International Urology and Nephrology (2020) 52:739–748
https://doi.org/10.1007/s11255-020-02416-y

NEPHROLOGY - ORIGINAL PAPER

The effects of depression and age on sleep disturbances in patients with non-dialysis stage 3–5 chronic kidney disease: a single-center study

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Received: 28 August 2019 / Accepted: 17 February 2020 / Published online: 2 March 2020

Abstract

Purpose Sleep disturbances have a negative impact on the prognosis of chronic kidney disease (CKD). However, information on the prevalence and predictors is limited. This study aimed to evaluate the prevalence and explore clinical factors affecting the quality of sleep in patients with non-dialysis CKD.

Methods Participants included 152 adult non-dialysis patients with stage 3–5 CKD. Demographic and clinical data were collected. Sleep quality and depression were assessed using the Pittsburgh Sleep Quality Index (PSQI) and Beck Depression Inventory (BDI), respectively. Sleep disturbances were defined as a PSQI score ≥ 5. Logistic regression was conducted to explore the independent factors of sleep disturbances. Clinical parameters were correlated with BDI scores using linear regression models.

Results The total prevalence of patients with sleep disturbances was 66.4%. Older age, higher BDI scores, lower estimated glomerular filtration rate (eGFR) changes per month (△eGFR/m) before the study, and lower serum magnesium levels were found in patients with sleep disturbances. BDI scores (odds ratio [OR] 1.224, 95% confidence interval [CI] 1.091–1.373, $p = 0.001$) and age (OR 1.041, 95% CI 1.013–1.069, $p = 0.003$) were independent predictors of sleep disturbances. Serum uric acid levels (β − 0.629, 95% CI − 1.244 to − 0.013, $p = 0.046$), △eGFR/m before the study (β − 0.454, 95% CI − 0.885 to − 0.024, $p = 0.039$), and daily protein intake (β − 0.052, 95% CI − 0.102 to − 0.002, $p = 0.043$) were negatively associated with BDI scores.

Conclusion A high overall prevalence of sleep disturbances was found in patients with non-dialysis stage 3–5 CKD. Depression, as a manageable predictor, should be managed, especially in elderly patients.

Keywords Chronic kidney disease · Pittsburgh Sleep Quality Index · Beck Depression Inventory · Sleep disturbances · Depression

Introduction

There is growing evidence that sleep disturbances may have adverse effects on the prognosis of patients with chronic kidney disease (CKD) [1–3]. Poor sleep quality was independently associated with decreased quality of life and higher mortality in hemodialysis (HD) and peritoneal dialysis (PD) patients [4, 5]. Compared to patients receiving dialysis, there are fewer studies focused on the prevalence and associated factors of sleep disorders in patients with non-dialysis CKD. Poor sleep quality promotes major risk factors for CKD, such as hypertension, diabetes, and cardiovascular disease, resulting in a rapid decline in renal function, rapid progression to end-stage renal disease (ESRD), and mortality [6–8]. Thus, a better understanding of sleep disturbances in patients with non-dialysis CKD may result in the development of various interventions to delay the progression of CKD.

Reduced sleep quality is a prominent lifestyle complaint and has a high prevalence in both dialysis and pre-dialysis patients with CKD [2, 9, 10]. Many studies have been conducted to explore risk factors related to sleep disturbances. Sex, depression, duration of dialysis, and hemoglobin levels were shown to be predictors of decreased sleep quality in HD patients [9]. Studies of PD patients showed reduced

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residual renal function (RRF), higher serum creatinine (Cr), higher serum magnesium (Mg), and higher serum ferritin were present in patients with excessive daytime sleepiness (EDS) [11]. However, there are limited studies of patients with non-dialysis CKD. The objective of this study was to estimate the overall prevalence of sleep disturbances and evaluate the clinical factors affecting the quality of sleep in patients with non-dialysis stage 3–5 CKD.

Material and methods

Subjects

We conducted a single-center cross-sectional study of patients with stage 3–5 CKD who were followed-up with at the outpatient clinic of the Nephrology Department of Tianjin First Center Hospital in Tianjin, China between November 2017 and October 2018. The exclusion criteria were patients who were aged < 18 or > 80 years, were undergoing renal replacement therapy, were using sedatives or hypnotics, were not willing to participate in the study, or had mental or psychiatric illness or unstable medical conditions that made them unable to complete the questionnaires.

