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The Effect of Factors Related to Poor Sleep Quality on Renal Failure Progression in Patients with Chronic Kidney Disease

Kronik Böbrek Hastalığı Olan Hastalarda Kötü Uyku Kalitesiyle İlgili Faktörlerin Böbrek Yetmezliğinin İlerlemesine Etkisi

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Abstract

Aim: In recent years, limited studies have been attempted to characterize the quality of sleep in patients with predialysis chronic renal disease (CKD), and the evidence has shown that insufficient sleep time or poor-quality sleep lead to the progression of CKD. In this study, we aimed to determine the factors related to poor quality of sleep in the patients with CKD and evaluate the effects of these factors on renal progression.

Material and Method: Patients with pre-dialysis CKD (E3-E5) over 18 years of age who did not have cardiovascular disease, obstructive sleep apnea, and active infection, started to be followed between June 2015 and November 2015, were included in the study. The quality of sleep these patients was measured using the Pittsburgh quality of sleep index (PSQI). At the end of the 4-year follow-up, the primary outcomes of the patients were accepted as ESRD, ESRD + mortality, and progression (25 ml/min reduction in GFR).

Results: Of the 179 patients followed in the study, 107 (59.8%) had good quality of sleep, 72 (40.2%) had poor quality of sleep. In the Binary Logistic Regression analysis performed to detect independent markers of poor quality of sleep; old age and female gender were found to be independent predictors of poor quality of sleep. It was found that poor quality of sleep did not affect renal progression conditions such as ESRD, ESRD + Mortality, and GFR≥ 25 ml/min decrease.

Conclusion: As a result, we determined that age and female gender are independent determinants of poor quality of sleep and poor quality of sleep increases mortality.

Keywords: Quality of sleep, chronic kidney disease, progression

Öz

Amaç: Son yıllarda, diyaliz öncesi KBH olan hastalarda uyku kalitesini karakterize etmek için sınırlı çalışmalar denenmiştir ve kanıtlar, yetersiz uyku süresinin veya düşük kaliteli uykunun KBH'nin ilerlemesine yol açtığını göstermiştir. Bu çalışmada kronik böbrek hastalarında kötü uyku kalitesi ile ilişkili faktörleri belirlemeyi ve bu faktörlerin böbrek progresyonu üzerindeki etkilerini değerlendirmeyi amaçladık.

Gereç ve Yöntem: Çalışmaya kardiyovasküler hastalığı olmayan, obstrüktif uyku apnesi ve aktif enfeksiyonu olmayan 18 yaş ve üzeri prediyaliz KBH (Evre 3-5) hastalar alınarak Haziran 2015 - Kasım 2015 tarihleri arasında izlenmeye başlandı. Bu hastaların uyku kalitesi Pittsburgh uyku kalitesi indeksi (PUQI) kullanılarak ölçüldü. 4 yıllık takip sonunda hastaların birincil sonlanmaları ESRD, ESRD + mortalite ve progresyon (GFH'de 25 ml / dk azalma) olarak kabul edildi.

Bulgular: Çalışmada izlenen 179 hastadan 107'si (% 59,8) iyi uyku kalitesine, 72'si (% 40,2) kötü uyku kalitesine sahipti. Kötü uyku kalitesinin bağımsız belirteçlerini tespit etmek için yapılan Binary Logistic Regression analizinde; yaşlılık ve kadın cinsiyetin kötü uyku kalitesinin bağımsız belirleyicisi olduğu bulundu. Kötü uyku kalitesinin ESRD, ESRD + Mortalite ve GFR≥ 25 ml / dk azalma gibi renal progresyon koşullarını etkilemediği bulundu.

Sonuç: Sonuç olarak, yaş ve kadın cinsiyetin kötü uyku kalitesinin bağımsız belirleyicileri olduğunu ve kötü uyku kalitesinin mortaliteyi artırdığını belirledik.

