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ORIGINAL RESEARCH

Prevalence and Assessment of Cognitive Dysfunction in Patients with End-StageRenal Disease: A Cross-Sectional Study.

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Abstract

Background: Cognitive functions include memory, executive functioning, attention, orientation, reasoning and language. Deficit in more than two areas of cognitive domains leads to cognitive impairment. Cognitive impairment in End Stage Renal Disease (ESRD) patients is common, with the likelihood that this may affect patient compliance, health care costs and clinical outcome and may also be a complication of ESRD.

Objective: This study has been aimed to find the prevalence and various parameters associated with cognitive functioning, discern vulnerability factors and compare brain imaging findings in a sample of End stage renal disease patients(ESRD).

Material & Methods: This is a cross-sectional hospital based where 89 patients over 20 years of age diagnosed with ESRD and undergoing haemodialysis for more than 6months were recruited within a period of 9 months. Cognitive functions were evaluated on the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA).

Results: The prevalence of cognitive dysfunction on MMSE was found to be 38.2% in our sample of 89 patients, and 58.4% on MoCA. Males more than females (MMSE p-value <0.022; MoCA p-value<0.023) showed cognitive impairment, while patients with diabetes (p-value<0.003 and p-value<0.002 on MMSE and MoCA respectively) and with increased pre-dialysis urea (p-value<0.011 and p-value <0.034 on MMSE and MoCA respectively) also showed significant association with cognitive impairment. Cerebral atrophy was more commonly associated with cognitive impairment (p-value<0.003 on MMSE; p-value<0.001 on MoCA) on neuroimaging findings.

Conclusion: Cognitive decline was statistically significant among male patients with ESRD, with high levels of pre-dialysis urea and concomitant diagnosis of diabetes mellitus. Patients with cerebral atrophy showed significant cognitive impairment.

Keywords: Cognition, Diabetes, Esrd, Mmse, Moca

Introduction

End Stage Renal Disease (ESRD) is the final stage in the progression of Chronic Kidney Disease (CKD), characterized by a Glomerular Filtration Rate (GFR) that falls below 15 ml/min/1.73 m^2, which is the level of renal function that requires the use of haemodialysis to manage the patient's condition [1].Renalimpairment is a common problem in the community, with estimates suggesting that 45% of adults over the age of 70 years have CKD [2].The incidence of kidney disease is increasing across all age groups, largely due to the rising prevalence of hypertension and diabetes. Individuals with End Stage Renal Disease (ESRD) are particularly vulnerable to cognitive decline, which can significantly impact their quality of life [3].As the Glomerular Filtration Rate (GFR) falls below 60 ml/min/1.73 m2, and especially below 30 ml/min/1.73 m2, patients with chronic kidney disease (CKD) face a range of complications that progressively worsen. These include anaemia, bone diseases, metabolic acidosis, heightened risk of infection, cardiovascular diseases, and neurological complications. Collectively, these complications can greatly diminish patients' quality of life [4].Cognitive dysfunction has long been recognized as a complication of End Stage Renal Disease (ESRD), although guidelines for early detection, prevention, and management of these impairments remain somewhat unclear. There is mounting evidence to suggest that cognitive dysfunction is not only common among ESRD patients, but it may also have significant implications for patient management and prognosis [5].Cognitive impairment among patients with ESRD has been found to have direct effect on patient's compliance, cost of treatment and outcome [6].Cognitive impairment is typically defined as a new deficit in at least two areas of cognitive functioning, which can include memory (such as difficulty registering or recalling new information), executive functioning (such as impaired planning or reasoning abilities), attention (including problems with concentration, rapid assimilation, and analysis), perceptual motor abilities (such as difficulty processing visual, tactile, or auditory information with motor activities), or language (such as word

