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Study of Cognitive Status in Patients with Chronic Kidney Disease: A Cross Sectional Study

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Abstract

Background: *There appears to be a pandemic of chronic kidney disease gripping the world, the full spectrum of which ranges from asymptomatic state to obvious kidney failure. The last decade has seen significant increase in the incidence, prevalence, and complications of CKD mostly because of the development of wider definitions for CKD by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative. There is ever growing interest in finding out the prevalence of cognitive impairment in patients with CKD which appears to be increasing not only because of increased incidence of CKD but also from increased survival of patients having CKD. Cognitive impairment is associated with an increased risk of death, which is mostly due to cerebro-vascular disease and prevalence of traditional and non-traditional vascular risk factors in chronic kidney disease (CKD). It is important to identify cognitive dysfunction in patients with CKD and take appropriate steps so as to improve outcome in such patients.*

Methods: *This was a cross-sectional, observational, questionnaire based study conducted in the department of General medicine of a tertiary care medical college situated in a semi-urban area. Cases were included in our study on the basis of a predefined criteria. Using a data collection form demographic details such as Age, Sex, Education, Occupation and socio-economic status of the patients were noted. Presence of systemic illnesses such as diabetes or hypertension and their duration was also noted down. Investigations such as complete blood count and renal function tests were noted in all the cases. Mini mental state examination (MMSE) & Montreal Cognitive Assessment Questionnaire (MoCA) was used to assess cognitive status. Patients were divided into 5 groups depending on stage of chronic kidney disease. Estimated glomerular filtration rate was calculated using modification of diet in renal disease equation. For statistical purposes p value less than 0.05 was taken as significant. SSPE 16 software was used for statistical analysis.*

Results: *Out of 50 studied cases there were 28 (56%) males and 22 (44%) females with an M: F ratio of 1:0.78. The most common affected age group was 41-50 years (28%) followed by 51-60 year (24%). In majority of the patients (78%) blood urea was found to be between 50-150 mg/dl whereas in 24 (48%) patients sr creatinine was between 3.0-6.0 mg/dl. Stage 5 and stage 4 renal disease was seen in 22 (44%)*

and 20 (40%) patients respectively. Most common etiological causes of CKD were found to be diabetes mellitus (38%) and a combination of diabetes and hypertension (28%). Mild cognitive impairment was seen in 27 (54%) patients and most common age group to be affected was found to be between 61-70 years (18%). Though males were more commonly affected by cognitive impairment the difference was not statistically significant (P=0.77). Similarly there was no statistically significant difference in cognitive impairment of patients with various stages of CKD (p=0.44). Patients with higher age group were found to be more likely to be affected by cognitive impairment (0.0001). MoCA was found to be a superior scale to detect mild cognitive impairment associated with chronic kidney disease patients.

Conclusion: *The study concluded that CKD is one of the important diseases seen among the common people. Hypertension and Diabetes are the common causes of this disease. Cognitive impairment was found to be more common in males and patients with stage 4 and stage 5 CKD but the difference was found to statistically insignificant (P>0.05).*

Keywords: *Chronic kidney disease, Risk Factors, Montreal Cognitive Assessment Questionnaire, Cognitive Impairment.*

Introduction

CKD can defined as kidney damage for more than three months, as defined either by structural or functional renal abnormalities[1]. The GFR may or may not be decreased in cases with CKD. It is usually manifested by either pathological abnormalities or altered markers indicative of kidney damage. The disease may manifest as abnormalities in composition of the blood or urine, or it may also present with various imaging abnormalities such as hyperechoic kidneys or loss of corticomedullary differentiation on ultrasonography[1]. Reasoning and perception induced acquiring of knowledge is cognition which affects almost all of the daily activities. Cognitive dysfunction may cause altered sensorium, intellectual dysfunction, attention deficit and inability to concentrate, memory loss and defective motor coordination[2].

