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Original Research Article

Quality of Sleep in Early Chronic Kidney Disease Patients: A Cross Sectional Study

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Abstract: Sleep disorders and their etiology in dialysis population have received increasing attention over the last decade. However there occurrence in predialysis patients which bears highest burden of Chronic kidney disease (CKD) population, is still a neglected area. This study aimed to measure the prevalence of 'poor sleep' in early CKD patients (stage 2-4) and to examine the association between quality of sleep and various demographic and biochemical parameters. Quality of sleep was measured using the Pittsburgh Sleep Quality Index (PSQI) in 100 prevalent CKD Stage 2-4 patients and daytime sleepiness, using Epworth Sleepiness Score (ESS). Other biochemical parameters were reviewed from case-records of patients. Sixty-two subjects were 'poor sleepers' defined as a global PSQI score of >5.There was no statistically significant correlation between quality of sleep and blood urea and serum creatinine however 'Poor sleep' correlated significantly with age (p= 0.014), BMI (p= 0.020), anemia (p=0.013) and ESS score (p<0.001). 'Poor sleep' is common in predialysis population. Quality of sleep decreases in the early stages of CKD and does not appear to be associated with the subsequent degree of renal failure. Large prospective longitudinal studies of quality of sleep in CKD patients are needed to examine the association between deterioration of renal function and quality of sleep while controlling for potential confounding variables.
Keywords: Chronic kidney disease; pre-dialysis; poor sleepers; sleep disturbances

INTRODUCTION:

Sleep disorders have been extensively investigated in dialysis patients [1-4]. However there occurrence in predialysis patients which bears highest burden of CKD population, is still a neglected area. Only few studies have assessed occurrence of sleep problems in these patients. The reported prevalence of 'poor sleep', including increased latency of sleep, sleep-wake complaints, sleep disordered breathing and excessive daytime sleepiness, is in the range of 50–80% which is as common as in dialysis population [5-8]. The objectives of this study were to measure the prevalence of 'poor sleep' in a prevalent population of early CKD patients and to examine the association between quality of sleep and various demographic and biochemical parameters.

MATERIAL AND METHODS:

This was a cross-sectional study of prevalent patients attending the Nephrology clinic at Kothari medical and research institute, Bikaner. The study subjects were recruited during the regular visits over a 6 month period. Only CKD patients of stage 2 to 4 (as per defined by K-DOQI classification [10]) were screened for the study. Renal function parameters and the other variables were evaluated from case records, at the time of enrolment. Patients were excluded if follow up period prior to enrolment, was less than 3 months (to define irreversible renal damage), if they were <12 years of age, if they were known case of hypothyroidism, depression, COPD stage 3 or 4 or any other psychiatric disease or if they were not competent to give informed consent. Overall 119 patients were included in the study. Seventeen patients were excluded by different exclusion criteria (09 patients) or due to unavailability of necessary biochemical investigations (08 patients). Two patients refused to participate in the

study. Rest 100 patients were included in the study. Hindi version of PSQI score was used to assess sleep quality. Daytime sleepiness was assessed by Epworth Sleepiness Score.

Renal function:

The measurements of renal function were the blood urea level, the serum creatinine level and the estimated creatinine clearance calculated using the Cockcroft–Gault equation [9].Only stage 2-4 CKD patients, were included in the study.

Day time sleepiness:

Day time sleepiness is a subjective parameter to assess the sleep deprivation. Epworth sleep scale is a validated instrument to measure the daytime sleepiness and thus subjective quality of sleep. All patients were subjected to the Epworth sleepiness scale (ESS) questionnaire [11]. ESS was developed by researchers in Australia and is being widely used by sleep professionals around the world to measure sleep deprivation. The subjects are asked to rate on a scale of 0-3 the chances that as part of his "usual way of life in recent times", he would doze off in each of the 8 different situations. ESS score ranges from 0-24, normal range is 2-9.Higher the score, higher is the day time sleepiness.

