

A Study of Serum Uric Acid at Presentation as an Indicator of Outcome among Acute Ischemic Cerebrovascular Accident (CVA) Patients

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Abstract:

Background: Stroke is the second leading cause of global mortality and a major contributor to long-term disability. Ischemic stroke accounts for approximately 87% of all strokes. Hyperuricemia, defined as elevated serum uric acid (SUA) levels, has shown conflicting associations with ischemic stroke outcomes in prior research. This study aimed to assess the association between SUA levels at presentation and clinical outcomes among patients with acute ischemic stroke (AIS).

Methodology: This observational cross-sectional study included 60 adult patients diagnosed with Acute Ischemic Cerebrovascular Accident via CT/MRI at Government General Hospital, Kadapa, from April 2023 to March 2024. Patients with hemorrhagic stroke, infection, liver/kidney disease, gout, or relevant comorbidities were excluded. Clinical data, including SUA, demographic variables, risk factors, duration of hospital stay, mortality, ECG changes, and re-admission, were recorded. Statistical analysis was performed using Epi Info v7.2.5.

Results: Hyperuricemia (>6.8 mg/dL) was observed in 20% of patients. Mean age was 57.25 years, and mean SUA was 6.15 mg/dL. Elevated Serum Uric Acid was significantly associated with longer hospital stays ($p < 0.05$) and hypertension ($p = 0.013$), but not with age, gender, smoking, or re-admission rates. Diagnostic accuracy analysis revealed a specificity of 100% and a positive predictive value of 100% for SUA >9 mg/dL in predicting mortality.

Conclusion: Elevated SUA is prevalent among AIS patients and is significantly associated with prolonged hospitalization and mortality. Although not linked with common vascular risk factors, hyperuricemia may serve as a potential prognostic biomarker. Regular monitoring of Serum Uric Acid levels in Acute Ischemic Cerebrovascular Accident patients is recommended.

Keywords: Acute Ischemic Stroke, Serum Uric Acid, Hyperuricemia, Stroke Outcomes.

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Introduction

Stroke stands as the world's second most prevalent cause of death, responsible for 11% of global mortalities and a significant contributor to disability worldwide. [1] In the United States, it ranks as the fifth leading cause of death, accounting for 17% of all fatalities. [2] As per the estimates from the global burden of disease, in 2016 alone, there were 9.5 million new cases of ischemic stroke, resulting in 2.7 million deaths.

Around half of the healthy life years lost due to ischemic stroke complications occur in individuals under 70 years of age. [3] With 77% of strokes occurring as initial events and 87% being ischemic, stroke poses a substantial public health challenge. [4] Ischemic stroke, characterized by the abrupt

interruption of blood flow to the brain, can arise from various factors such as vessel blockage, atherosclerosis affecting cerebral circulation and embolism. These factors trigger cerebral inflammation, ultimately leading to cell death. So, prioritizing the prevention of ischemic stroke is imperative in mitigating its burden. [5]

Hyperuricemia is elevation of uric acid in the plasma. It has no accepted single cut-off value, but values above 6.8mg/dL are usually considered increased in adults. [6] Hyperuricemia has positive association with stroke morbidity and mortality as per certain previous studies. [7,8] As per the Rotterdam Cohort study done on 4,385 participants, uric acid was considered a risk factor for stroke. [9]

One study by Chamorro et al. showed good clinical 2 outcomes among patients with acute ischemic stroke (AIS) and increasing uric acid levels. [10] Certain studies indicated worsening outcomes among AIS patients with elevated serum uric acid (SUA) levels. [11,12] This implies the data was inconsistent and conflicting and needs more research. Hence the current study was undertaken. The current study was done at GMC, GGH, Kadapa, which is a tertiary care center with 1200 beds. All facilities are available in the department to conduct the study.

Aim: To study the association between serum uric acid at presentation and the clinical outcome among acute ischemic cerebrovascular accident patients.

Objectives: To study serum uric acid as a predictor of cerebrovascular accident and to study the risk factors of cerebrovascular accident, to follow up the patient for a 7day period.

Methodology: It was an Observational cross sectional study done in 60 patients who were prospectively enrolled from the ICU and General Medicine Department at Government General Hospital, Kadapa between a periods from April 2023 to March 2024.

Patients aged more than 18 years with acute ischemic stroke - confirmed by CT/MRI scan of brain were included. Patients with subarachnoid hemorrhage, extra dural hemorrhage, sub dural hemorrhage, Intra cerebral hemorrhage, with previous history of Transient ischemic attack, malignancies, dyslipidemia and fever or any focus of infection, Liver and kidney disease, with alcoholism and

with gout history or using medications for gout were excluded from the study.

