



BMJ Open Sleep quality and associated factors among patients with chronic kidney disease in Nigeria: a cross-sectional study

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ABSTRACT

Objective Poor sleep quality adversely affects the overall well-being and outcomes of patients with chronic kidney disease (CKD). However, it has not been well studied in Africans with CKD. We determined the prevalence of poor sleep quality and associated factors among patients with CKD.

Design This was a cross-sectional study that involved patients with CKD.

Settings The study was carried out in the outpatient clinic of nine hospitals in Nigeria.

Methods Sleep quality, depressive and anxiety symptoms and quality of life (QoL) were assessed among 307 patients with CKD using Pittsburgh Sleep Quality Index Questionnaire, Hospital Anxiety Depression Scale Questionnaire and 12-item Short Form Health Survey Quality of Life Questionnaire, respectively. The prevalence of poor sleep quality and associated factors were determined. A $p < 0.05$ was considered as statistically significant.

Results The mean age of the study participants was 51.40 ± 15.17 years. The male:female ratio was 1.5:1. One hundred and twenty-one (39.4%) of the patients were on maintenance haemodialysis (MHD). The prevalence of poor sleep quality, anxiety symptoms and depressive symptoms among the patients was 50.2%, 37.8% and 17.6%, respectively. The prevalence of poor sleep quality in the CKD stages 3, 4, 5 and 5D was 38.1%, 42.6%, 52.2% and 58.7%, respectively. The prevalence of poor sleep quality was significantly higher in MHD patients compared with predialysis CKD (59.5% vs 43.6%; $p = 0.008$). Factors associated with poor sleep quality were CKD stage ($p = 0.035$), anaemia ($p = 0.003$), pruritus ($p = 0.045$), anxiety symptoms ($p \leq 0.001$), depressive symptoms ($p \leq 0.001$) and reduced QoL ($p \leq 0.001$). On multivariate analysis, factors associated with poor sleep were anxiety (AOR 2.19; 95% CI 1.27 to 3.79; $p = 0.005$), anaemia (AOR 5.49; 95% CI 1.43 to 21.00; $p = 0.013$) and reduced physical component of QoL (AOR 4.11; 95% CI 1.61 to 10.47; $p = 0.003$).

Conclusion Poor sleep quality is common among patients with CKD especially in the advanced stage. The significant factors associated with poor sleep quality were QoL, anaemia and anxiety symptoms. These factors should be adequately managed to improve the overall outcomes of patients with CKD.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The study provided evidence on the need to routinely assess sleep quality in patient with chronic kidney disease in Nigeria.
- ⇒ A validated, but subjective method of assessment of sleep quality was used.
- ⇒ Participants provided responses about their previous sleep experiences which could introduce recall bias.

INTRODUCTION

Chronic kidney disease (CKD) is a chronic illness that has a negative impact on physical, mental, economic well-being and quality of life (QoL) of the patients, their caregivers and family members.^{1–3} The quality and duration of sleep are factors that affect both physical and mental well-being of individuals.^{4,5} Sleep deprivation is associated with adverse cardiovascular, endocrine, metabolic and inflammatory consequences in the general population.⁶ Previous studies established the association between duration of sleep, cardiovascular outcomes and mortality.^{7,8}

Poor sleep quality is common in both predialysis patients with CKD and those with end-stage renal disease (ESRD) on renal replacement therapy (RRT).^{9–14} Previous reports showed that the prevalence of poor sleep quality in patients with CKD was between 37% and 87%.^{9–14} It is caused by interplay of multiple factors in patients with CKD. These factors include medication side effects, high level of daytime melatonin, tyrosine deficiency, uraemia, stress, anxiety, depression, restless leg syndrome and change in normal body temperature rhythm and dialysis treatment.¹⁵

Poor sleep quality has been identified as a novel cardiovascular risk factor for development and progression of CKD.^{16,17} Sleep

disturbances and deprivation are associated with increase in sympathetic nervous system stimulation, heart rate, fluid retention, blood pressure, vascular non-compliance, endothelial dysfunction, which may cause progression of CKD to ESRD.¹⁶

Despite the impact of sleep quality on overall well-being and outcomes of patients with CKD, it has not received the deserved attention in CKD management. Mental well-being of patients with CKD which includes sleep quality is not routinely assessed during their evaluation and management. This leads to loss of opportunity for intervention, which may improve their overall outcomes. Presently, there are limited data on sleep quality among patients with CKD in Africa including Nigeria.¹⁸

The aim of this study was to determine the prevalence of poor sleep quality and associated factors among patients with CKD. The information from this study will provide the basis to advocate for regular mental health evaluation in CKD management with the aim of improving their overall QoL and outcomes.

