

# Neuropsychiatric complications in chronic kidney disease: Role of gender, clinical, and sociodemographic factors

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## ABSTRACT

**Introduction:** Patients with chronic kidney disease (CKD) frequently experience neuropsychiatric conditions, such as depression, anxiety, and cognitive impairment, which not only significantly diminish their quality of life, but also contribute to longer hospitalizations, poor treatment adherence, and increased mortality. This hospital-based cross-sectional study aimed to investigate neuropsychiatric complications in CKD patients, focusing on gender differences, and clinical and other sociodemographic factors. **Materials and Methods:** Diagnosis of CKD was based on the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, and patients aged 18 years or above were included. Delirium was assessed using the Confusion Assessment Method (CAM) Scale. Those without delirium underwent evaluation using the Hindi Mental Status Examination (HMSE), Brief Psychiatric Rating Scale (BPRS), and Hospital Anxiety and Depression Scale (HADS) to identify cognitive and psychiatric symptoms. **Results:** Among the 104 participants, 50% were male, with a predominant age group over 45 years (61.5%). A majority portion of the cohort was married (72.1%), employed (57.7%), and identified as Christian (56.7%). The majority of CKD cases were diagnosed as stage 5 (87.5%) and on dialysis treatment. Delirium was present in 19.2% of participants. In those without delirium, anxiety affected 46.3%, depression impacted 50.0%, and cognitive dysfunction was present in 11.1%. A gender-based analysis revealed no significant differences in age or illness duration; however, males exhibited a higher level of education ( $P < 0.02$ ). While females tended to display more severe psychiatric symptoms ( $P < 0.06$ ), males had more cognitive dysfunction ( $P < 0.08$ ); however, these differences did not reach statistical significance. Socioeconomic status (SES) comparisons demonstrated that lower SES correlated with a reduced number of years of education ( $P < 0.00$ ). **Conclusion:** Anxiety and depression were prevalent in nearly half of CKD patients, without gender or socioeconomic disparities. This underscores the imperative need for holistic, multidisciplinary interventions to effectively manage these conditions and enhance overall quality of life.

**Keywords:** Anxiety, chronic kidney disease, cognitive impairment, depression, gender

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## Introduction

Chronic kidney disease (CKD) is defined by the Kidney Disease: Improving Global Outcomes (KDIGO) as lasting abnormalities in kidney structure or function for more than

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3 months, accompanied by a glomerular filtration rate (GFR) below 60 ml/min/1.73 m<sup>2</sup>.<sup>[1]</sup> CKD poses a significant health challenge with associated heightened morbidity and mortality rates. Studies conducted in India reveal varying CKD prevalence, ranging from 0.8%<sup>[2]</sup> to as high as 7% for stage 1 disease,<sup>[3]</sup> approximately equivalent to 800 cases per million population.<sup>[4]</sup> Major contributors to CKD include well-established risk factors, such as diabetes mellitus, hypertension, glomerulonephritis, and idiopathic causes.

Physical manifestations, such as anemia, mineral and bone disorder, hypertension, heart failure, dyslipidemia,<sup>[5]</sup> as well as neuropsychiatric symptoms,<sup>[6]</sup> develop as direct consequences of CKD. Importantly, neuropsychiatric complications are not confined to advanced stages but have been documented in earlier CKD phases, encompassing cognitive impairment, depression, anxiety, acute confusional states,<sup>[7,8]</sup> sleep disturbances,<sup>[9,10]</sup> sexual dysfunction,<sup>[11]</sup> and, distressingly, even suicide.<sup>[12]</sup> A study conducted in India among hemodialysis patients revealed alarmingly high rates of depression (61.3%) and anxiety (28%).<sup>[13]</sup> McQuillan *et al.*,<sup>[14]</sup> in a comprehensive review, underscored the widespread prevalence of neuropsychiatric complications in CKD, including cognitive impairment, delirium, and depression. Furthermore, they highlighted the association of these neuropsychiatric disturbances with heightened mortality rates, increased hospitalization rates, and suboptimal adherence to treatments.

