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A study on cognitive functions in chronic kidney disease patients in a government medical college, Kerala

Muhammad[1*], CV Shaji[2], KA Kabeer[3], S Gomathy[4]
[1] Senior Resident, Department of Neurology, Govt TDMC Alappuzha, Kerala, India
[2, 4] Professor and Head, Department of Neurology, Govt TDMC Alappuzha, Kerala, India
[3] Associate Professor, Department of Neurology, Govt TDMC Alappuzha, Kerala, India

Abstract
Introduction: Cognitive impairment (CI) is more common in patients with CKD than in the general population. But it remains poorly recognized clinically and, therefore, underconsidered in the care of renal disease patients.
Methodology: This was an Observational study on 50 CKD patients, over 1-year period., conducted at Nephrology and Medicine wards. Cognitive assessments were done using MoCA scale. MoCA score of various stages of CKD were compared.
Results: The mean age of the study group was 47.14 ± 10.8. Male to female ratio was 3:2. Etiologies of CKD were diabetes (38%), systemic hypertension (18%), chronic glomerulonephritis (14 %). Mean years of schooling was 8.74 ± 2.74 years. 46% of patients had stage 5 CKD and 18% had stage 4. 50% of patients were on hemodialysis (HD). Mean MoCA score observed was 25.40 ± 2.76. MoCA score of < 26 was observed in 26 out 50 patients. No significant difference between mean MoCA scores of males and females. Pearson correlation between MoCA score, eGFR and HD, showed more cognitive impairment in those on HD and with advanced CKD.
Among the various cognitive tests assessed most common abnormality was for word fluency (78%) followed by Trail making test (56%) and abstraction (54%).
Conclusion: CI is more in patients with advanced CKD patients and in those on HD. Most of the abnormality observed were in non - amnestic domains of cognition. Most of the abnormality observed were in non - amnestic domains of cognition.

Keywords: CKD, MoCA, cognitive impairment

Introduction
Chronic kidney disease (CKD) is a worldwide public health problem and is more prevalent in the elderly population. Cognitive impairment (CI) is common in all stages of CKD. CI can potentially affects multiple areas of patient care including compliance with treatment plans and quality of life. Although CI is more common in patients with CKD than in the general population, it remains poorly recognized clinically and, therefore, under-considered in the care of renal disease patients.
Several factors may be responsible for the high prevalence of CI in this population. As the prevalence of CKD worldwide continues to increase, patients with CI also on the rise.
High prevalence of subcortical white matter lesions load and high incidence rate for stroke in patients with CKD. Subcortical white matter lesions formation secondary to small vessel cerebrovascular disease, is likely to be accelerated in CKD because of clustering of multiple vascular risk factors, including hypertension, diabetes, hyperlipidemia, elevated oxidative stress, and an elevated inflammatory state. Small vessel cerebrovascular disease can lead to vascular dementia (VaD) with a pattern of cognitive deficits characterized by impairment in domains related to attention, executive function and processing speed with relatively preserved memory.
As most of the current dementia screening tools, rely heavily on memory deficits, this non-amnestic pattern of Cognitive deficits likely to be missed, particularly in the early stages.
The purpose of this study is to perform cognitive assessment in inpatient CKD and HD patients with no history of dementia, stroke or neurodegenerative disease and characterize the cognitive deficits using Montreal cognitive assessment scale (MoCA).
MoCA covers the assessment of non-amnestic domains particularly executive function, hence was recommended as a screening test in the evaluation of cognitive functions in CKD patients [1].

Materials and Methods
Site and study design
This was a descriptive study, carried out at department of Nephrology and Medicine, Govt. T.D Medical college, Alappuzha, from April 2017 to March 2018. The approval from the ethical committee was obtained for the study.

Study population
Patients with CKD who were admitted in department of Nephrology and Medicine, during the study period were considered as the study subjects. A total of 50 patients participated in the study.

Inclusion criteria
All CKD patients above the age of 18 years and less than 60 years

The exclusion parameters are as follows

History of Stroke History of Dementia Presence of neurodegenerative disease Presence of chronic liver disease Psychiatric illness Delirium visual and auditory disorders that prevented them from performing the tests Patient refusal A proforma was used to collect the data. Cognitive assessment was done using Montreal cognitive assessment scale (MoCA). Stage of CKD was determined based on eGFR, which was calculated using creatinine clearance estimate by Cockcroft –Gault equation.

Cockcroft – Gault equation

Creatinine clearance = Sex * [(140-age) / (serum creatinine)] *(weight / 72) sex: use '1' for men and 0.85 for females

Statistical analysis

Data were entered in Microsoft Excel and was analysed using SPSS software.

Quantitative variables were expressed in mean with standard deviation. Qualitative variables were expressed as proportions or percentages. Spearman correlation and linear regression analysis were done to find out correlation, and a P value of < 0.05 was considered as statistically significant.

