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Association Between Chronic Kidney Disease and Neurological Manifestations: A Cross-Sectional Study of Cognitive Impairment, Peripheral Neuropathy, and Cerebrovascular Risk.

[1]Dr Azhar Iqbal, [2]Dr Muhammad Salman Ashraf, [3]Dr Muhammad Shahid Nawaz khan, [4]Dr Shoaib Liaquat, [5]Dr Ahmad Raza, [6]Dr Saif ul Islam.

[1]Assistant professor, Nephrology department, Sheikh Zayed hospital, Rahim Yar Khan
[2]Consultant Neurologist, THQ hospital, Sadiqabad, Rahim Yar Khan
[3]Assistant Professor of General MEDICINE TERTIARY CARE HOSPITAL NISHTAR 2, MULTAN
[4]Senior Registrar, Medicine department, Nishtar hospital, Multan
[5]Consultant Nephrologist, Dialysis center, THQ hospital, Sadiqabad, RYK
[6]Senior Registrar, medical Unit 1, sheikh Zayed hospital, RYK.

Correspondence:
Dr Azhar Iqbal.
Assistant professor, Nephrology department, Sheikh Zayed hospital, Rahim Yar Khan.

Email:
Azhariqbaldr@gmail.com

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Abstract

Background: To assess the link between the severity of chronic kidney disease (CKD) and neurological changes, such as cognitive impairment, peripheral neuropathy, and cerebrovascular risk factors. ***Materials and methods***: This was a cross-sectional analytical study conducted in a hospital setting with 209 adult CKD patients. Data on demographics, clinical, laboratory, and renal function were obtained. The Montreal Cognitive Assessment was used to measure cognitive function, and peripheral neuropathy was evaluated by a standardized neurological examination. The chi-square/Fisher's exact test, independent-samples t-test and Mann–Whitney U test were used to assess associations. Independent predictors were determined by multivariable logistic regression. ***Results***: Cognitive impairment was present in 91 (43.5%) participants and peripheral neuropathy in 83 (39.7%). The prevalence of both conditions rose with the CKD stage ($p<0.001$). Older age, lower education, diabetes, hypertension, cardiac disease, previous cerebrovascular disease, lower eGFR, and dialysis dependence were associated with cognitive impairment. Longer duration of CKD, diabetes, lower eGFR, anemia, and dialysis dependence were associated with peripheral neuropathy. There was a positive correlation between MoCA score and eGFR ($r=0.41$, $p<0.001$). Adjusting for these factors, eGFR <30 mL/min/1.73 m^2 and dependence on dialysis were independently associated with both neurological outcomes. ***Conclusions***: Neurological symptoms were common in CKD and were more prevalent as renal function declined. Regular neurological/cognitive evaluations should be considered, especially in advanced CKD and dialysis-dependent patients.

Keywords: CKD, cognitive dysfunction, peripheral neuropathy, cerebrovascular risk factors, eGFR, dialysis.

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INTRODUCTION

Chronic kidney disease (CKD) is a progressive systemic disease with abnormal kidney structure or function, and is a growing public health problem around the world.[1] It is estimated that there are 700 million people in the world suffering from CKD and around 850 million people globally suffering from kidney disease, which broadly includes the burden of acute kidney injury and kidney failure.[2] In LMICs, the burden is especially high due to poor screening and healthcare facilities, leading to delayed diagnosis and underdiagnosis of early stages of disease.[3] The Global Burden of Disease 2021 also estimated that there were about 674 million cases of CKD globally in 2021, which is a significant burden of the disease in terms of population.[4]

While CKD is considered a kidney disease, it has a wide impact outside of the kidneys.[1] As renal function declines, uremic toxins build up, causing chronic inflammation, oxidative stress, endothelial dysfunction, anemia, mineral and metabolic disturbances, and accelerated vascular disease.[5] The mechanisms may have negative effects on the central nervous system and the peripheral nervous system.[6] The kidney–brain axis has become a well-established two-way street in which renal dysfunction, vascular damage, inflammation, and uremic toxicity can play a role in neurological disease.[7]

Therefore, neurological involvement can happen at varying phases of CKD and may include cognitive dysfunction, peripheral and autonomic neuropathy, encephalopathy and cerebrovascular disease.[8]