MATERIALS AND METHODS

Study design

This was a cross-sectional study that was conducted over a 9-month period between September 2021 and May 2022. The study was carried out among patients with CKD in the nephrology departments of nine hospitals in seven States of Nigeria.

Sample size calculation

The sample size was determined using the formula for single proportion.¹⁹ The prevalence of poor sleep quality in patients with CKD used in this calculation was 77.8% based on report from a previous study.¹² The confidence interval was taken as 95% and the power of the study was 80%. The minimum sample size for this study was 293 after including 10% attrition.

Study participants

Participants for this study were selected from the nephrology departments of nine participating health institutions, which were conveniently selected. These institutions were located in 7 out of 36 states in Nigeria and representing both Southern and Northern regions of the country. Sample size for each institution was determined using proportional allocation that was based on their respective patient population, which ranged from 30 to 150. Within the respective nephrology department, patients were selected using systematic sampling with the weekly patient population list serving as the sampling frame. Only those who met the inclusion criteria were recruited for the study after screening.

Inclusion criteria for the study were stages 3–5 patients with CKD determined by Kidney Disease Improving Global Outcome classification guideline who were yet to commence maintenance dialysis, patients with CKD who were receiving maintenance haemodialysis (MHD)

in the hospital, and the absence of established diagnosis of mental health illness. Clinically unstable patients with CKD and those with acute illness were excluded from the study.

A researcher-administered questionnaire was used to obtain sociodemographic and clinical information from study participants. The 12-item Short Form Health Survey (SF-12) questionnaire was used to assess QoL while the Health Hospital Anxiety and Depression Scale were used to assess study participants for anxiety and depressive symptoms.^{20–21} Sleep qualities of study participants were assessed with Pittsburgh Sleep Quality Index (PSQI).²² PSQI contains 24 questions and seven components (first component: subjective sleep quality, second component: sleep latency, third component: sleep duration, fourth component: habitual sleep efficiency, fifth component: sleep disturbances, sixth component: use of sleeping medication, seventh component: daytime dysfunction). In every domain of the scale, scoring was performed within a range of 0–3. The sum of the scores of these seven components constituted the total index score. High scores indicated that sleep quality is impaired. In this scale, the total value can be between 0 and 21. Good quality was defined as PSQI score of 0–5 while poor quality sleep was defined as PSQI score ≥ 6 .²²

The SF-12 is a multipurpose short form survey with 12 questions that assesses mental and physical functioning and overall health-related QoL. Reverse scoring was done for 4 items after which 35 indicator variables were created. Weighting of indicator variables and computation of aggregate scores for physical and mental summary scales were done. Each summary scale score was transformed to the norm-based scoring. A formal check of the accuracy of scoring was done to eliminate errors. Reduced QoL score was taken as value less 50.²³

Hospital Anxiety and Depression Scale is a 14-item scale. Each item was scored from 3 to 0 ('yes definitely' to 'not at all') with reversal of the scoring system for items 7 and 10. Anxiety score was based on items 2, 4, 6, 8, 11, 12 and 14 while depression score was based on items 1, 3, 5, 7, 9, 10 and 13. The total score range for both anxiety and depressive symptoms is 0–21. Non-case is designed as score of 0–7, borderline case as score of 8–10 and case as score of ≥ 11 . CKD stage was based on Kidney Disease Improving Global Outcomes.²⁴ Anaemia was defined as packed cell volume less than 36%.²⁵

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Data analysis

Data generated were analysed using the SPSS V.21.0. Missing data for individual variables occurred randomly and was less than 5%. These were automatically excluded during data analysis. Discrete variables were presented as frequency and percentages. Continuous variables were

presented as means and SD. Subgroup analysis was done between predialysis and dialysis patients using χ^2 was used to find association between categorical variables. Multi-variable logistic regression analysis was used to determine factors associated of poor sleep quality. A $p < 0.05$ was considered as statistically significant.