CKD is a significant public health concern in the northeastern region of India.<sup>[15,16]</sup> Despite its relatively high prevalence, there is a notable dearth of studies focusing on the neuropsychiatric complications experienced by CKD patients in this specific geographic area. CKD has been documented to be more prevalent in women<sup>[17]</sup> and persons of lower socioeconomic status (SES)<sup>[18]</sup> across different ethnicities including Indians. Additionally, anxiety and depression are also known to be more common in women. Whether the gender differences in the prevalence of neuropsychiatric symptoms are reflected in patients with CKD is not exactly known. In this study, we aimed to bridge this knowledge gap by assessing the neuropsychiatric profiles of CKD patients in the northeastern region and to evaluate the presence of gender or socioeconomic differences.

## Methodology

A hospital-based analytical cross-sectional study was conducted, involving individuals diagnosed with CKD according to the KDIGO criteria, in a tertiary care teaching hospital at Shillong, Meghalaya, in the northeastern region of India. Sociodemographic data, including age, gender, marital status, employment, habitat, education, family type, religion, and SES, were collected. Clinical details encompassed past psychiatric and medical history, family psychiatric and medical history, CKD stage, dialysis treatment, and the presence of other comorbid medical conditions, such as hypertension, diabetes, and delirium. The Confusion Assessment Method for the

Intensive Care Unit (CAM-ICU)<sup>[19]</sup> was employed to assess the presence or absence of delirium. Those who were found to have no delirium were evaluated for cognitive function using the Hindi Mental Status Examination (HMSE),<sup>[20]</sup> with a cut-off of  $\leq 23$  to detect ant cognitive decline.<sup>[21]</sup> The items in the HMSE questionnaire encompass questions in both English and Hindi,<sup>[22]</sup> and it has shown reliability and validity in the Indian rural population. Psychiatric illness severity was measured by the Brief Psychiatric Rating Scale (BPRS), with scores indicating mild (31–40), moderate (41–52), and severe symptoms (above 52).<sup>[23,24]</sup> Additionally, the Hospital Anxiety and Depression Scale (HADS)<sup>[25]</sup> was used, with a recommended cut-off of  $\geq 8$  for identifying the presence of anxiety and/or depression.<sup>[26]</sup>

**Sample size:** The sample size was calculated considering the prevalence of psychiatric complications in patients with CKD, which is around 18%. Using a 95% confidence interval and a finite population correction factor for a population size of 1,000,000, the sample size required is 101. On the basis of the sample size estimations, 104 patients with CKD (diagnosed as per the KDIGO guideline) were recruited prospectively from the Department of General Medicine.

The study received approval from the Institutional Ethics Committee under Project No. P166/12/77. Before their involvement in the study, all participants provided informed written consent, ensuring transparency and adherence to ethical standards. The study was designed in accordance with the 2013 revision of the Declaration of Helsinki and reported in compliance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

## Statistical analysis

Data analysis was performed utilizing STATA 14.1 (Texas Inc.). Descriptive statistics were employed to summarize sociodemographic and clinical parameters, presented as counts and percentages. The comparison of means utilized the “*t*” statistic, while the Chi-square statistic was employed for comparing categorical variables. A level of  $P < 0.05$  is considered statistically significant.

## Results

The sociodemographic and clinical characteristics of the study cohort are summarized in Table 1. Of the 104 participants, 50% were male, the majority of participants were married (72.1%) and employed (57.7%), and 29.8% were students. Additionally, 51.9% hailed from rural areas. A higher proportion of the participants (54.8%) had completed intermediate-level education, and 63.4% belonged to nuclear families. The predominant religious affiliation was Christian (56.7%), and 50% of the participants were classified under a low SES.