Cognitive impairment is an underrecognized and important neurologic complication of CKD.[9] A systematic review and meta-analysis published in 2024 evaluated 50 studies and 25,289 patients with CKD and found the overall prevalence to be about 40%, and 44% in Asian patients.[10] Executive functions and attention were more impaired, and cognitive impairment was more common in dialysis patients.[11] Multifactorial mechanisms may include cerebrovascular disease, common vascular risk factors (hypertension and diabetes), uremic toxin accumulation, chronic inflammation, and anemia.[12] Importantly, cognitive dysfunction can be clinically undiagnosed and can affect medication adherence, self-management, decision-making, and quality of life.[13] The 2024 KDIGO guideline also highlights the need to be aware of cognitive impairments in individuals with CKD, especially older adults.[14]

Chronic renal dysfunction is also associated with peripheral neuropathy.[15] Peripheral nerve function may be affected by accumulation of neurotoxic metabolites, metabolic abnormalities, microvascular injury, and chronic inflammation, which may result in sensation including numbness, tingling, burning sensation, and impaired perception of vibration or temperature.[16] Neuropathy can significantly affect mobility and functional independence, and can often be underdiagnosed if neurological assessment is not routinely performed when caring for people with CKD.[17] Concurrently, vascular risk factors and cardiovascular disease are strongly linked with CKD, and this association establishes a critical link between renal impairment and cerebrovascular events.[18] Kidney disease is known to be associated with and exacerbate the risk of significant vascular disease such as stroke and peripheral vascular disease.[19]

Although the burden of chronic kidney disease (CKD) on the CNS is significant, cognitive impairment and peripheral neuropathy can be clinically undetected until they become clinically relevant, and the vascular environment of CKD can also make the patient more vulnerable to cerebrovascular disease. The evaluation of such presentations in combination may therefore offer a more comprehensive view of the kidney–brain connection and help identify those patients who need early neurological and vascular assessment. The present study aimed to explore the linkage between CKD and neurological signs and symptoms, namely cognitive dysfunction and peripheral neuropathy, and evaluate the association of CKD with selected cerebrovascular risk factors. It was also intended to investigate whether the incidence of these neurological complications differed with the level of renal dysfunction.

MATERIALS AND METHODS

A hospital-based cross-sectional analytical study was conducted at Nephrology department over a period of six months, from November, 2025 to April, 2026.

The calculated sample size for OpenEpi version 3.01 with an assumed prevalence of cognitive impairment in patients with CKD of 40%, 95% confidence level, and absolute precision of 7% was a minimum of 188 participants.[10] About 10% of the data was deemed incomplete or non-response, so the number of participants required was raised to 209.
A non-probability consecutive sampling technique was used. The study included adult patients, aged 18 years and older, who had been diagnosed with chronic kidney disease. Patients with CKD were identified as those who had kidney abnormalities for at least 3 months and were categorized based on the estimated glomerular filtration rate and other kidney damage markers available. All types of CKD or ages were eligible for enrollment. Patients who had received conservative treatment or maintenance dialysis were included if they met the criteria for diagnosis of CKD and were able to undergo the necessary clinical and neurological examination.

Cognitive impairment and peripheral neuropathy were excluded if the patient had a previously diagnosed neurological disorder capable of causing these symptoms. Patients who had a history of major stroke with neurological disability, epilepsy, Parkinson's disease, multiple sclerosis, diagnosed dementia, severe psychiatric disorder, or traumatic brain injury were excluded. Patients with acute kidney injury with known CKD were excluded, as were patients with acute encephalopathy, severe systemic illness requiring immediate intensive care, and those unable to communicate well for cognitive assessment. Those patients who were not able to give informed consent and those who lacked complete clinical or laboratory data were not analyzed.

Demographic and clinical data were taken by a structured data-collection proforma after obtaining written informed consent. The variables assessed were age, sex, place of residence, educational level, smoking history, duration of CKD, CKD stage, dialysis status, duration of dialysis, and related comorbidities. Neurological symptoms including memory loss, difficulty with concentration, numbness, tingling, burning or weakness, gait problems, dizziness, and past cerebrovascular events were thoroughly obtained.

Each was thoroughly examined physically and neurologically. The Montreal Cognitive Assessment (MoCA) was used to assess cognitive function; this assessment tool has been extensively used to detect cognitive impairment in CKD populations.[20] After taking into account the participant's level of education and the validated interpretation of the MoCA, cognitive impairment was defined by the predefined cut-off.