The extent and nature of cognitive dysfunction in Chronic Kidney Disease is not clear. With proper use of dialysis, CKD-associated cognitive impairment is reversible to a large extent (Orientation & Attention show significant improvement)[3,4]. Cognitive impairment must be differentiated with the neurodegenretive disorders which may co-exist particularly in elderly population. These conditions needs to be differentiated from CKD related cognitive impairment so as to properly manage these conditions [5,6,7.]

Identifying pattern of cognitive impairment associated with CKD is important for proper management of patients and improving the outcome. For assessment of cognitive functions brief cognitive screening tests, such as the Mini-Mental State Examination (MMSE) &Montreal Cognitive Assessment Questionnaire can be used for screening purpose[8].

The Montreal Cognitive Assessment (MoCA) is a screening tool for assessment of cognitive dysfunction that tests cognitive domains including episodic memory, attention, visuospatial ability, language orientation and executive functions. Reitan developedit (in 1944) particularly for the US Army for intelligence testing and today is a proven diagnostic tool in the clinical setting for evaluation of cognitive dysfunctions in brain damage. Lower scores indicate better cognitive function and higher scores suggest progressive cognitive impairment. The test can be quickly completed in absence of any cognitive impairment[9].

MMSE- The most widely used method for the initial assessment and progress evaluation in CKD is the Mini-Mental State Examination (MMSE), developed by Folstein et al in 1975[10]**.** It is commonly used for the diagnosis and treatment of dementia and Alzheimer's disease, as it is simple and requires only little time to implement. By using an interview technique, the MMSE gathers orientation, memory (visual and auditory), attention, language comprehension, and visuo-

construction on a minimum dimension. It thus allows only a general, global statement of the cognitive performance.

Because of the lack of data and conflicting results, here we evaluated the cognitive status among CKD patients (stages 3-5) with a specific and sensitive tool like MoCA and MMSE to investigate any change with declining kidney function.

Materials and Methods:

This was an observational and cross sectional study which was conducted in the department of general medicine of a tertiary care medical college. The institutional ethical committee duly approved the study and consent was obtained from all the cases included in this study. 50 cases of chronic kidney disease were included in this study on the basis of a predefined inclusion and exclusion criteria. A uniform patient data collection form was used to obtain the sociodemographic details of the patients such as Age, Sex, Education and occupation of the patients. History of smoking or alcoholism was also noted. History of systemic illnesses such as diabetes or hypertension and their duration was also noted. History of CKD, medications and laboratory reports were all reviewed in detail.

The cognitive status of the patients was checked by interviewing the patient with Montreal cognitive assessment questionnaire. It assesses different cognitive domains: cognitive domains including episodic memory, attention, visuospatial ability, language orientation and executive functions. Time required for assessment of MoCA is approximately ten minutes. The maximum possible score is 30 points. One point needs to be added for a person who had twelve years or fewer of formal education, for a possible maximum of 30 points. Score of twenty six or above is assumed to be normal.

Statistical analysis was done using SSPE 16 software. For statistical purposes p value of less than 0.05 was taken as statistically significant.

Inclusion criteria

- Patients having age between 19-79 years
- Patients with chronic kidney disease (stage 3-5)
- Minimum 3 months of disease duration

Exclusion criteria

Patients with

- Psychiatric disorders
- Neurological disorders
- Pregnant and lactating patients
- Blind patients
- Severe diabetic complication
- Patients younger than 18 years.
- Patients older than 80 years.
- Renal transplant patients
- Patients with acute kidney disease.
- Documented cases of hyponatremia.

Results

The present study compromised of 50 cases of chronic kidney disease admitted to the department of general medicine. Out of these 50 patients there were 28 (56%) males and 22 (44%) females with a M: F ratio of 1:0.78.

