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PILL BURDEN, SLEEP QUALITY, ANXIETY, DEPRESSION IN PATIENTS WITH DIABETIC AND NON - DIABETIC CHRONIC KIDNEY DISEASE

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ABSTRACT:

Background: Chronic kidney disease (CKD) has a significant impact upon the quality of life of patients due to multiple factors. One of major stress is due to medication effects which may affect in patients with chronic kidney disease quality of life. In patients with chronic kidney disease, anxiety disorders are often perceived to represent the symptoms of depression and sleep disturbances.

Aim and objectives: Therefore the present study evaluated the role of Pill burden, sleep quality, anxiety and depression in patients with diabetic and Non -diabetic chronic kidney disease**.**

Materials and methods: The present study was conducted in 198 pre dialysis CKD patients of 1 to 5 stages with and without Diabetes mellitus**.** Sleep quality was assessed by using Pittsburgh Sleep Quality Index (PSQI) which is a standard self- reported scale for assessment of sleep quality. Anxiety and depression scores were calculated by using Hospital Anxiety and Depression scale (HADS).

Results: With increasing severity of disease burden, CKD patients were found to have more increase in pill burden, reduction in sleep quality, increase in anxiety and depression. This progression was found to be more significant in diabetic CKD patients when compared to non- diabetic CKD patients.

Conclusion: The present study findings conclude that patients with advanced stages of CKD experience a high symptom burden that impacts on their daily life. Diabetic CKD patients have been found to be more prone to altered sleep quality, anxiety and depression than non- diabetic CKD patients.

Keywords: Chronic kidney disease, Diabetes mellitus, Pill burden, sleeps quality, anxiety and depression.

INTRODUCTION

Chronic Kidney Disease (CKD) is progressive loss of kidney structure and function with an evidence of kidney damage with abnormal glomerular filtration rate (GFR) below 60 ml/min/1.73 m^2 body surface area for at least 3 months [1,2]. It is a worldwide public health problem and due to increasing incidence and prevalence, CKD is usually associated with high costs, poor outcomes and coexisting diseases such as hypertension and diabetes mellitus [3]. Management of CKD includes pharmacotherapy, dialysis, life style modifications, organ transplants and immunosuppressive therapy [4]. Chronic kidney disease patients have a high pill burden due to severe chronic illness along with multiple co morbidities such as hypertension and diabetes mellitus. Consequently, these patients have to take more number of pills on an average of 19-20 tablets/day [5, 6]. At the same time poly pharmacy is unavoidable because of multiple comorbid conditions [1]. Because of multiple co morbidities different classes of medications which includes secondary hyperparathyroidism medications such as Alfacalcidol and Cinacalcet; hypertensive medications like Alpha blockers, ACE inhibitors, Beta blockers, Calcium channel blockers (CCB'S) and Diuretics; cardio vascular medications such as anticoagulants, anti-platelets, antiarrhythmic and cholesterol-lowering drugs;

phosphate binders(non-calcium binders includes Sevelamer and Lanthanum; calcium binders involves Calcium acetate and Calcium carbonate) were administered to these patients which indirectly results in pill burden [7]. Patients with end-stage renal disease (ESRD) have various types of sleep disturbances ranging from 50% to 80% by subjective manner and in up to 50% of cases as objectively documented with polysomnography [8,9]. Assessment of quality of sleep is performed by using The Pittsburgh Sleep Quality Index (PSQI). It is a self-reported questionnaire that consists of 19 individual items, creating 7 components that produce global score ranging from 0 to 21. A lower score indicates healthier sleep quality. A score of 5 or greater is indicative of poor sleep quality and person is advised to maintain sleep hygiene and patient counseling to improve healthier sleep quality [10,11]. Anxiety and Depression are most common mood disturbances in chronic diseases and it may be due to physical and physiological illness, high number of medications for a longer duration, financial burden to continue treatment etc. Anxiety and depression scores are calculated by using Hospital Anxiety and Depression scale (HADS). The Hospital Anxiety and Depression Scale (HADS) is a widely used self-report measure for screening anxiety and depression in hospital, outpatient, and community settings. Total of 14 questions are included in HADS scale, in which 7 questions for Anxiety score and 7 questions for Depression score. A score 7 or <7 indicates the normal level, >7 indicates for abnormal i.e., anxiety or depression [12,13.] A few studies have reported that older CKD patients are significantly prone to restless sleep. Because SQ is a modifiable risk factor and there are implications that improving sleep quality can also cure anxiety and depression and improve quality of life [(14, 15)]. Hence, the present study determined the pill burden, sleep quality, anxiety and depression in chronic kidney disease patients with or without diabetes.

