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STUDY OF COGNITIVE IMPAIRMENT IN ELDERLY PATIENTS WITH CHRONIC KIDNEY DISEASE

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ABSTRACT
Background: Cognitive impairment (CI) represents a significant global public health issue affecting approximately 50 million people worldwide. Individuals with chronic kidney disease (CKD) are particularly vulnerable to developing CI, which can adversely impact quality of life, medication adherence, mortality risk, and healthcare resource utilization. Thus, the present study aims to investigate the prevalence of CI among elderly patients diagnosed with CKD.
Materials and Method: A hospital-based cross-sectional study included 70 CKD patients aged over 65 years, assessing cognitive impairment using (Montreal Cognitive Assessment) MoCA. Clinical data, including glomerular filtration rate (eGFR) and biomarkers, were collected and analyzed.
Results: Patients had an average age of 69.5 years, with a majority at CKD stages 4 and 5. CI, defined by MoCA scores ≤ 24, was prevalent in 81.1% of patients. Higher hemoglobin levels ($r = 0.493$, $p = 0.0005$) and eGFR ($r = 0.488$, $p = 0.0005$) correlated significantly with better cognitive function. Progressive CKD stages showed a decline in eGFR, with Stage V indicating severe renal impairment.
Conclusion: The present study highlights the association between CKD severity, clinical biomarkers, and CI in elderly patients. Lower eGFR levels independently correlate with impaired cognitive function, particularly affecting executive function. Early detection of cognitive decline in CKD may improve patient outcomes through targeted interventions and enhanced care strategies. Further research is needed to optimize screening tools and interventions for CI in this vulnerable population.

Keywords: Chronic Kidney Disease, Cognitive impairment, Montreal Cognitive Assessment, Glomerular filtration rate

INTRODUCTION
Chronic kidney disease (CKD) involves gradual and irreversible kidney damage, impairing its ability to function effectively. This condition's prevalence has surged due to a rise in hypertension, diabetes mellitus, and obesity rates. [1]

Cognitive impairment (CI) can result from CKD related conditions such as hypertension, anaemia, vascular dysfunction, uremia, proteinuria, systemic inflammation and oxidative stress. This impairment exhibits as difficulties with memory, learning, concentration, and decision-making, which are common among CKD patients. [2] Globally, around 50 million people experienced severe cognitive impairment in 2015, with 60% residing in low- and middle-income countries. By 2030 and 2050, 82 million and 152 million respectively are expected to have this predominance. [3]

Limited research has explored the link between CKD prior to kidney failure and cognitive outcomes, indicating that older adults with severely impaired kidney function tend to exhibit poorer cognitive function compared to those without CKD. However, there is a lack of understanding regarding which cognitive domains are specifically affected in CKD, as previous studies predominantly relied on global cognitive screening tools rather than assessments targeting specific domains. [4]

Tests such as the Mini-Mental State Examination (MMSE), modified Mini –Mental State Examination, Six-Item Cognitive Screen Test, Montreal Cognitive Assessment (MoCA), Cognitive Screening interview for Dementia, Trials Making Test, and Digit Symbol Substitution Task can be used to assess cognitive dysfunction. The MMSE, for instance, is particularly helpful in determining the degree and course of CI in individuals over time, providing valuable insights into their response to treatment. [5]

CI in CKD significantly impacts quality of life, healthcare utilization, medical costs, and hospitalization rates, leading to suboptimal medical care. It also presents difficulties for informed consent when it comes to decisions on the start, continuation and transplantation of dialysis. Thus, identifying CI in CKD patients is crucial to mitigate associated morbidities. [6]
Therefore, the present study aims to assess the prevalence of CI among elderly patients with CKD using the score, and to investigate the correlation between CI severities. Understanding the extent of CI in elderly CKD patients is crucial for early detection and prevention of progressive cognitive decline. This can ultimately enhance the quality of life for older adults by initiating timely interventions in the early stages of CKD.