Data collection

Baseline demographic including age, sex, Charlson comorbidity index, diabetes mellitus (DM) status, cardiocerebral vascular disease (CVD) history, smoking and drinking history, marital status, educational status, and original disease were filled out. Medication data on antihypertensive drug use, such as angiotensin converting enzyme inhibitors or angiotensin II receptor blockers (both combined as RAS inhibitors), calcium channel blockers, β receptor blockers, or diuretics, were recorded at the time the questionnaires were also filled out. DM was confirmed by medical records or oral glucose tolerance tests. CVD was defined by any of the following conditions: coronary heart disease, myocardial infarction, angioplasty, coronary artery bypass, heart failure, or stroke. Biochemical data, blood pressure, and body mass index were measured and collected in the morning during an outpatient visit within one week of the initiation of the study. Biochemical data, including hemoglobin (Hb), sodium (Na), potassium (K), chlorine (Cl), calcium (Ca), inorganic phosphorus (P), Mg, blood urea nitrogen (BUN), Cr, uric acid (UA), albumin (Alb), total cholesterol (TC), triglycerides (TG), and venous carbon dioxide (CO_2) were collected. The estimated glomerular filtration rate (eGFR) was calculated using the CKD Epidemiology Collaboration equation. The change in eGFR per month (△eGFR/m) was calculated using the eGFR values from the three months prior to the study initiation. Spot urine and 24-h urine samples were collected within one week of the initiation of the study. The degree of hematuria, according to the dipstick, were coded on a scale of 0–4 and recorded to the nearest 0.5. The 24-h urine protein, daily salt intake, and daily protein intake were calculated by measuring the protein, Na, BUN, and Cr levels in the 24-h urine samples.

Questionnaires

Enrolled patients were required to answer two questionnaires. The questionnaires were explained to all participants by a specially trained nurse before they were filled out. A Chinese version of the Pittsburgh Sleep Quality Index (PSQI) questionnaire, which was developed by Buysse et al., was used to assess the sleep quality of patients with CKD [12, 13]. The Beck Depression Inventory (BDI) questionnaire was used to estimate symptoms of depression.

The PSQI contained 19 self-rated questions grouped into seven components of sleep (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction). Each component was scored on a scale of 0–3, yielding a total score of 0–21. Higher scores indicated lower quality of sleep. Sleep disturbances were defined as a total PSQI score ≥ 5. The PSQI score has been widely used to assess sleep quality in both dialysis and pre-dialysis patients with CKD [9, 11, 14–17].

The BDI score has been used in CKD populations to measure depressive symptoms [9, 16, 18–20]. It contains 21 self-reported items. Each item is assigned a value from 0–3, in which 0 means the absence of a problem and 3 means the extreme severity of a problem, yielding a total score of 0–63. Higher scores indicate more severe depression.

Statistical analysis

Normally distributed continuous variables are presented as mean ± standard deviation, non-normally distributed continuous variables (△eGFR/m, Charlson comorbidity index, UB score of spot urine, and 24-h urine protein) are presented as medians and interquartile ranges, and categorical variables are presented as frequencies and percentages. Comparisons of continuous variables between two groups were analyzed using independent sample *t* tests or the Mann–Whitney *U* test, as appropriate. The chi-squared test was used for categorical variables. Univariate and multivariate logistic regression analyses were performed to derive the odds ratios (ORs) of clinical predictors of sleep disturbance in patients with CKD. The parameters with $p < 0.05$, according to the univariate model, were then added to the multivariate model. By setting smaller *p* values (using $p < 0.05$ instead of $p < 0.2$)

in the multivariate model selection, we avoided the inclusion of weak or non-covariates. The parameters predicting sleep disturbance were subjected to receiver operating characteristics (ROC), showing the area under the curve (AUC) with a 95% confidence interval (CI) and the cut-off point. The association between clinical parameters and BDI scores were analyzed using univariate and multivariate linear regression. All statistical analyses were conducted using SPSS version 22 (IBM, Japan) and STATA version 14 (StataCorp LP, College Station, TX, USA). A p value < 0.05 was considered statistically significant.

Results

Patient characteristics

A total of 152 patients were included in the study. Figure 1 shows the flow diagram of participant recruitment. The range of PDSI scores among patients with non-dialysis stage 3–5 CKD was 1–20 with a mean value of 6.64 ± 3.91. The total prevalence of patients with sleep disturbances in this cohort was 66.4% (101/152). Table 1 shows the clinical characteristics and laboratory data of all patients and compares differences between patients with and without sleep disturbances. For all patients, the mean age was 53.8 ± 15.5 years, 65.8% of the patients were men, the mean eGFR was 32.4 ± 15.7 mL/min/1.73m^2, and 16.4% and 15.1% of patients had a history of DM and CVD, respectively. The change of eGFR in the three months prior to the study initiation was relatively stable with a range of -1.01 to 1.27 mL/min/1.73m^2. The BDI scores ranged from 0 to 30 and the mean score was 5.48 ± 5.43. Compared with patients who did not experience sleep disturbances, older age (56.5 ± 14.8 vs. 46.3 ± 15.2, $p = 0.002$), higher BDI scores (6.65 ± 6.01 vs. 3.16 ± 2.92, $p < 0.001$), lower △eGFR/m (-2.00 [-1.00, 0.68] vs. 0.68 [-1.01, 1.97], $p = 0.040$), and lower serum Mg levels (0.88 ± 0.13 vs. 0.97 ± 0.19, $p = 0.045$) were present in the patients with sleep disturbances.