Materials and Methods:

A prospective study was conducted in 198 pre dialytic CKD patients in the department of nephrology at Sri Venkateswara Institute of Medical Sciences, Tirupati. The patients were recruited for the study based on inclusion and exclusion criteria after obtaining the written inform consent from patient's or their guardian. The study included CKD patients of stages 1 to 5 with diabetes(n=98) and without diabetes(n=100) in pre dialytic stage. Based on severity of disease CKD patients were sub grouped as stage 1 and 2 are considered as mild, stages 3 and 4 as moderate and stage 5 patients as severe group. Non-diabetic CKD patients were further sub divided into three groups as Mild stage patients (n=31), Moderate stage patients (n=38) and Severe stage patients (n=31). Diabetic CKD patients were further sub divided into three groups as Mild stage patients (n=30), Moderate stage patients (n=38) and Severe stage patients (n=30). The study excluded dialysis and transplant patients, Pregnant and lactating women, Pediatric age group and those who were unwilling to participate in study. Demographic details such as age, gender, diagnosis, co morbid conditions, and number of medications per prescription were obtained from patient medical records. Sleep quality score was assessed by using Pittsburgh sleep quality index (PSQI). The obtained score of each patient was categorized into mentioned groups and mean of each group is used to check the quality of sleep in various stages of patients. Anxiety and depression score were obtained by using Hospital Anxiety and Depression Score (HADS). GFR was calculated by using Modification of diet in Renal disease (MDRD) study equation(15)

$GFR = 186(S_{cr})^{-1.154}(age)^{-0.203}$ (0.742 if female) (1.21 if African-American)

STATISTICAL ANALYSIS:

Data distribution was tested using Kolmogorov Smirnov test. Continuous variables were expressed as mean ± standard deviation (SD) and as frequency (number [%]) for categorical data. Categorical variables were tested using Chi-square test. Differences among two groups studied were analyzed by student t test. Differences among three groups studied were analyzed by analysis of variance (ANOVA). Pearson's correlation analysis was done to test the correlations among variables. Statistical analysis was performed using Microsoft Excel spread sheets and SPSS software for windows version 25.0(SPSS Inc., Chicago, IL, USA). A *P* value of < 0.05 was considered statistically significant.

RESULT:

The present study included 198 pre dialysis CKD patients of 1 to 5 stages and assessed on

parameters such as pill burden, sleep quality, anxiety and depression over a period of 6 months. Chronic Kidney Disease patients were divided into 3 categories namely mild CKD (stage 1 and 2), moderate CKD (stage 3 and 4) and severe CKD (stage 5). eGFR was calculated by using MDRD formula. Among 198 patients there are diabetic (n=98) and non –diabetic (n=100), patients.

Demographic data was collected and shown in **table 1 a & b.** Among 198 patients middle age and elderly age CKD patients predominated as compared to younger age. Among 198 patients of all stages, 122 patients were male which constitutes about 61.62% and 76 patients were females which constitutes 38.88% showing that males being more in number in comparison to females.

Table 1 a: Age distribution of the CKD patients

Age distribution(in years)	NO.OF PATIENTS n (%)
20 – 40	34 (17 %)
41 – 60	88 (45%)
61 – 100	76 (38%)

Table 1 b: Gender distribution of the CKD patients

GENDER(n=198)	Non-Diabetic(n=100)	Diabetic (n=98)	P value
Males (n=122)	55 (55.0%)	67 (68.0%)	0.059†
Females (n= 76)	45 (45.0%)	31 (32.0%)	0.065†

