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Association between uric acid and cognitive function in maintenance hemodialysis patient

Avisek Maity[1], Ajay Kumar Sowthiri[2]

[1]Associate Professor, Department of Nephrology, Nil Ratan Sircar Medical College and Hospital, Kolkata, West Bengal, [2]Research Associate, Renal Science Dialysis and Transplantation Technology Apollo Dialysis Clinics, Ramanathapuram, Tamil Nadu, India

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ABSTRACT

Background: Chronic kidney disease (CKD) is an independent risk factor for cognitive dysfunction. Hyperuricemia is prevalent in CKD patients and has been associated with cognitive dysfunction. Hyperuricemia has been associated with an increased risk for cerebral microvascular disease. **Aims and Objectives:** The study aimed to evaluate the association between uric acid level and cognitive function in maintenance hemodialysis patients. **Materials and Methods:** The study was conducted on 90 maintenance hemodialysis patients. Serum uric acid (sUA) level was measured in patients on maintenance hemodialysis and cognitive performance was assessed by the Standardized Mini-Mental State Examination score. **Results:** There was a significant association between sUA level and cognitive function in hemodialysis patients. Patient with higher sUA levels was found to have poor cognitive function ($P<0.05$). There was a significant negative correlation between sUA and cognitive function which revealed an increase in sUA will decrease the cognitive function ($P<0.05$). In our study, there was a significant association between sUA and cognitive function in hemodialysis patients. Patients with hyperuricemia had poor cognitive function. **Conclusion:** In our study, there was a significant association between sUA and cognitive function in hemodialysis patients. Patients with hyperuricemia had poor cognitive function.

Key words: Uric acid; Cognitive; Hyperuricemia; Chronic kidney disease

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INTRODUCTION

Uric acid is a metabolic breakdown of purine and a heterocyclic compound composed of carbon, nitrogen, oxygen, and hydrogen with the formula $C_5H_4N_4O_3$. It exerts beneficial functions due to its antioxidant properties, which may be particularly relevant in the context of neurodegenerative disease. Cognition refers to thinking skills, intellectual skills to perceive, acquire, understand and respond to information, the ability to pay attention, remember, process information, solve problems, organize and reorganize information, and communicate and act on the information.[1-3] All these abilities work in a close, interdependent fashion to allow you to function in your environment.[4,5]

Cognitive impairment is a deficit in one or more key brain functions, such as memory, learning, concentration, and decision-making. Chronic kidney disease (CKD) is an independent risk factor for cognitive dysfunction.[1,6] When compared to the general population, those with CKD, which is defined as having a glomerular filtration rate of <60 mL/min/1.73 m^2 or having a kidney damage marker, such as albuminuria, are significantly more likely to experience cognitive impairment. Depending on the CKD stage and the technique used to detect cognitive impairment, the incidence of cognitive impairment in people with CKD ranges from an astounding 10–40%.[1]

Hyperuricemia is prevalent in patients with CKD which has been associated with cognitive dysfunction. Cognitive decline in patients with kidney disease may be caused by various factors such as clinical and subclinical cerebrovascular disease.[7,8] Hyperuricemia is characterized by the presence of serum uric acid (sUA) levels above

Address for Correspondence:
Dr. Avisek Maity, Associate Professor, Department of Nephrology, Nil Ratan Sircar Medical College and Hospital, Kolkata - 700 014, West Bengal, India. **Mobile:** +91-9163653344. **E-mail:** avisek.maity@yahoo.com

6.8–7 mg/dL. Hyperuricemia has also been associated with vascular cognitive impairment in patients with maintenance hemodialysis.[9,10]

In the current study, we have monitored patients on the maintenance of hemodialysis. The sUA levels were estimated and cognitive performance was assessed using Standardized Mini-Mental State Examination (SMMSE) score. The present study supports the hypothesis that patients with hyperuricemia have poor cognitive function.

Aims and objectives

This study was designed to evaluate the relationship between hyperuricemia and cognitive impairment in patients undergoing maintenance hemodialysis.

MATERIALS AND METHODS

The study was conducted at the Dialysis Unit, Department of Nephrology, Mercy Hospital, Kolkata. The sample size of the study is 90 patients with maintenance hemodialysis (α error 5% with the power of 80%). The patients were followed up from May 2017 to July 2018.

Inclusion criteria

CKD end-stage kidney disease patients on maintenance hemodialysis with an age of more than 18 years were included in the study.

Exclusion criteria

The patients on peritoneal dialysis with acute kidney injury, psychiatric disorders, and acute cerebral vascular disease were excluded from the study.

Statistical analysis

Mean, standard deviation, frequency distribution, and percentages were used in interpreting the demographic data of the subjects. Statistical analysis was performed using both non-parametric and parametric tests. The Chi-square (χ^2) test with an alpha error of 5% was employed for categorical data, whereas parametric tests such as the Z-test were utilized for continuous variables. A $P<0.05$ was considered statistically significant. In addition, odds ratios were calculated to assess the strength of association between risk factors and coronary artery calcification. Higher odds ratios indicated a greater association between the risk factor and the outcome.

RESULTS

Demographic data of the subjects specifically age, sex, and diagnosis were collected and collated from their respective medical records. sUA level was measured in patients with CKD stage 5 on maintenance hemodialysis and cognitive performance by SMMSE score was recorded and the relationship between uric acid and cognitive impairment was studied. The SMMSE measures various domains of cognitive function including orientation to time and place; registration; concentration; short-term recall; naming familiar items; repeating a common expression; and the ability to read and follow written instructions, write a sentence, construct a diagram, and follow a three-step verbal command.