RESULTS

Three hundred and seven patients with CKD with a mean age of 51.40 ± 15.17 years participated in this study. The male:female ratio was 1.5:1. About half of the patients had tertiary education while 68.7% were married. Forty-six per cent of the participants were between ages 40 and 60 years while majority (81.4%) were employed. Among the patients with CKD, 63 (20.5%) had CKD stage 3, 54 (17.6%) had CKD stage 4, 69 (22.5%) had CKD stage 5 while 121 (39.4%) had CKD stage 5D. The common aetiologies of CKD in this study were hypertension (34.5%), diabetes mellitus (25.7%) and chronic glomerulonephritis (21.2%) (table 1).

The prevalence of poor sleep quality was significantly higher in MHD patients compared with predialysis CKD (59.5% vs 43.6%; $p = 0.008$). Also, depression was significantly higher in the MHD patients (23.8% vs 13.3%; $p = 0.022$). Reduced QoL was also significantly lower in the MHD group compared with the predialysis CKD group ($p < 0.001$) (table 2).

The prevalence of poor sleep quality in the CKD stages 3, 4, 5 and 5D was 38.1%, 42.6%, 52.2% and 58.7%, respectively. Significant factors associated with poor sleep quality were anaemia ($p = 0.003$), pruritus ($p = 0.045$), CKD stage ($p = 0.035$), anxiety ($p \leq 0.001$), depression ($p \leq 0.001$) and reduced QoL ($p \leq 0.001$) (table 3).

A higher proportion of patients on MHD had score of 2 points and 3 points when compared with predialysis patients with CKD for the various components of the sleep quality assessment (figure 1).

On multivariate analysis, factors associated with poor sleep were anxiety (AOR 2.19; 95% CI 1.27 to 3.79; $p = 0.005$), anaemia (AOR 5.49; 95% CI 1.43 to 21.00; $p = 0.013$) and reduced physical component of QoL (AOR 4.11; 95% CI 1.61 to 10.47; $p = 0.003$) (table 4).

DISCUSSION

This study determined the prevalence of poor sleep quality and associated factors among patients with CKD. Poor sleep quality was found in about half of the patients with CKD and was more common in those with advanced CKD. The significant factors associated with poor sleep among the patients with CKD were QoL, anaemia and anxiety symptoms.

The prevalence of poor sleep quality in this study was 50.2% which is significantly higher than 25.7% reported among the general population in Nigeria by Ogunsemi *et al.*²⁶ The finding of this study suggests that CKD is associated with poor sleep quality. The prevalence of poor sleep

Table 1 Sociodemographic parameters of study participants (N=307)

Characteristic	n (%)
Age (years)	
Mean age	51.40±15.17 years
<40	76 (24.8)
40–60	141 (46.1)
>60	89 (29.1)
Gender	
Male	185 (60.3)
Female	122 (39.7)
Level of education	
No education	7 (2.3)
Primary	37 (12.1)
Secondary	95 (30.9)
Tertiary and above	157 (51.1)
Not stated	11 (3.6)
Marital status	
Single	52 (16.9)
Married	211 (68.7)
Widow	23 (7.5)
Separated	7 (2.3)
Divorced	2 (0.7)
Not stated	12 (3.9)
Aetiology of CKD	
Hypertension	106 (34.5)
Diabetes mellitus	79 (25.7)
Chronic glomerulonephritis	65 (21.2)
HIVAN	17 (6.6)
ADPKD	13 (4.2)
Obstructive uropathy	10 (3.3)
SLE	7 (2.3)
Others	10 (3.3)
CKD stage	
3	63 (20.5)
4	54 (17.6)
5	69 (22.5)
5D	121 (39.4)
ADPKD, autosomal dominant polycystic kidney disease; CKD, chronic kidney disease; HIVAN, HIV-associated nephropathy; SLE, systemic lupus erythematosus.	