Independent predictors of sleep disturbances in patients with non-dialysis stage 3–5 CKD

As shown in Table 2, higher BDI scores (OR 1.209, 95% CI 1.091–1.339, $p < 0.001$), older age (OR 1.036, 95% CI 1.012–1.061, $p = 0.003$), lower △eGFR/m (OR 0.866, 95% CI 0.756–0.922, $p = 0.038$), and diuretic drug usage (OR 0.230, 95% CI 0.055–0.960, $p = 0.044$) were found to be associated with sleep disturbances after univariate logistic regression analysis. These four parameters were put into a multivariate model and only higher BDI score (OR 1.224, 95% CI 1.091 to 1.373, $p = 0.001$) and older age (OR 1.041, 95% CI 1.013–1.069, $p = 0.003$) appeared significant. BDI

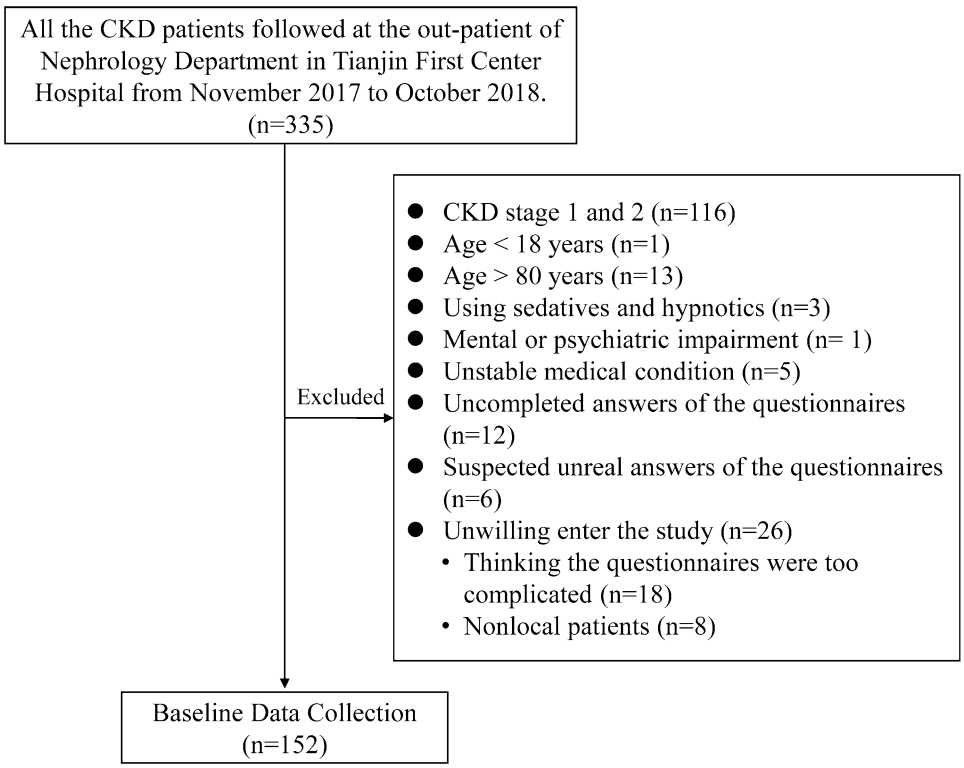

Fig. 1 Flow diagram of participant recruitment

Table 1 Clinical characteristics and laboratory data between sleep disturbance patients and non-sleep disturbance patients ($n=152$)