Gender	Mild	Moderate	P value
Non-Diabetic Males	13 (42.0%)	28 (74.0%)	0.013*
Diabetic Males	17 (57.0%)	32 (84 .0%)	0.056†
Non-Diabetic Females	18 (58. 0%)	10 (26.0%)	0.062†
Diabetic Females	13 (43. 0%)	06 (16.0%)	0.053†
Gender	**Mild**	**Severe**	**P value**
Non-Diabetic Males	13 (42.0%)	14 (45.0%)	0.895†
Diabetic Males	17 (57.0%)	18 (60.0%)	0.762†
Non-Diabetic Females	18 (58. 0%)	17 (55.0%)	0.886†
Diabetic Females	13 (43. 0%)	12 (40.0%)	0.842†
Gender	**Moderate**	**Severe**	**P value**
Non-Diabetic Males	28 (74.0%)	14 (45.0%)	0.018*
Diabetic Males	32 (84 .0%)	18 (60.0%)	0.078†
Non-Diabetic Females	10 (26.0%)	17 (55.0%)	0.053†
Diabetic Females	06 (16.0%)	12 (40.0%)	0.052†

PSQI - The Pittsburgh Sleep Quality Index , e GFR- estimated glomerular filtration rate

* Significant at the 0.05 probability level. † NS- Not significant at the 0.05 probability level

Comparison of the variables between non diabetic and diabetic CKD patients by using student t test was presented as mean ± SD and is shown in the **Table 2.** In the present study the mean number of pills per day and number of classes of pills per day were more in diabetic group compared to non diabetic group which was found to be statistically significant($p < 0.05$). The present study compared the sleep scores between non-diabetic and diabetic CKD patients by using PSQI score. The findings were that diabetic CKD patients are having more PSQI score than non-diabetic CKD patients which was found to be statistically significant($p < 0.05$). In PSQI score, a score of 5 and below indicates normal or good sleep quality and a score above 5 resembles poor sleep quality. As the score increases, it indicates that the sleep of patient was depleted or poor sleep. The present study observations indicates diabetic CKD patients were more tend to have poor sleep than non- diabetic CKD patients. In comparison of anxiety scores between non-diabetic and diabetic CKD patients, both diabetic and non-diabetic were having same anxiety scores which was not statistically significant ($p=0.908$). Both the severe groups have same mean anxiety score. The present study compared the depression scores between non-diabetic and diabetic CKD patients and found that both diabetic and non-diabetic are having same depression scores which was not statistically significant ($p=0.706$).

Table 2: Comparison of the variables between non diabetic and diabetic CKD patients

Variable	Non-Diabetic(n=100)	Diabetic (n=98)	P value
Age (Years)	51.78±14.16	57.75±12.17	0.002*
Weight (KG)	59.57±10.25	63.74±12.50	0.011*
S . Creatinine (mg/dL)	3.31±2.87	2.92±2.06	0.281†
e GFR (ml/min/1.73 m²)	52.90±50.99	49.75±44.47	0.644†
Mean No. of pills per day	9.64±3.74	11.41±3.56	0.001*
Mean No. of classes of pills per day	6.45±2.67	7.51±2.45	0.004*
PSQI score	8.96±3.10	10.19±3.25	0.007*
Anxiety score	7.29±3.43	7.23±3.31	0.908†
Depression score	8.57±3.29	8.38±3.48	0.706†

PSQI - The Pittsburgh Sleep Quality Index , e GFR- estimated glomerular filtration rate

* Significant at the 0.05 probability level. † NS- Not significant at the 0.05 probability level

Comparison of the variables across the Non diabetic CKD patients by using one way ANOVA was shown in **table 3.** The present study found a statistically significant progressive increase in the mean pill number and mean classes of pill per day among Mild, Moderate stage and Severe stage Non diabetic CKD patients (p <0.001). In the study, statistically significant progressive increase in PSQI score among Mild , Moderate and Severe stage Non diabetic CKD patients (p =0.010) was observed. These findings suggest that all the patients of non-diabetic CKD are having a poor quality of sleep. Among the three groups of Non diabetic CKD, severe group have the least sleep quality (10 ± 3) followed by moderate group (9±3) and the mild group has comparatively better sleep quality (8±3) than the other two groups. The present study found a non-statistical significant progressive increase in the Anxiety score among Mild , Moderate and Severe stage non diabetic CKD patients (p=0.195). In the present study a statistically significant progressive increase in Depression score among Mild , Moderate stage and Severe stage non diabetic CKD patients was observed (p =0.002). However the scores in Moderate and Severe stage non diabetic CKD patients are same indicating a depressive and anxiety states in both the groups.