METHODOLOGY

This hospital-based cross sectional in Bangalore Medical and Research Institute-affiliated facilities. A total of 70 patients were included in the research. The patients who met the inclusion and exclusion criteria were enrolled after receiving approval and clearance from the institutional ethical committee.

Criteria of Inclusion:

Patients aged over 65 years who were willing to provide informed consent and diagnosed with CKD were enrolled in the study.

Criteria of Exclusion:

Patients below the age of 65 years who were not willing to provide informed consent were not included in the study. Additionally, patients with neurological or psychiatric illnesses, as well as those with acute kidney injury, were also excluded from the study.

Methodology:

Clinical examination and investigations was done and data was collected using proforma. Glomerular filtration rate was calculated using 2021 modified MDRD equation. In this study, patients was assessed with detailed clinical history and basic clinical examination. Cognitive assessment was done using MOCA scoring system (annexure-3). Level of cognitive impairment was correlated with glomerular filtration rate.

RESULTS:

In this study, 70 CKD patients aged over 65 years were included. The average age of the participants was 69.5 years, with a standard deviation of 5 years. The majority of the patients were male, constituting 71.4% of the cohort. Most participants, approximately 81.4%, were classified under CKD stages 4 and 5, indicating advanced kidney disease. A significant proportion of the patients had comorbid conditions, with 95.7% being hypertensive and 64% diagnosed with diabetes. CI, assessed using the MoCA with a cutoff score of ≤ 24, was prevalent among 81.1% of the patients. Specifically, 11 patients exhibited mild CI, 29 had moderate CI, and 17 experienced severe CI.

Table 1: Classification of demographic data.

Descriptive Statistics					
	N	Minimum	Maximum	Mean	SD
Age	70	65.0	84.0	69.5	5.0
Height	70	134.0	176.0	163.5	8.9
Weight	70	42.0	78.0	61.2	9.1
Hemoglobin	70	5.5	15.0	10.3	2.4
Urea	70	23.00	275.00	86.0	52.7
Creat	70	.69	10.77	4.2	2.5
Hba1c	5	13.6	69.0	47.1	23.1
If yes duration DM	44	2.0	16.0	7.8	4.0
If yes duration HTN	66	0.00	15.00	6.1	3.8
If yes duration IHD	7	1.0	6.0	3.3	1.8
IPTH	68	98.0	1227.0	303.2	266.0
TSAT	18	6.55	94.00	35.0	28.2
LVEF	51	35	64	57.3	6.2
Egfr	70	3.6	115.1	21.0	15.7
Moca Score	70	15.0	24.0	20.3	2.9

The table 1 summarizes demographic and clinical data for 70 individuals, showing the following means (ranges): age 69.5 years (65.0–84.0), height 163.5 cm (134.0–176.0), weight 61.2 kg (42.0–78.0), hemoglobin 10.3 g/dL (5.5–15.0), urea 86.0 mg/dL (23.0–275.0), creatinine 4.2 mg/dL (0.69–10.77), HbA1c 47.1 mmol/mol (13.6–69.0), parathyroid hormone 303.2 pg/mL (98.0–1227.0), transferrin saturation 35.0% (6.55–94.0), left ventricular ejection fraction 57.3% (35%–64%), eGFR 21.0 mL/min/1.73 m² (3.6–115.1), and MoCA score 20.3 (15.0–24.0). This provides an overview of their health characteristics.

Table 2: Correlation of MOCA score with clinical parameters

		Moca Score
Hb	r-value	493
	p-value	0005
	N	70
Urea	r-value	380
	p-value	001
	N	70
Egfr	r-value	488
	p-value	0005
	N	70

The table 2 displays the correlations of the MoCA score with various clinical parameters. The MoCA score shows a significant positive correlation with hemoglobin levels ($r = 0.493$, $p = 0.0005$), indicating that higher hemoglobin levels tend to be associated with better cognitive function as measured by the MoCA. Conversely, it demonstrates a negative correlation with urea levels (r = -0.380, p = 0.001), suggesting that higher urea levels may be related with poorer cognitive performance. Additionally, there is a significant positive correlation between MoCA score and eGFR (r = 0.488, p = 0.0005), implying that better kidney function, as indicated by higher eGFR, correlates with better cognitive function. These findings highlight the potential interplay between cognitive health and these clinical biomarkers in the studied population.