Characteristic	Total ($n=152$)	Sleep disturbance ($n=101$)	Non-sleep disturbance ($n=51$)	p value*
Age, year	53.8 ± 15.5	56.5 ± 14.8	48.3 ± 15.5	0.002
Gender, male, *n* (%)	100 (65.8%)	64 (63.4%)	36 (70.6%)	0.469
PSQI score	6.64 ± 3.91	8.52 ± 3.43	2.92 ± 1.09	< 0.001
BDI score	5.48 ± 5.43	6.65 ± 6.01	3.16 ± 2.92	< 0.001
Baseline eGFR, mL/min/1.73m^2	32.4 ± 15.7	32.7 ± 16.3	31.9 ± 14.5	0.768
△eGFR/m, mL/min/1.73m^2	0.00 [− 1.01, 1.27]	− 2.00 [− 1.00, 0.68]	0.68 [− 1.01, 1.97]	0.040
Charlson comorbidity score	2.00 [0.00, 3.00]	1.00 [0.00, 3.00]	2.00 [0.00, 3.00]	0.964
DM, *n* (%)	25 (16.4%)	16 (15.8%)	9 (17.6%)	0.819
CVD history, *n* (%)	23 (15.1%)	16 (15.8%)	7 (13.7%)	0.814
Smoking history, *n* (%)	47 (30.9%)	31 (30.7%)	16 (31.4%)	1.000
Drinking history, *n* (%)	43 (28.3%)	32 (31.7%)	11 (21.6%)	0.253
Marital status				0.259
Married, *n* (%)	136 (89.5%)	92 (91.1%)	44 (86.3%)	
Unmarried, *n* (%)	11 (7.2%)	5 (5.0%)	6 (11.8%)	
Divorced, *n* (%)	2 (1.3%)	1 (1.0%)	1 (2.0%)	
Widowed, *n* (%)	3 (2.0%)	3 (3.0%)	0 (0.0%)	
Educational status				0.693
Elementary school and below, *n* (%)	17 (11.2%)	12 (11.9%)	5 (9.8%)	
Junior high school, *n* (%)	59 (38.8%)	42 (41.6%)	17 (33.3%)	
High school, *n* (%)	31 (20.4%)	19 (18.8%)	12 (23.5%)	
College and above, *n* (%)	45 (29.6%)	28 (27.7%)	17 (33.3%)	
Original disease				0.835
Glomerulonephritis, *n* (%)	79 (52.0%)	53 (52.5%)	26 (51.0%)	
Diabetic nephropathy, *n* (%)	23 (15.1%)	14 (13.9%)	9 (17.6%)	
Hypertensive nephrosclerosis, *n* (%)	41 (27.0%)	27 (26.7%)	14 (27.5%)	
Others, *n* (%)	9 (5.9%)	7 (6.9%)	2 (3.9%)	
SBP, mmHg	139.1 ± 17.4	140.2 ± 16.7	136.8 ± 18.6	0.263
DBP, mmHg	87.4 ± 10.2	88.1 ± 10.9	86.2 ± 8.7	0.287
BMI, kg/m^2	24.9 ± 4.4	24.8 ± 4.2	25.2 ± 4.7	0.525
Blood parameters				
Hb, g/dL	12.4 ± 2.1	12.3 ± 2.3	12.5 ± 1.8	0.522
Na, mEq/L	140.4 ± 2.6	140.4 ± 2.6	140.6 ± 2.8	0.627
K, mEq/L	4.68 ± 0.70	4.67 ± 0.68	4.71 ± 0.74	0.758
Cl, mEq/L	103.4 ± 3.5	103.2 ± 3.4	103.8 ± 3.6	0.322
Ca, mg/dL	2.25 ± 0.23	2.23 ± 0.26	2.29 ± 0.16	0.153
P, mg/dL	1.23 ± 0.23	1.23 ± 0.23	1.22 ± 0.24	0.737
Mg, mg/dL	0.90 ± 0.15	0.88 ± 0.13	0.97 ± 0.19	0.045
BUN, mmol/L	12.3 ± 6.7	12.4 ± 6.8	12.0 ± 6.4	0.770
UA, mg/dL	6.58 ± 1.68	6.54 ± 1.75	6.68 ± 1.55	0.624
Alb, g/L	41.0 ± 5.4	41.4 ± 5.3	40.3 ± 5.7	0.268
TC, mmol/L	5.10 ± 1.38	5.09 ± 1.44	5.10 ± 1.28	0.999
TG, mmol/L	1.83 ± 1.20	1.87 ± 1.18	1.76 ± 1.25	0.687
CO_2, mEq/L	24.7 ± 3.4	24.7 ± 3.7	24.7 ± 2.8	0.963
UB score of spot urine	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00 [0.00, 1.00]	0.293
24-h urine protein, g/day	1.11 [0.32, 2.70]	0.99 [0.31, 2.88]	1.39 [0.34, 2.71]	0.728
Daily salt intake, g/day	3.88 ± 2.08	3.75 ± 2.30	4.14 ± 1.53	0.389
Daily protein intake, g/day	61.1 ± 22.1	58.1 ± 17.5	67.3 ± 28.9	0.055
Treatment				
RASi, *n* (%)	42 (27.6%)	24 (23.8%)	18 (35.3%)	0.178

Table 1 (continued)

Characteristic	Total ($n=152$)	Sleep disturbance ($n=101$)	Non-sleep disturbance ($n=51$)	p value*
CCB, *n* (%)	92 (60.5%)	60 (59.4%)	32 (62.7%)	0.728
β-Blocker, *n* (%)	48 (31.6%)	30 (29.7%)	18 (35.3%)	0.580
Diuretic, *n* (%)	9 (5.9%)	3 (3.0%)	6 (11.8%)	0.061