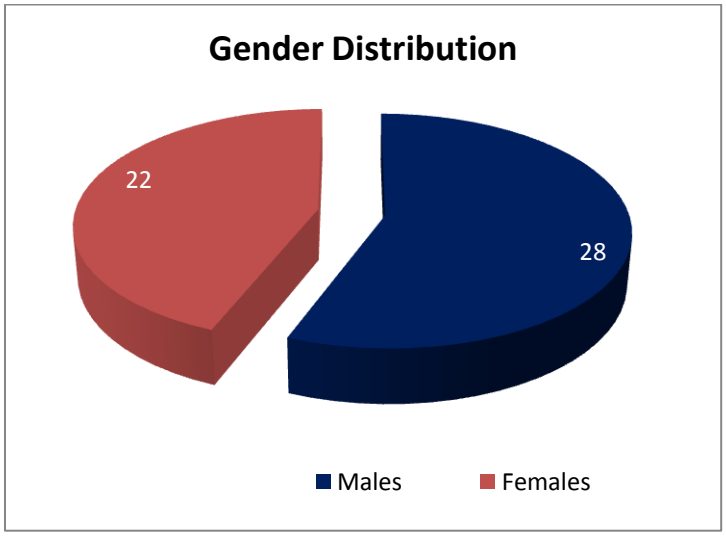

Figure 1: Gender Distribution of the studied cases.

The analysis of the age groups of the patients showed that the most common affected age group was 41-50 years (28%) followed by 51-60 year (24%) and 61-70 years (22%). The mean age of the patients was 50.18±14.81.

Table 1: Age distribution of the studied cases

SL NO.	AGE GROUP IN YRS	NO. OF CASES	PERCENTAGE
1	18-30	03	6%
2	31-40	07	14%
3	41-50	14	28%
4	51-60	12	24%
5	61-70	11	22%
6	71-80	2	4%
7	81-90	1	2%
8	91-100	0	0%
	TOTAL	50	100%

In our study, out of 50 patients, maximum number of patients had education qualification up to high school (34%) followed by upper primary (22%).Only one patient (02%) was not educated. Out of 50 patients, 05 patients (10%) were degree holders.

Table 2: Educational Qualification of the studied cases

Education Qualification	No.Of Patients	Percentage
No Qualification	01	02%
Lower Primary (1-4)	07	14%
Upper Primary(5-8)	11	22%
High School(8-10)	17	34%
PUC (11-12)	09	18%
Degree	05	10%
Total	50	100%

The analysis of kidney function test showed that majority of the patients had blood urea level between 50-100 mg/dl (42%) whereas 24 (48%) patients had serum creatinine level between 3.0-6.0 mg/dl. The range of serum creatinine levels in the study was 1.6mg/dl -18.4 mg/dl. Mean creatinine value was 5.72 mg/dl± 2.70mg/dl

Table 3: Renal Function tests in the studied cases

	Range	No of Patients	Percentage
Blood Urea	20-50	4	8%
	50-100	21	42%
	100-150	18	36%
	>150	07	14%
	TOTAL	50	100%
Serum Creatinine	1.5-3.0	11	22%
	3.0-6.0	24	48%
	>6.0	15	30%
	TOTAL	**50**	**100%**

Using the serum creatinine, GFR was calculated using Cockgroft Gault formula. Out of 50 patients 8 patients (16%) had stage 3 chronic renal disease whereas stage 4 and stage 5 renal disease was seen in 20 (40%) and 22 (44%) patients respectively.

Table 4: Distribution based on Creatinine clearance

Stage	No.Of Cases	Percentage
Stage 1 [Signs of mild kidney disease with normal or better GFR;GFR->90%]	00	00
Stage 2 [Mild kidney disease with reduced GFR; GFR 60-89%]	00	00
Stage 3 [Moderate chronic renal insufficiency; GFR 30-59%]	08	16
Stage 4 [Severe chronic renal insufficiency; GFR 15-29%]	20	40
Stage 5 [End stage renal disease; GFR <15%]	22	44
TOTAL	50	100

Diabetic nephropathy (38%), hypertensive nephrosclerosis (28%) and IgA nephropathy (10%) were the other common causes of CKD in our study. In 04% of the cases, etiology was either unknown or analgesic nephropathy.