Table 2 outlines the clinical profile of the study participants. We found that 10.6% of the participants had a history of past psychiatric issues, and 56.7% reported previous medical

**Table 1: Sociodemographic profile of the study population**

Variables	n (%)
Age	
<45	40 (38.5)
>45	64 (61.5)
Gender	
Male	52 (50)
Female	52 (50)
Marital status	
Single	16 (15.4)
Married	75 (72.1)
Divorced/widow	13 (12.5)
Employment	
Unemployed	7 (6.7)
Employed	60 (57.7)
Student	31 (29.8)
Housewife	6 (5.8)
Habitation	
Urban	50 (48.1)
Rural	54 (51.9)
Education	
Primary	38 (36.5)
Intermediate	57 (54.8)
Graduate and above	9 (8.7)
Family	
Nuclear	66 (63.4)
Joint	21 (20.2)
Extended	17 (16.4)
Religion	
Hindu	27 (26.0)
Muslim	11 (10.6)
Christian	59 (56.7)
Others	7 (6.7)
Socioeconomic status	
Lower	52 (50)
Middle and upper	52 (50)

**Table 2: Clinical profile of the study population**

Variables	n (%)
Past psychiatric history	
Yes	11 (10.6)
No	93 (89.4)
Past medical history	
Yes	59 (56.7)
No	45 (43.3)
Family psychiatric history	
Yes	8 (7.7)
No	96 (92.3)
Family medical history	
Yes	22 (21.2)
No	82 (78.8)
CKD stage	
1	2 (1.9)
2	3 (2.9)
3	1 (1.0)
4	7 (6.7)
5	91 (87.5)
On dialysis treatment	
Yes	84 (80.8)
No	20 (19.2)
Hypertension	
Yes	30 (28.9)
No	74 (71.1)
Diabetes mellitus	
Yes	29 (27.9)
No	75 (72.1)

conditions. A family history of psychiatric illness was present in 7.7%, while 21.2% had a family history of medical conditions. Medical comorbidities were prevalent in 72.1% of the patients. The majority (87.5%) were at stage 5 of CKD, and most of them (80.8%) were undergoing dialysis treatment.

Evaluation of neuropsychiatric symptoms revealed the presence of delirium in 19.2%, anxiety in 46.3%, depression in 50%, and cognitive dysfunction in 11.1%, respectively. When considering the severity of psychiatric symptoms, 24.1% had mild, 8.4% had moderate, and 1.2% had severe symptoms [Table 3].

Comparison by gender is summarized in Table 4. No significant gender differences were observed for mean age ( $P = 0.30$ ), duration of illness ( $P = 0.89$ ), or age at disease onset ( $P = 0.29$ ); however, males were found to have greater number of years of education ( $P < 0.02$ ). Females were also more likely to have more severe psychiatric symptoms ( $P < 0.06$ ), while cognitive dysfunction ( $P < 0.08$ ) was more likely among males; however, the differences were not statistically significant.

Comparison by SES revealed no significant differences in the age of onset, CKD illness duration, and prevalence of psychiatric illness ( $P > 0.05$  for all); however, CKD patients with lower SES had a lower number of years of formal education ( $P < 0.001$ ) [Table 5].

## Discussion

This cross-sectional observational study aimed to assess clinical, sociodemographic features, and the presence of neuropsychiatric conditions in CKD patients. In our study, which comprised mainly of subjects with advanced CKD, depressive and anxiety disorders were observed in 50% and 46.3% of patients, respectively. Comparatively, a systematic review and meta-analysis, encompassing 216 studies with 55,982 CKD patients, demonstrated a prevalence of 26.5% for depressive symptoms when assessed through screening questionnaires. Clinically significant depression, evaluated through clinical interviews, was found in 21.4% of cases.<sup>[27]</sup> Notably, the prevalence of depression in CKD patients in our study was substantially higher than these figures, being three to four times more prevalent compared to the general population and two to three times more prevalent than other chronic conditions, such as diabetes, coronary artery disease, and chronic obstructive pulmonary disease.<sup>[28,29]</sup> The higher prevalence rate observed in our study may be explained by the greater number of subjects with stage 5 CKD, than what is seen in the population.