Anahtar Kelimeler: Uyku kalitesi, kronik böbrek hastalığı, progresyon

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INTRODUCTION

Chronic Kidney Disease (CKD) is an important public health problem that has become an epidemic in the world and in our country.[1] The prevalence of CKD in adults in our country is 15.7%.[2] The burden of CKD includes not only expensive renal replacement therapy but also the low quality of life, cardiovascular events, mortality, and deaths, resulting in significant social and economic burdens.[3-5] Sufficient quality is required for sleep, which is a basic physiological process.[6] Chronic kidney disease (CKD), especially end-stage kidney disease (ESRD); associated with poor quality of sleep, sleep disturbance, and excessive daytime sleepiness.[7-11] Poor quality of sleep has been reported to be associated with cardiovascular risks, including obesity, hypertension, and diabetes mellitus, known risk factors for CKD.[6,12-14] However, the underlying mechanisms for the relationship between quality of sleep and CKD are unknown. Sleep disorders can contribute to CKD progression through activation of the sympathetic nervous system and/or increased inflammation, which can indirectly lead to glomerular endothelial damage.[15-17] In recent years, limited studies have been attempted to characterize sleep in predialysis CKD, and the evidence has shown that insufficient sleep time or poor-quality sleep causes the progression of CKD. A direct possibility is the negative impact of sleep disorders on CKD, supported by the fact that, under normal physiological conditions, the key hormones that regulate body fluid balance and blood pressure are elegantly modulated by the sleep-wake cycle.[18,19]

In this study, we aimed to determine the factors related to poor quality of sleep in Chronic Kidney Patients and to examine its effect on renal progression.

MATERIAL AND METHOD

Patients with pre-dialysis CKD (E3-E5) over 18 years of age who did not have cardiovascular disease, obstructive sleep apnea, and active infection, started to be followed between June 2015 and November 2015, were included in the study. During this time, puki tests were conducted. The quality of sleep of these patients was measured using the Pittsburgh quality of sleep index (PSQI). Those with a sleep score of 5 or upper were considered to have poor quality of sleep, and those with a sleep score under 5 were considered to have good quality of sleep. After approximately 4 years, the data of the patients were obtained from the outpatient records. Patients with unknown prognosis and who did not continue their follow-up to our hospital were excluded from the study. Clinical, laboratory and demographic data were obtained from patient records. At the end of the 4-year follow-up, the primary outcomes of the patients were accepted as ESRD, ESRD + mortality, and progression (25 ml/min reduction in GFR). The etiology of CKD of patients was recorded. The relationship between the demographic information recorded and the routine biochemistry tests with the quality of sleep were evaluated. The effect of poor quality of sleep on ESRD, ESRD + mortality, and renal progression were examined. The study permit was obtained from the University of Health Sciences Konya Training and Research Hospital Specialization in Medicine Training Board with the decision dated 05.12.2019 and numbered 48929119/774.

Statistical Analysis

The analysis of the study was done with Statistical Package for the Social Sciences (IBM) version 22.0. The Kolmogorov Smirnov test was performed to determine whether the data were normally distributed. In two groups comparisons, a T-test was performed for normally distributed numerical data and Mann-Whitney U test performed for skewed distributed numerical data. In the comparison of categorized data, the Chi-Square test or Fisher exact test was used according to their suitability. Normally distributed data were expressed as mean ± standard deviation and non-normally distributed data were expressed as median (minimum-maximum). Binary Logistic Regression analysis (Forward conditional method) was performed to determine the parameters showing the poor quality of sleep independently. In univariate analyzes, parameters ($p<0.05$) associated with poor quality of sleep were included in the logistic regression model.

RESULTS

The study was started with 201 patients. It was completed with 179 patients since 22 patients did not come for regular control over a period of approximately 4 years. During this period, 66 patients started receiving dialysis treatment, 15 patients underwent kidney transplantation, and 12 patients died. The remaining 86 patients were followed up in the nephrology outpatient clinic as predialysis CKD.

As the most common primary causes of kidney diseases in our study, 55 patients (30.7%) were DM and 36 patients (20.1%) were HT. Other etiologies were as follows; 19 (10.6%) glomerulonephritis, 10 (5.6%) tubulointerstitial diseases, 16 (8.9%) cystic kidney diseases, and 43 (24.1%) unknown.

