ORIGINAL ARTICLE

Examining the Relationship Between Chronic Kidney Disease Severity and Cognitive Decline: A Cross-Sectional Analysis in Adult Patients

Gokul. P. Reghunathan[1], L. Lavanya[2], Venkatraman Natarajan[3], Raman K[4]

[1] Final year postgraduate, Department of Psychiatry, Saveetha medical college Hospital, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai,602105, India
[2] Assistant professor, Department of Psychiatry, Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai - 602105, India.
[3] Associate Professor, Department of Psychiatry, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai,602105, India
[4] Professor, Department of Psychiatry, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai,602105, India

ABSTRACT

Introduction: Chronic kidney disease (CKD) is a gradual loss of kidney function characterized by reduced GFR or elevated albuminuria, with a global prevalence of 9.37% in 2019. Cognitive decline, a common but underdiagnosed complication of CKD, affects approximately 10% to 40% of patients depending on the stage and assessment method. This study investigates the association between CKD stages and cognitive decline. **Methods:** This cross-sectional study involved 140 CKD patients aged 18-65 years at Saveetha Medical College. Participants were selected based on confirmed CKD diagnosis, excluding those with prior mental illness or severe health issues. Cognitive function was assessed using the Mini-Mental State Examination (MMSE) and Brief Cognitive Rating Scale (BCRS). Data collection included structured interviews and record analysis, analyzed using SPSS version 26. **Results:** Of the 140 participants, 40.7% were aged 51-65 years, and 57.9% were male. Cognitive decline was observed in 23.57% of patients, with 22.1% exhibiting mild and 1.4% severe impairment. A significant correlation between CKD stage and cognitive decline was found, with 30.2% of stage 5 patients affected compared to 14.3% in stage 1. These findings suggest a graded decline in cognitive function with increasing CKD severity. **Discussion:** CKD-related cognitive decline is associated with inflammation, uremic toxins, anemia, and oxidative stress. Advanced CKD stages notably increase the risk of cognitive impairment. Early intervention and comprehensive management, including controlling blood pressure and albuminuria, are crucial to mitigating cognitive deterioration in CKD patients. **Trial Registration:** The study was registered with the Institutional Ethical Committee (SMCH-IEC), Saveetha Medical college and Hospital: SMC/IEC/2023/06/041

Malaysian Journal of Medicine and Health Sciences (2024) 20(SUPP13): 46-50.doi:10.47836/mjmhs.20.s13.10

Keywords: Chronic kidney disease, cognitive decline, MMSE, CKD stages, cognitive impairment, uremic toxins, inflammation.

Corresponding Author:
L. Lavanya, MD
Email: lavanyadhanasekar226@gmail.com
Tel : +91 9840531866

INTRODUCTION

Chronic kidney disease (CKD) is a gradual loss of kidney function with reduced GFR or elevated albuminuria. According to the research done in 2019, the global prevalence of CKD was 9.37% and incidence was 0.05% (1). Cognitive decline is one of the most underdiagnosed complications of chronic kidney disease which accounts for 1/3rd of cases (2). The prevalence of cognitive damage in CKD patients is around 10% to 40%, subjective to the method of assessment and the CKD stage (3, 4). Chronic kidney disease (CKD) is an independent risk factor for cognitive impairment and recent study shows that cognitive decline is more common in CKD patients than controls (5).

85% of patients with end stage disease had cognitive impairment such as memory loss, executive impairment or language deficits (6). A study done by Murray et.al,

showed that around 87% of CKD patients had cognitive impairment and only 13% had normal cognition (7). Newly identified independent risk factors for cognitive decline are reduced eGFR and albuminuria. Accumulation of uremic toxins, anaemia, systemic inflammation and oxidative stress are the probable reason behind the pathophysiology of cognitive decline in CKD (8). Even though studies are more, there exist lacunae in the association of CKD stages with cognitive decline. So this study is done to find out the association between stages of CKD and cognitive decline.

MATERIALS AND METHODS

This cross-sectional study was meticulously designed and executed following approval from the Institutional Review Board (IRB) of Saveetha medical college and hospital. Ethical considerations were paramount, ensuring that all procedures adhered to the highest standards of research ethics. Each participant provided informed written consent, affirming their voluntary participation after being thoroughly briefed on the study's aims, procedures, and potential risks.

