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Risk Factors for Cognitive Impairment among CKD Patients in Usmanu Danfodiyo University Teaching Hospital, Sokoto

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ABSTRACT

Introduction: The association between cognitive impairment and chronic kidney disease has been documented. Cognitive impairment in CKD may affect adherence to treatment, including diet, medications and quality of life, furthermore, it is an independent risk factor for mortality. Hence the need to identify risk factors for cognitive impairment among CKD patient in our study.

Methods: All consecutively seen, eligible and consenting CKD patients ≥18 years with no barrier to Neuropsychological assessments were recruited between June – August, 2019. Structured proforma was used for data collection including the Montreal Cognitive Assessment tool (MoCA). SPSS version 20.0 was used for data analysis.

Results: 40 participants were recruited with M:F ratio of 3:1. Mean age was 45.03±12.89 years. 89.7% of the CKD patients were cognitively impaired using MoCA scores of 26 as cut off. Significant difference was seen in the MoCA scores of cognitively impaired compared to cognitively normal patients. (17.69±3.28 and 27.75±1.26; p = < 0.001). BMI and systolic blood pressure were found to be associated with cognitive impairment (p = 0.004 and p = 0.047 respectively). No association was found with waist circumference, diastolic blood pressure, aetiology of CKD, duration of diagnosis of CKD and eGFR.

Conclusion: Cognitive impairment may be common in our CKD patients and its assessment with emphasis on risk factors should form part of evaluation of all CKD patients.

INTRODUCTION

Cognition is the mental action or process of acquiring knowledge and understanding through thought, experience, and the senses [1]. Cognitive impairment is an inclusive term to describe any characteristic that acts as a barrier to the cognitive process [2]. Chronic kidney disease (CKD), defined by persistent reduction in glomerular filtration rate (GFR) and/or the presence of other signs of kidney damage, is staged based on GFR and albuminuria categories [3]. The population based prevalence of CKD in Nigeria is between 2.5–26% [4], which is higher than the reported prevalence of 12.1–19.9% in Africa [5], and it is more than the global prevalence of 11-13% [6]. The association between cognitive impairment and chronic kidney disease has been documented in the literature [7,8]. Cognitive impairment in CKD may affect adherence to treatment, including diet and medications [9], besides it is an independent risk factor for mortality [10,11]. CKD patients with cognitive impairment should be identified to reduce morbidity and improve their quality of life [12], in addition, early intervention will slow the progression of cognitive impairment [13], hence the need to

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identify risk factors for cognitive impairment among CKD patient in our study.

SUBJECTS AND METHOD

Ethics Statement

Approval for this study was obtained from the health research ethical committee of the Usmanu Danfodiyo University Teaching Hospital, Sokoto. Informed consent was taken from each participant prior to inclusion in the study.

Study population

Consecutive patients with CKD e” 18 years and eligible, seen at the medical outpatient department of the Usmanu Danfodiyo University Teaching Hospital Sokoto were recruited.

Clinical and Demographic data

All consecutively seen and consenting patients with CKD with no evidence of uraemic encephalopathy, previous overt stroke, significant head trauma, visual impairment, hearing impairment or overt dementia were included. Biodata and other clinical variables as they relate to CKD were obtained with an interviewer administered structured proforma. As at the time of administering the Neuropsychological tests, hypoglycaemia was ruled out by pre-testing RBS, and those with low RBS were equally excluded. Only participants with laboratory results of parameters which is usually requested for follow up, which include Packed cell volume, Serum Calcium, Uric acid and Phosphate were included. Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI 2009 equation.

Neuropsychological testing

The Montreal Cognitive Assessment (MoCA) tool was used to evaluate the cognitive function of the participants because previous studies have demonstrated high sensitivity of MoCA score with cognitive function [14,15]. MOCA of <26 was taken as the cut-off for cognitive impairment in the normal general population across many ethnic groups. Besides, it has less susceptibility to educational and cultural artifacts thus enabling its use in our environment [16]. More importantly, systematic review on cognitive function in CKD incorporating many studies used <26 score of MoCA as the cut in their various studies [14].

Statistical analysis

Data of each participants were decoded and de-identified with Excel spread sheet. It was later transferred to Statistical Package for Social sciences version 20.0. Data exploration was done and normality test was carried out using Shapiro-wilk test. Normally distributed continuous variable such as age and MoCA scores were presented as means and standard deviation, and were compared using t-test. Categorical variables of various risk factors were categorized based on cognitive state and were explored using chi-square. Data was summarized using tables.

RESULTS

Forty (40) participants were recruited, M: F – 3;1. Age range of 20-71, mean of 45.03±12.89 years. The mean score of MoCA was 18.72±4.39 (95% CI: 17.29-20.14). Using the cut off score of 26 for MoCA, 89.7% were cognitively impaired, 80% M; 20% F.