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finding or phrasing difficulties) [7].There is some evidence that patients with certain ethnic backgrounds have higher prevalence of CKD [8].Several Indian studies have shown a direct correlation between CKD and cognitive impairment, ranging from 44% in relatively younger people to almost 90% in frail and older [9,10,11].Patients reaching End Stage Renal Disease (ESRD) face a heavy burden of comorbidities and geriatric conditions, including peripheral vascular disease, atherosclerosis, depression, diabetes mellitus, hypertension, and biochemical abnormalities such as hypoalbuminemia. These factors are well-established risk factors for poor outcomes in ESRD patients and have also been associated with an increased risk of cognitive impairment [12].A deeper understanding of the neuropathological mechanisms underlying cognitive decline in patients with End Stage Renal Disease (ESRD) could be gained by identifying the relationships between abnormal regions of the brain [13].Slowing down cognitive decline in patients with End Stage Renal Disease (ESRD) may be possible by targeting low blood pressure and reducing albuminuria with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. However, cognitive dysfunction can also limit opportunities for future kidney transplantation [14].There is no denying that the prevalence of Chronic Kidney Disease (CKD) is on the rise, particularly among the elderly population. In fact, individuals over the age of 60 now account for half of all new cases of End Stage Renal Disease (ESRD), with an even greater impact on frail older individuals with higher vascular risk factors, as compared to younger populations [12,15].The objective of this study was to examine the prevalence of cognitive impairment in persons with ESRD and it was hypothesised that the prevalence of cognitive impairment would be higher in persons with ESRD [16]. We set out to compare the Mini mental status examination (MMSE) with Montreal cognitive Assessment (MoCA), and to determine common factors that might be associated with cognitive impairment in ESRD patients.

Material and Methods

Study design: This is a hospital-based, cross-sectional study which was carried out at a tertiary care hospital in Northern India during January 2021 and September 2021. This study was approved by the Institute Ethics Committee.

Inclusion criteria for participants:

1. Patients aged 20 years and above.
2. Diagnosed with ESRD, and undergoing dialysis at the Nephrology department of the hospital for more than 6 months were taken through consecutive purposive sampling within a period of 9 months.

Exclusion criteria for participants:

Patients with recognised mental health difficulties, intellectual disabilities, history of any co-morbid psychiatric disorder currently on medication before the diagnosis of ESRD, patients who were unable to participate in the study due to the severity of the physical disease, patients with alcohol and drug dependence, were excluded from the study.

A total of 89 patients diagnosed as ESRD were recruited during the period mentioned above.

Informed consent: They were informed that their participation would be entirely voluntary and this will not have any effect on the follow up and treatment. The details of this study were explained to the patients and informed written consent was obtained.Withdrawal of subject consent at any stage of the study was accepted and confidentiality was maintained.

Data Collection: Thesociodemographic data of the patient was collected andother co-morbidity Hypertension and Diabetes) were noted.The are standardised scalesfor assessing cognitive functioning, and have been used Indian population.The participants were assessed using subcategories of both scales (06 for MMSE and 07 for MOCA), and total scores were calculated for each participant on both scales.

- MoCAis designed as a rapid screening test for cognitive dysfunction to assess different cognitive domains and a score less than 26 suggests cognitive impairment.
- MMSE assesses different mental abilities including a person's memory, attention, registration, recall, visual-spatial and language with a maximum score of 30 points. A score of 25-30 suggests no cognitive impairment,20-24 mild cognitive impairment, 10-19as moderate cognitive impairment and less than 10 suggests severe cognitive impairment.

Renal function test was also performed on the participants before dialysis. 52 participants agreed to get their MRI done and the scores of both the scales were compared with the MRI findings, which included cerebral atrophy, cerebral microbleeds, and white matter change. Normality of the data was checked using Shapiro Wilk test and Kolmogorov-Smirnov Test and it was found that the MoCA and MMSE data was not normally distributed. Results were statistically analysed with help of STATA version 15.0(STATA Corporation college Station, Texas, USA).The data were analysed usingchi-square test, Mann-Whitney test and Kruskal Wallis test. The p-value <0.05 (Confidence Interval of 95%) was taken as statistically significant.