Of the 179 patients followed in the study, 107 (59.8%) had good quality of sleep and 72 (40.2%) had poor quality of sleep. 34.7% of the patients with poor quality of sleep had a diagnosis of DM. Patients with poor quality of sleep had 51.4% ESRD, 54.2% ESRD + Mortality, 71.9% renal progression. 62.5% of patients with poor quality of sleep were female gender (**Table 2**).

In comparison between poor quality of sleep and good quality of sleep groups, significant differences were found in age, body mass index, waist circumference, systolic blood pressure, pulse pressure, albumin, mortality, and gender.

Binary Logistic Regression analysis was performed to determine the factors that independently affect poor quality of sleep. Old age (OR=0.966 P: 0.014) and female gender (OR=1.910 P: 0.049) were found to be independent predictors of poor quality of sleep (**Table 3**). It was found that poor quality of sleep did not affect renal progression conditions such as ESRD, ESRD + Mortality, and GFR≥ 25 ml/min decrease. (P: 0.312), (P: 0.173), (P: 0.228), respectively.

Tablo 1. Demographic and Biochemical Parameters

PARAMETERS	Good quality of sleep (n:107)	Poor quality of sleep (n:72)	P
Age (year)	55 (19-83)	60 (22-88)	0.003
Sleep score	2 (0-4)	8 (5-19)	<0.001
Follow-up time (month)	42.5 (1-52)	34.5 (1-51)	0.222
BMI (kg/m^2)	28.9 (13.5-48)	30.5 (19.2-53.1)	0.018
Waist circumference (cm)	95.6±15.2	100.4±14.7	0.039
SBP (mm/Hg)	136.5±19.6	143.2±22.2	0.039
DBP (mm/Hg)	88.8±13.3	90.1±13.6	0.527
BP (mm/Hg)	47.5±15.7	53.1±16.4	0.025
MDRD 0 (ml/min)	34.4±13.6	32.9±13.5	0.499
MDRD 4 (ml/min)	38.6±16.0	39.6±159	0.787
Albumin (g/dl)	4 (1.8-4.7)	3.9 (1.6-4.6)	0.046
Hb (g/dl)	12.8±1.9	12.5±1.9	0.363
Üric acid (mg/dl)	7.1±1.7	7.2±1.6	0.734
Calcium (mg/dl)	8.9±0.7	8.9±0.7	0.368
Phosporus (mg/dl)	3.6±1.2	3.8±0.7	0.274
Parathormone (ng/L)	158.1 (10.3-799.0)	142.91 (41.8-616.3)	0.860
Total cholesterol(mg/dl)	205.9±50.8	207.6±506	0.835
LDL cholesterol (mg/dl)	131.5 (48-273)	127 (64-228)	0.901
HDL cholesterol (mg/dl)	42.7±12.2	41.7±11.3	0.585
Triglycerides (mg/dl)	176.9±103.6	179±104.3	0.863
CRP (mg/l)	3.44 (3.28-201.0)	3.76 (3.28-78.2)	0.838
HCO3 (mEq/l)	21.0±3.4	21.6±3.5	0.422
Proteinuria (g/day)	1.3(0.01-13.92)	2.2 (0.10-12.72)	0.142

LDL: low density lipoprotein **HDL**: High density lipoprotein **BMI**: Body mass index **SBP**: Systolic blood pressure **DBP**: Diastolic blood pressure **Hb**: Hemoglobin **PTH**: Parathormone **CRP**: C-reactive protein **BP**:Blood pressure