quality in this study falls between 37% and 87% that has been reported among CKD population in some previous studies.^{9–14, 27} The prevalence in this study is higher than 37% and 36.2% reported by Yamamoto *et al.*⁹ and Tu *et al.*²⁷ respectively. However, it is lower than 68.6% and 87% reported by Zubair and Butt²⁸ and Edalat-Nejad and Qlich-Khani,¹⁴ respectively. These differences may be

Table 2 Comparison between predialysis and maintenance HD patients

	Predialysis CKD group (n=181) n (%)	Maintenance HD group (n=126) n (%)	P value
Sleep quality			
Good	102 (56.4)	51 (40.5)	0.008
Poor	79 (43.6)	75 (59.5)	
Depression			
Present	24 (13.3)	30 (23.8)	0.022
Absent	157 (86.7)	96 (76.2)	
Anxiety			
Present	60 (33.1)	56 (44.4)	0.055
Absent	121 (66.9)	70 (55.6)	
Quality of life (PCS)			
Reduced	61 (33.7)	68 (54.0)	<0.001
Not reduced	120 (66.3)	58 (46.0)	
Quality of life (MCS)			
Reduced	55 (30.4)	57 (45.2)	<0.001
Not reduced	126 (69.6)	69 (54.8)	

CKD, chronic kidney disease; HD, haemodialysis; MCS, Mental Component Score; PCS, Physical Component Score.

partly related to the differences in clinical characteristics of the study population. While Tu *et al*²⁷ included patients with CKD in early stages, that is, stages 1 and 2, Edalat-Nejad and Qlich-Khani¹⁴ and Zubair and Butt²⁸ studied patients who were only on MHD. This study involved both predialysis patients with CKD in stages 3–5 and patients with ESRD on MHD. Other factors that may contribute to these varied prevalence rates in the various studies are differences in the sociodemographic characteristics, behavioural factors, environmental factors and method of assessment of sleep quality.

There was a significant association between the prevalence of poor sleep quality and CKD stage in this study. This agrees with a report that showed increasing trend in the prevalence of poor sleep quality across CKD stages.¹⁸ However, some previous studies did not find a significant association between poor sleep quality and renal function.^{10 27 29} In this study, the prevalence of poor sleep quality among predialysis CKD and MHD patients were 43.6% and 59.5%, respectively. In fact, the proportion of study participants with higher scores in the various components of the sleep quality assessment was more common in HD patients compared with predialysis patients with CKD. The significantly higher prevalence of poor sleep quality in the MHD patients is similar to report by Mujahid *et al*.³⁰ However, this finding is different from report of Shafi and Shafi¹¹ who did not find any significant difference in the prevalence of poor sleep quality between MHD and predialysis population.

Table 3 Factors associated with sleep quality among study participants (N=307)

	Good sleep quality PSQI scores 0–5 (n=153) n (%)	Poor sleep quality PSQI score ≥6 (n=154) n (%)	P value
Age (years)			
Mean age	51.48±15.52	51.32±14.87	
<40	38(50)	38(50)	0.638
40–60	67 (47.5)	74 (52.5)	
>60	48 (53.9)	41 (46.1)	
Gender			
Male	90 (48.6)	95 (51.4)	0.346
Female	63 (51.6)	59 (48.4)	
Category of patient			
Pre-HD	102 (56.4)	79 (43.6)	0.004
HD	51 (40.5)	75 (59.5)	
Stage of CKD			
3	39 (61.9)	24 (38.1)	
4	31 (57.4)	23 (42.6)	0.035
5	33 (47.8)	36 (52.2)	
5D	50 (41.3)	71 (58.7)	
Depressive symptoms			
Present	15 (27.8)	39 (72.2)	<0.001
Absent	138 (54.5)	115 (45.5)	
Anxiety symptoms			
Present	39 (33.6)	77 (66.4)	<0.001
Absent	114 (59.7)	77 (40.3)	
Quality of life (PCS)			
Reduced	48 (31.4)	81 (52.6)	<0.001
Not reduced	105 (68.6)	73 (47.4)	
Quality of life (MCS)			
Reduced	108 (70.6)	75 (48.7)	<0.001
Not reduced	45 (29.4)	79 (51.3)	
Anaemia			
Present	138 (47.8)	151 (52.2)	0.003
Absent	15 (83.3)	3 (16.7)	
Pruritus			
Present	22 (36.1)	39 (63.9)	0.045
Absent	129 (53.5)	112 (46.5)	

CKD, chronic kidney disease; HD, haemodialysis; MCS, Mental Component Score; PCS, Physical Component Score; PSQI, Pittsburgh Sleep Quality Index.