Table 5 : Etiology of chronic kidney disease

Etiology	**Severity Of Chronic Renal Failure**			**Total**
	STAGE 3	**STAGE 4**	**STAGE 5**	
Diabetes Mellitus	03	11	05	19
Diabetes+Hypertension	03	02	09	14
Chronic Glomerulonephritis	01	02	03	06
IgA Nephropathy	00	02	03	05
Contrast-induced nephropathy	00	02	02	04
OTHERS	01	01	00	02
Total	08	20	22	50

The Montreal Cognitive Assessment was calculated in all the cases. Scores ≥26 was taken as normal and score <26 was taken as abnormal. 23 patients (46%) had normal MoCA score. Whereas 27 patients (54%) had MoCA score in abnormal range suggestive of cognitive impairment.

Table 6 : Cognitive status of the studied cases.

Cognitive status	Moca score	No. Of patients	Percentage
Normal	≥26	23	46%
Mild impairment	<26	27	54%
Total		50	100%

The analysis of age groups of the patients with respect to normal or abnormal cognitive status showed that the mean age of patients with normal MocA score was 44.26 +/- 11.63 whereas mean age of patients with abnormal MocA score was found to be 57.23 +/- 12.58. The difference in age in these 2 groups was found to be statistically "highly significant" (P=0.0001).

Table 7: Age wise distribution of patients with cognitive status

Age group	**Normal**		**Abnormal**	
	No.of patients	**Percentage**		**No.of patients**
18-30	03	06%	00	00%
31-40	04	08%	03	06%
41-50	10	20%	04	08%
51-60	04	08%	08	16%
61-70	02	04%	09	18%
71-80	00	00%	02	04%
81-90	00	00%	01	02%
Total	**23**	**46%**	**27**	**54%**
	Mean Age= 44.26 +/- 11.63		**Mean Age = 57.23 +/- 12.58**	
	P= 0.0001 (Highly Significant)			

The gender wise distribution of Cognitive impairment showed that 16 (32%) patients with cognitive impairment were males whereas 11 (22%) were females. Though it appears that males were affected by cognitive impairment but the difference was not found to be statistically significant (P=0.77)

Table 8: Gender wise distribution of patients with cognitive status

Gender	Normal		Abnormal	
	No.of patients	Percentage	No.of patients	Percentage
Male	12	24%	16	32%
Female	11	22%	11	22%
Total	23	46%	27	54%

Cognitive impairment was seen more in almost in patients of all levels of education status ,however it was more among patients lesser educational qualification like lower and higher primary.

Table 9: Education of patients with cognitive status

EDUCATION STATUS	**NORMAL**		**ABNORMAL**	
	NO.OF PATIENTS	**PERCENTAGE**	**NO.OF PATIENTS**	**PERCENTAGE**
NA	00	00%	01	02%
LOWER PRIMARY	00	00%	07	14%
UPPER PRIMARY	02	04%	09	18%
HIGH SCHOOL	11	22%	06	12%
PUC	06	12%	03	06%
DEGREE	04	08%	01	02%

The analysis of stage of renal failure and cognitive status of the patients showed that 14 (28%) patients had stage 5 CKD whereas 10 (20%) and 3 (6%) patients had cognitive impairment. There was no statistically significant difference in incidence of cognitive impairment across various stages of CKD (P=0.44).

Table 10: Stage of CKD and cognitive status

Stage	**No. Of patients with abnormal cognitive status**	**Percentage**
Stage 3	03	06%
Stage 4	10	20%
Stage 5	14	28%
Total	27	54%

The analysis of education status of the patients showed that the MMSE scores of cases across the educational status were comparable and there was no significant difference in mean MMSE scores of the cases across educational status.

Table 11: Cognitive status based MMSE score (According to education status)

Sl.no	**Education status**	**Mmse score(mean ± sd)**
1	Lower primary	26.57 ± 1.71
2	Upper primary	24.82 ± 2.71
3	High school	27.05 ± 1.74
4	PUC	26.77 ± 2.43
5	Degree	28.40 ± 1.25

Discussion

Chronic kidney disease is more likely to occur in males as compared to females. Total patients included in the study are 50 in numbers, out of which 28 were male(56%) and 22 were females (44%), which was concordant with the CKD

registry of India report where males constituted 68% of the total CKD patients and CMC Vellore study where 62% were males. Though the males were more commonly affected the gender difference was not found to be statistically significant. A study by Odagiri G et al results concordant with the study ie gender is not statistically significant with cognitive status[11].