Tablo 2. Relationship of sleep quality with renal progression and mortality

Parameters	Good quality of sleep (n:107)	Poor quality of sleep (n:72)	P
DM			
Yes	28 (26.2%)	25 (34.7%)	0.144
No	79 (73.8%)	47 (65.3%)	
Mortality	4 (33.3%)	8 (66.7%)	0.053
ESRD			
Yes	52 (48.6%)	37 (51.4%)	0.312
No	55 (51.4%)	35(48.6%)	
ESRD+Mortality			
Yes	56 (52.3%)	45 (62.5%)	0.173
No	51 (47.7%)	27 (37.5%)	
Progression			
Yes	70 (65.4%)	52 (71.9%)	0.228
No	37 (34.6%)	20 (28.1%)	
Gender			
Female	47 (43.9%)	45 (62.5%)	0.011
Male	60 (56.1%)	27 (37.5%)	
Smoking			
Yes	11 (10.3%)	7 (9.7%)	0.454
No	96 (89.7%)	65 (90.3%)	

ESRD: End-stage renal disease

Tablo 3. Binary logistic regression analysis for ındependent determinants of poor sleep quality

	MODEL-1 (FC) (forward conditional) R ^{2}=0.043			MODEL-2(FC) (forward conditional) R ^{2}=0.066		
	P	EXP(b)	95% cı	P	EXP(b)	95% cı
Age	0.009	0.964	(0.938-0.991)	0.014	0.966	(0.940-0.993)
Gender (female)	-------	------	------	0.049	1.910	(1.004-3.633)

The parameters with p <0.5 were included in the table.

DISCUSSION

In this study, which we conducted with approximately a 4-year follow-up of 179 predialysis CKD patients, we found that the prevalence of poor quality of sleep was 40.2%. In this study, we found that age and female gender are independent determinants of poor quality of sleep. In our study, a significant relationship was found between poor quality of sleep and mortality (P=0.05); 66.7% (8 of 12 patients) of patients who resulted in mortality during 4 years of follow-up were patients with poor quality of sleep.

In the studies conducted, the prevalence of sleep disorders detected based on surveys in predialysis chronic kidney patients shows a wide range of 14% - 85%.[20-24] The prevalence of poor quality of sleep in the patient group in our study was close to the middle of this range. This wide range may be due to patient population, lifestyle, socioeconomic status, genetics, method of assessing quality of sleep, geography and climate differences, CKD etiological causes, and comorbidities of patients rather than polysomnographic objective sleep measurements.

In their study, Ricardo et al. conducted the Pittsburgh quality of sleep index test on 431 patients followed for 5 years. In the study, they did not find a significant relationship between poor quality of sleep, insufficient sleep time, and the risk of ESRD. However, they found a significant relationship between insufficient sleep time and e-GFR decrease. In the study, it was found that daytime sleepiness, which was measured subjectively, was associated with a high risk of death for any reason. Epworth Sleepiness Scale was used to determine daytime sleepiness.[25] Sleep disorders (especially irregular breathing, restless legs syndrome, insomnia, and excessive daytime sleepiness) are common in ESRD patients and are associated with impaired quality of life and increased mortality.[26] In our study, a significant relationship was found between poor quality of sleep and mortality. During the 4-year follow-up, 66.7% of the patients who resulted in mortality consisted of CKD patients with poor quality of sleep.

Yamamoto et al. found a significant relationship between poor quality of sleep and ESRD in the study conducted prospectively with 1601 CKD patients by using the Pittsburgh quality of sleep index test. In addition, in this study, a significant relationship was found between short (<5 hours) and long sleep time (> 8 hours) with ESRD risk.[27] In our study, we did not find a significant relationship between poor quality of sleep and renal progression states such as ESRD, ESRD+mortality, and e-GFR ≥ 25 ml/min reduction. Shafi ST. et al. did not find a significant relationship between GFR reduction and quality of sleep in their study.[28] Kurella and Kumar, on the other hand, found a significant relationship between GFR reduction and quality of sleep in their studies with their friends.[20,29] In our study, no significant relationship was found between GFR reduction and quality of sleep. These discordant

findings may be related to the differences in the number and characteristics of the study population and the detection of exposure. There are several potential explanations for the relationship between insufficient sleep and a faster decline in e-GFR. Experimental sleep deprivation has been shown to cause acute increases in blood pressure and heart rate, activation of the sympathetic nervous system.[30] increased salt retention[31,32] and changes in glucose metabolism.[33] Indeed, in general populations, short sleep time (5-7 hours) has been associated with an increased risk for adverse outcomes, including hypertension[34] type 2 diabetes mellitus[35,36] and coronary artery disease. These are all CKD risk factors.