Majority of HD patients in Nigeria are not optimally dialysed due to financial cost of RRT which is beyond their reach.^{31 32} Suboptimal dialysis may contribute to higher prevalence of poor sleep quality in MHD patients

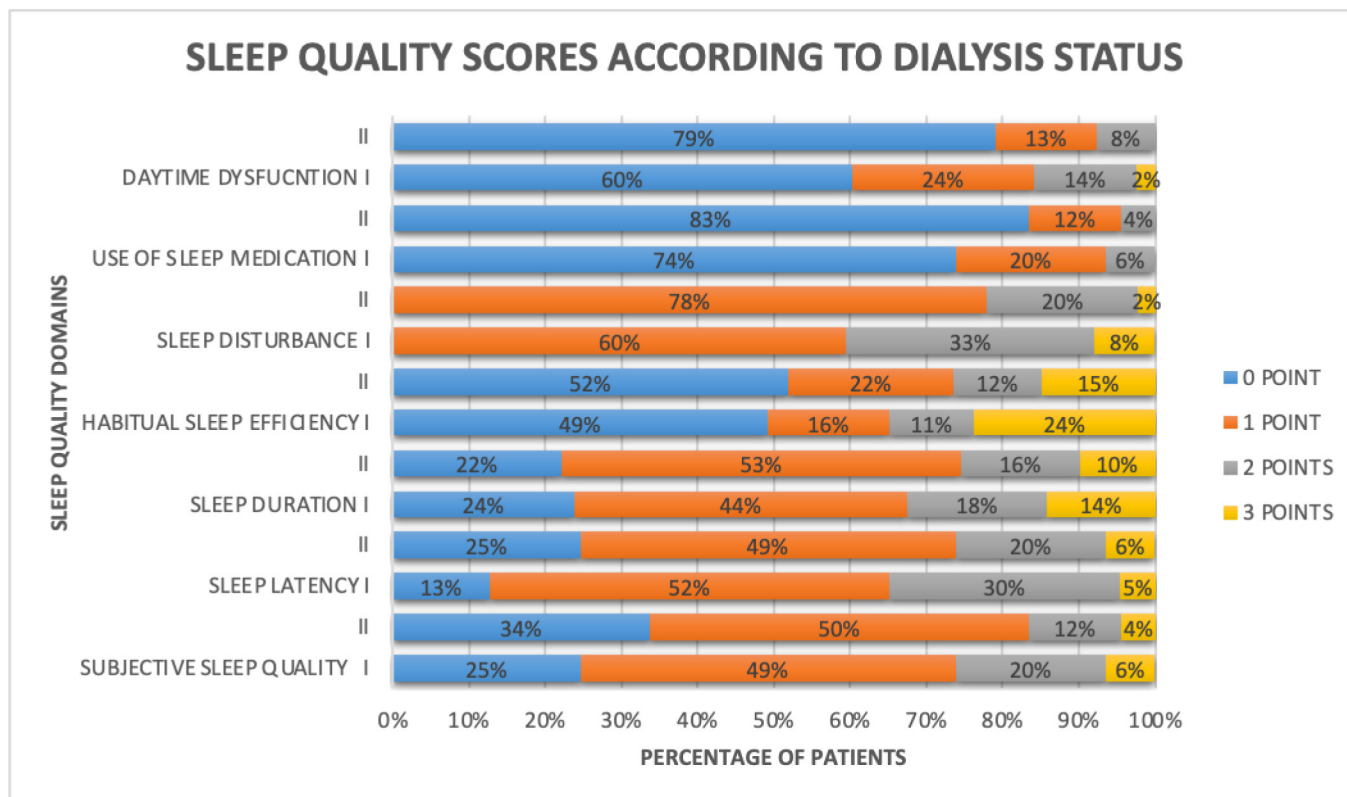


Figure 1 Sleep quality scores according to dialysis status. CKD, chronic kidney disease.