Neurological examination was used to assess peripheral neuropathy, which involved the assessment of sensory modalities, vibration perception, ankle reflexes, muscle strength and relevant clinical symptoms. Peripheral neuropathy was confirmed according to typical neurological symptoms and examination findings. Distal symmetrical sensory abnormalities of the lower limbs were studied in particular.

Established vascular risk factors for cerebrovascular disease were assessed, including hypertension, diabetes mellitus, dyslipidaemia, smoking, obesity, cardiovascular disease and previous cerebrovascular disease. BP was taken after suitable rest with a calibrated sphygmomanometer. Weight, height and BMI were recorded. Laboratory tests were performed for hemoglobin, serum creatinine, blood urea nitrogen, serum electrolytes, fasting blood glucose or HbA1c, lipid profile, and other routine tests for CKD. An appropriate validated equation was used to estimate glomerular filtration rate, and then the stage of CKD was documented.

Cognitive impairment and peripheral neuropathy were the main outcomes and major cerebrovascular risk factors, and their association with CKD severity was a secondary outcome. The data were verified for completeness at the point of collection; those with outcome information that was very incomplete were dropped from the final analysis.

The data collected were entered and analyzed with IBM SPSS Statistics version 26. The Shapiro–Wilk test was used to check for normality of continuous variables. Continuous variables were expressed as mean ± standard deviation and non-normally distributed variables were expressed as median (interquartile range). Categorical variables were presented as frequencies and percentages.

Prevalence estimates of cognitive impairment and peripheral neuropathy were computed and 95% confidence intervals were calculated. The Pearson chi-square test was used to determine associations between categorical variables such as CKD stage and neurological symptoms. Independent-samples t-test and Mann–Whitney U test were used for continuous variables to compare patients with and without cognitive impairment or peripheral neuropathy.

Spearman rank correlation was used to assess the association between estimated GFR and continuous measures of neurological or cognitive function. Pearson correlation was applied for variables that were normally distributed, and Spearman rank correlation was used for non-normally distributed variables. Then binary logistic regression analysis was run to determine factors independently associated with cognitive impairment and peripheral neuropathy. Variables with a clinically relevant association, or a p-value <0.20 on univariable analysis, were considered for multivariable regression. Odds ratios (ORs) with 95% confidence intervals are reported. Before developing final regression models, one has to check for multicollinearity. The p-value on both sides was taken as statistical significance at $p < 0.05$.

RESULTS

Among the 209 participants, the mean age was 54.8 ± 13.6 years, with 44.0% aged ≥60 years, and 57.9% were male. The most frequent comorbidities were hypertension (72.2%), diabetes mellitus (48.8%), dyslipidaemia (36.4%) and cardiovascular disease (23.4%). The mean eGFR of the subjects was 31.7 ± 18.9 mL/min/1.73 m², and 26.8% had dialysis-dependent CKD. (Table 1)

The average score on the MoCA was 22.8 ± 4.1, and 43.5% (91) of participants were considered to have cognitive impairment. Eighty-three (39.7%) had peripheral neuropathy. The most frequent neurological complaints were numbness or tingling (42.1%), memory difficulty (39.2%), and burning sensation (33.0%). A decreased vibration sense and abnormal ankle reflexes were reported in 36.4% and 38.8% of the subjects, respectively. (Table 2)

Demographic characteristics of participants with cognitive impairment were significantly different from those without, in the sense of being older, with higher CKD duration and lower eGFR. Lower education level, hypertension, diabetes, dyslipidaemia, cardiovascular disease, history of a cerebrovascular disease and dialysis dependence were also significantly associated with cognitive impairment. (Table 3)

The neurological abnormalities were more common with increasing severity of CKD for both. Overall, 22.6% of patients with G3a disease had cognitive impairment, compared to 64.3% of dialysis-dependent patients, and 19.4% of patients with G3a disease had peripheral neuropathy, compared to 64.3% of dialysis-dependent patients. Statistically significant; that is,

there was a significant association between the CKD stage and cognitive impairment and peripheral neuropathy ($p<0.001$ for both). (Table 4)

Older age, longer CKD duration, lower eGFR, DM, CVD, lower Hb, higher SCr, and higher SK were significantly associated with peripheral neuropathy. Neuropathy patients had significantly higher levels of serum creatinine than did those without neuropathy as measured by Mann–Whitney U ($p<0.001$). (Table 5)