PSQI Pittsburgh Sleep Quality Index, *BDI* Beck Depression Inventory, *eGFR* estimated glomerular filtration rate, *ΔeGFR/m* eGFR change per month, *DM* diabetes mellitus, *CVD* cardiocerebral vascular disease, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *BMI* body mass index, *Hb* hemoglobin, *Na* sodium, *K* potassium, *Cl* chlorine, *Ca* calcium, *P* phosphorus, *Mg* magnesium, *BUN* blood urea nitrogen, *UA* uric acid, *Alb* albumin, *TC* total cholesterol, *TG* triglyceride, CO_2 venous carbon dioxide, *UB* urine blood, *RASi* RAS inhibitor, *CCB* calcium channel blocker, *β-blocker* β receptor blocker

*Independent sample *T* test or Mann–Whitney *U* test (△eGFR/m, Charlson comorbidity score, UB score of spot urine and 24-h urine protein) as appropriate

score showed a higher Wald value, which indicated it was a better predictor for sleep disturbances. The relationships between BDI and PDSI scores and between age and PDSI scores were plotted in Figs. 2 and 3.

Clinical factors associated with BDI scores

Linear regression analysis was used to assess the association of clinical factors with BDI score and the results are shown in Table 3. △eGFR/m (β −0.454, 95% CI −0.885 to −0.024, $p=0.039$), UA (β −2.028, 95% CI −1.244 to −0.013, $p=0.046$), and daily protein intake (β −0.052, 95% CI −0.102 to −0.002, $p=0.043$) showed significant inverse correlations with BDI score after multivariate analysis.

ROC analysis

For predicting sleep disturbances, the AUCs for BDI score and age were 0.690 (95% CI 0.603–0.772, $p<0.001$) and 0.657 (95% CI 0.564–0.750, $p=0.002$), respectively. The cut-off values for indicating sleep disturbances were BDI score > 5.5 and age > 51.5 years. The synergistic AUC for combining BDI score and age to predict sleep disturbances increased to 0.750 (95% CI 0.670–0.830, $p<0.001$). The ROC curves were plotted in Fig. 4.

Discussion

In the present study, we found that the overall prevalence of patients with sleep disturbances in the non-dialysis stage 3–5 CKD population with a mean eGFR 32.4 ± 15.7 mL/min/1.73m^2 was 66.4%. Depression and older age had a prominent impact on sleep quality. Serum UA levels, previous △eGFR/m, and daily protein intake were negatively associated with severity of depression.

The prevalence of sleep disorders reported by different studies varied greatly among many populations. In HD patients, 63.6–87% were reported as having sleep disorders by multiple studies [21–24]. He et al. [21] reported that sleep disturbances affected 63.6% of patients receiving maintenance HD who were > 40 years old when assessed by PSQI score. Another study found poor sleep was more common in HD patients, and the prevalence was as high as 87% when defined as total PSQI score ≥ 5 [24]. There were fewer studies focusing on PD patients than on HD patients. Li et al. [25] reported that the prevalence of continuous ambulatory peritoneal dialysis patients with sleep disorders was 47.6%. Another study showed that the prevalence of poor sleep quality, as defined by a PSQI score ≥ 5, was 74.49%, and daytime sleepiness occurred in 22.45% of prevalent PD patients [11]. Studies in patients with pre-dialysis CKD were even more limited, and the reported prevalence ranged from 14% to 84.6% [17, 26–29]. In the early stages of CKD, Ogna et al. [26] reported that moderate-to-severe sleep disordered breathing (SDB) occurred in 37.3% of patients and 15.3% had severe SDB. De Santo et al. [30] followed 220 patients with CKD for up to 4 years and found that sleep disturbances affected 84.6% of patients. Different populations, dialysis modalities and dosages, age ranges, comorbidities, ethnicities, and assessment methods resulted in inconsistent results. Our results are comparable with previous studies.

Patients with sleep disturbances were older and had higher BDI scores than patients without sleep disturbances. We also found that BDI scores and age were independent predictors of sleep disturbances according to logistic regression analysis. ROC analysis showed BDI scores > 5.5 and age > 51.5 years indicated sleep disturbances in patients with non-dialysis CKD in this cohort. Several studies have focused on discovering risk factors for poor sleep quality in dialysis patients [1, 31–33]. However, studies including only non-dialysis patients are still limited, even though eGFR has not been shown to be associated with sleep disorders [18].

Table 2 Associated clinical factors for sleep disturbances (PSQI ≥ 5) ($n = 152$)