Table 3: Comparison of the variables across the non diabetic CKD patients

Variable (n=100)	Mild non diabetic (n=31)	Moderate non diabetic (n=38)	Severe non diabetic (n=31)	P value
Age (Years)	46.80 ±14.11	55.21±13.71	52.54 ±13.77	0.045*
Weight (KG)	58.87 ± 12.60	62.28 ± 9.38	58.93 ± 7.89	0.087†
S Creatinine (mg/dL)	0.81 ±0.27	2.52 ±0.99	6.78 ±2.48	< 0.001
e GFR (ml/min/1.73 m²)	118.63 ± 41.20	34.77 ± 11.76	9.99 ± 3.05	< 0.001*
Mean No. of pills per day	5.48± 1.60	10.60 ± 2.89	12.61 ± 2.29	< 0.001*
Mean No. of classes of pills per day	3.61 ± 1.11	6.97 ± 2.13	8.64 ± 1.76	< 0.001*
PSQI score	7.83 ± 2.65	8.86 ± 3.41	10.19 ± 2.72	0.010*
Anxiety score	6.41 ±3.00	7.44 ±3.50	7.96 ±3.66	0.195†
Depression score	6.90 ±3.37	9.05 ±3.06	9.64 ± 2.90	0.002*

Comparison of the variables across the diabetic CKD patients by using one way ANOVA was shown in **table 4.** The present study found a statistically significant progressive increase in the mean pill number and mean classes of pill per day among Mild, Moderate and Severe stage diabetic CKD patients (p <0.001). In the study, found a statistically significant progressive increase in PSQI score among Mild, Moderate and Severe stage diabetic CKD patients (p <0.001) these findings suggest that all the patients of diabetic CKD are having a poor quality of sleep. Among the three groups of diabetic CKD, severe group have the least sleep quality (12 ± 2) followed by moderate and mild group has comparatively better sleep quality (9 ± 3). The present study found a non-statistical significant progressive increase in the Anxiety score among Mild, Moderate and Severe stage diabetic CKD patients (p=0.195). In the present study a statistically significant progressive increase in Depression score among Mild, Moderate and Severe stage diabetic CKD patients was observed (p =0.005).

Table 4: Comparison of the variables across the diabetic CKD patients

Diabetic Variables (n=98)	Mild diabetic (n=30)	Moderate diabetic (n=38)	Severe diabetic (n=30)	P value
Age (Years)	51.63 ±13.13	59.89 ±10.24	61.16 ±11.51	0.003*
Weight (KG)	63.75 ± 15.53	67.98 ± 11.20	58.38 ± 8.28	0.006*
S . Creatinine (mg/dL)	0.88 ±0.28	2.57 ±0.83	5.42 ± 1.52	< 0.001*
e GFR (ml/min/1.73 m²)	108.15 ± 33.53	33.12 ± 10.94	12.41 ± 2.61	< 0.001*
Mean No. of pills per day	7.30 ± 1.72	12.26 ± 2.60	14.46 ± 1.67	< 0.001*
Mean No. of classes of pills per day	4.90 ± 1.49	7.86 ± 1.89	9.66± 1.18	< 0.001*
PSQI score	9.23 ± 3.39	9.36 ± 3.05	12.20 ± 2.44	< 0.001*
Anxiety score	6.33 ±3.12	7.73±3.76	7.50 ± 2.77	0.195†

PSQI - The Pittsburgh Sleep Quality Index , e GFR-estimated glomerular filtration rate

* Significant at the 0.05 probability level. † NS- Not significant at the 0.05 probability level

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Comparison of the variables between mild non diabetic and diabetic CKD patients by using student's t test was shown in **table 5**. The present study found a statistically significant increase in the mean pill number and mean classes of pill per day in mild diabetic CKD patients compared with mild non diabetic CKD patients (p <0.05). In the present study, found an increase in PSQI score in mild diabetic CKD patients compared with mild non diabetic CKD patients which is not statistically significant (p = 0.078) These findings suggest that all the patients of Mild CKD group are having a poor quality of sleep. In the present study, non statistically significant difference in Anxiety score between mild diabetic CKD patients compared with

mild non diabetic CKD patients which is not statistically significant (p = 0.908) was found. In the present study, non statistically significant difference in Depression score between mild diabetic CKD patients compared with mild non diabetic CKD patients (p = 0.706) was found.