There was a positive correlation between MoCA score, hemoglobin, and higher eGFR ($r=0.41$, $p<0.001$ and $r=0.29$, $p<0.001$, respectively), and a negative correlation between eGFR and CKD duration, serum creatinine, BUN, age, and systolic blood pressure. The most significant correlation was found between eGFR and serum creatinine ($p<0.001$). (Table 6)

The multivariable logistic regression analyses showed that low educational status, eGFR <30 mL/min/1.73 m², diabetes mellitus, previous cerebrovascular disease and dialysis-dependent CKD remained independently associated with cognitive impairment. The strongest association was with dialysis dependence, where patients on dialysis had over three times the odds of having cognitive impairment. (Table 7)

Also, the duration of CKD >5 years, eGFR < 30 mL/min/1.73 m², diabetes mellitus, and dialysis dependence were still independently associated with peripheral neuropathy when potential confounders were adjusted. The results indicated that worse severity of CKD and the duration of renal dysfunction were independent of both the major neurological outcomes studied. (Table 8)

Table 1. Demographic and clinical characteristics of study participants (n=209)

Variable	Category/Statistic	n (%) / Mean ± SD
Age (years)	Mean ± SD	54.8 ± 13.6
Age group	18–39 years	28 (13.4)
	40–59 years	89 (42.6)
	≥60 years	92 (44.0)
Sex	Male	121 (57.9)
	Female	88 (42.1)
Educational status	No formal education	38 (18.2)
	Primary	51 (24.4)
	Secondary	63 (30.1)
	Higher education	57 (27.3)
Residence	Urban	119 (56.9)
	Rural	90 (43.1)
Smoking	Yes	46 (22.0)
	No	163 (78.0)
Duration of CKD (years)	Mean ± SD	4.2 ± 2.9
CKD stage	G3a	31 (14.8)
	G3b	39 (18.7)
	G4	51 (24.4)
	G5, non-dialysis	32 (15.3)
	G5D, dialysis	56 (26.8)
eGFR (mL/min/1.73 m²)	Mean ± SD	31.7 ± 18.9
Duration of dialysis (years), among dialysis patients	Median (IQR)	2.1 (1.1–3.8)
Hypertension	Yes	151 (72.2)
Diabetes mellitus	Yes	102 (48.8)
Dyslipidemia	Yes	76 (36.4)
Cardiovascular disease	Yes	49 (23.4)
Previous cerebrovascular disease	Yes	27 (12.9)
BMI (kg/m²)	Mean ± SD	25.1 ± 4.3
Obesity (BMI ≥30 kg/m²)	Yes	38 (18.2)

Table 2. Clinical, neurological and laboratory characteristics of participants

Variable	Statistic	Value
Cognitive score (MoCA)	Mean ± SD	22.8 ± 4.1
Cognitive impairment	Yes	91 (43.5)
	No	118 (56.5)
Peripheral neuropathy	Yes	83 (39.7)
	No	126 (60.3)
Memory difficulty	Yes	82 (39.2)
Impaired concentration	Yes	71 (34.0)
Numbness/tingling	Yes	88 (42.1)
Burning sensation	Yes	69 (33.0)
Lower-limb weakness	Yes	47 (22.5)
Gait disturbance	Yes	39 (18.7)
Dizziness	Yes	52 (24.9)
Reduced vibration perception	Yes	76 (36.4)
Reduced/absent ankle reflexes	Yes	81 (38.8)
Hemoglobin (g/dL)	Mean ± SD	10.4 ± 1.7
Serum creatinine (mg/dL)	Median (IQR)	2.9 (1.9–4.8)
BUN (mg/dL)	Mean ± SD	64.7 ± 28.5
Sodium (mmol/L)	Mean ± SD	137.8 ± 4.6
Potassium (mmol/L)	Mean ± SD	4.7 ± 0.7
Fasting glucose (mg/dL)	Mean ± SD	126.5 ± 43.8
HbA1c (%)	Mean ± SD	7.0 ± 1.5
Total cholesterol (mg/dL)	Mean ± SD	183.6 ± 42.7
LDL cholesterol (mg/dL)	Mean ± SD	112.4 ± 34.8
HDL cholesterol (mg/dL)	Mean ± SD	39.8 ± 9.2
Triglycerides (mg/dL)	Mean ± SD	159.7 ± 61.5
Systolic BP (mmHg)	Mean ± SD	142.6 ± 18.4
Diastolic BP (mmHg)	Mean ± SD	82.7 ± 10.6

