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Original Article

Association between Cognitive Dysfunction and Other Clinical Characteristics in Chronic Kidney Disease Patients Undergoing Hemodialysis

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Abstract

Background: Cognitive impairment commonly occurs in individuals with chronic kidney disease (CKD), especially in advanced stages, yet they are poorly diagnosed. Early diagnosis and intervention help contain and mitigate the progress of cognitive impairment.

Aims: This study aimed to evaluate the prevalence of cognitive impairment in patients with CKD on hemodialysis and its relationship with sociodemographic and clinical variables.

Materials and Methods: A cross-sectional study was done in inpatients diagnosed as CKD stage 5, between 18 and 60 years of age, and on hemodialysis treatment for more than 6 months in the nephrology ward of a tertiary care hospital, Goa, over a period of 1 year. The sample size was 71 collected by purposive sampling technique. The Addenbrooke's Cognitive Examination-Revised Questionnaire and the Clinical Dementia Rating Scale were used to assess cognitive functioning.

Results: The prevalence of cognitive impairment in patients with CKD undergoing hemodialysis was 45.1%. It was found that cognitive function was significantly associated with age, education, occupation, diabetes mellitus, serum creatinine levels, and drugs such as calcium channel blockers and insulin.

Conclusion: Our study found that the cognitive impairment is common but often undiagnosed in dialysis patients. Thus, early identification, careful monitoring, and appropriate treatment are required to avoid complications, longer independent living, and decrease caregiver burden with improved compliance with medication.

Key words: Chronic kidney disease, Cognitive impairment, Hemodialysis, Sociodemographic correlates

INTRODUCTION

Chronic kidney disease (CKD) is a spectrum of different pathophysiologic processes associated with abnormal kidney function, and a progressive decline in glomerular filtration rate. The term chronic renal failure indicates the process of continuing significant irreversible reduction in nephron number, and typically corresponds to CKD stages 3–5.[1] The reported prevalence of CKD in different regions of India ranges from 1% to 13%. Recently, 17% prevalence has been reported in the data from the International Society of Nephrology's Kidney Disease Data Center Study. Parts of the states of Andhra Pradesh, Odisha, and Goa have high levels of CKD of unknown etiology, which is a chronic interstitial nephropathy with insidious onset and slow progression.[2] Several causative factors have been proposed such as water-borne agrochemicals, silica, chemical flavors in betel nuts, and pesticides.[3]

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The lives of thousands of patients with end-stage renal disease (ESRD) have been prolonged due to the widespread availability of dialysis which includes hemodialysis, peritoneal dialysis, or transplantation.[1] In India, hemodialysis is the most common modality followed by transplantation, and peritoneal dialysis is third. In India, it is estimated that about 120,000 patients are on hemodialysis.[2]

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Cognitive impairment in those on dialysis is an increasingly important public health problem considering the aging ESRD population and the escalating prevalence of diabetes and vascular disease.[4] A study by Pereira *et al.*, comparing the cognitive performance of dialysis patients with that of the general population, found that those on dialysis had worse performance in executive function, considered to be associated with vascular disease and risk factors.[4] Evidence shows that early hemodialysis improves cognitive abilities in patients with CKD. However, a large number of hemodialysis patients develop moderate-to-severe cognitive impairment.[5]

Cognitive assessment in individuals with CKD is important as patients have to process and understand significant amounts of information of this complex illness in order to duly comply with the treatment. Early diagnosis and treatment can help reduce number of hospitalizations, decrease complications, prolong independent living,[6] and also mitigate the progress of Cognitive Impairment.[7] It will also help the individual if practitioners are aware that noncompliance may be due to cognitive impairment rather than negligence.[8] Goa has a high prevalence of CKD; however, there is dearth of data on cognitive functioning in this group. Thus, with this objective in mind, the present study was conducted to assess the cognitive impairment in patients with CKD on hemodialysis, and its relationship with sociodemographic and clinical characteristics.

MATERIALS AND METHODS

A cross-sectional study was conducted in admitted patients diagnosed with CKD stage 5, between 18 and 60 years of age, and on hemodialysis treatment for more than 6 months in the nephrology ward of a tertiary care hospital, Goa, over a period of 1 year (January 2020–December 2020). A total of 71 patients were included in the study by purposive sampling technique. Ethical clearance was obtained from the institutional ethical committee. Informed consent was taken from a patient and their relatives. Confidentiality was maintained throughout the study.

Patients with CKD on hemodialysis for more than 6 months, between 18 and 60 years of age, and those willing to participate in the study were included. While, the patients diagnosed with acute kidney injury, those with history of psychiatric illness, and those receiving medication for same and with history of substance use were excluded.