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Results

As seen in table 1, eighty-nine (89)ESRD patients study participants, 67.4% were male and 32.6% were female. The mean age of study participants was 51.1 years, with the majority 36% being aged between 41-50 years. Almost half (48.3%)of the participants had achieved secondary school education. Just over two-thirds (68.5%) were employed or retired from a job and almost 90% were married. More than half of participants were rural dwellers. Most of the study participants (75.3%) belonged to a middle-class family. Our study was to evaluate the cognitive functions of patients with End Stage Renal Disease (ESRD) undergoing haemodialysis at a tertiary centre in Northern India. Our findings revealed that the majority of participants (36.0%) belonged to the age group of 31-40 years, while 20.2% were aged between 51-60 years. Similar findings have been reported by Goyal et al[18] where the majority belonged to the age group 41-60 years (55.1%). It is worth noting that only a quarter of our study sample was over the age of 60 years, which could explain the relatively lower incidence of cognitive impairment we observed secondary school education. Just over two-thirds (68.5%) were employed or retired from a job and almost 90% were married. More than half of participants were rural dwellers. Most of the study participants (75.3%) belonged to a middle-class family.our study was to evaluate the cognitive functions of patients with End Stage Renal Disease .

Table 1: Sociodemographic data of study participants

Sociodemographic data		Percentage
Gender	Male	67.4%
	Female	32.6%
Age range (years)	21-30	4.5%
	31-40	14.6%
	41-50	36%
	51-60	20.2%
	61-70	13.5%
	71-80	11.2%
Education	Illiterate/Primary School	25.8%
	Secondary School (year 8-10)	48.3%
	High School (year 11-12)	24.7%
	College / University (Bachelor or higher degree)	1.1%
Occupation	Employed/retired	68.5%
	Unemployed	31.5%
Marital Status	Married	88.8%
	Unmarried	11.2%
Geography	Urban	46.1%
	Rural	53.9%
Socioeconomic Status	Upper Class	1.1%
	Middle Class	75.6%
	Lower Class	23.6%

The overall prevalence of cognitive impairment on MMSE was 38.2% in the sample, with a higher prevalence observed among males (41.6% of men) compared to females (31.03% of women) Cognitive impairment on MoCA was found in 58.4% of the sample. Consistent with MMSE scoring, more males (58.3%) than females (58.6%) were observed to have cognitive impairment on MoCA. The presence of diabetes and elevated urea levels were both significantly associated with prevalence of cognitive impairment assessed on MMSE as well as MoCA.

Table 2: Gender distribution on MMSE and MoCA

Psychometric tests	Male, N=60	Female, N=29	Total, N=89	p-value
MMSE, (IQR)	24 (22-26)	24 (23-26)	24 (23-26)	0.531
MMSE score <25	25 (41.6%)	9 (31.0%)	34 (38.2%)	**0.022***
MoCA, median (IQR)	24 (21-27)	24 (22-26)	24 (21-26)	0.860
MoCA score<26	35 (58.3%)	17 (58.6%)	52 (58.4%)	**0.023***

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However, no other factors were found to be significantly associated with cognitive impairment. Therefore, we found no statistical association of cognitive impairment with age, literacy, employment, marital status, rurality, socioeconomic status, creatinine levels and hypertension.[22]havereported a close association between ESRD and cognitive decline. In this study, we established that 38.2% of ESRD patients rated on the MMSE and 58.4% of patients rated on MoCA, showed significant cognitive impairment. This finding is somewhat higher than the 16.0% to 38.0% suggested by some reports[8].However, if psychometric testing on MMSE is considered, our results are compatible with previous reports. Our observation suggests that patients with ESRD show demonstrable: The sociodemographic data of the patient was collected and other co-morbidity Hypertension and Diabetes) were noted.The are standardised scales for assessing cognitive functioning, and have been used Indian population. The participants were assessed using subcategories of both scales (06 for MMSE and 07 for MOCA), and total scores were calculated for each participant on both scales finding is somewhat higher than the 16.0% to 38.0% suggested by some reports[8].However, if psychometric testing on MMSE is considered, our results are compatible with previous reports.Our observation suggests that patients with ESRD the .