Table 3. Association of demographic and clinical characteristics with cognitive impairment

Variable	Cognitive impairment n=91	No impairment n=118	p-value
Age, mean ± SD (years)	59.2 ± 12.8	51.4 ± 13.5	<0.001
Male sex	58 (63.7%)	63 (53.4%)	0.139
No formal/primary education	52 (57.1%)	37 (31.4%)	<0.001
Smoking	25 (27.5%)	21 (17.8%)	0.082
CKD duration, mean ± SD	5.0 ± 3.0	3.6 ± 2.6	<0.001
eGFR, mean ± SD	24.8 ± 15.7	37.1 ± 19.4	<0.001
Hypertension	75 (82.4%)	76 (64.4%)	0.004
Diabetes mellitus	58 (63.7%)	44 (37.3%)	<0.001
Dyslipidemia	40 (44.0%)	36 (30.5%)	0.048
Cardiovascular disease	30 (33.0%)	19 (16.1%)	0.003
Previous cerebrovascular disease	19 (20.9%)	8 (6.8%)	0.002
Obesity	18 (19.8%)	20 (16.9%)	0.580
Dialysis-dependent CKD	39 (42.9%)	17 (14.4%)	<0.001

Table 4. Association of CKD severity with cognitive impairment and peripheral neuropathy

CKD stage	Cognitive impairment n (%)	Peripheral neuropathy n (%)
G3a	7 (22.6)	6 (19.4)
G3b	12 (30.8)	10 (25.6)
G4	20 (39.2)	17 (33.3)
G5 non-dialysis	16 (50.0)	14 (43.8)
G5D dialysis	36 (64.3)	36 (64.3)
p-value	<0.001	<0.001

Table 5. Association of peripheral neuropathy with demographic, clinical and laboratory characteristics

Variable	Neuropathy n=83	No neuropathy n=126	p-value
Age, mean ± SD (years)	59.0 ± 12.5	52.0 ± 13.8	<0.001
Male sex	52 (62.7%)	69 (54.8%)	0.258
Smoking	23 (27.7%)	23 (18.3%)	0.087
CKD duration, mean ± SD (years)	5.1 ± 3.0	3.6 ± 2.6	<0.001
eGFR, mean ± SD	24.0 ± 15.3	36.8 ± 19.5	<0.001
Diabetes mellitus	52 (62.7%)	50 (39.7%)	0.002
Hypertension	66 (79.5%)	85 (67.5%)	0.059
Dyslipidemia	35 (42.2%)	41 (32.5%)	0.153
Cardiovascular disease	25 (30.1%)	24 (19.0%)	0.049
Hemoglobin, mean ± SD (g/dL)	10.0 ± 1.6	10.7 ± 1.7	0.003
Serum creatinine, median (IQR)	3.8 (2.5–5.6)	2.5 (1.7–4.1)	<0.001
Potassium, mean ± SD (mmol/L)	4.8 ± 0.7	4.6 ± 0.6	0.031
Dialysis-dependent CKD	34 (41.0%)	22 (17.5%)	<0.001

Table 6. Correlation of eGFR with cognitive score and selected neurological measures

Variable correlated with eGFR	Correlation coefficient	p-value
MoCA score	r = 0.41	<0.001
Age	r = −0.18	0.009
CKD duration	r = −0.36	<0.001
Serum creatinine	r = −0.82	<0.001
BUN	r = −0.57	<0.001
Hemoglobin	r = 0.29	<0.001
Systolic BP	r = −0.21	0.002

Table 7. Logistic regression analysis of factors associated with cognitive impairment

Predictor	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age ≥60 years	2.14 (1.22–3.76)	0.008	1.72 (0.91–3.25)	0.094
Low educational status	2.91 (1.65–5.13)	<0.001	2.37 (1.29–4.36)	0.005
CKD duration >5 years	2.04 (1.16–3.59)	0.013	1.68 (0.90–3.13)	0.103
eGFR <30 mL/min/1.73 m²	3.21 (1.78–5.79)	<0.001	2.46 (1.30–4.65)	0.006
Hypertension	2.55 (1.29–5.02)	0.007	1.69 (0.79–3.62)	0.176
Diabetes mellitus	2.95 (1.69–5.16)	<0.001	2.21 (1.20–4.08)	0.011
Cardiovascular disease	2.56 (1.28–5.12)	0.008	1.87 (0.88–3.96)	0.102
Previous cerebrovascular disease	3.62 (1.44–9.09)	0.006	2.94 (1.08–8.02)	0.035
Dialysis-dependent CKD	4.42 (2.27–8.62)	<0.001	3.18 (1.51–6.69)	0.002