in this study which is similar to a report by Terzi *et al.*³³ Conditions such as pain, anxiety, depression which are more common in HD patients may also have significantly contributed to the higher prevalence of poor sleep quality compared with predialysis patients.^{2 34} In addition, patients with advanced stages of CKD especially those on MHD usually have elevated levels of inflammatory cytokines, orexin and reduced level melatonin which can cause sleep disturbances by altering the circadian rhythm.^{35–37}

There was a significant association between poor sleep quality, anxiety and depressive symptoms. This is similar to findings from some previous studies.^{12 27 38–42} Those with anxiety were twice more likely to have poor sleep quality compared with those without anxiety. The significant association between poor sleep quality, depression and anxiety may be related to the fact that sleep disturbances are common features of both depression and anxiety. This underscores the need to routinely assess patients with CKD for depressive and anxiety symptoms. There are both non-pharmacological and pharmacological interventions which have been reported to be useful in the management of these conditions in patients with CKD.^{41 43} Early diagnosis and management of anxiety and depressive illness in patients with CKD may improve their sleep quality.

There was no significant difference in the prevalence of poor sleep quality between male and female patients with CKD in this study. This is similar to reports from some previous studies.^{11 13 14 35} However,

this finding is at variance to the report of some other studies that reported significantly higher prevalence of poor sleep quality in female patients with CKD.^{28 29 39} Also, there was no significant association between poor sleep quality and age in this study. This is similar to some previous reports.^{13 18 27 29} Older age was reported to be significantly associated with sleep quality in some previous studies.^{12 28 38} The findings in this study suggest that sleep quality should be assessed in patients with CKD irrespective of their sociodemographic characteristics.

Poor sleep quality was associated with anaemia in our study. Patients with CKD with anaemia had sixfold increased risk of having poor sleep quality in this study. This is in keeping with previous reports.^{11 12 39 44 45} Carneiro *et al.*³⁸ reported no association between anaemia and sleep quality in HD patients. However, this difference may be due to the relatively small sample size in their study. The link between sleep quality, insomnia and anaemia is not well understood. However, a plausible explanation is that anaemia is associated with fatigue which may lead to poor quality of sleep.

There was an association between mental and physical components of QoL and poor sleep quality in this study, which agrees with some previous reports.^{14 29} Pruritus was found to be significantly associated with poor sleep quality. This is corroborated by the report of systematic review by Huang *et al.*⁴² that showed that pruritus is one of the significant factors associated with poor sleep quality among patients with CKD. This finding is not surprising because

**Table 4** Factors associated with sleep quality among study participants (n=307)

	AOR (95%CI)	P value
Age		
≤40 years (ref)	1	
>40 years	1.18 (0.65 to 2.16)	0.591
Gender		
Male (ref)	1	
Female	0.85 (0.51 to 1.44)	0.555
Anxiety symptoms		
Absent (ref)	1	
Present	2.19 (1.27 to 3.79)	0.005
Depressive symptoms		
Absent (ref)	1	
Present	2.03 (0.96 to 4.29)	0.064
Pruritus		
No (ref)	1	
Yes	1.77 (0.94 to 3.35)	0.080
Anaemia		
Absent (ref)	1	
Present	5.49 (1.43 to 21.00)	0.013
CKD stage		
3 (ref)	1	
4	1.04 (0.45 to 2.39)	0.924
5	1.09 (0.49 to 2.43)	0.838
5D	1.06 (0.50 to 2.26)	0.871
Quality of life (PCS)		
Not reduced (ref)	1	
Reduced	4.11 (1.61 to 10.47)	0.003
Quality of life (MCS)		
Not reduced (ref)	1	
Reduced	1.51 (0.82 to 2.76)	0.188

AOR, Adjusted Odd Ratio; CKD, chronic kidney disease; MCS, Mental Component Score; PCS, Physical Component Score.

pruritus-induced scratching may cause sleep interruption and poor sleep quality. The systematic review by Huang *et al*⁴² also reported an association between sleep quality in patients with CKD, gastrointestinal symptoms, anthropometric indices, cardiovascular risk factors such as blood pressure, dyslipidaemia which were not considered in this study.