Observations and Results

A total of 50 patients were studied of which 28 (56%) patients were between 50-59 years. 22% were less than 40 years. Youngest was 20 years, and oldest was 59 years. 30 out 50 patients were males. Most common etiology observed was diabetes mellitus in 38 % of cases followed by systemic hypertension in 18 % of cases [Figure 1). Most common associated co-morbidity was systemic hypertension (in 70% cases). Mean number of years of schooling was 8.74 ± 2.74 years.

Most of the study patients were in stage 5 (46%) followed by stage 4 (18%) [Table 1]. Mean duration of CKD was 22.42 months. 50 % of patients (25 out of 50) were on hemodialysis. Out of these 25 patients, 19 had stage 5 and 6 had stage 4 CKD. 52 % of patients (23% males, 23% females) had abnormal MoCA score (ie, < 26), suggestive of CI. Mean MOCA Score observed was 25.40 ± 2.76 [Table 2]. Mean MoCA score of males and females were 25.37 and 25.45 respectively.

Pearson correlation study between stage of CKD and MoCA score showed correlation Coefficient (r) of – 0.441, with a significant P – value (0.001). This implies that MoCA score decreases with increasing the stage of the CKD. Means cognitive impairment was more in advanced CKD patients [Figure 2, Table 3].

Comparison of MoCA score of stage 1 and stage 5 CKD was done using independent sample t-test. It showed significant P - value of 0.029. MoCA score < 26 (suggestive of CI) was seen in 26 patients, of which 16 patients stage 5 CKD. Linear regression analysis between eGFR and MoCA shows decline in eGFR is associated with reduction in MoCA Score (R – value 0.124, P-value 0.01) [Table 4]. Independent sample t-test was done to compare MoCA score of patients on HD Versus non – HD group, showed CI more in HD group [Table 5].

Most common cognitive abnormality was for word fluency (in 78%) followed by TMT (Trail Making Test) (in 56%) and abstraction (in 54%). Visuospatial / executive function (VS/EF) Score was impaired in 58% of patients [Figure 3]. Among this VS/EF, testing abnormalities was more for TMT (in 56% cases) followed by CDT (in 38% cases). Attention was also tested using digit span, random A and serial 7 substraction tests, showed abnormality in 32%, 32% and 44% respectively. Though five item recall was affected in 44% of patients, majority of them (36%) had only problem in recalling one item out of five [Table 6].

Discussion

This was an Observational study conducted among diagnosed CKD patients over a period of 1 year. Assessment of various cognitive functions using MOCA scale were done in 50 CKD patients.

In this study 30 patients (60%) were males and 20 were females. This study was comparable to a study done by Paraizo *et al* [2] in which 55.6 % were males and 44.4 % were females. Mean age of the study population in our study was 47.14 ± 10.8 with 56 % patients belong to 50 – 59 years of age. 22 % patients belong to 40 – 49 years of age group and another 22% patients belong to the age group of less than 40 years. Mean age group of patients in Paraizo *et al* study was 56.74 ± 7.63 years. Most common etiology found in our study was DM, seen in 19 out of 50 (38 %) patients followed by systemic hypertension (in 18% cases). Systemic hypertension was the etiology in 18 % of cases followed by CGN (in 14%). In the remaining patients' causes were – vascular (in 12%), CTID (in 12%) and Reflux (in 6%). These observations were comparable to the study by Iyasere *et al*. [3], who observed DM as the most common etiology for CKD (in 64%).

Most common comorbid condition noted was systemic hypertension (in 70% of cases) followed by retinopathy (in 60 % cases) and DM (in 50 % cases). PN was observed in 36% and CAD in 18% of cases. Paraizo *et al*. [2] and Angermann *et al*. [4] also observed hypertension as the most common co morbidity (in 93.1% and 94.7% respectively).

Mean number of years of schooling observed in our study was 8.74 ± 2.74 years. Most of the patients (90%) had formal education of more than 4 years. This was comparable to the studies done by Paraizo *et al*. [2], in which mean age of study group was 5.4 ± 2.9 years, and 84.3% patients had education of 4 years of more. In Angermann *et al*. [4] study 62.3% of patients had formal education of 12 years or less.

23 out 50 patients (46%) had stage 5 CKD and 18% had stage 4 disease. 10%, 12%, 14% of patients had stage 1, 2 and 3 respectively. Mean duration of CKD was 22.42 months. 25 out 50 patients (50%) were on maintenance HD. Out of these 25 patients, 19 had stage 5 and 6 had stage 4 disease. Duration of HD in most of the patients (20 out of 25, 80%) were 12 months or less, with mean duration of 10.32 months.