A questionnaire prepared noted the detailed collection of Age, Gender, BMI, Smoking, Uric acid levels, Presence of diabetes and hypertension, Artery involved, Mortality rate, Duration of hospital stay, ECG findings, Re admission need. CT was done to confirm the diagnosis and ECG was also done. The other investigations done include complete blood count, Liver Function Tests, Renal Function Tests with electrolytes, urine routine and microscopy.

Ethical clearance: The permission from the Institutional Ethical Committee attached to GGH, Kadapa was taken before conducting the study. Every patient and their relatives were explained the whole process and advantages of availing their data for the study.

Statistical analysis: The data were entered in Excel 2023 and data analysis were done using statistical software called Epi Info version 7.2.5. 1st prevalence of high uric acid levels were assessed. Then all parameters were compared between patients with high and normal uric acid levels. Numerical parameters were compared using students T test and categorical parameters were compared using chi square test. P value <0.05 was considered as statistically significant. Diagnostic accuracy of uric acid levels at a cut of value above 9 in detecting mortality was assessed.

Results: Mean age was 57.25 years in the current study. Mean BMI was 25.38 kg.m² in the current study. Mean duration of hospital stay was 7.5 days in the current study. Mean uric acid was 6.15 mg.dl in the current study.

Table 1: Levels of Uric Acid in the Study Population

Uric acid levels	Frequency	Percent
More	12	20.00%
Normal	48	80.00%
Total	60	100.00%

Table 2: Re admissions in the Study Population

Re admission	Frequency	Percent
No	54	90.00%
Yes	6	10.00%
Total	60	100.00%

Table 3: ECG Changes in the Study Population

ECG Changes	More	Normal	Total
No	3	32	35
Yes	9	16	25
Total	12	48	60

Table 4: Duration of hospital stay in the Study Population

Duration of hospital stay	Uric acid levels		Total
	More	Normal	
5	1	12	13

6	0	23	23
7	0	12	12
10	0	1	1
12	1	0	1
13	2	0	2
14	5	0	5
15	2	0	2
17	1	0	1
Total	12	48	60
Chi-Square 54.2308		df 8	

Table 5: Artery involved in the Study Population

Artery involved	Uric acid levels		
	More	Normal	Total
ACA	6	17	23
Lacunar	1	5	6
MCA	4	16	20
Others	1	10	11
Total	12	48	60

Table 6: Statistics in the Study Population

Statistic	Value	95% CI
Sensitivity	75.00%	19.41% to 99.37%
Specificity	100.00%	93.62% to 100.00%
Disease prevalence (*)	6.67%	1.85% to 16.20%
Positive Predictive Value (*)	100.00%	29.24% to 100.00%
Negative Predictive Value (*)	98.25%	91.12% to 99.67%
Accuracy (*)	98.33%	91.06% to 99.96%

Table 7: Age & Uric Acid in the Study Population

Means			
Group	Obs	Mean	Std Dev
More	12.0000	5.9833	9.4046
Normal	48.0000	5.617	9.2021
Method	DF	t Value	Pr > t
Pooled	58	0.77	0.4454

Table 8: Re admission rate & Uric Acid in the Study Population

Uric Acid	Re admission		
	No	Yes	Total
FN	1	0	1
TN	50	6	56
TP	3	0	3
Total	54	6	60
Chi-Square 0.4762		df 2	Probability 0.7881

Table 9: Gender & Uric Acid in the Study Population

Gender	Uric Acid levels		
	More	Normal	Total
Female	4	19	23
Male	8	29	37
Total	12	48	60
Chi-square 0.1586		2-tailed p 0.6904	

Table 10: Hypertension & Uric Acid in the Study Population

Hypertension	Uric Acid levels		
	More	Normal	Total
No	3	31	34

Yes	9	17	26
Total	12	48	60
Chi-square 6.1256		2-tailed p 0.01332	

Table 11: Smoking & Uric Acid in the Study Population

Smoking	Uric Acid levels		
	More	Normal	Total
No	9	36	45
Yes	3	12	15
Total	12	48	60
Chi-square 0.0000		2-tailed p 1.00000	

Discussion:

Maousd et al. [13] did a cross-sectional study on patients admitted to Firoozgar Hospital from 2010 to 2011 with acute ischemic stroke. The study was done on clinical records and SUA levels of these patients. The study included 55 patients with acute stroke, comprising 25 females and 30 males with a mean age of 67 years. In the current study also, males were more compared to females, implying males are more prone to stroke. Mean age in the present study was 57 years.