Table3: Sociodemographic and medical factors associated with cognitive status of the participants on MMSE and MoCA

	MMSE			MoCA		
Demographics	**No cognitive impairment**	**Cognitive impairment**	**p-value**	**No cognitive impairment**	**Cognitive impairment**	**p-value**
Age (years), mean±SD	50.8±14.9	51.6±12.7	0.813	50.2±16.1	51.8±12.5	0.584
Education, (%)						
Illiterate/Primary School	13 (23.6%)	10 (29.4%)	0.523	9 (24.3%)	14 (26.9%)	0.686
Secondary School	25 (45.4%)	18 (52.9%)		17 (45.9%)	26 (50%)	
High School	16 (29.1%)	6 (17.6%)		11 (29.7%)	11 (21.2%)	
College	1 (1.8%)	0 (0%)		0 (0%)	1 (1.9%)	
Employment status(%)						
Employed/retired, (%)	37 (67.3%)	24 (70.6%)	0.96	25 (67.6%)	36 (69.2%)	0.414
Unemployed	18 (32.7%)	10 (29.4%)		12 (32.4%)	16 (30.8%)	
Marital status(%)						
Married, (%)	48 (87.3%)	31 (91.2%)	0.571	31 (83.8%)	48 (92.3%)	0.21
Unmarried,(%)	7 (12.7%)	3 (8.8%)		6 (16.2%)	4 (7.7%)	
Locality (%)						
Rural residence,(%)	28 (50.9%)	20 (58.8%)	0.467	22 (59.5%)	26 (50%)	0.378
Urban residence, (%)	27 (49.1%)	14 (41.2%)		15 (40.5%)	26 (50%)	
Socioeconomic status, (%)						
Upper Class	1 (1.8%)	0 (0%)	0.659	0 (0%)	1 (1.9%)	0.249
Middle Class	42 (76.4%)	25 (73.5%)		31 (83.8%)	36 (69.2%)	
Lower Class	12 (21.8%)	9 (26.5%)		6 (16.2%)	15 (28.8%)	
Hypertension, (%)						
Yes	26 (47.3%)	18 (52.9%)	0.603	17 (46%)	27 (51.9%)	0.578
No	29 (52.7%)	16 (47.1)	(0.27)	20 (54%)	25 (48.1%)	(0.31)
Diabetes, (%)						
Yes	7 (20.6%)	30 (47.6%)	0.003*	15 (41.6%)	30 (58.4%)	0.040
No	25 (45.4%)	27 (79.4%)	-8.63	22 (58.4%)	22 (41.6%)	(0.425)
Renal Functions, (pre-dialysis)						
Urea, mean±SD	67.64±17.68 (55)	79.29±24.45 (34)	0.011*	66.49±18.33 (37)	77.59±27.34 (52)	0.034*
Creatinine, mean±SD	4.7±0.2	5.5±0.4	0.078	4.6±0.2	5.2±0.3	0.157

*Statistically significant

In ESRD patients exhibiting cognitive impairment or a history of delirium (n=52), MRI brain scans were performed and in these patients 36.5% had cerebral atrophy, 17.3% had cerebral microbleeds, 21.2% had white matter changes