A predesigned semi-structured questionnaire was used to obtain the sociodemographic details, spreadsheet for medical history and treatment details including duration and frequency of undergoing hemodialysis, and laboratory investigation of patients having serum creatinine and hemoglobin levels. The Mini-International Neuropsychiatric Interview (M.I.N.I.) Plus was used in our study to rule out psychiatric illnesses and substance use disorders. M.I.N.I. is a short-structured diagnostic interview developed by psychiatrists and clinicians in the US and Europe for DSM-IV and ICD-10 disorders.[6] The Clinical Dementia Rating Scale was used to assess the severity of cognitive impairment. The score of 4.5–9 indicates mild, 9–15.5 indicates moderate, and >15.5 indicates severe impairment.[9,10] The Addenbrooke's Cognitive Examination-Revised Questionnaire was used to assess cognitive functions. Cut scores were:

- Global score<78
- Orientation/attention<17
- Memory<15
- Verbal fluency<8
- Language<22
- Visuospatial ability<13.[4,11]

Data were entered into Microsoft Excel (Windows 7; Version 2007), and an analysis was done using the Statistical Package for the Social Sciences for Windows software (version 22.0). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, and frequencies and percentages for categorical variables, were calculated. The association between variables was analyzed by using Chi-square test for categorical variables. Bar charts and pie charts were used for visual representation of the analyzed data. The level of significance (P) was set at 0.05.

RESULTS

Total of 84 patients were screened during the study period, of which 12 patients did not fit in the inclusion criteria and 1 denied consent leaving 71 participants as the final sample. Table 1 shows the distribution of sociodemographic and various clinical variables. The mean age of the sample was 46.37 (SD = 10.66). Majority of the participants were male. The mean duration of CKD was 48.40 (SD = 14.5) months, and the mean duration of receiving hemodialysis was 36.16 (SD = 21.21) months. The mean hemoglobin of the sample was 8.63 (SD = 1.74)/dL, while the mean serum creatinine level was 8.42 (SD = 3.01) mg%. 45.1% of all the participants were detected with cognitive impairment. Majority of the participants had impaired verbal fluency.

Table 2 demonstrates the association between cognitive impairment with sociodemographic and clinical variables. There was a significant association between cognitive impairment and age, years of education, occupation, diabetes mellitus, and use of medications such as calcium

Table 1: Distribution of sociodemographic and various clinical variables

Sociodemographic finding	Number (n)	Percentage
Age		
≤30	8	11.3
31–40	11	15.5
41–50	21	29.6
51–60	31	43.7
Sex		
Male	44	62
Female	27	38
Locality		
Urban	31	43.7
Rural	40	56.3
Years of education		
0–5	11	15.5
6–10	20	28.2
11–15	29	40.8
16–20	11	15.5
Occupation		
Professional	6	8.5
Semi-professional	4	5.6
Clerical/farm/shop	9	12.7
Skilled worker	4	5.6
Semi-skilled worker	20	28.2
Unskilled workers	10	14.1
Unemployed	18	25.4
Duration of CKD (in months)		
6–18	27	38
19–30	3	4.22
31–42	10	14.08
43–54	6	8.45
55–66	9	12.67
>66	16	22.53
Duration of hemodialysis (in months)		
6–18	26	36.6
19–30	9	12.7
31–42	11	15.5
43–54	8	11.3
55–66	7	9.9
>66	10	14.1
Frequency of hemodialysis		
Once a week	7	9.9
Twice a week	44	62
Thrice a week	20	28.2
Comorbidities		
Diabetes mellitus	27	38
Hypertension	55	77.5
Others	5	7
Drugs		
Calcium channel blockers	36	50.7
Alpha 1 antagonists	40	56.3
Potassium channel blockers	11	15.5
Insulin	27	38
Vitamin D	71	100
Calcium	71	100
Hemoglobin level (g/dL)		
<7	17	23.9
7–8	27	38
9–11	22	31
>11	5	7
Serum creatinine (mg %)		
>5	8	11.3
5–8	27	38
8–12	26	36.6
>12	10	14.1
Severity of cognitive impairment		
No impairment	40	56.3
Mild impairment	17	23.9
Moderate impairment	11	15.5
Severe impairment	3	4.2
Prevalence of cognitive impairment by		
Domains		
Fluency	62	87.3
Orientation/attention	14	19.7
Memory	14	19.7
Visuospatial ability	19	26.8
Language	35	49.3
Cognitive impairment		
Present	32	45.1
Absent	39	54.9

CKD: Chronic kidney disease

channel blockers and insulin, which is described in detail during discussion.