Mean uric acid was 6.15 mg/dl in the current study. Masoud et al reported that mean SUA as 5.94 mg/dl, and around half of the patients were hyperuricemic, while in the present study 20% of patients had hyperuricemia. One large 10 years follow up study by Yenyan et al also showed the prevalence of hyper-uricemia as 20.1% [14] this finding was similar to the present study. Another study done in Bangkok population by Uaratanawong S showed that prevalence of hyperuricemia as 24%. [15] One study done in developing country by Conen D showed the prevalence of hyperuricemia as 35.2% among men and 8.7% among women. [16] As per all the above mentioned studies, the prevalence of hyperuricemia is considered to be higher among patients with acute stroke.

ARIC study showed that hyperuricemia is no longer is associated with ischemic stroke (IS) after adjusting for confounder like diuretic-treated hypertension. [17] One case-cohort study done in 2020 [18] showed the relationship between hyperuricemia and IS in a community-based population that enrolled in national Reasons for Geographic and Racial Differences in Stroke study [19] apart from quantifying blood pressure role and other confounders. One meta-analysis done in 2017 [20] showed significant dose-response relationship between more uric acid and stroke risk, reporting rise in stroke risk by around 10% for every 1 mg/dL increase in uric acid levels.

One study demonstrated no relation between SUA and stroke occurrence. [21] Bansal et al. investigated 50 patients with ischemic thrombotic cerebrovascular disease, finding that thirty percent exhibit-

ed hyperuricemia. Their conclusion suggested that elevated serum uric acid levels might play a role in the development of ischemic thrombotic cerebrovascular disease, particularly among patients under 40 years of age. [22]

Cazzato et al. found no difference in SUA between patients with stroke and controls and their results showed that hyperuricemia was not a high risk factor in stroke. [23] Chen et al included 226 hemodialysis patients and followed them for around 18 months, and 43 patients experienced AIS, and SUA was found to be inversely related to AIS morbidity among hemodialysis patients. [24]

Jaskamal et al [25] did a study on association between elevated SUA and an increased risk of cardiovascular disease and AIS, among other medical conditions. AIS, the second most common cause of mortality globally, occurs due to reduced blood flow to the brain caused by thrombosis, embolism, or systemic hypoperfusion.

In the study of Masoud et al- there is a significant negative correlation between age and SUA. There is significant correlation between gender and SUA, SUA being more among males compared to females. In the current study, no association was found between age, gender and SUA. One study found a weak significant positive link between age of patients and SUA levels. [26] Some of the previous studies showed that there were significant differences in SUA levels between men and women. Another study by Conen et al, showed high prevalence of hyperuricemia is higher among men compared to women and higher alcohol consumption among men could be cause of this difference. [27] In the current study, no association between SUA and gender was found, probably due to less incidence of alcoholism.

In the study of Masoud et al. Hyperuricemia was more correlated with increased levels of TGs and and LDL cholesterol. There was no significant link between SUA and presence of DM, HTN, smoking, similar to the current study. In the current study, patients with dyslipidemia were excluded. Hence lipid profile was not assessed. Some previous studies have noted a significant association between

insulin resistance, systolic and diastolic blood pressure, and serum uric acid levels. [28] A study by Bonora et al. indicated no significant association between smoking and uric acid levels. They investigated 957 young men and found a significant positive correlation between serum uric acid levels & levels of serum triglycerides, total cholesterol, and LDL cholesterol. Hence, significant association with cardiovascular risk, mortality and morbidity rate. Previous studies, including those involving patients with gout, have reported associations between uric acid and triglyceride levels. [29]

Studies involving healthy individuals in developing countries have shown a close association between serum uric acid levels and serum triglyceride levels. Chammaro et al. reported an association between serum uric acid levels and serum triglyceride levels. The underlying mechanism of this strong association between serum uric acid and triglyceride levels remains poorly understood. While some studies have suggested genetic factors contributing to gout and hypertriglyceridemia, most researchers believe that hyperuricemia and hypertriglyceridemia may reflect aspects of a patient's lifestyle as part of metabolic syndrome. [30]

Conclusion: The present study showed that prevalence of hyperuricemia among patients with acute stroke was high. There was significant association between serum uric acid levels and duration of hospital stay, re admission need and mortality rate.

There is no significant association between uric acid level and presence of diabetes mellitus, hypertension and smoking. Due to high prevalence of hyperuricemia in patients with ischemic stroke, it can be considered as a risk factor for ischemic stroke. We recommend to check uric acid levels serially to monitor patient's health condition.

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