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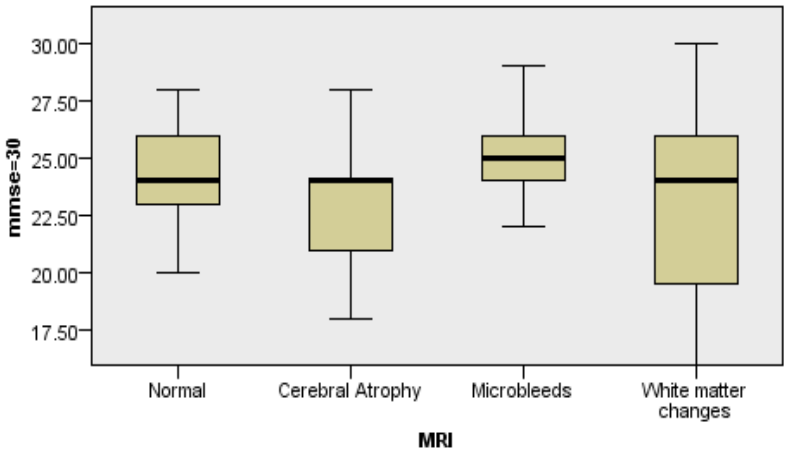
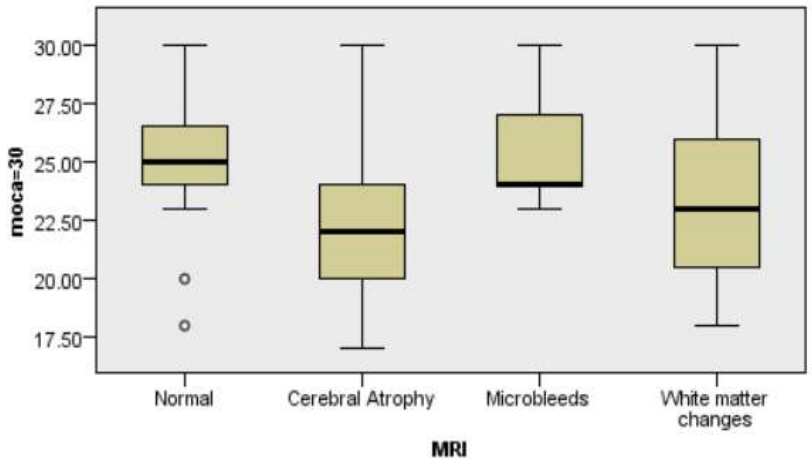
and 25% had normal MRI finding. As seen in Figure 1 the distribution of MMSE across the various categories of MRI findings was same, thus there was no significant differences across the samples. MMSE is considered, our results are compatible with previous reports. Our observation suggests that patients with the our .

Figure 1: Association between MMSE and MRI findings (Kruskal Wallis Test, N=52, p=0.262)



Similar findings were seen with MoCA scores and there was no significant differences across the samples. The MoCA scores were same across the various categories of MRI findings (Figure 2).

Figure 2: Association between MoCA and MRI findings (Kruskal Wallis Test, N=52, p=0.104)



Discussion

The primary objective of our study was to evaluate the cognitive functions of patients with End Stage Renal Disease (ESRD) undergoing haemodialysis at a tertiary centre in Northern India. Our findings revealed that the majority of participants (36.0%) belonged to the age group of 31-40 years, while 20.2% were aged between 51-60 years. Similar findings have been reported by Goyal et al[18]where the majority belonged to the age group 41-60 years (55.1%). It is worth noting that only a quarter of our study sample was over the age of 60 years, which could explain the relatively lower incidence of cognitive impairment we observed compared to other studies with a predominantly older cohort. It is also important to mention that the majority of our study participants came from a rural background. This could be attributed to a lack of early preventive measures, poor knowledge about the illness, and delayed detection and treatment of renal disease, which can contribute to the progression of renal failure[20]. The gender distribution showed that males were more commonly affected by ESRD than females, which is a similar finding to Elhadadet al[21].Severalstudies[9,10,11,22]havereported a close association between ESRD and cognitive decline. In this study, we established that 38.2% of ESRD patients rated on the MMSE and 58.4% of patients rated on MoCA, showed significant cognitive impairment. This finding is somewhat higher than the 16.0% to 38.0% suggested by some reports[8].However, if psychometric testing on MMSE is considered, our results are compatible with previous reports. Our observation suggests that patients with ESRD show demonstrable decline in performance in attention, recall and executive function. These results are also consistent with reports from other studies[17,18].Although this study was not designed to assess the relationship between cognitive performance and GFR, as the focus of our study was ESRD, other studies have shown a graduated association between ESRD and cognitive impairment[23].The high prevalence of cognitive impairment in patients with End Stage Renal Disease

