Nocturia in Adult Korean Men. Sci Rep. 2017;7:41714.

18. Akerla J, Pesonen JS, Poyhonen A, Hakkinen J, Koskimaki J, Huhtala H, et al. Impact of lower urinary tract symptoms on mortality: a 21-year follow-up among middle-aged and elderly Finnish men. Prostate Cancer Prostatic Dis. 2019;22(2):317-323.

19. Kupelian V, Fitzgerald MP, Kaplan SA, Norgaard JP, Chiu GR, Rosen RC. Association of nocturia and mortality: results from the Third National Health and Nutrition Examination Survey. J Urol. 2011;185(2):571-577.

20. Bosch JL, Weiss JP. The prevalence and causes of nocturia. J Urol. 2013;189(1 Suppl):S86-92.

21. Zermann DH, Janitzky A, Hohne M, Schubert J. Frequency and nocturia after successful renal transplantation: a normal situation? BJU Int. 2006;97(3):555-558.

22. Mitsui T, Moriya K, Morita K, Iwami D, Kitta T, Kanno Y, et al. Risk Factors for Lower Urinary Tract Dysfunction and Symptoms After Successful Renal Transplantation. Ann Transplant. 2015;20:757-763.

23. Van der Weide MJ, Van Achterberg T, Smits JP, Heesakkers JP, Bemelmans BL, Hilbrands LB. Causes of frequency and nocturia after renal transplantation. BJU Int. 2008;101(8):1029-1034.

24. van Doorn B, Kok ET, Blanker MH, Westers P, Bosch JL. Determinants of nocturia: the Krimpen study. J Urol. 2014;191(4):1034-1039.

25. Kim SO, Kim JS, Kim HS, Hwang EC, Oh KJ, Kwon D, et al. Age related change of nocturia in women. Int Neurourol J. 2010;14(4):245-249.

26. Kujubu DA, Aboseif SR. An overview of nocturia and the syndrome of nocturnal polyuria in the elderly. Nat Clin Pract Nephrol. 2008;4(8):426-435.

27. Natsume O. Diuretic pattern in adults with nocturnal polyuria: the possible contribution of blood pressure to the worsening of nocturnal polyuria. Int J Urol. 2007;14(9):822-827.

28. Mizerski A, Ostrowska Clark K, Ostrowski M, Ciechanowski K, Kaminski M, Sulikowski J, et al. Postoperative adaptation of urinary bladder to variable volume of urine in the initial period following kidney transplantation. Transplant Proc. 2003;35(6):2174-2175.

29. Weiner ID, Wingo CS. Hypokalemia--consequences, causes, and correction. J Am Soc Nephrol. 1997;8(7):1179-1188.

30. Kupelian V, Wei JT, O'Leary MP, Norgaard JP, Rosen RC, McKinlay JB. Nocturia and quality of life: results from the Boston area community health survey. Eur Urol. 2012;61(1):78-84.

31. Tikkinen KA, Johnson TM, 2nd, Tammela TL, Sintonen H, Haukka J, Huhtala H, et al. Nocturia frequency, bother, and quality of life: how often is too often? A population-based study in Finland. Eur Urol. 2010;57(3):488-496.

32. Eppenberger L, Hirt-Minkowski P, Dickenmann M. Back to work? Socioeconomic status after kidney transplantation. Swiss Med Wkly. 2015;145:w14169.

33. Brekke FB, Waldum-Grevbo B, von der Lippe N, Os I. The effect of renal transplantation on quality of sleep in former dialysis patients. Transpl Int. 2017;30(1):49-56.

34. Burkhalter H, Denhaerynck K, Huynh-Do U, Binet I, Hadaya K, De Geest S, et al. Change of sleep quality from pre- to 3 years post-solid organ transplantation: The Swiss Transplant Cohort Study. PLoS One. 2017;12(10):e0185036.

35. Teng S, Zhang S, Zhang W, Lin X, Shang Y, Peng X, et al. Symptom Experience Associated With Immunosuppressive Medications in Chinese Kidney Transplant Recipients. J Nurs Scholarsh. 2015;47(5):425-434.

36. Liaveri PG, Dikeos D, Ilias I, Lygkoni EP, Boletis IN, Skalioti C, et al. Quality of sleep in renal transplant recipients and patients on hemodialysis. J Psychosom Res. 2017;93:96-101.

37. Parker KP. Sleep disturbances in dialysis patients. Sleep Med Rev. 2003;7(2):131-143.

38. Sabbatini M, Pisani A, Crispo A, Nappi R, Gallo R, Cianciaruso B, et al. Renal transplantation and sleep: a new life is not enough. J Nephrol. 2008;21 Suppl 13:S97-101.

39. Noohi S, Khaghani-Zadeh M, Javadipour M, Assari S, Najafi M, Ebrahiminia M, et al. Anxiety and depression are correlated with higher morbidity after kidney transplantation. Transplant Proc. 2007;39(4):1074-1078.

40. Baines LS, Joseph JT, Jindal RM. Emotional issues after kidney transplantation: a prospective psychotherapeutic study. Clin Transplant. 2002;16(6):455-460.

41. Fung JJ, Alessiani M, Abu-Elmagd K, Todo S, Shapiro R, Tzakis A, et al. Adverse effects associated with the use of FK 506. Transplant Proc. 1991;23(6):3105-3108.

42. Randomised trial comparing tacrolimus (FK506) and cyclosporin in prevention of liver allograft rejection. European FK506 Multicentre Liver Study Group. Lancet. 1994;344(8920):423-428.

43. Rohde KA, Schlei ZW, Katers KM, Weber AK, Brokhof MM, Hawes DS, et al. Insomnia and Relationship With Immunosuppressant Therapy After Lung Transplantation. Prog Transplant. 2017;27(2):167-174.