Parameter	Univariate				Multivariate			
	Wald	OR	95% CI	*p* value	Wald	OR	95% CI	*p* value
BDI score	13.13	1.209	1.091–1.339	< 0.001	11.831	1.224	1.091–1.373	0.001
Age, year	8.883	1.036	1.012–1.061	0.003	8.533	1.041	1.013–1.069	0.003
Gender, male	0.782	0.721	0.349–1.489	0.376				
Baseline eGFR, mL/min/1.73m^2	0.089	1.003	0.982–1.025	0.766				
ΔeGFR/m, mL/min/1.73m^2	4.289	0.866	0.756–0.922	0.038	2.434	0.885	0.759–1.032	0.119
Charlson comorbidity score	0.172	0.679	0.799–1.157	0.679				
DM	0.080	0.878	0.358–2.153	0.777				
CVD history	0.118	1.183	0.453–3.090	0.731				
Smoking history	0.007	0.969	0.468–2.004	0.932				
Drinking history	1.690	1.686	0.767–3.709	0.194				
Marital status	0.000	1.006	0.530–1.907	0.996				
Educational status	1.061	0.839	0.601–1.172	0.303				
Original disease	0.049	1.039	0.742–1.454	0.825				
SBP, mmHg	1.256	1.011	0.991–1.032	0.262				
DBP, mmHg	1.137	1.019	0.985–1.054	0.286				
BMI, kg/m^2	0.409	0.975	0.903–1.053	0.522				
Hb, g/dL	0.415	0.995	0.979–1.011	0.520				
Na, mEq/L	0.240	0.968	0.848–1.104	0.624				
K, mEq/L	0.097	0.925	0.565–1.513	0.925				
Cl, mEq/L	0.051	0.951	0.860–1.050	0.321				
Ca, mg/dL	2.066	0.216	0.027–1.747	0.151				
P, mg/dL	0.114	1.312	0.273–6.309	0.735				
Mg, mg/dL	2.106	0.020	0.000–1.268	0.065				
BUN, mmol/L	0.087	1.008	0.957–1.061	0.769				
UA, mg/dL	0.244	0.951	0.778–1.162	0.621				
Alb, g/L	1.227	1.037	0.973–1.105	0.268				
TC, mmol/L	0.000	1.000	0.731–1.367	0.999				
TG, mmol/L	0.166	1.081	0.744–1.570	0.684				
CO_2, mEq/L	0.002	0.997	0.882–1.128	0.963				
UB score of spot urine	0.671	1.117	0.858–1.454	0.413				
24-h urine protein, g/day	0.001	1.002	0.884–1.136	0.974				
Daily salt intake, g/day	0.739	0.916	0.749–1.119	0.390				
Daily protein intake, g/day	3.083	0.981	0.959–1.002	0.079				
RASi	2.229	0.571	0.274–1.191	0.135				
CCB	0.158	0.869	0.435–1.737	0.691				
β-Blocker	0.489	0.775	0.379–1.584	0.484				
Diuretic	4.067	0.230	0.055–0.960	0.044	1.839	0.292	0.049–1.729	0.175

Normative aging is associated with a reduced ability to initiate and maintain sleep and sleep disruption is a common complication of "normal aging" [34]. Other studies have shown that advanced age is associated with sleep disturbances in patients with non-dialysis CKD, like the general population, which is consistent with our results [27, 35, 36]. Mounting evidences have indicated that depression dramatically affects sleep quality in patients with CKD [9, 37, 38]. A study including 326 patients with CKD (stage 1–5) who were not on dialysis showed that depressive symptoms, as assessed by BDI scores, were associated with sleep quality among patients with early-stage CKD [18].

Further analysis was conducted to explore the association of clinical factors for depression in patients with CKD. The results of this study showed that previous eGFR changes and serum UA levels were correlated with severity of depression.

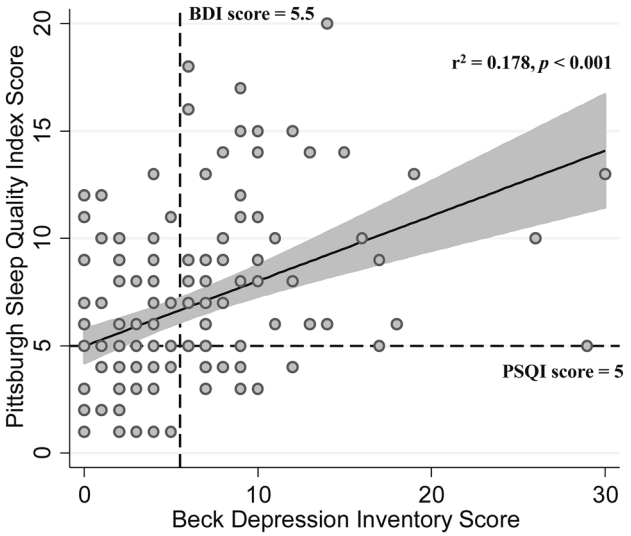

Fig. 2 Correlation between Pittsburgh Sleep Quality Index Score and Beck Depression Inventory Score. The BDI score showed a positive correlation with PDSI score in non-dialysis CKD patients with $r^2 = 0.178$, $p < 0.001$