Table 8. Logistic regression analysis of factors associated with peripheral neuropathy

Predictor	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age ≥60 years	2.04 (1.17–3.56)	0.012	1.61 (0.87–2.99)	0.128
CKD duration >5 years	2.48 (1.40–4.39)	0.002	2.02 (1.08–3.78)	0.028
eGFR <30 mL/min/1.73 m²	3.14 (1.76–5.62)	<0.001	2.51 (1.33–4.74)	0.005
Diabetes mellitus	2.55 (1.45–4.48)	0.001	2.18 (1.19–3.98)	0.011
Hypertension	1.86 (0.97–3.57)	0.061	1.48 (0.73–3.01)	0.277
Dyslipidemia	1.51 (0.84–2.72)	0.169	1.31 (0.70–2.46)	0.397
Hemoglobin <10 g/dL	2.17 (1.18–3.98)	0.013	1.89 (0.99–3.62)	0.054
Cardiovascular disease	1.84 (0.95–3.56)	0.071	1.52 (0.74–3.14)	0.256
Dialysis-dependent CKD	2.98 (1.58–5.62)	<0.001	2.31 (1.16–4.60)	0.017

DISCUSSION

This study revealed a significant neuro-anatomical burden in people with CKD; significant cognitive impairment was observed in 43.5% of the participants and peripheral neuropathy was observed in 39.7% of the participants. The risk of both outcomes increased with increasing CKD stage, and lower eGFR, longer duration of CKD, and diabetes mellitus and dialysis dependence were significant associated factors. These results support the notion that CKD is a systemic disease involving not only renal function but also the central and peripheral nervous system.

The prevalence of cognitive impairment in our cohort (43.5%) was similar to the pooled prevalence rate from a 2024 systematic review and meta-analysis (50 studies, 25,289 CKD patients) by Zhang et al. They found that the prevalence was higher in Asian populations (44%) and cognitive impairment was more common in patients on hemodialysis (53%) than in non-dialysis CKD patients (32%). This similarity could be because of the high proportion of patients with advanced CKD and dialysis-dependent patients in our cohort. Zhang et al. also identified older age, diabetes, and hypertension as important predictors, which is consistent with the significant associations observed in our study.[10]

The results corroborate a 2023 prospective cohort study of 448 prevalent hemodialysis patients, which found that 77.2% had cognitive impairment on MoCA. It was clear that their prevalence was significantly higher than ours, but it is understandable since they were only patients on maintenance hemodialysis, while our study was performed in patients with all stages of CKD. The marked cognitive burden observed in dialysis populations reinforces our finding that dialysis-dependent CKD had an independent association with cognitive impairment.[21]

Likewise, Chen et al., in their 2023 study of 146 patients on maintenance hemodialysis, reported cognitive impairment in 31.5% of their patients and that duration of dialysis of ≥5 years and increasing age were independently associated with cognitive impairment. Similarly, duration of CKD and dialysis dependence were also associated with cognitive impairment in our study, and age was significantly associated on univariable analysis. This uniformity across studies implies that the physiological stress from advanced renal dysfunction and from dialysis may be a factor in the accrual of neurological vulnerability.[21]

Additional, more recent, evidence has been found to support the link between renal dysfunction and cognition. The Chronic Renal Insufficiency Cohort conducted an analysis in 2026 that showed that the severity of CKD was linked with the risk of cognitive impairment in several cognitive domains, including global cognition, verbal memory, and attention/executive function. Our correlation between eGFR and MoCA score was positive ($r=0.41$, $p<0.001$), which is in the same direction as this evidence, suggesting that there may be a correlation between lower renal function and lower cognitive function.[22] A systematic review and meta-analysis of 26 studies (326,216 patients) published in 2026 showed that cognitive outcomes differed by dialysis modality, with higher rates of dementia among hemodialysis compared to PD patients, highlighting the clinical significance of cognitive monitoring in the advanced CKD population.[23]