The study included a total of 140 patients diagnosed with chronic kidney disease (CKD), all aged between 18 and 65 years. These participants were carefully selected based on specific inclusion criteria to ensure a representative sample. The inclusion criteria mandated that participants must have a confirmed diagnosis of CKD. Exclusion criteria were also rigorously applied: patients with a previous history of mental illness were excluded to avoid confounding variables related to pre-existing cognitive deficits. Additionally, non-cooperative patients and those who were seriously ill were excluded to ensure that the data collected was reliable and that participants could fully engage with the study protocols
.
Data collection was conducted through two primary methods: structured interviews and thorough record analysis. The interviews allowed researchers to gather detailed demographic and clinical information directly from the participants, ensuring accuracy and comprehensiveness. The record analysis involved a meticulous review of each patient's medical history and existing health records to corroborate the information provided during interviews and to obtain additional clinical data.

To assess cognitive function, two standardized and widely recognized tools were employed: the Mini-Mental State Examination (MMSE) and the Brief Cognitive Rating Scale (BCRS). The MMSE is a 30-point questionnaire that evaluates various cognitive domains, including arithmetic, memory, and orientation, providing a quantitative measure of cognitive impairment. The BCRS complements this by offering a detailed evaluation of cognitive decline across several scales, such as concentration, recent and past memory, orientation, and functioning. Together, these tools provided a robust and comprehensive assessment of each participant's cognitive status.

The collected data was systematically recorded in a structured format using Microsoft Excel, ensuring organized and efficient data management. At the conclusion of the data collection phase, the data was analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 26. This sophisticated statistical tool facilitated detailed analysis, enabling the researchers to identify patterns, correlations, and statistically significant findings related to cognitive decline in CKD patients.

Statistical analyses
All data obtained was entered in MS excel format. Data was analysed at the end of the study using a statistical software using SPSS version 26.

ETHICAL CLEARANCE

The study was registered with the Institutional Ethical Committee (SMCH-IEC), Saveetha Medical college and Hospital: SMC/IEC/2023/06/041

RESULTS

The study included 140 patients diagnosed with chronic kidney disease (CKD), aged between 18-65 years, with a majority (40.7%) in the 51-65 age group. The gender distribution revealed that 57.9% were male. Participants were predominantly from semi-urban areas (39.3%), followed by rural (31.4%) and urban (29.3%) areas. Most participants lived in nuclear families (59.3%) and had varying educational backgrounds, with 20.7% being illiterate and 17.9% having completed high school. In terms of occupation, 22.1% were electricians, and 15% were unemployed. A significant portion (26.4%) belonged to the lower-income group, earning less than Rupees 3907 per month.

Regarding CKD staging, 54.3% of the patients were in stage 5, with the rest distributed across stages 1 to 4. Treatment varied, with 54.3% undergoing dialysis and 45.7% receiving conservative management. The duration of CKD ranged, with 33.5% having the disease for more than five years. Among those on dialysis, 42.1% received it twice a week. Comorbid conditions were common, with systemic hypertension (30.7%) and diabetes mellitus (15%) being the most prevalent.

Cognitive decline was assessed using the Mini-Mental State Examination (MMSE). Results indicated that 23.57% of CKD patients experienced cognitive decline, with 22.1% showing mild and 1.4% severe cognitive impairment. Cognitive decline was significantly associated with the stage of CKD. Specifically, 30.2% of patients in stage 5 exhibited cognitive decline compared

to 14.3% in stage 1, demonstrating a clear correlation between advanced CKD stages and increased cognitive impairment. The study found a graded decline in cognitive function with increasing CKD severity, supporting the notion that severe kidney failure is an independent risk factor for cognitive decline. These findings underscore the importance of early intervention and management strategies aimed at mitigating cognitive deterioration in CKD patients, particularly those in advanced stages of the disease.

Table I: Prevalence of cognitive decline By MMSE

	Frequency (N)	Percentage (N %)
Cognitive Decline	33	23.57%
No Cognitive Decline	107	76.43%
Total	140	100%

Table II: Prevalence of severity of cognitive decline

MMSE	Frequency	Percentage
No decline	107	76.4%
Mild	31	22.1%
Severe	2	1.4%
Total	140	100%

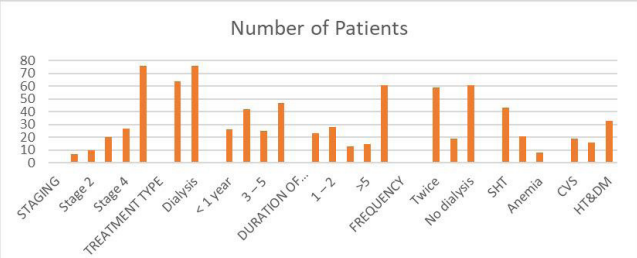

Fig. 1: Depicting different stages, treatment type, duration of illness, duration of dialysis, frequency, comorbidity