Quality of sleep:

Quality of sleep was measured using the Pittsburgh Sleep Quality Index (PSQI) [12]. This self-administered questionnaire assesses quality of sleep during the previous month and contains 19 self-rated questions yielding seven components: subjective sleep quality sleeps latency, sleep duration, sleep efficiency, and sleep disturbance, use of sleep medications and daytime dysfunction. Each component is scored from 0 to 3, yielding a global PSQI score between 0 and 21, with higher scores indicating lower quality of sleep. A global PSQI score>5 indicates that a person is a 'poor sleeper' having severe difficulties in at least two areas or moderate difficulties in more than three areas.

Other variables:

Data regarding age, sex, educational level, associated co-morbidities, Erythropoietin and *i.v.* iron usage, hemoglobin, blood urea, serum creatinine, serum albumin were drawn by reviewing case records. BMI was directly measured.

STATISTICAL ANALYSIS:

The data collected from the subjects, analyzed using SPSS software version 17 for Windows. Student's *t*-test was used to compare the means of normally distributed variables between 'good sleepers' (global PSQI $\leq$5) and 'poor sleepers' (global PSQI >5), and the Mann–Whitney *U* test was used for variables that were not normally distributed. Differences among categorical variables were analyzed using the Chi-square or two-tailed Fisher's exact test as appropriate. Pearson correlation coefficients were used to examine associations between continuous variables. The level of significance was p=0.05 for all comparisons and correlation was labeled highly significance if p value was less than 0.001.

RESULTS:

Univariate analysis

Baseline characteristics of 100 recruited patients are shown in table 1. Male: female ratio was 58:42. Twenty, thirty seven and forty three patients belonged to CKD stage II, III and IV, respectively. Among associated co-morbidities, 89 patients were hypertensive among which 57 patients were hypertensive for more than 5 years duration, most likely suffering from hypertensive nephropathy. Thirty eight patients were diabetic, 33 patients had coronary artery disease, while 14 patients had history of cerebrovascular accident. Sixty two patients were 'poor sleepers' (global PSQI>5).Excessive daytime sleepiness (ESS score>9) was seen in 45 patients. Among PSQI domains, Subjective sleep quality and sleep latency were maximally affected.

Bivariate analysis:

Correlation PSQI domain with biochemical parameters

Characteristics of 'good' vs. 'poor' sleepers are shown in table 2. Compared to 'good sleepers' 'poor sleepers' comprised of older population, were obese and more patients had post secondary education, though results were not statistically significant. 'Poor sleep' quality group had statistically significant lower hemoglobin level. Although blood urea, serum creatinine and serum albumin level were also low, results were not statistically significant. More patients belonged to higher CKD stages but with poor statistical significance.

Table 1: Baseline demographic and laboratory of study population

Variable		**'n'**	**Mean (±SD)**
Age			48.18 (±14.50)
Sex	female	42	
	Male	58	
BMI			23.91 (±4.70)
CKD stage II/III/IV		20/37/43	
Post-secondary education		43	
Hypertension		89	
Diabetes		38	
Coronary artery disease		33	
Cerebrovascular accident		14	
Erythropoietin usage		26	
i.v. iron usage		24	
Hemoglobin (gm/dl)			10.44 (±2.19)
Blood urea (mg/dl)			88.12 (±31.39)
Serum creatinine (mg/dl)			3.06 (±1.29)
Serum albumin (gm/dl)			3.41 (±0.68)
ESS score			9.03±4.24
Global PSQI			8.60 (±5.30)
Subjective sleep quality			1.72 (±0.96)
Sleep latency			1.75 (±0.96)
Sleep duration			1.32 (±0.79)
Sleep efficiency			0.96 (±0.95)
Sleep disturbance			1.32 (±0.57)
Use of sleep medication			0.88 (±1.18)
Daytime dysfunction			0.69 (±0.96)

Table 2: Characteristics of 'good sleepers' compared with 'poor sleepers'