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(ESRD) has significant implications for their treatment, including future transplantation and withdrawal of dialysis, as well as their quality of life. Moreover, the association between ESRD and type 2 diabetes mellitus could also contribute to the increased risk of cognitive dysfunction. Moran et al. have reported that type 2 diabetes mellitus is associated with brain atrophy, lower total grey and white matter, which could be another potential cause for the high prevalence of cognitive impairment in ESRDpatients[24].The pathogenesis of cognitive dysfunction in patients with Chronic Kidney Disease (CKD) is not yet fully understood, but some researchers have suggested that it may be related to the faulty kidney-brain axis[32].The accumulation of uraemic toxins, chronic inflammation, and oxidative stress in patients with End Stage Renal Disease (ESRD) is associated with vascular changes, endothelial dysfunction, and neuronal damage, which may lead to cerebral changes. In addition to kidney dysfunction, haemodialysis may also contribute to these changes[7,8].Several studies have reported a strong correlation between cognitive decline and cerebral atrophy, similar to the findings of our study. However, patients undergoing haemodialysis may be at an even higher risk of cognitive impairment due to their older age and the high prevalence of stroke and other vascular risk factors. These factors can contribute to chronic inflammation, oxidative stress, and vascular changes that can lead to neuronal damage and cognitive dysfunction in patients with ESRD[25].While the mechanism underlying cognitive impairment in people with ESRD is not understood, duration of dialysis and late diagnosis play an important part, amongst other matters. It is crucial to recognize the implications of cognitive impairment in patients with ESRD, as it can lead to negative outcomes such as higher mortality rates, increased withdrawal from dialysis, frequent hospitalization, and disability. Therefore, regular cognitive screening is necessary to identify patients with cognitive decline and provide timely interventions to improve their quality of life. Additionally, healthcare providers should focus on preventive measures such as controlling blood pressure, reducing albuminuria, and managing comorbidities and risk factors associated with cognitive impairment to slow down the progression of cognitive decline in ESRD patients. Screening for cognitive dysfunction in patients with ESRD can be improved by including caregiver interviews, as they often detect cognitive deficits before they become apparent to clinicians. Furthermore, assessments should be available to clinicians to help establish the degree of impairment. Preventive measures should focus on modifying vascular risk factors, preventing and managing diabetes, which have shown promise in the general population and may be reasonably extended to patients with ESRD. Kidney transplantation has been shown to reverse cognitive impairment in dialysis patients in one prospective study, while some researchers suggest that dialysis predicts better cognitive functioning, others have been unable to reach this conclusion[26].Larger, purposeful studies must be designed to delineate the various factors involved in cognitive impairment in ESRD patients, so that firm guidelines can be drawn up.

Conclusion

This study highlights the differences in the rates of cognitive impairment between the MMSE and MoCA tests,. Additionally, patients with ESRD and diabetes, as well as those with higher levels of urea, were significantly associated with cognitive dysfunction. In summary, our study identified several risk factors for cognitive dysfunction in patients with ESRD, including diabetes, male gender, and elevated urea levels. Interestingly, age was not found to be a significant risk factor in our younger cohort. being the best predictor of cognitive impairment. These results emphasize the need for early diagnosis and treatment of cognitive impairment in ESRD patients to improve their quality of life and reduce the burden of disease. Further research is needed to explore potential interventions to prevent or manage cognitive dysfunction in this population.

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Conflict of Interest

None. There is no conflict of interest between any authors.

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