Table 1: Sociodemographic variables based on cognitive function categorization

Sociodemographic Variables		Cognitively Impaired	Cognitively Normal	Test statistics	P value
Age (Years)		45.91±13.26	39.00±9.63	t = 1.007	0.320
Sex	Male	28	2	χ^2= 1.820	0.223
	Female	7	2		
Education	Tertiary	12	2	χ^2= 4.440	0.326
	Secondary	9	1		
	Primary	1	1		
	Informal	10	0		
	Others	3	0		
Occupation	Civil servant	9	1	χ^2= 2.374	0.494
	Business	14	1		
	Farmer	6	0		
	Unemployed	6	2		

Table 2: Clinical details of CKD as it relates to cognitive function categorization

Clinical Details		Cognitively Impaired	Cognitively Normal	Test statistics	P value
Duration of <2		23	4	χ^2= 0.726	1.000
Diagnosis of 2-5		5	0		
CKD (Years) >5		2	0		
Aetiology of CKD	CGN	14	0	χ^2= 8.131	0.077
	Hypertension	9	1		
	Type 2 DM	4	3		
	Obstructive uropathy	5	0		
	HIV	1	0		
	Others	2	0		
Type of treatment	Conservative	15	4	χ^2= 4.980	0.197
	Haemodialysis	19	0		
	Transplant	1	0		

Table 3: Anthropometric variables based on cognitive function categorization

Anthropometry		Cognitively Impaired	Cognitively Normal	Test statistics	P value
BMI(Kg/m^2)	Underweight	4	0	χ^2= 15.15	0.004
	Normal weight	23	0		
	Overweight	7	2		
	Class I obesity	0	1		
	Class II obesity	0	1		
	Class III obesity	1	3		
Waist Circumference (cm)	High	19	3	χ^2= 0.626	0.618
	Normal	16	1		
Systolic BP(mmHg)	< 140	20	0	χ^2= 4.692	0.047
	$\geq$ 140	15	4		
Diastolic BP(mmHg)	< 90	20	1	χ^2= 1.492	0.318
	$\geq$ 90	15	3		

Table 4: Stage of CKD and laboratory parameters based on cognitive function categorization

Laboratory Evaluation		Cognitively Impaired	Cognitively Normal	Test statistics	p value
eGFR (CKD-EPI)	1	3	0	χ^2= 2.967	0.685
(Stage)	2	2	1		
mL/kg/1.73m2	3	11	1		
	4	13	2		
	5	6	0		
Packed cell volume (%)	< 20	6	1	χ^2= 2.195	0.313
	20-30	26	2		
	> 30	3	1		
Calcium(mMol/L)	< 2.20	25	3	χ^2= 1.521	0.559
	2.20-2.55	4	1		
	> 2.55	1	0		
Phosphate(mMol/L)	< 0.87	2	0	χ^2= 1.377	0.651
	0.87-1.45	8	0		
	> 1.45	20	4		
Uric acid(mg/dL)	< 3	1	0	χ^2= 4.650	0.407
	3-7	14	1		
	> 7	5	0		

Table 5: Relationship between medications and cognitive function

Medications		Cognitively Impaired	Cognitively Normal	Test Statistics	P-Value
Antihypertensives					
Calcium channel blocker	Yes	13	4	4.034	0.045
	No	15	0		
ACEI/ARB	Yes	20	3	0.022	0.882
	No	8	1		
Methyldopa	Yes	5	2	2.116	0.146
	No	23	2		
Diuretics	Yes	9	2	0.495	0.482
	No	19	2		
Antidiabetic agents*					
Biguanides	Yes	3	1	0.016	0.898
	No	5	2		
Sulphonylurea	Yes	4	1	0.244	0.621
	No	4	2		
Insulin	Yes	4	3	2.357	0.308
	No	3	0		
Others					
Erythropoietin	Yes	12	2	0.385	0.535
	No	23	2		
Calcium carbonate	Yes	1	0	0.117	0.732
	No	34	4		
Calcium lactate	Yes	25	2	0.774	0.379
	No	10	2		
Haematinics	Yes	31	2	4.103	0.043
	No	4	2		
Calcitriol	Yes	23	2	0.385	0.535
	No	12	2		

The mean MoCA scores of the cognitively impaired compared to cognitively normal were 17.69±3.28 and 27.75±1.26 respectively (t=6.028, p<0.001).