The age of the patients varied from 18 to 85 yrs with majority of patients falling within 41-60 years group. The mean age was 50.18 years± 14.81yrs. Because of the documented age related decline in GFR, the prevalence of CKD increases with age. This was seen in our study too with a majority of patients in the age group of 41-60 years with a mean of 50.18 ± 14.81 years. Patients with affected cognition was found to have a higher mean age than patients with normal cognition and the difference was statistically highly significant (P=0.0001).

The mean age in the CKD registry of India report was 48.3±16.6 years and CMC Vellore study[12] was 38.2±14.5 years, and other studies like N.P SINGH[13] had mean age of 41.1± 12.1, Michel Dahan[14] had mean age of 48.7± 13.5.In our study, out of 50 patients, maximum number of patients had education qualification up to high school (34%) followed by upper primary (22%). Only one patient (02%) was not educated. Out of 50 patients, 05 patients (10%) were degree holders.

Diabetic nephropathy (38%), hypertensive nephrosclerosis (28%) and IgA nephropathy (10%) were the other common causes of CKD in our study. In 04% of the cases, etiology was unknown/analgesic nephropathy.CMC Vellore study[12], where CGN was the diagnosis in 70.5%. Thus even with the epidemic of non-communicable diseases like diabetes and hypertension in developing countries, CGN still continues to be the most common cause of CKD.

In our study, 23 patients (46%) had normal MoCA score,27 patients(54%) had MoCA score in abnormal range. Studies by Madan P et al[15], Williams UE et al[16], Etgen T et al[17] and Khatri M et al[18] etc showed similar results with the study. Elderly population was found to be more susceptible for development of cognitive impairment as compared to relatively young patients with CKD. In our study of 50 patients , patients having cognitive impairment belonged to age group of 51-70 consisting of 34 % of the cases with cognitive Impairment .In a study by Tiffin-Richards FE[19] et al reveal negative association between the MoCA total score and age. When comparing educational status, in our study of 50 patients, Populations with lower education qualification have more cognitive impairment. Better cognitive status was seen in educated cases. A study by Odagiri G et al results concordant with the study ie level of education is significantly associated with cognitive status .In our study, we found that kidney disease of higher stages had more cognitive impairment than with those with stage 3 kidney damage. Though the difference was not statistically significant (p=0.44). The relation of stage of CKD and cognitive impairment was not found to be statistically significant and cognitive impairment was seen in all stages of CKD. A study by Kurella M et al concluded that advanced stages of CKD were associated with an increased risk for cognitive impairment[20]. The MMSE score in our study of 50 patients was within normal range in all groups according to education status.

Conclusion

Our study found that CKD is one of the significant diseases seen among the common people and individuals with Hypertension and Diabetes are more commonly affected as compared with individuals without any systemic illness. Males are more affected than Females though the difference was not statistically significant. Cognitive impairment was more among patients lower educational status as compared with patients with higher educational status. Moreover cognitive impairment was found to be more common in older patients. However MMSE scoring didn't reveal any cognitive impairment in any study group. MoCA scoring was superior to

the well-established Mini-Mental State Examination (MMSE) screening test, since the MoCA not only assesses executive functioning, which may be particularly important in the CKD population, but also have a better sensitivity for mild cognitive dysfunction.