MoCA score of < 26, (suggestive of CI) was observed in 26 patients (52%), 6 Patients had score of 6 or less. Mean MoCA score of whole sample was 25.40 ± 2.76.

Mean MoCA score after excluding 2 patients with education < 4 years was 25. 437.Mean MoCA score of males and females were 25.37 and 25.45 respectively.

Paraizo *et al* [2] and Iyasere *et al*. [3] showed CI in 73.6% and 60.56% of patients respectively. Mean MoCA score was 21.83 ± 4.16 in the former and 24 in the latter.

Correlation between MoCA score and stage of CKD was done using spearman correlation which showed an r-value of -0.441, with a significant P-value (0.001).

This suggests that MoCA score declines as CKD progresses to advanced stage.

Mean MoCA score of satge 1 CKD was 27.60 ± 1.52, compared to stage 5 CKD (score of 24.22 ± 3.16). CI observed was 51% in a study by C. E. Rodríguez -Angarita *et al*. [5] on patients with moderate CKD. It reach about 70% in patients with severe CKD / dialysis [6].

Spearman correlation study between MoCA score and eGFR also showed significant positive correlation, with an r-value of 0.353. This implies that MoCA score falls in correlation with decline in eGFR. This was further supported by linear regression analysis, which showed an R-value of 0.124, with a significant P value (0.012). These observations were supported by the REasons for Geographic and Racial Differences in Stroke (REGARDS) Study [7], which reported an 11% increase in the risk of CI for every 10 mL decrease in eGFR below 60 mL/min/1.73 m2. Also supported by CRIC COG study by Yaffe K *et al*. [8].

Pearson correlation analysis shows negative correlation between MoCA score and HD, with an r - value of -0.367. This implies that MoCA score is lower in patients on HD. This is supported by observations made by Murray AM *et al*, [6] that CI was more in advanced CKD/dialysis patients. A follow-up study by Osasuyi Iyasere *et al*. [3] showed faster decline in MoCA scores in the dialysis group compared with CKD group. Study by Lee *et al*. [9] also showed significantly lower MoCA score in HD patients.

Independent sample t-test was done to compare MoCA scores of HD versus non-HD group showed greater cognitive decline in HD group. Mean MoCA score of HD group was 24.4 ± 3.08 compared to 26.4 ± 1.98 in non-HD group (with significant P-value of 0.009).

Visuospatial / executive function (VS/EF) Score was impaired in 58% of patients. Among this VS/EF testing abnormalities was more for TMT (in 56% cases) followed by CDT (in 38% cases). Copying a cube was abnormal in 36% of cases.

This is comparable to the study by Lee *et al* [9] which showed executive dysfunction in 43% of patients and visuospatial problem with 50% of cases.

Forward digit span (FDS) and backward digit span (BDS) testing for attention, showed abnormalities in 32% of cases. Both impaired in 8% of patients and BDS alone was impaired in 24% of cases. Similar observation by Lee *et al*. [9] showed attention testing abnormalities using FDS and BDS in 40% of cases. However, Paraizo *et al*. [2] reported abnormal FDS score in 45.80% and abnormal BDS score in 22.20%. Attention was also tested using random A test and serial 7 substraction test, which showed abnormalities in 32% and 44% of patients respectively. Among the tests for attention abnormality was more for serial 7 substraction test.

Naming was normal in all (100%) patients. Studies by Paraizo *et al*. [2] and Iyasere *et al*. [3] also didn't show any alteration in naming. It was the only cognitive test in the MoCA which everyone answered correctly. Repetition was abnormal in 8% of patients. 78% of patients had decreased word fluency per 1 minute. They only able to say 11 words or less in 1 minute. Lee *et al* showed language abnormality in 40% of patients and Paraizo *et al*. [2] reports decreased verbal fluency in 29% of cases.

27 out of 50 (54%) had problem with abstraction. Of this 36% of patients were able to say similarities of one group of objects. 44% patients had problem with recall, however 36% patients had problem with recalling one item out of five. 12% of patients had problem with orientation, in which 8% of patients scored 5 out of 6 and 4% of patients scored 4 out of 6.

Most common abnormality was for word fluency (in 78%) followed by TMT (in 56%) and abstraction (in 54%). Though recall was affected in 44% of patients, majority of them (36%) had only problem in recalling one item out of five.

Conclusion

It was observed that CI is common in CKD patients, which can negatively affects their health-related quality of life. CI is often under-diagnosed due to the patients' unawarenessof their cognitive deficits, as they do not subjectively experience any cognitive deficits. Therefore, screening tests would be more appropriate for identifying these patients. MoCA is a good screening tool to assess the global cognition of individuals with CKD, as it tests both amnestic (memory) and non-amnestic (attention, visuospatial, executive functions etc) cognitive domains. Interventions on modifiable risk factors for CI may delay its progression and improve quality of life.

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