Table 5: Comparison of the variables between mild non diabetic and diabetic CKD patients

Variable	Mild Non-Diabetic(n=100)	Mild Diabetic (n=98)	P value
Age (Years)	51.78±14.16	57.75±12.17	0.002*
Weight (KG)	59.57±10.25	63.74±12.50	0.011*
S . Creatinine (mg/dL)	3.31±2.87	2.92±2.06	0.281†
e GFR (ml/min/1.73 m²)	52.90±50.99	49.75±44.47	0.644†
Mean No. of pills per day	9.64±3.74	11.41±3.56	0.001*
Mean No. of classes of pills per day	6.45±2.67	7.51±2.45	0.004*
PSQI score	8.96±3.10	10.19±3.25	0. 078†
Anxiety score	7.29±3.43	7.23±3.31	0.908†
Depression score	8.57±3.29	8.38±3.48	0.706†

PSQI - The Pittsburgh Sleep Quality Index, e GFR-estimated glomerular filtration rate

* Significant at the 0.05 probability level. † NS-Not significant at the 0.05 probability level

Comparison of the variables between moderate non diabetic and diabetic CKD patients by using students t test was shown in **table 6.** The present study found a statistically significant increase in the mean pill number and mean classes of pill per day in moderate diabetic CKD patients compared with moderate non diabetic CKD patients (p <0.05). In the present study, found an increase in PSQI score in moderate diabetic CKD patients compared with moderate non diabetic CKD patients which is not statistically significant (p = 0.503) These findings suggest that all the patients of Moderate CKD group are having a poor quality of sleep. In the present study, found no significant difference in Anxiety score in moderate diabetic CKD patients compared with moderate non diabetic CKD patients (p = 0.729). In the present study, found no statistically significant difference in Depression score in moderate diabetic CKD patients compared with moderate non diabetic CKD patients (p = 0.462).

Table 6: Comparison of the variables between moderate non diabetic and diabetic CKD patients

Variable	Moderate Non-Diabetic(n=38)	Moderate Diabetic (n=38)	P value
Age (Years)	55.21 ±13.71	59.89 ±10.24	0.096†
Weight (KG)	62.28 ± 9.38	67.98 ±11.20	0.019*
S . Creatinine (mg/dL)	2.52 ±0.99	2.57 ±0.83	0.793†
e GFR (ml/min/1.73 m²)	34.77 ± 11.76	33.12±0.94	0.530†
Mean No. of pills per day	10.60 ± 2.89	12.26 ± 2.60	0.011*
Mean No. of classes of pills per day	6.97 ± 2.13	7.86 ± 1.89	0.057†
PSQI score	8.86 ± 3.41	9.36 ± 3.05	0.503†
Anxiety score	7.44 ±3.50	7.73 ±3.76	0.729†
Depression score	9.05 ±3.06	8.47 ±3.72	0.462†

PSQI - The Pittsburgh Sleep Quality Index, e GFR-estimated glomerular filtration rate

* Significant at the 0.05 probability level. † NS-Not significant at the 0.05 probability level

Comparison of the variables between severe non diabetic and diabetic CKD patients by using students t test was shown in **table 7**. The present study found a statistically significant increase in the mean pill number and mean classes of pill per day in severe diabetic CKD patients compared with severe non diabetic CKD patients (p <0.05). These findings suggest that all the patients of severe diabetic CKD patients are having a poor quality of sleep compared to severe non diabetic CKD patients which is statistically significant (p = 0.004). In the present study, found non statistically significant difference in Anxiety score in severe diabetic CKD patients compared with severe non diabetic CKD patients (p = 0.577). In the present study, found non statistically significant difference in Depression score in severe diabetic CKD patients compared with severe non diabetic CKD patients (p = 0.873).