Table 3: Comparison of severity and MOCA score

Moca Score	N	Mean	SD	F value	p value
Normal	13	21.5	2.3	5.67	0.002
Mild	11	21.5	2.9		
Moderate	29	20.5	2.2		
Severe	17	18.1	3.4		

The table 3 compares MoCA scores across severity levels: Normal (Mean = 21.5), Mild (Mean = 21.5), Moderate (Mean = 20.5), and Severe (Mean = 18.1). Significant differences in scores were found among these groups (F = 5.67, p = 0.002), indicating varying cognitive function across severity levels.

Table 4: Comparison of Hb level and MOCA score level.

(I) Hb		MD (I-J)	p-value	95% C.I	
				LB	UB
Normal	Mild	-.0070	1.000	-2.867	2.853
	Moderate	1.0212	.657	-1.309	3.351
	Severe	3.4208*	.004	.849	5.993
Mild	Moderate	1.0282	.693	-1.444	3.500
	Severe	3.4278*	.007	.727	6.129
Moderate	Severe	2.3996*	.021	.267	4.532

The table 4 examines the relationship between hemoglobin (Hb) levels and MoCA scores across severity categories: Normal, Mild, Moderate, and Severe. Each comparison shows the mean difference (MD) in MoCA scores between Hb levels, along with corresponding p-values to indicate statistical significance. Significant findings include higher MoCA scores associated with Normal compared to Severe Hb levels (MD = 3.4208, p = 0.004), Mild compared to Severe Hb levels (MD = 3.4278, p = 0.007), and Moderate compared to Severe Hb levels (MD = 2.3996, p = 0.021). These results suggest that lower Hb levels correlate with poorer cognitive function as measured by MoCA, highlighting a potential association between hemoglobin status and cognitive performance across varying severity levels.

Table 5: Classification of Urea status

Urea	N	Mean	SD	p value
Normal	49	21.0	2.6	0.001
Abnormal	21	18.6	2.9	

The table 5 categorizes individuals based on their urea status and compares associated mean values and standard deviations (SD) between groups. Among 70 participants, 49 were classified under the Normal urea category, showing a mean urea level of 21.0 mg/dL with a SD of 2.6. In contrast, 21 participants fell into the abnormal urea category, where the mean urea level was lower at 18.6 mg/dL with a slightly higher SD of 2.9. A statistically significant difference in urea levels between these two groups is indicated by the p value of 0.001. This suggests that individuals with abnormal urea levels tend to reveal lower mean values associated to normal urea levels, highlighting potential implications for clinical assessment and management of urea-related conditions.

Table 6: Comparison of EGFR with stages of CKD

(I) Egfr		MD (I-J)	p-value	95% C.I	
				LB	UB
Stage 3 & below	Stage IV	1.2605	.198	-.475	2.996
	Stage V	4.7692*	.0005	2.986	6.553
Stage IV	Stage V	3.5087*	.0005	2.112	4.905

The table 6 examines the relationship between eGFR levels and stages of chronic kidney disease (CKD): Stage 3 & below, Stage IV, and Stage V. Each comparison shows the mean difference (MD) in eGFR between CKD stages, accompanied by p-values indicating statistical significance. Significant findings include Stage V demonstrating significantly higher eGFR levels compared to both Stage 3 & below (MD = 4.7692, p = 0.0005) and Stage IV (MD = 3.5087, p = 0.0005). These results highlight the progressive decline in kidney function as CKD advances, with Stage V representing the most severe impairment in renal function among the stages analyzed.