Conflict of Interest: none

Bibliography

1. Matovinović MS. 1. Pathophysiology and Classification of Kidney Diseases. EJIFCC. 2009;20(1):2-11. Published 2009 Apr 20.
2. Borson S. Cognition, aging, and disabilities: conceptual issues. Phys Med RehabilClin N Am. 2010;21(2):375-82.
3. O'Lone E, Connors M, Masson P, Wu S, Kelly PJ, Gillespie G, Parker D, Whiteley W, Strippoli GFM, Palmer S, Craig JC, Webster AC. Cognition in people with end-stage kidney disease treated with hemodialysis: a systematic review and meta-analysis. Am J Kidney Dis. 2016;67(6):925–35.
4. Masson P, Wu S, Duthie FA, Kelly PJ, Craig JC, Gillespie D, Parker D, Palmer S, Whiteley W, Webster AC. Cognition in kidney transplant recipients: a systematic review and meta-analysis. Nephrol Dial Transplant. 2016;31(Suppl 1):i565.
5. Salmond CH, Sahakian BJ. Cognitive outcome in traumatic brain injury. Curr Opin Crit Care. 2005;11(2):111–6.
6. Tatemichi TK, Desmond DW, Stern Y, Paik M, Sano M, Bagiella E. Cognitive impairment after stroke: frequency, patterns, and relationship to functional abilities. J Neurol Neurosurg Psychiatry. 1994;57:202–7.
7. Ringholz GM, Appel SH, Bradshaw M, Cooke NA, Mosnik DM, Schulz PE. Prevalence and patterns of cognitive impairment in sporadic ALS. Neurol. 2005;65(4):586–90.
8. Tombaugh TN, McIntyre NJ. The mini-mental state examination: a comprehensive review. J Am Geriatr Soc. 1992 Sep;40(9):922-35.
9. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, Cummings JL, Chertkow H. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005 Apr;53(4):695-9.
10. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12:189-98
11. Odagiri G, Sugawara N, Kikuchi A, Takahashi I, Umeda T, Saitoh H, et al: Cognitive function among hemodialysis patients in Japan. Annals of General Psychiatry 2011; 10(20): 1-5.
12. Dharan KS, John GT, Neelakantan N, Korula A, Balakrishnan N, Kirubakaran MG, Jacob CK. Spectrum of severe chronic kidney disease in India: a clinicopathological study. Natl Med J India. 2006 Sep-Oct;19(5):250-2.
13. Singh NP, Chandreshekar, M Nair, Gopal K, Ajita J et al The cardiovascular and hemodynamic effects of erythropoietin in chronic renal failure. JAPI 1999; 47: 284-89.
14. Dahan M, Siohan P, Viron B, Michel C, Paillole C, R G Mignon et al . Relationship between left ventricular hypertrophy, myocardial contractility and overload condition in haemodialysis patients: An echocardiographic study. Am J Kid Dis 1997; 30; 780-85.
15. Madan P, Kalra OP, Agarwal, Tandon OP: Cognitive Impairment in Chronic Kidney Disease. Nephrology Dialysis Transplantation 2007; 22: 440–444.
16. Williams UE, Owolabi MO, Ogunniyi A, Ezunu EO: Prevalence and Pattern of

Neurocognitive Impairment in Nigerians with Stages 3 to 5 Chronic Kidney Disease. ISRN Neurology 2013; 1-6.

17. Etgen T, Chonchol M, Forstl H, and Sander D: Chronic Kidney Disease and Cognitive Impairment: A Systematic Review and Meta-Analysis. American Journal of Nephrology 2012 May; 35: 474–482.
18. Khatri M, Nickolas T, Moon YP, Paik MC, Rundek T, Elkind MSV: CKD Associates with Cognitive Decline. Journal of the American Society of Nephrology 2009; 20: 2427–2432.
19. Tiffin-Richards FE, Costa AS, Holschbach B, Frank RD, Vassiliadou A, Kruger T, et al: The Montreal Cognitive Assessment (MoCA) - A Sensitive Screening Instrument for Detecting Cognitive Impairment in Chronic Hemodialysis Patients. Plos One 2014 Oct; 9(10): 1-9.
20. Kurella M, Chertow GM, Fried LF, Cummings SR, Harris T, Simonsick E, et al: Chronic Kidney Disease and Cognitive Impairment in the Elderly: The Health, Aging, and Body Composition Study. Journal of the American Society of Nephrology 2015; 16: 2127–2133.