DISCUSSION

Almost 90% of the study participants were cognitively impaired with male predominance. There was a statistically significant difference between the MoCA scores of the cognitively impaired to cognitively normal participants. The mean age of the cognitively impaired was 45.91±13.26 years and the MoCA score was 17.69±3.28, indicating poor cognitive function, comparing our cohorts cognitive performance to that of Gluhm et al, among healthy adults between the 4th and 6th decade of life, the MoCA scores ranged between 27.8-27.0, indicating better cognitive function [16].

Categorizing the participants based on their cognitive performance, revealed a statistically significant difference in the body mass index and systolic blood pressure. While it seems a paradox that the underweight and especially 'normal weight' patients were cognitively impaired compared to overweight and obesse who were cognitively normal, however, in patients with CKD, there is the possibility of water retention [17], thus patients that are underweight resulting from malnutrition tend to have normal body mass, if not overweight, furthermore, those that are 'normal' weight and possibly overweight may tend towards overweight and obesity respectively. Besides, water retention has been associated with inflammation and endothelial injury [17], which are substrates for cognitive dysfunction [18,19]. This may be the likely case scenario in our cohort, more so that the weight measured were not lean body weight. Another possible explanation may be malnutrition in CKD, which may be associated with albuminuria and subsequent water retention. Malnutrition and albuminuria have equally been associated with cognitive decline [20,21]. More participants with elevated systolic blood pressure were significantly cognitively impaired. This finding may explain the vascular mechanism responsible for cognitive dysfunction and CKD [22]. Furthermore,

There is a statistically significant difference between cognitively impaired (76%) and cognitively normal (24%) who are on calcium channel blockers thus pointing to the primary aetiology for which these potent antihypertensives is being taken. Therefore, this may be explained by the fact that apart from diabetes, hypertension is an independent and/or co-risk factor for the development of cognitive dysfunction. This is further highlighted by the findings in our cohorts (Table 2) with over 90% of them may have primary and/or secondary hypertension [23]. Apart from calcium channel blockers, intake of hematinics was also found to be significantly associated with cognitive impairment, as 91% were cognitively impaired. This is an indirect association as most patients with CKD have anaemia, thus warranting intake of hematinics and anemia has been associated with cognitive dysfunction and this is ameliorated with treatment [24,25].

CONCLUSION

Our study revealed that cognitive impairment may be common in our CKD patients and weight loss as a result of malnutrition possibly and anaemia from many aetiologies are likely risk factors for cognitive impairment in our environment. Hence, the need to encourage adequate and balanced nutrition in addition to optimal blood pressure control, and active management and or prevention of anaemia among CKD patients.

LIMITATIONS

The sample was small limiting discovery of other risk factors for cognitive impairment and lack of neuroimaging to delineate those with subclinical stroke which may also be responsible for cognitive dysfunction.

REFERENCES

1. Oxford Dictionaries. cognition - definition of cognition in English from the Oxford dictionary. www.oxforddictionaries.com. http://www.oxforddictionaries.com/definition/english/cognition. Published 2017. Accessed July 30, 2016.
2. Stanley Coren. Sensation and Perception. *In*: Freedheim DK, Weiner IB, eds. Hand Book of Psychology: Vol 1, History of Psychology. Canada: John Wiley & Sons, Inc.; 2003:150-dc21. http://arsmath.org/msl/Library/psychology/common/Handbook-of-Psychology-Volume-1-Histoty-of-Psychology. pdf#page=106. Accessed April 9, 2019.
3. Kidney disease: Improving global outcomes (KDIGO) CKD work group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease - Johns Hopkins University. https://jhu.pure.elsevier.com/en/publications/kidney-disease-improving-global-outcomes-kdigo-ckd-work-group-kdi-4. Accessed November 25, 2019.
4. Chukwuonye II, Ogah OS, Anyabolu EN, *et al.* Prevalence of chronic kidney disease in Nigeria: systematic review of population-based studies. Int J Nephrol Renovasc Dis. 2018:11-165. doi:10.2147/IJNRD.S162230
5. Kaze AD, Ilori T, Jaar BG, Echouffo-Tcheugui JB. Burden of chronic kidney disease on the African continent: a systematic review and meta-analysis. BMC