DISCUSSION

In our study, the prevalence of cognitive impairment in patients with CKD undergoing hemodialysis was 45.1%. A similar study done by Joseph *et al.* in India found cognitive impairment in 44% of the patients,[12] while Reddy and Yadla[13] and Sehgal *et al.*[14] found a prevalence of around 30%. However, most of the foreign studies show a higher prevalence ranging from 70% to 80.9%.[5,15,16] Reasons for lower prevalence in our study could be a smaller sample size and lower mean age of our participants. Few other studies also found a lower prevalence.[17,18]

We found that 23.9%, 15.5%, and 4.2% had mild, moderate, and severe cognitive impairment, respectively, while 56.3% had no impairment. In most of the other similar studies, the prevalence of mild cognitive impairment (MCI) was higher.[16,19-21] Previous studies also found that for dialysis population, uremic toxin accumulation, injury to vascular endothelial, hormonal deficiency, malnutrition, anemia, and dyslipidemia were closely related to cognition dysfunction.[22] Furthermore, traditional causes such as age, education years, and hypertension are also implicated. Therefore, patients on hemodialysis have more exposures to susceptibility factors of MCI.

The present study found that 87.3% of the participants had cognitive impairment in fluency, 49.3% in language, 19.7% in each memory and orientation/attention, and visuospatial impairment in 26.8%. It was seen that maximum impairment was in executive functioning (fluency and visuospatial) followed by language. Other similar studies found executive function deficits in 9–56.8%, memory in 9–42.2%, language

Table 2: Association between cognitive impairment with sociodemographic and clinical variables

Variable	Cognitive impairment		χ^2, *P*
	Present (*n* = 32), *n* (%)	Absent (*n* = 39), *n* (%)	
Age			
≤30		8 (100)	0.0017*
31–40	4 (36.4)	7 (63.6)	
41–50	9 (42.9)	12 (57.1)	
51–60	19 (61.3)	12 (38.7)	
Sex			
Male	19 (43.2)	25 (56.8)	0.683
Female	13 (48.1)	14 (51.9)	
Locality			
Urban	12 (38.7)	19 (61.3)	0.343
Rural	20 (50)	20 (50)	
Years of education			
0–5	10 (90)	1 (9.1)	0.001*
6–10	14 (70)	6 (30)	
11–15	8 (27.6)	21 (72.4)	
16–20		11 (100)	
Occupation			
Professional	1 (11.1)	6 (100)	0.004*
Semi-professional	2 (50)	4 (100)	
Clerical/farm/shop	11 (55)	8 (88.9)	
Skilled worker	8 (80)	2 (50)	
Semi-skilled worker	10 (55.6)	9 (45)	
Unskilled worker		2 (20)	
Unemployed		8 (44.4)	
Duration of CKD			
6–18	13 (48.14)	14 (51.85)	0.174
19–30	3 (100)	0	
31–42	4 (40)	6 (60)	
43–54	2 (33.33)	4 (66.66)	
55–66	5 (55.55)	4 (44.44)	
>66	7 (43.75)	9 (56.25)	
Duration of hemodialysis			
6–18	11 (42.3)	15 (57.7)	0.861
19–30	5 (55.6)	4 (44.4)	
31–42	4 (36.4)	7 (63.6)	
43–54	3 (37.5)	5 (62.5)	
55–66	3 (42.9)	4 (57.1)	
>66	6 (60)	4 (40)	
Frequency of hemodialysis			
Once a week	2 (28.6)	5 (71.4)	0.237
Twice a week	18 (40.9)	26 (59.1)	
Thrice a week	12 (60)	8 (40)	
Comorbidities			
Diabetes	20 (74.1)	7 (25.9)	<0.001*
No diabetes	12 (27.3)	32 (72.7)	
Hypertension	27 (49.1)	28 (50.9)	0.207
No hypertension	5 (31.3)	11 (68.8)	
Others	2 (40)	3 (60)	0.813
None	30 (45.5)	36 (54.5)	
Drugs			
Calcium channel blockers	25 (61.1)	14 (38.9)	0.006*
No calcium channel blockers	10 (28.6)	25 (71.4)	
Alpha 1 agonists	11 (35.5)	20 (64.5)	0.153
No alpha 1 agonists	21 (52.5)	19 (47.5)	
Potassium channel blockers	6 (54.5)	5 (45.5)	0.492
No potassium channel blockers	26 (43.3)	34 (56.7)	
Insulin	19 (70.4)	8 (29.6)	0.001*
No insulin	13 (29.5)	31 (70.5)	
Blood parameters (mean value)			
Hemoglobin	8.80	8.50	0.475
Creatinine	7.59	9.09	0.036*

*Significant findings *P*=0.05. CKD: Chronic kidney disease

in around 2%, and attention in 42.2%.[16,18,23,24] Our results which show a significant impairment in executive functioning can be explained by the concept of reno-cerebro-vascular disease and accelerated vascular cognitive impairment in a dialyzed population.[20] Majority of participants had lower education status unlike the foreign studies which can be a reason for higher prevalence of language impairment as compared to other studies.