Anxiety is also a prevalent psychiatric condition in CKD patients, although it has been comparatively less researched than depression. In a longitudinal study involving 50 CKD patients undergoing hemodialysis, 45.7% exhibited symptoms of anxiety according to the HADS; the prevalence of anxiety was similar to what we observed in our study. After a 16-month follow-up, 30% of these patients continued to experience symptoms of anxiety.<sup>[30]</sup> In a cross-sectional study encompassing 208 pre-dialysis CKD patients, the prevalence of anxiety, as measured by the HADS, was 24.8% in patients at CKD stage 3, 29.9% in those at stage 4, and 34.3% in patients at stage 5.<sup>[31]</sup> Given the high rates of undiagnosed psychiatric illnesses

in CKD patients, screening for their early identification is important, as appropriate treatment and management can alleviate their overall well-being and impact their quality of life.

CKD is an independent risk factor for cognitive impairment and dementia.<sup>[32]</sup> In this study, cognitive impairment was identified in 11.1% of patients after excluding patients with delirium. Studies using the Mini-Mental Scale Examination (MMSE) report the prevalence of cognitive impairment in individuals with CKD to range from 8.3 to 51%.<sup>[33-35]</sup> Cognitive dysfunction can potentially compromise CKD patients' capacity to make informed decisions and comprehend the complexities of their treatment,<sup>[36]</sup> including adherence to fluid and dietary restrictions (28,29). Moreover, patients experiencing cognitive impairment face an elevated risk of hospitalization, mortality, and a diminished quality of life.<sup>[37]</sup> Holistic care encompassing multidisciplinary approaches, including close involvement of caregivers, is crucial for managing these patients and improving their overall quality of life.

The association between CKD and cognitive impairment is multifaceted and can be attributed to several factors. Firstly, common risk factors in CKD patients, such as cerebrovascular disease, dementia, and cardiovascular disease, contribute to the higher incidence of cognitive impairment and were higher with those with lower estimated (GFR).<sup>[38]</sup> Secondly, vascular damage, uremic toxicity, oxidative stress, and inflammation may cause cognitive dysfunction.<sup>[39]</sup> Lastly, hemodialysis itself has been implicated in cognitive dysfunction in patients with CKD.<sup>[40]</sup> Collectively, these factors have the potential to impact cognitive function, highlighting the intricate interplay between renal health and cognitive well-being in CKD patients. Although the female gender is a risk for cognitive dysfunction,<sup>[41]</sup> our finding of males showing more cognitive dysfunction needs to be interpreted with caution.

**Table 3: Neuropsychiatric symptoms of the study population**

Variables	n (%)
Delirium (104)	
Yes	20 (19.2)
No	84 (80.8)
Anxiety (n=82) HADS-A ≥8	
Yes	38 (46.3)
No	44 (53.7)
Depression (n=82) HADS-D ≥8	
Yes	41 (50)
No	41 (50)
Cognitive dysfunction (n=81) HMSE ≤23	
Yes	9 (11.1)
No	72 (88.9)
Psychiatric symptoms severity (n=83) BPRS	
No symptoms	55 (66.3)
Mild	20 (24.1)
Moderate	7 (8.4)
Severe	1 (1.2)

HADS: Hospital Anxiety and Depression Scale; HADS-A: Anxiety; HADS-D: Depression; (data available for analysis n=82); HMSE: Hindi Mental Status Examination (data available for analysis n=81); BPRS: Brief Psychiatric Rating Scale (data available for analysis n=83)