Table 1 shows the stages of cognitive impairment that relate to SMMSE scores. A total score of 30 indicates no impairment. Scores between 26 and 30 are considered normal in the general population. Patients who score between 25 and 20 have mild cognitive impairment (MCI) and will be experiencing problems with the instrumental activities of daily living, such as shopping, finances, medication use, and meal preparation, but can usually live on their own with support. Those who score between 20 and 10 have a moderate cognitive impairment, usually cannot live independently, and are starting to have problems with basic activities, such as grooming, dressing, and using the toilet. Scores between 9 and 0 denote severe cognitive impairment. Pre-dialysis blood samples of uric acid were collected and assessed. Table 2 shows that with elevated levels of serum uric, there is an increase in the incidence of cognitive impairment.

There is a significant association between sUA level and cognitive function in hemodialysis patients (Table 3). Patients with higher sUA levels were found to have poor cognitive function ($P<0.05$).

There is a significant negative correlation between sUA and cognitive function (Table 4). This shows that an increase in sUA will decrease cognitive function ($P<0.05$).

DISCUSSION

The etiology of cognitive impairment in CKD is intricate and includes endothelial failure, arterial calcification and other structural alterations in the arteries, poor autoregulation as well as other humoral elements unique to renal disease.[5] Recently, the field of nephrology has garnered a scientific interest in studying MCI. According to studies, CKD is an independent risk factor for cognitive

Table 1: Standardized mini-mental state examination

Score	Description	Stage
30–26	Could be normal	Could be normal
25–20	Mild	Early
19–10	Moderate	Middle
9–0	Severe	Late

Table 2: Serum uric acid cognitive function cross-tabulation

Variables/Parameters	Cognitive function			Total
	Normal	Mild cognitive dysfunction	Moderate cognitive dysfunction	
Serum uric acid				
<9 mg/dl				
Count	52	26	6	84
% within serum uric acid	61.9	31.0	7.1	100.0
>9 mg/dl				
Count	2	1	3	6
% within serum uric acid	33.3	16.7	50.0	100.0
Total				
Count	54	27	9	90
% within serum uric acid	60.0	30.0	10.0	100.0

Table 3: Chi-square tests

Variables	Value	Df	Asymp. Sig. (sided)
Pearson Chi-square	11.429[a]	2	0.003
Likelihood ratio	6.968	2	0.031
linear-by-linear association	6.279	1	0.012
N of valid cases	90		

Table 4: Cognitive score versus uric acid

n	Pearson Correlation	Sig (2-tailed)
90	−0.213	0.04

deterioration. MCI initiates early on in the course of CKD and parallels kidney function decline in renal function.[11,12] Controlling cardiovascular risk factors in accordance with current standards of care is a rational way to avoid this.[8] While cognitive impairment is clearly important, its exact clinical consequences in the context of CKD as well as its prevalence and measurement have to be determined. Moreover, there is a dearth of information on therapies that might reduce cognitive impairment in CKD patients. However, the link between the kidney and the brain is reciprocal, with patients experiencing a faster loss in renal function following a brain infarction. There is uncertainty on the pattern of cognitive impairment in CKD.

Hyperuricemia has been recognized as an independent cardiovascular risk factor in epidemiological studies. In this article, we critically revise the evidence on the relationship between sUA levels and cognitive function in patients. Remarkably, research conducted previously included 676 hemodialysis patients in adulthood from 20 Italian centers assessed the frequency and trends of cognitive impairment in five areas: Language, perceptual-motor, executive function, complex attention, learning and memory, and learning. Ten neuropsychological tests have been used in this study to evaluate cognitive function.[6,12-15] According to the study, 71.1% of hemodialysis patients are thought to be impaired in at least one area, and patients frequently suffer several impairments at once, with 45.2% of patients being affected on two or more domains. Cognitive impairment is also quite widespread in this patient population.[8,9]

In our study, 90 subjects were assessed. The study shows that patients with elevated uric acid levels were found to have moderate cognitive function of 50% and mild cognitive function of 16.7% in the maintenance hemodialysis population. There was a significant association between sUA levels and cognitive functions in hemodialysis patients. Patients with higher sUA levels were found to have poor cognitive function ($P<0.05$). Odagiri et al.,[7] found that the prevalence of cognitive impairment based on the MMSE was 18.8% in HD and we observed that 30% of our study population had a mild cognitive dysfunction. Dr. Archanaa[16] found that as sUA level goes high cognitive function test scores reduce. Afsar et al.[1] also reported that serum uric levels are independently and inversely associated with cognitive dysfunction in CKD patients.

Limitations of the study

Limitations of our study warrant consideration. The sample size may limit generalizability, and larger multicenter studies are warranted to validate our findings across diverse patient populations.

CONCLUSION

In our study, there was a significant association between sUA and cognitive function in hemodialysis patients. Patients with hyperuricemia had poor cognitive function.

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DATA AVAILABILITY STATEMENT

The datasets generated during the study are available from the corresponding author on reasonable request.

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Authors' Contributions:
AM, AKS- Conceptualization, design of the study, clinical protocol, the definition of intellectual content, literature survey, prepared the first draft of the manuscript and subsequent edition/revision, implementation of the study protocol, data collection, statistical analysis, interpretation, created tables and figures.

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Orcid ID:
Avisek Maity- https://orcid.org/0000-0003-1300-2243
Ajay Kumar Sowthiri- https://orcid.org/0009-0001-1600-2882

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Remark: Reprint request should be directed to the corresponding author Dr. Avisek Maity (avisek.maity@yahoo.com)