We found a statistically significant prevalence of cognitive impairment to be increased with increasing age group. This has been consistent with other similar studies.[19,25] Gesualdo *et al.* and Pei *et al.* found that age and cognitive impairment have a negative correlation.[5,22] Age was found to be a strong risk factor for executive functioning decline in a study by Drew *et al.*[26]

It was noticed that the years of education and cognitive impairment have a statistically significant association showing that less education status is a risk factor for cognitive impairment. Similar results were found in other studies.[16,17,21,25,26] Chen *et al.* found that there are differences in age-related gray matter atrophy between the high and the low education groups in the anterior regions (left medial orbitofrontal superior gyrus and left anterior cingulated and paracingulate) and age-related white matter damage in the forceps major and superior longitudinal fasciculus.[27]

We found that the impaired cognition was associated with lower occupation status. There are no similar studies done to assess the association of occupation with cognitive impairment. Participation in cognitive stimulating activities throughout a major part of a person's adult life may contribute to cognitive reserve, and conceal the effects of neurodegeneration on cognitive function at older ages. Furthermore, environmental stimulation may increase the level of neurotrophins in brain tissue, which may protect or repair existing neurons as well as actively promote neurogenesis. This pathway, which is called as differential preservation, may enhance neural reserve that protects against the adverse effects of brain deterioration due to aging, stress, and neurodegenerative disease.[28]

Among the participants who had diabetes, the prevalence of cognitive impairment was 74.1%. A significant association was found between the two variables in this study. A similar study done by Reddy and Yadla and Fadili *et al.* found a prevalence of 16.1% and 30.8%, respectively.[13,17] The risk factors for cognitive dysfunction in type 2 diabetes patients include glycemic control, hypoglycemia, inflammation, depression, and macro- and microvascular pathology along with aging process.[29]

The present study found that cognitive impairment was significantly associated with the use of insulin therapy and calcium channel blockers. There is a lack of data available studying the association between medications and impaired cognition in hemodialyzed patients currently. Cardiovascular disease has been shown to be associated with impaired cognitive function. Thus, the association between insulin and cognitive function may be the reflection of the "Insulin resistance syndrome."[30] Older hypertensive patients taking calcium channel blockers are significantly more likely to experience cognitive decline. This can be probably due to vulnerability to ischemia during periods of reduced cerebral blood flow induced by these agents.[31]

There was a significant association between creatinine levels and cognitive functioning. The mean serum creatinine level among those who had impaired cognition was 7.59. Griva *et al*. in their study found that the mean serum creatinine was 11.15 (SD = 1.47) among cognitively impaired participants. The mean creatinine among participants with cognitive impairment was 10.24 (SD = 2.7) and that among those without cognitive impairment was 11.15 (SD = 2.66).[32] Elias *et al*. found that higher levels of serum creatinine were associated with lower global cognitive performance in CKD patients.[33] Our finding was statistically significant; however, this finding was inconsistent with other studies. This can be due to other confounders such as age of the patient, duration of CKD, and duration of receiving hemodialysis. However, future studies may give us better clarification between the association of serum creatinine and cognitive impairment.

Limitations

The following were the limitations in our study: (1) Sample was selected using purposive sampling. (2) The cause–effect relationship could not be established. (3) Due to COVID-19 restrictions, we could not complete our targeted sample size and could collect only 71 samples. (4) Our study was restricted only to a tertiary health-care level. (5) The data before and after receiving hemodialysis were not included. Furthermore, comparison with other treatment modalities for ESRD was not considered in our study to get a clearer picture of association of hemodialysis and cognitive impairment.

CONCLUSION

This study found that the cognitive impairment is common but often remains undiagnosed in dialysis patients. The cognitive functions were significantly affected by age, years of education, occupation, diabetes mellitus, and use of medications such as calcium channel blockers and insulin. Thus, early identification, careful monitoring, and appropriate interventions are required. This will help to prolong independent living, decrease caregiver burden, and reduce number of hospitalizations with improved compliance with medication. Future studies are required to compare cognitive impairments in hemodialysis patients with the quality of life, psychological impact, and overall functioning.

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