Nephrol. 2018;19(1):125-131. doi:10.1186/s12882-018-0930-5

6. Hill NR, Fatoba ST, Oke JL, *et al*. Global prevalence of chronic kidney disease - A systematic review and meta-analysis. PLoS One. 2016;11(7):e0158765. doi:10.1371/journal.pone.0158765
7. Kurella Tamura M, Wadley V, Yaffe K, et al. Kidney Function and Cognitive Impairment in US Adults: The Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study. Am J Kidney Dis. 2008;52(2):227-234. doi:10.1053/j.ajkd.2008.05.004
8. Elias MF, Elias PK, Seliger SL, Narsipur SS, Dore GA, Robbins MA. Chronic kidney disease, creatinine and cognitive functioning. Nephrol Dial Transplant. 2009; 24(8):2446-2452. doi:10.1093/ndt/gfp107
9. Murray AM, Knopman DS. Cognitive impairment in CKD: No longer an occult burden. Am J Kidney Dis. 2010;56(4):615-618. doi:10.1053/j.ajkd.2010.08.003
10. Griva K, Stygall J, Hankins M, Davenport A, Harrison M, Newman SP. Cognitive impairment and 7-year mortality in dialysis patients. Am J Kidney Dis. 2010;56(4):693-703. doi:10.1053/j.ajkd.2010.07.003
11. Kurella M, Chertow GM, Luan J, Yaffe K. Cognitive impairment in chronic kidney disease. J Am Geriatr Soc. 2004;52(11):1863-1869. doi:10.1111/j.1532-5415.2004.52508.x
12. Kurella M, Luan J, Yaffe K, Chertow GM. Validation of the Kidney Disease Quality of Life (KDQOL) Cognitive Function subscale. Kidney Int. 2004;66(6):2361-2367. doi:10.1111/j.1523-1755.2004.66024.x
13. Etgen T, Chonchol M, Frstl H, Sander D. Chronic kidney disease and cognitive impairment: A systematic review and meta-analysis. Am J Nephrol. 2012;35(5):474-482. doi:10.1159/000338135
14. Amatneeks TM, Hamdan AC. Montreal Cognitive Assessment for cognitive assessment in chronic kidney disease: a systematic review. J Bras Nefrol. 2019; 41(1):112-123. doi:10.1590/2175-8239-JBN-2018-0086
15. Tiffin-Richards FE, Costa AS, Holschbach B, *et al*. The Montreal Cognitive Assessment (MoCA) - A sensitive screening instrument for detecting cognitive impairment in chronic hemodialysis patients. PLoS One. 2014; 9(10):e106700. doi:10.1371/journal. pone.0106700
16. Gluhm S, Goldstein J, Loc K, Colt A, Liew C Van, Corey-Bloom J. Cognitive performance on the mini-mental state examination and the montreal cognitive assessment across the healthy adult lifespan. Cogn Behav Neurol. 2013;26(1):1-5. doi:10.1097/WNN.0b013e31828b7d26
17. Mitsides N, Alsehli FMS, Mc Hough D, *et al*. Salt and Water Retention Is Associated with Microinflammation and Endothelial Injury in Chronic Kidney Disease. Nephron. 2019;143(4):234-242. doi:10.1159/000502011
18. Marottoli FM, Katsumata Y, Koster KP, Thomas R, Fardo DW, Tai LM. Peripheral inflammation, apolipoprotein E4, and amyloid-â interact to induce cognitive and cerebrovascular dysfunction. ASN Neuro. 2017;9(4):1759091417719201. doi:10.1177/1759091417719201
19. Gorelick PB, Scuteri A, Black SE, *et al.* Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the american heart association/american stroke association. Stroke. 2011;42(9):2672-2713. doi:10.1161/STR.0b013e3182299496
20. Zheng K, Wang H, Hou B, *et al.* Malnutrition-inflammation is a risk factor for cerebral small vessel diseases and cognitive decline in peritoneal dialysis patients: a cross-sectional observational study. BMC Nephrol. 2017;18(1):366-371. doi:10.1186/s12882-017-0777-1
21. Tamura MK, Muntner P, Wadley V, *et al.* Albuminuria, kidney function, and the incidence of cognitive impairment among adults in the United States. Am J Kidney Dis. 2011;58(5):756-763. doi:10.1053/j.ajkd. 2011.05.027
22. Helmer C, Stengel B, Metzger M, *et al.* Chronic kidney disease, cognitive decline, and incident dementia: The 3C Study. Neurology. 2011;77(23):2043-2051. doi:10.1212/WNL.0b013e31823b4765

23. Etgen T, Sander D, Bickel H, Förstl H. Mild cognitive impairment and dementia: the importance of modifiable risk factors. Dtsch Arzteblatt Int. 2011;108(44):743-750. doi:10.3238/arztebl.2011.0743
24. Kurella Tamura M, Vittinghoff E, Yang J, *et al.* Anemia and risk for cognitive decline in chronic kidney disease. BMC Nephrol. 2016; 17(1):13. doi:10.1186/s12882-016-0226-6
25. Singh NP, Sahni V, Wadhwa A, *et al.* Effect of improvement in anemia on electro neurophysiological markers (P300) of cognitive dysfunction in chronic kidney disease. Hemodial Int. 2006;10(3):267-273. doi:10.1111/j.1542-4758.2006.00107.x