Table 7: Comparison of the variables between severe non diabetic and diabetic CKD patients

Variable	Severe Non-Diabetic(n=31)	Severe Diabetic (n=30)	P value
Age (Years)	52.54 ±13.77	61.16 ±11.51	0.010*
Weight (KG)	56.93 ± 7.89	58.38 ± 8.28	0.487†
S . Creatinine (mg/dL)	6.78 ± 2.48	5.42 ± 1.52	0.012*
e GFR (ml/min/1.73 m²)	9.99 ± 3.05	12.41 ± 2.61	0.002*
Mean No. of pills per day	12.61 ± 2.29	14.46 ± 1.67	0.001*
Mean No. of classes of pills per day	8.64 ± 1.76	9.66 ± 1.18	0.010*
PSQI score	10.19± 2.72	12.20 ± 2.44	0.004*
Anxiety score	7.96 ±3.66	7.50 ± 2.77	0.577†
Depression score	9.64 ± 2.90	9.76 ± 3.00	0.873†

PSQI - The Pittsburgh Sleep Quality Index, e GFR-estimated glomerular filtration rate

* Significant at the 0.05 probability level. † NS- Not significant at the 0.05 probability level

Pearson's correlation analysis between Pill burden, sleep quality, anxiety score and depression score in non diabetic and diabetic groups was shown in **table 8 a & b.** A positive correlation between pill burden, PSQI score and depression scores was observed in both non- diabetic and diabetic CKD patients which was found to be statistically significant ($p<0.05$). But there was positive correlation between anxiety scores and other variables such as pill burden, PSQI score, and depression scores which was not statistically significant in both Non- Diabetic and Diabetic CKD patients ($p>0.05$).

Table 8 a: Pearson's correlation analysis between Pill burden, sleep quality, anxiety score and depression score in non diabetic CKD patients

Non diabetic Parameters		Mean No. of pills per day	Mean No. of classes of pills per day	PSQI score	Anxiety score	Depression score
Mean No. of pills per day	r	1.000	0.968	0.275	0.114	0.333
	Sig		**0.001***	**0.006***	0.258†	**0.001***
Mean No. of classes of pills per day	r		1.000	0.279	0.131	0.314
	Sig			**0.005***	0.195†	**0.001***
PSQI score	r			1.000	0.344	0.276
	Sig				0.001*	**0.005***
Anxiety score	r				1.000	0.325
	Sig					**0.001***
Depression score	r					1.000
	Sig					

Table 8b: Pearson's correlation analysis between Pill burden, sleep quality, anxiety score and depression score in diabetic CKD patients

Diabetic Parameters		Mean No. of pills per day	Mean No. of classes of pills per day	PSQI score	Anxiety score	Depression score
Mean No. of pills per day	r	1.000	0.951	0.324	0.192	0.243
	Sig		**0.001***	**0.001***	0.058†	**0.016***
Mean No. of classes of pills per day	r		1.000	0.351	0.179	0.284
	Sig			**0.001***	0.078†	**0.005***
PSQI score	r			1.000	0.331	0.184
	Sig				**0.001***	0.070†
Anxiety score	r				1.000	0.421
	Sig					**0.001***
Depression score	r					1.000
	Sig					

DISCUSSION:

A total of 198 CKD patients were included in the present study. Among 198 CKD patients middle and elderly aged CKD patients predominated. Among 198 CKD patients, 122 were male and 76 were female. Based on the severity of CKD , Patients were divided into three groups as mild (stage 1-2), moderate (stage 3 - 4), and severe (stage 5), which were further sub divided as diabetic (n=98) and non – diabetic (n=100) CKD patients.

Due to increased pill burden in CKD patients leads to take numerous pills or other forms of medications on frequent basis. Therefore, high pill burden increases the chances of hospitalization, medication errors and elevated costs for not only pharmaceuticals as well as the treatment for adverse events in CKD patients which is more so for Diabetic patients in addition to CKD. In the present study, there was a progressive increase in number of pills per day and number of classes of pills per day with increasing severity of CKD burden in both diabetic and non – diabetic CKD patients, which was found to be statically significant ($P< 0.05$). Further, among diabetic and non – diabetic CKD patients in the present study there was more pill burden in diabetic CKD patients when compared to non – diabetic CKD patients which was also statistically significant($p<0.05$). This is in concordance with other studies [15,16]. This increase in pill burden in diabetic CKD patients could be attributed to more elderly CKD patients in diabetic group when compared to non – diabetic group. Therefore pill burden is an important concern for the patients [16] .