In an epidemiological study in the general population, sleep disorders were more common in women.[37] Similarly, in our study, our group with poor quality of sleep had a higher female/male ratio, and the female gender was an independent determinant of poor quality of sleep. In a study involving both predialysis CKD patients and patients receiving renal replacement therapy, female sex was found to be associated with lower quality of sleep.[38] In the study by Iliescu et al., there was no relationship between quality of sleep and gender.[39]

Some studies in CKD patients found a significant relationship between age and quality of sleep[23,40] while some studies did not find a relationship between age and quality of sleep.[38] Our study showed that the group with poor quality of sleep was older.

Although serum phosphorus levels were higher in the group with poor quality of sleep, it was not statistically significant. Calcium levels are similar in groups with both good quality of sleep and poor quality of sleep, but PTH was higher in those with good quality of sleep. In a study conducted by Sabbatini, no relationship was found between quality of sleep and PTH levels in various stages of CKD patients.[40] However, Liet et al. reported a relationship between calcium x phosphorus product with poor quality of sleep in patients receiving continuous outpatient peritoneal dialysis treatment.[41] One view of this relationship is that the high calcium x phosphorus product is associated with secondary hyperparathyroidism[42] coronary calcification, and increased cardiovascular mortality.[43] Insufficient quality of sleep in these patients may result from underlying vascular calcification and atherosclerosis. Another view is that increased calcium x phosphorus product or phosphorus causes itching[44] and itching causes poor quality of sleep.

In this study, BMI, waist circumference, SBP, PP, and albumin levels also differed significantly between the groups with good and poor quality of sleep. Waist circumference is an obesity measurement parameter and obesity can be a risk factor for progression to ESRD. A decrease in the amount of sleep can promote weight gain.[21] In healthy adults, short sleep has a significant effect on neuroendocrine control of appetite.[33] At the same time, obesity is the main cause of obstructive sleep apnea. Poor sleep can increase the risk and severity of hypertension.[21] Sleep deprivation can also disrupt the natural release of cardiac sympathovagal balance and plasma renin levels.

In some previous studies, BMI was found to be the independent determinant of quality of sleep in hemodialysis patients[45] and predialysis CKD patients.[23] The causal relationship between poor quality of sleep and obesity and hypertension may be bidirectional and become a vicious circle; the goal should be to break the loop. Data showing that improving quality of sleep may delay the progression of CKD;[43] requires the physician to consider modifiable factors related to poor quality of sleep such as high blood pressure, obesity, and increased waist circumference.

Limitations of the Study

There are some limitations to our study. First, we analyzed quality of sleep data using a subjective assessment, PSQI and used single time point measurements. The use of polysomnographic measurements prevents reporting bias and identifies certain forms of sleep disorders. It would also be better if a suitable control group was included. If 22 patients who were excluded from the study at the end of the 4-year follow-up were included in the study, it would increase the strength of our study.

The strength of our study is that it was performed in a homogeneous study population (only from patients with predialysis CKD and a single-center that prevents potential variability from different centers).

CONCLUSION

As a result, we determined that age and female gender are independent determinants of bad quality of sleep and bad quality of sleep increases mortality.

Our study has shown that pre-dialysis CKD patients have a high prevalence of poor quality of sleep and SBP, BMI, and waist circumference are potentially correctable factors.

In this study, it has been shown that medical treatments alone will not be sufficient to increase the quality of life of patients with CKD, and it will be beneficial to provide a good sleep quality and to correct the factors that impair sleep quality. There is a need for future studies to reassess quality of sleep by correcting the causes that impair quality of sleep.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study permit was obtained from University of Health Sciences Konya Training and Research Hospital Specialization in Medicine Training Board with the decision dated 05.12.2019 and numbered 48929119/774.
Informed Consent: All patients signed the free and informed consent form.
Referee Evaluation Process: Externally peer-reviewed.
Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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