Surprisingly, sleep quality is not routinely assessed in the management of patients with CKD despite its high prevalence among this population and the adverse impact on them.^{9 12 46 47} In a prospective study that involved 11 351 dialysis patients from seven countries, poor sleep quality was found to be associated with higher risk of mortality.⁴⁷ Poor sleep quality was found to be associated with markers of cardiovascular

damage such left ventricular hypertrophy, early and late diastolic peak flow ratio in predialysis patients.¹² It also contributed to cardiac autonomic dysfunction in these patients.³ Yamamoto *et al*⁹ reported that poor sleep quality is associated with progression of CKD to ESRD in a prospective study involving 1601 predialysis patients. Possible mechanisms for this association include activation of sympathetic nervous system, dysregulation of renin–angiotensin–aldosterone pathway and increased arterial wall stiffness.¹⁶ It also predisposes to other known cardiovascular risk factors such as hypertension, diabetes and obesity which may contribute to CKD progression. Therefore, it is expedient that sleep quality be regularly assessed in patients with CKD and necessary intervention be put in place to improve the sleep quality and overall outcomes in these patients. Both non-pharmacological and pharmacological interventions have been shown to improve sleep quality in CKD. For instance, a randomised control trial by Chen *et al*⁴⁸ showed that cognitive–behavioural therapy improved the sleep quality in patients on MHD possibly by reducing levels of inflammatory markers such as interleukin-18 and C reactive protein. Pharmacological treatment with exogenous melatonin has been reported to improve sleep quality in patients on MHD.^{49 50}

The limitation of the study was that sleep quality was assessed using Pittsburgh Sleep Quality questionnaire; a validated but subjective method of assessment compared with the use of polysomnography which is an objective method of assessment. Second, the study participants provided responses about their previous sleep experiences which could have introduced recall bias. Third, chronic peritoneal dialysis patients were not part of this study because the main mode of RRT in Nigeria are haemodialysis and kidney transplantation. Lastly, information such as iron deficiency which may be associated with restless leg syndrome with consequent effect on sleep quality among the study participants was not obtained. The strength of the study lies in the fact that it assessed sleep quality and its association with QoL and psychological problems such as anxiety and depression in some CKD population in Nigeria which has not been previously done. Also, it has provided evidence on the need to assess sleep quality among patient with CKD and institute appropriate care in routine clinical practice in Nigeria.

In conclusion, poor sleep quality is common among patients with CKD especially in the advanced stage. It was associated with advanced CKD (both stages 5 and 5D), pruritus, anaemia, reduced QoL and depressive and anxiety symptoms. Sleep quality and other psychological problems such as anxiety and depression should be routinely assessed and managed appropriately in order to improve the overall outcomes of our patients with CKD.

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Contributors OA was involved in study design, data acquisition, data analysis, data interpretation and manuscript drafting. IRE was involved in study design, data acquisition, data analysis and data interpretation. MM was involved in study design, data acquisition, data analysis and data interpretation. OSO was involved in study design, data acquisition, data analysis and data interpretation. OCO was involved in study design, data acquisition, data analysis and data interpretation. AAA was involved in study design, data acquisition, data analysis and data interpretation. EIO was involved in study design, data acquisition, data analysis and data interpretation. SDA was involved in study design, data acquisition, data analysis and data interpretation. OGE was involved in study design, data acquisition, data analysis and data interpretation. JF was involved in study design, data acquisition, data analysis and data interpretation. AD was involved in study design, data acquisition, data analysis and data interpretation. MOO was involved in study design, data acquisition, data analysis and data interpretation. BO was involved in study design, data acquisition, data analysis and data interpretation. All authors revised and approved the final draft. OA is the guarantor of the study.

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Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study involves human participants and ethical approval for this study was obtained from the Human Research and Ethics and Committee of the Delta State University Teaching Hospital, Nigeria. The approval reference number was DELSUTH/HREC/2021/040/0549. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

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