In the present study, the quality of sleep was affected significantly ($p <0.05$) with increasing severity of CKD burden and pill burden in both diabetic and non – diabetic CKD patients. In comparison of sleep scores between non-diabetic and diabetic groups, diabetic CKD patients are having more PSQI score than non-diabetic group which was found to be statistically significant ($p <0.05$). The present study observations indicates that diabetic CKD patients are more tend to have poor sleep than non- diabetic CKD patients. This is in line with other studies [11,17,18]. This poor sleep quality could be attributed to more pill burden in diabetic CKD patients when compared to non – diabetic CKD patients which would have led to the disturbance. Further PSQI score was progressively increased with increasing severity of CKD in both diabetic and non - diabetic patients which was statically significant ($p<0.05$). These findings suggest that in addition to CKD, the diabetic state might contribute to increased pill burden along

with severity of CKD and hence showed a progressive increase indicating poor sleep quality.

In the present study, anxiety and depression score was recorded from Hospital Anxiety and Depression Scale (HADS). In the present study, from the HAD scale the trend of anxiety and depression score was progressively increased with increasing severity of CKD burden in both diabetic and non - diabetic CKD patients but was not statically significance ($p>0.05$). In the present study a statistically significant progressive increase in Depression score among Mild , Moderate and Severe stage non diabetic and diabetic CKD patients was observed. In HADS scale, depression and anxiety scores of 7 and below comes under normal and a score above 7 is considered as depressive and anxiety state. However the anxiety and depression score is less than 7 in mild non diabetic and diabetic group and more than 7 in moderate and severe non diabetic and diabetic groups indicating a depressive and anxiety states in both moderate and severe non diabetic and diabetic groups. These findings are similar to the findings of other studies [13,19,20.]. When compared between diabetic and non - diabetic patients the trend of anxiety was more in diabetic CKD patients compared with non diabetic CKD patients but was not statically significance ($p = 0.908$). In comparison of depression scores between non-diabetic and diabetic CKD patients, both diabetic and non-diabetic are having same depression scores and was not statistically significant ($p=0.706$). In the present study as depression and anxiety scores are above 7 in both non-diabetic and diabetic CKD patients, it indicates a depressive and anxiety state. Anxiety and Depression in pre-dialysis CKD patients is associated with poor clinical outcome and with faster decline in kidney function in pre-dialysis CKD patients. These are in line with other study findings [21,22]. Few studies reported that, certain factors such as religious belief, lack of exercise and severity of CKD are associated with anxiety and depression states in CKD patients [23,24].

Correlation analysis between Pill burden, sleep quality, anxiety score and depression score in non diabetic and diabetic groups was shown. A positive correlation between pill burden, PSQI score and depression scores was observed in both are non-diabetic and diabetic CKD patients which was found to be statistically significant. These findings suggest that with increased pill burden there was reduction in sleep quality in both non- diabetic and diabetic CKD patients. Also a positive correlation was found between pill burden, anxiety, and depression indicates that with increased pill burden, increased anxiety and depression in both diabetic and non- diabetic CKD patients. The positive correlation between anxiety and depression indicated that with increased anxiety, there may be an increase depression in both Diabetic and Non- Diabetic CKD patients.

CONCLUSION: Increased pill burden, reduction in sleep quality, increase in anxiety and depression were observed with increasing disease burden in both diabetic and non- diabetic CKD patients. Moreover the diabetic state is found to be associated with increased pill burden which led to poor sleep quality as compared to non- diabetic CKD patients. As observed from the findings that moderate and severe stage diabetic and non-diabetic CKD patients have increase in the mean pill number and mean classes of pill per day, PSQI score , anxiety and depression scores compared to Mild stage diabetic and non- diabetic CKD patients.

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