**Table 4: Comparison of clinical variables and psychiatric symptoms across gender**

Variable	Male mean (±SD) n (%)	Female mean (±SD) n (%)	t	df	P
Education in years (n=104)	8.4 (4.7)	6.2 (4.7)	2.37	102	0.02
Age (n=104)	49.3 (15.1)	46.1 (15.7)	1.04	102	0.30
Duration of illness (n=104)	3.8 (3.5)	3.7 (3.8)	0.13	102	0.89
Age of onset (n=104)	45.6 (14.2)	42.5 (15.7)	1.07	102	0.29
Score on psychiatric symptoms severity (BPRS)(n=83)	25.3 (7.5)	29.1 (10.3)	-1.94	81	0.06
Score on cognitive dysfunction (HMSE) (n=81)	25.7 (3.8)	27.0 (2.9)	-1.76	79	0.08
Anxiety (HADS-A) (n=82)	7.5 (5.0)	9.3 (5.4)	-1.54	79	0.13
Depression (HADS-D) (n=82)	7.9 (4.9)	8.7 (5.5)	-0.71	79	0.48

HADS: Hospital Anxiety and Depression Scale; HADS-A: Anxiety; HADS-D: Depression; HMSE: Hindi Mental Status Examination; BPRS: Brief Psychiatric Rating Scale

**Table 5: Comparison of clinical variables and psychiatric conditions by socioeconomic status**

Variable	Lower Mean (±SD) n (%)	Middle and upper Mean (±SD) n (%)	t	df	P
Education (n=104)	4.9 (4.0)	9.7 (4.2)	-6.02	102	0.00
Duration of illness (years)	3.1 (2.9)	4.3 (4.2)	-1.76	102	0.08
Age of onset (n=104)	43.1 (15.5)	44.9 (14.6)	-0.62	102	0.54
Score on psychiatric symptoms severity (BPRS) (n=83)	26.6 (8.8)	28.02 (9.7)	-0.72	81	0.48
Score on cognitive dysfunction (HMSE score) (n=81)	26.7 (2.7)	26.1 (4.1)	0.70	79	0.49
Anxiety (HADS-A) (n=82)	8.9 (5.6)	7.9 (4.9)	0.81	79	0.42
Depression (HADS-D) (n=82)	8.6 (5.2)	8.1 (5.2)	0.41	79	0.69

HADS: Hospital Anxiety and Depression Scale; HADS-A: Anxiety; HADS-D: Depression; HMSE: Hindi Mental Status Examination; BPRS: Brief Psychiatric Rating Scale



It is noteworthy that our analysis revealed higher rates of depression and anxiety. This finding underscores the impact of psychiatric complications on the decision-making process related to treatment compliance as CKD demands a lot of restrictions in terms of diet, and compliance to dialysis and other treatments. Understanding these factors is crucial for healthcare providers in tailoring interventions and support strategies, particularly in addressing the concerns or preferences that may influence decisions around dietary modifications, dialysis initiation, or refusal in CKD patients. Importantly, our study found no significant gender or socioeconomic differences in the prevalence of psychiatric illnesses in CKD patients. However, a recent study found a higher prevalence of anxiety and depression in females and those in lower income group.<sup>[42]</sup>

### Limitation

This study has a few limitations. Firstly, the study's reliance on a relatively small sample size from a single center may constrain the generalizability of the findings. Secondly, the lack of a contemporary non-CKD control group limits the ability to compare the prevalence of neuropsychiatric conditions observed in CKD patients with those in the general population. Thirdly, selection bias may have influenced the composition of the study population, as participants were recruited from a hospital setting. Fourthly, the cross-sectional design of the study limits the ability to establish causality or examine temporal relationships between CKD and neuropsychiatric symptoms.

### Conclusion

CKD significantly impacts mental health, often leading to psychiatric complications. Our study in northeast India found similar neuropsychiatric complication prevalence across genders. Recognizing this high prevalence enables healthcare providers to develop processes for early identification and tailored interventions. Timely diagnosis and management can alleviate psychiatric complications, enhancing overall well-being in CKD patients. Adopting a multidisciplinary approach, involving mental health professionals, nephrologists, and social workers, is crucial. This collaborative effort acknowledges the complex interplay between physical and mental health, fostering a personalized strategy to optimize health and resilience in CKD patients.

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### Conflicts of interest

There are no conflicts of interest.

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