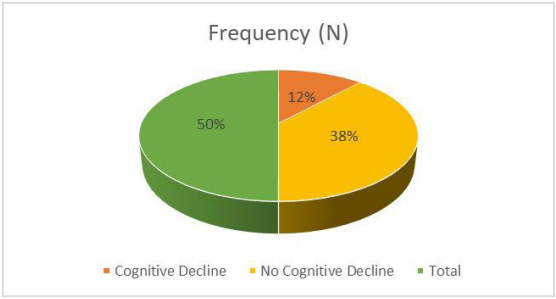

Fig. 2: Depicting cognitive decline by MMSE

Table III: Prevalence of cognitive decline in stage 1-5

	Staging				
	Stage1	Stage2	Stage3	Stage4	Stage5
Cognitive decline	1	1	3	5	23
%	14.3%	10.0%	15.0%	18.5%	30.2%
No Cognitive decline	6	9	17	22	53
%	85.7%	90.0%	85.0%	81.4%	69.7%
Total	7	10	20	27	76
Chi - square	4.445				
Df	4				
P Value	Significant				

Table IV: Prevalence of severity of cognitive dysfunction in stage 1-5

Stage		Mild	Severe	No imp
Stage 1	No	1	0	6
	%	14.3%	0	85.7%
Stage 2	No	1	0	9
	%	10%	0	90%
Stage 3	No	3	0	17
	%	15%	0	85%
Stage 4	No	5	0	22
	%	18.5%	0	81.5%
Stage 5	No	21	2	53
	%	27.6%	2.6%	69.8%
Chi square – 5.248			P value – 0.731	

DISCUSSION

CKD have been found to be linked with cognitive decline due to the increased levels of inflammatory markers. Other than inflammatory markers factors such as anemia, uremic toxins, albuminuria, oxidative stress, dyslipidemia in CKD patients affect cognition (9, 10).

A majority of the study group belongs to age group between 51-65 Years which contributes to 40.70% and 57.90% of the patients were male in our study.

We have noticed around 23.57% of our CKD subjects had cognitive decline. Kurella et al, found that elevated risk of cognitive decline was found in elderly CKD patients (11). In the present study, among the 33 subjects with cognitive decline, 31 had mild cognitive decline and 2 had severe cognitive decline.

In the present study, it was noted that there was statistical significance in the prevalence of cognitive decline with CKD stage. 30.2% of patients in stage 5 CKD had cognitive decline when compared to 14.3% of patients with cognitive decline in stage. Madan P et.al, also noted similar findings that decline in cognitive function is related with increasing severity of CKD from stage 3 to 4 and stage 4 to 5 (12).

We have found that in stage 5, 27.6% had mild and 2.6% had severe cognitive impairment. Increasing severity of CKD is associated with graded decline in cognitive function. Zijlstra LE et.al, have also showed that severe kidney failure is associated with increased cognitive impairment and decline over time (13). Severe kidney failure is now considered as an independent risk factor for cognitive decline (14).

So, treatment should be aimed at lowering blood pressure and albuminuria to prevent or postpone cognitive decline. Early commencement of dialysis can prevent excessive accumulation uremic toxins to prevent cognitive impairment.

CONCLUSION

The study concluded that chronic kidney disease (CKD) patients are at a significantly higher risk of cognitive decline compared to the general population. The data revealed a clear association between the severity of CKD and the extent of cognitive impairment, with patients in more advanced stages of CKD exhibiting higher rates of cognitive decline. Specifically, the prevalence of cognitive impairment was notably higher in patients in stage 5 of CKD, where 30.2% of these patients experienced cognitive decline compared to just 14.3% in stage 1. This demonstrates that as CKD progresses, the risk and severity of cognitive impairment increase substantially.

Several factors contribute to this phenomenon, including the accumulation of uremic toxins, systemic inflammation, oxidative stress, anemia, and dyslipidemia, all of which are exacerbated in more severe stages of CKD. These pathological processes negatively impact brain function, leading to cognitive deficits. The study also highlighted that a significant proportion of CKD patients with cognitive impairment had mild cognitive decline (22.1%), while a smaller percentage experienced severe cognitive decline (1.4%).

Given these findings, it is imperative to address cognitive health proactively in CKD patients. Early detection and intervention are crucial, as they can help mitigate the progression of cognitive impairment. Treatment strategies should focus on controlling blood pressure, reducing albuminuria, managing anemia, and starting dialysis at appropriate times to minimize the accumulation of uremic toxins. Additionally, comprehensive management plans that include cognitive assessments and tailored interventions could potentially improve the quality of life for CKD patients.

Overall, the study underscores the importance of recognizing cognitive decline as a significant and prevalent complication of CKD. It calls for heightened awareness among healthcare providers and the implementation of targeted strategies to prevent or slow cognitive deterioration in this vulnerable patient population. This approach not only aims to enhance cognitive function but also to improve overall patient outcomes and well-being.