DISCUSSION

CKD is emerging as a significant global public health issue. The current prevalence of CKD may be attributed to changes in its underlying pathogenic mechanisms. Similar to other chronic conditions, CKD may independently contribute to cognitive impairment. A number of variables, including demographics like age, education level, gender, and ethnicity (Hispanic and African American), can affect cognitive performance. Pschosocial elements including anxiety, despair, exhaustion, identity loss, and insomnia also play a role.

There have been few research on the risks of dementia and CI in people with CKD. In the Cardiovascular Health Cognition Study, **Seliger et al.,** [7] discovered that older individuals with CKD had a higher chance of getting dementia. Both a continuous variable and a dichotomous variable were used to evaluate kidney function.

In the present study, the mean age of participants was 69.5 years. Similarly, in the study by **Paraizo et al.,** [8] the sample consisted of adult, non-elderly individuals with a mean age of 56.74 ± 7.63 years. Additionally, numerous studies have demonstrated that older age is a risk factor for CI, attributed to neurotransmitter dysregulation that occurs with aging. [9, 10]

Furthermore, the current study found significant positive correlations between MoCA scores and clinical biomarkers. Higher hemoglobin levels (r = 0.493, p = 0.0005) and higher estimated eGFR (r = 0.488, p = 0.0005) were associated with better cognitive function. **Gela et al.,** [11] also reported that reduced eGFR is a strong predictor of CI. Specifically, CI was 3.9 times more common in patients with lower eGFR than in those with eGFR ≥60 mL/min/m^2.

This increased risk is likely due to the accumulation of neurotoxic waste products in the blood as kidney function declines. CI in patients with CKD is associated with elevated levels of uremic toxins, neuropeptide Y, parathyroid hormone, decreased kidney neurotrophins, increased homocysteine, and vascular damage in the central nervous system

The present study underscores the correlation between eGFR levels and CKD stages, showing a gradual decline in kidney function as CKD progresses, with Stage V indicating the most severe renal impairment. **Aggarwal et al.,** [6] similarly found that as CKD stage advances, eGFR decreases and serum creatinine levels rise, correlating with a decline in MMSE and MoCA scores. This aligns with results from studies by **Stevens et al.,** [12] and **Kurella et al.,** [13] further supporting the finding of the present study.

Another study conducted by **Gela et al.,** [12] found that CKD Patients had a greater prevalence of CI than the healthy controls. This findings were found to be consistent with a similar study conducted in Nigeria. [14] This may be due to the retention of waste products in the blood, such as urea and electrolytes, resulting from decreased glomerular filtration rate or glomerular capillary abnormalities. Additionally, this study identified an independent association between lower eGFR levels and impaired cognitive function across various domains, particularly in tests of executive function. This association remained significant even after accounting for sociodemographic and clinical factors. These findings suggest the potential importance of screening older patients with advanced CKD for cognitive impairment. However, further research is necessary to establish optimal screening tools and determine the sensitivity and specificity of various cut points for screening.

Limitations of the Study:

- Small sample size
- Single centre research
- No comparison between healthy and CKD patients.

CONCLUSION

CKD is a prevalent condition that leads to various symptoms and comorbidities in older adults. Among these, cognitive impairment is notably common, with its severity often correlating with the level of kidney dysfunction. While the precise mechanisms behind cognitive impairment in CKD patients are not yet fully understood, they seem to involve a complex interplay of pathophysiological processes. This cognitive decline can have significant impacts for both patients and those who care for them. Lifestyle interventions, particularly increased physical activity and exercise, show promise in improving cognitive function in this at-risk population.

Furthermore, these findings emphasize the complex relationship between kidney function, clinical biomarkers, and cognitive impairment in elderly CKD patients, suggesting possibilities for further research and targeted interventions to improve cognitive outcomes in this vulnerable group.