Variable	**"good sleepers" (PSQI score ≤ 5) n= 38**	**"poor sleepers" PSQI score >5) n= 62**	**p value**
Age(n)	43.66 (±15.32)	50.95 (±13.36)	0.014
Females(n)	18	24	0.412
BMI (kg/m^2)	22.53(±4.53)	24.76 (±4.63)	0.020
Post-secondary education(n)	14	29	0.407
CKD stage II(n)	12	08	0.051
CKD stage III(n)	14	23	0.051
CKD stage IV(n)	12	31	0.051
Hemoglobin (gm/dl)	11.13 (±1.97)	10.04(±2.22)	0.013
Blood urea (mg/dl)	82.29 (±28.65)	91.69 (±32.66)	0.147
Serum creatinine (mg/dl)	2.88 (±1.20)	3.17(±1.33)	0.276
Serum albumin	3.46 (±0.76)	3.39 (±0.65)	0.617
ESS score	5.66 (±1.51)	11.10 (±4.05)	<0.001

DISCUSSION:

Prevalence of 'poor sleep' in the present study was 62%. The results are in comparison to few studies done on predialysis population [5-8]. Also, similar prevalence has been found in dialysis patients [1-4]. Consideration is to be given to the fact that our study included only stage II to IV patients so that ESRD population wasn't confounding factor and still found similar prevalence of "sleep problems". In this regard, this study further strengthens the fact that sleep disorders originate early during course of disease and are not a manifestation of ESRD [5].

In this study "quality of sleep" was negatively affected by age, BMI and anemia. These factors are clearly associated with "poor sleep" in dialysis population [2, 13-16] and correction of anemia may improve quality of sleep and HR QoL [14-16]. However results are in contrast to study by Iliescu EA, which is till now the most comprehensive study available regarding predialysis population [8]. This study measured "quality of sleep" in 120 CKD patients, not on dialysis. Age, sex, BMI, BUN and serum creatinine were not associated with "poor quality of sleep". The presence of depression was the only significant predictor of decreased quality of sleep among the independent variables considered (odds ratio=3.07, p=0.026). However, in this study, almost half study population (59) comprised of ESRD group which is excluded from our study. Also, depressive patients were not considered in our study. So results of these 2 studies are not comparable.

Our study didn't find association between "quality of sleep" and renal function parameters (blood urea and serum creatinine). This is the most controversial aspect in regards to sleep disorders in CKD population. Studies in dialysis population have found clear association between these two variables while results in predialysis population are equivocal. Above mentioned study didn't find positive correlation. However, a 3year long prospective study by Sabbatini M *et al.;* [6], found that there was significant deterioration in quality of sleep with progression of renal disease ($p<0.0001$).

It is also to be highlighted that prevalence of sleep disorders are similar in both predialysis and dialysis population. Our study is first study to report relationship between "quality of sleep" and anemia and obesity (higher BMI) in early CKD population, so it is clearly evident that some common (mentioned above) as well as intrinsic factors other than uraemia, might also play role in genesis of sleep abnormalities in these patients. More longitudinal studies, focusing on pathogenesis of disease, are required to throw more light on this aspect.

In our study Epworth Sleepiness Score (ESS) positively correlated with poor quality of sleep with very high statistically significance. ESS is a tool to measure daytime sleepiness which in turn, indirectly reflects poor sleep during night [11].

Potential limitations of this study include its cross-sectional nature. Therefore, direction and causality cannot be inferred. Also, some potential confounding Variables, which could have affected "quality of sleep" in these patients, were not considered, including lifestyle habits, income, nutrition, use of anti-hypertensive medications, functional status, psychiatric syndromes and daily life stress. One of such factor, post secondary education was associated poorer sleep quality but it didn't reach statistically significant level. In our study, only known cases of depression were excluded, not taking into consideration of undiagnosed subjects and subjects with new onset of depression. This was potential confounding factor in study since depression is clearly associated with "poor quality" of sleep [08].

CONCLUSION:

In conclusion, the results of this study suggest that 'poor sleep' is common in CKD patients and that quality of sleep decreases in the early stages of CKD. We hypothesize that the causes of decreased quality of sleep in CKD patients are multiple and interrelated and probably not due uraemia, itself. Large prospective longitudinal studies of quality of sleep in CKD patients are needed to confirm the high prevalence of decreased quality of sleep in this population and examine the association between renal function and quality of sleep. Polysomnographic studies of CKD patients are needed to assess the prevalence of OSA and PLMS.

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