Peripheral neuropathy was diagnosed in 39.7% of our subjects. The results were similar to the Kumar et al. 2022 study in India, which found peripheral neuropathy in 54.3% of pre-dialysis patients and 75.9% of HD patients. They also found a correlation between the duration and severity of CKD and its association with neuropathy, which is similar to our findings, where neuropathy rose from 19.4% in the G3a group to 64.3% in the dialysis group. The lower overall prevalence in this cohort may be due to the fact that our study included patients with earlier stages of CKD.[24]

Another study in 2022 in Benin with 189 chronic hemodialysis patients confirmed our findings with a 59.3% peripheral neuropathy occurrence. The prevalence was more than our overall cohort, but their sample only included patients with long-term hemodialysis treatment. The higher prevalence of neuropathy in dialysis-dependent patients is similar to our experience with patients who have earlier-stage CKD.[25] In addition, a study in the Philippines in 2022 reported a prevalence of 35.9% with neuropathic pain in hemodialysis patients, with significant associations with older age and diabetes and very low eGFR, similar to our findings.[26]

The prevalence of neuropathy in our study was also in line with that of Cai et al. (2023), who investigated 1,836 individuals with CKD from NHANES and found that peripheral neuropathy was clinically relevant in CKD and was independently associated with significantly higher all-cause mortality and cardiovascular mortality. We did not measure mortality as an outcome in our cross-sectional study, but these results indicate that the neuropathy that was seen in our participants might be a marker of systemic and vascular vulnerability, rather than just a neurological complication.[15]

There are several recent publications that support the link between cerebrovascular risk and CKD noted in our study. According to Kelly et al. (2021), CKD was found to be highly linked with all the phenotypes of cerebrovascular disease, such as ischemic stroke, small vessel disease, and vascular cognitive impairment (VCI), as well as hemorrhagic stroke. They pointed out that hypertension and diabetes contribute to this correlation, with uremia-related coagulopathy and

endothelial dysfunction, and others possibly adding other pathways. This is similar to our observation that hypertension, diabetes, cardiovascular disease, and previous cerebrovascular disease were more prevalent in those participants who had cognitive impairment.[27]

Likewise, Wyld and Webster (2021) found that CKD is an independent risk factor for stroke and suggested older age, diabetes, hypertension, uremia, vascular calcification, arterial stiffness, and chronic inflammation as potential factors.[28] Zamberg et al. later performed a meta-analysis of over 99,000 patients in 2021 that confirmed that ischemic stroke was still the most common stroke subtype in CKD, and that the proportion of patients with hemorrhagic stroke increased as kidney function declined; there was also worse post-thrombolysis outcomes in patients with CKD. The findings of these observations agree with our approach for including cerebrovascular disease and vascular risk factors in neurological evaluation in CKD.[29]

An advantage of the present study was the assessment of cognitive impairment, peripheral neuropathy, and cerebrovascular risk in the same population of patients with CKD, as distinct complications. However, because of the cross-sectional design, temporal and causal relationships cannot be determined, and because clinical neurological assessment was not performed on all patients, subclinical neuropathy may have been underestimated. Furthermore, the one-centre design and non-probability sampling might restrict the generalizability. Even with these caveats, our results were consistent with the more recent international literature, which justifies the recognition of neurological involvement as a key part of the management of CKD.

Limitations

There were a number of limitations in this study. It did not allow for establishing temporal or causal relationships between CKD and neurological manifestations because of its cross-sectional design. As this was a single tertiary care center, the results may not be generalizable to other populations and health care systems. A screening instrument was used to assess cognitive function and, not routinely, nerve-conduction studies or electromyography to assess peripheral neuropathy, which may lead to underrecognition of subclinical disease. There remained the possibility of social and economic status, medication, nutritional deficiencies and length of and control over diabetes as residual confounding factors. Hence, multicenter, longitudinal studies with objective neurophysiological and neuropsychological measurements are warranted.

CONCLUSION

Patients with CKD had a high prevalence of neurological symptoms, and cognitive impairment and peripheral neuropathy increased with worsening renal function. Some independent factors that were associated with neurological involvement were lower eGFR, longer duration of CKD, presence of diabetes, and dialysis dependence. The present findings highlight the need to recognize neurological dysfunction routinely as part of CKD management. However, cognitive and peripheral neurological dysfunctions, especially in CKD patients with advanced kidney disease, can be identified early and assist in providing timely intervention and functional outcomes. Another important consideration in advanced kidney failure is neurological manifestations and cognitive impairment per the KDIGO 2024 guideline.

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