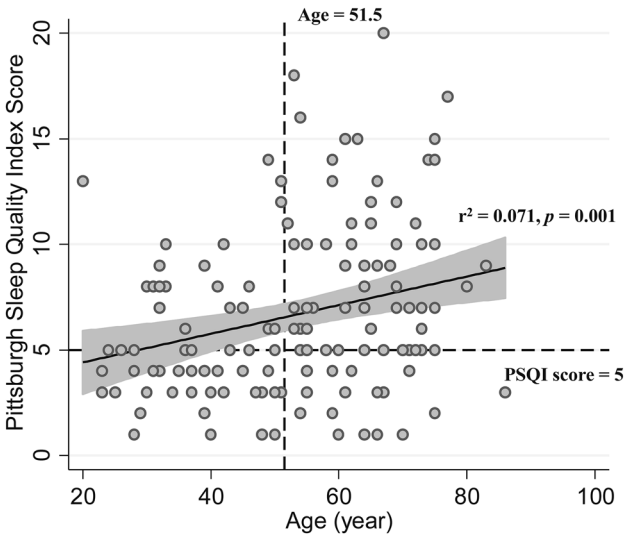

Fig. 3 Correlation between Pittsburgh Sleep Quality Index Score and age. Age showed a positive correlation with PDSI score in non-dialysis CKD patients with $r^2 = 0.071$, $p = 0.001$

However, this study did not prove that baseline eGFR and previous eGFR changes had an impact on sleep disturbances. McMullan et al. [6] conducted a large prospective study of middle-aged women with 11 years of follow-up and discovered that shorter sleep duration was significantly and independently associated with a rapid decline in renal function. The results of some studies [39–41] may provide an explanation for why sleep disturbances have detrimental effects on renal function of non-dialysis patients. Younger women who had a sleep duration of ≤ 5 h per night were more likely to develop hypertension by a hazard ratio of 1.20 compared with participants who reported a sleep duration of at least 7 h [39]. Patients with CKD who do not sleep well are more likely to develop DM [40]. In a large cohort of 6,834 participants, short sleep duration, especially ≤ 5 h, was shown to be a predictor of proteinuria [41]. Sleep disturbances were significantly associated with hypertension, diabetes, and proteinuria, which are the most important risk factors for progression of CKD. These result in a rapid decline of renal function that can be described as eGFR slope or ΔeGFR/m as used in our study. Our study showed that the change of eGFR in the 3 months before the study initiation was significantly inversely correlated with depression. Rapid deterioration of renal function may influence one's emotions. Patients with depression should be followed-up with to observe the longitudinal changes of renal function.

An interesting discovery of this study is the association of serum UA levels and depression, which, to our knowledge, is the first time this has been reported. Limited previous studies reported a relationship between serum UA and cognitive impairments in patients with CKD [42, 43]. A study of 247 patients with CKD had a mean Cr level of 239.0 ± 134.1 μmol/L [42]. Cognitive function was assessed using the Standardized Mini-Mental State Examination. The results showed that higher serum UA was associated with worse cognitive function. Another study reported a similar association in patients with CKD [43]. Our study demonstrated an inconsistent result. Serum UA levels were inversely correlated with BDI scores, indicating lower UA levels predict more severe depression. This inverse correlation between serum UA and depression has also been found in other populations, such as community-dwelling older adults with impaired fasting glucose or diabetes [44], patients with hypertension [45], the general population [46], and participants between the ages of 18–65 years from the general population [47]. Researchers have shown that oxidative stress plays an important role in depression [48]. Serum UA as an antioxidant could reduce oxidative damage to DNA. Decreased serum UA levels will induce increased production of ROS and may cause oxidative damage to the DNA, which may be involved in the pathogenesis of depression [46]. The exact effect of serum UA on depression in the CKD population needs to be further explored. We also found daily protein intake was negatively associated with BDI scores. A low protein diet is recommended for conservative management of CKD. In clinical practice, we should pay

Table 3 Linear regression for BDI score with clinical factors ($n = 152$)