ACKNOWLEDGEMENT

The authors thank the Dean of Saveetha Medical College Hospital and Director of Saveetha Institute of Medical and technical sciences university for their support and permission to publish this original article

REFERENCES

1. Drew DA, Weiner DE, Sarnak MJ. Cognitive impairment in CKD: pathophysiology, management, and prevention. American Journal of Kidney Diseases. 2019 Dec 1;74(6):782-90. Murray AM, Tupper DE, Knopman DS, Gilbertson DT, Pederson SL, Li S, et al. Cognitive impairment in hemodialysis patients is common. Neurology. 2006; 67(2):216–23. https://doi.org/10.1053/j.ajkd.2019.05.017
2. Sarnak MJ, Tighiouart H, Scott TM, Lou KV, Sorensen EP, Giang LM, Drew DA, Shaffi K, Strom JA, Singh AK, Weiner DE. Frequency of and risk factors for poor cognitive performance in hemodialysis patients. Neurology. 2013 Jan 29;80(5):471-80. https://doi.org/10.1212/WNL.0b013e31827f0f7f
3. Tamura MK, Yaffe K. Dementia and cognitive impairment in ESRD: diagnostic and therapeutic strategies. Kidney international. 2011 Jan 1;79(1):14-22. https://doi.org/10.1038/ki.2010.336
4. Etgen T, Chonchol M, Furstl H, Sander D. Chronic kidney disease and cognitive impairment: a systematic review and meta-analysis. American journal of nephrology. 2012 May 3;35(5):474-82. https://doi.org/10.1159/000338135

5. Kuo YT, Li CY, Sung JM, Chang CC, Wang JD, Sun CY, Wu JL, Chang YT. Risk of dementia in patients with end-stage renal disease under maintenance dialysis—a nationwide population-based study with consideration of competing risk of mortality. Alzheimer's Research & Therapy. 2019 Dec;11:1-2.
No DOI
6. Murray AM, Tupper DE, Knopman DS, Gilbertson DT, Pederson SL, Li S, Smith GE, Hochhalter AK, Collins AJ, Kane RL. Cognitive impairment in hemodialysis patients is common. Neurology. 2006 Jul 25;67(2):216-23.
https://doi.org/10.1212/01.wnl.0000225182.15532.40
7. Six I, Flissi N, Lenglet G, Louvet L, Kamel S, Gallet M, Massy ZA, Liabeuf S. Uremic toxins and vascular dysfunction. Toxins. 2020 Jun 18;12(6):404.
https://doi.org/10.3390/toxins12060404
8. Watanabe K, Watanabe T, Nakayama M. Cerebro-renal interactions: impact of uremic toxins on cognitive function. Neurotoxicology. 2014 Sep 1;44:184-93.
https://doi.org/10.1016/j.neuro.2014.06.014
9. Tamura MK, Xie D, Yaffe K, Cohen DL, Teal V, Kasner SE, Messй SR, Sehgal AR, Kusek J, DeSalvo KB, Cornish-Zirker D. Vascular risk factors and cognitive impairment in chronic kidney disease: the Chronic Renal Insufficiency Cohort (CRIC) study. Clinical journal of the American Society of Nephrology. 2011 Feb 1;6(2):248-56.
DOI: 10.2215/CJN.02660310
10. Kurella M, Chertow GM, Fried LF, Cummings SR, Harris T, Simonsick E, Satterfield S, Ayonayon H, Yaffe K. Chronic kidney disease and cognitive impairment in the elderly: the health, aging, and body composition study. Journal of the American Society of Nephrology. 2005 Jul 1;16(7):2127-33.
DOI: 10.1681/ASN.2005010005
11. Madan P, Kalra OP, Agarwal S, Tandon OP. Cognitive impairment in chronic kidney disease. Nephrology Dialysis Transplantation. 2007 Feb 1;22(2):440-4.
https://doi.org/10.1093/ndt/gfl572
12. Zijlstra LE, Trompet S, Mooijaart SP, van Buren M, Sattar N, Stott DJ, Jukema JW. The association of kidney function and cognitive decline in older patients at risk of cardiovascular disease: a longitudinal data analysis. BMC nephrology. 2020 Dec;21:1-0.
No DOI
13. Chaiben VB, Silveira TB, Guedes MH, Fernandes JP, Ferreira JH, Beltrгo J, Leal GF, Erbano LH, Bosch NL, Pecoits Filho R, Moraes TP. Cognition and renal function: findings from a Brazilian population. Brazilian Journal of Nephrology. 2018 Sep 13;41(2):200-7.
https://doi.org/10.1590/2175-8239-JBN-2018-0067