Parameter	Univariate				Multivariate			
	β	T	95% CI	p value	β	T	95% CI	p value
Age, year	0.013	0.434	− 0.044 to 0.069	0.665				
Gender, male	− 1.608	− 1.744	− 3.431 to 0.214	0.083				
Baseline eGFR, mL/min/1.73m^2	− 0.029	− 1.048	− 0.085 to 0.026	0.296				
ΔeGFR/m, mL/min/1.73m^2	− 0.331	− 2.138	− 0.637 to − 0.025	0.034	− 0.454	− 2.097	− 0.885 to − 0.024	0.039
Charlson comorbidity score	− 0.472	− 1.936	− 0.954 to 0.010	0.055				
DM	0.431	0.361	− 1.924 to 2.785	0.718				
CVD history	− 0.412	− 0.334	− 2.848 to 2.024	0.739				
Smoking history	− 0.233	− 0.244	− 2.122 to 1.656	0.808				
Drinking history	− 0.735	− 0.750	− 2.670 to 1.201	0.454				
Marital status	− 0.178	− 0.213	− 1.835 to 1.479	0.832				
Educational status	0.121	0.279	− 0.738 to 0.981	0.780				
Original disease	0.350	0.796	− 0.518 to 1.217	0.427				
SBP, mmHg	− 0.025	− 0.994	− 0.076 to 0.025	0.322				
DBP, mmHg	− 0.003	-0.057	− 0.089 to 0.084	0.954				
BMI, kg/m^2	− 0.188	− 1.873	− 0.387 to 0.010	0.063				
Hb, g/dL	− 0.028	− 1.360	− 0.070 to 0.013	0.176				
Na, mEq/L	− 0.329	− 1.944	− 0.664 to 0.005	0.054				
K, mEq/L	0.499	0.770	− 0.783 to 1.782	0.443				
Cl, mEq/L	− 0.139	− 1.066	− 0.396 to 0.119	0.288				
Ca, mg/dL	− 3.476	− 1.727	− 7.457 to 0.505	0.086				
P, mg/dL	2.287	1.114	− 1.775 to 6.349	0.267				
Mg, mg/dL	3.125	0.539	− 8.492 to 14.741	0.592				
BUN, mmol/L	0.072	1.082	− 0.059 to 0.202	0.281				
UA, mg/dL	− 0.532	− 2.042	− 1.047 to − 0.017	0.043	− 0.629	− 2.028	− 1.244 to − 0.013	0.046
Alb, g/L	− 0.011	− 0.122	− 0.185 to 0.163	0.903				
TC, mmol/L	− 0.365	− 0.803	− 1.269 to 0.538	0.424				
TG, mmol/L	0.244	0.464	− 0.799 to 1.287	0.644				
CO_2, mEq/L	− 0.038	− 0.219	− 0.379 to 0.304	0.827				
UB score of spot urine	0.254	0.750	− 0.415 to 0.923	0.454				
24-h urine protein, g/day	− 0.178	− 1.089	− 0.503 to 0.146	0.278				
Daily salt intake, g/day	− 0.159	− 0.586	− 0.697 to 0.380	0.560				
Daily protein intake, g/day	− 0.055	− 2.207	− 0.105 to − 0.006	0.030	− 0.052	− 2.055	− 0.102 to − 0.002	0.043
RASi	− 0.039	− 0.039	− 1.991 to 1.914	0.969				
CCB	0.160	0.177	− 1.626 to 1.947	0.860				
β-Blocker	0.242	0.255	− 1.636 to 2.120	0.799				
Diuretic	− 0.392	− 0.210	− 4.092 to 3.307	0.834				

close attention to a low protein diet's impact on the symptoms of depression among patients with CKD.

The major limitation of this study was that it was a single-center study with a small sample size; its findings may be difficult to generalize to other populations. Although the present study provides promising evidence of clinical factors associated with sleep disturbances that may have adverse effects on the prognosis of CKD patients, more prospective, multicenter, large-scale trials in this field need to be conducted in the future.

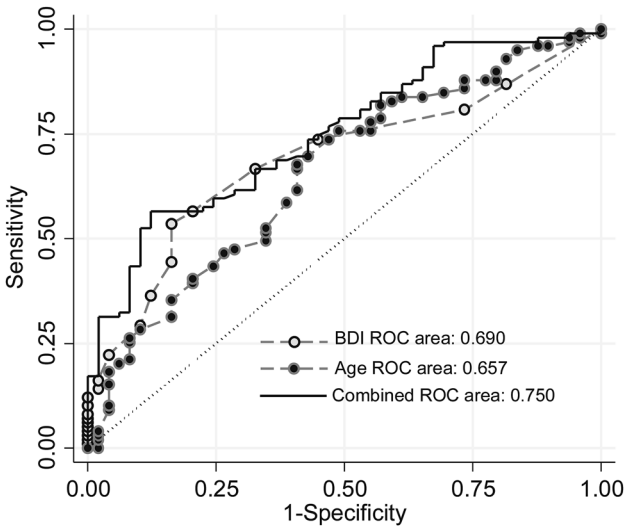

Fig. 4 ROC curves for BDI and age predicting sleep disturbances in non-dialysis stage 3–5 CKD patients

Conclusion

This study demonstrated a high overall prevalence of sleep disturbances in patients with non-dialysis CKD. Depression, as a manageable predictor, should be managed, especially in elderly patients.

Acknowledgements We thank all the doctors at the division of Nephrology in our hospital, Tianjin, China, for their work.

Author contributions YYH and WXC drafted the manuscript. XCW critically reviewed the manuscript. XYS and YL collected the data. WYZ critically reviewed data management. JPL performed English editing. WXC performed statistical analysis. YKT critically reviewed the statistical data. All authors read and approved the final manuscript.

Funding Tianjin Health Bureau funded this study (Grant No. A0102).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Tianjin First Center Hospital, 2015008S) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Written informed consent was obtained from each patient before the study began.

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