

Association between Serum Uric Acid Levels and Stroke Severity in Acute Ischemic Stroke: A Cross-Sectional Study

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Abstract

Introduction: Ischemic stroke represents a significant global health burden. Studies have suggested a potential link between serum uric acid levels and stroke risk through mechanisms such as oxidative stress and inflammation. This study aimed to evaluate the association between serum uric acid levels and severity of acute ischemic stroke.

Methods: A hospital based cross-sectional study was conducted in a tertiary care hospital from November 2020 to October 2021, after ethical approval (Reference no:1317/2078/79). The study included adults with acute ischemic stroke confirmed by neuroimaging within 7 days of presentation. The study excluded patients with hemorrhagic stroke, malignancies, those receiving chemotherapy, recent surgery or trauma and medications affecting serum uric acid level. Purposive sampling technique was used for data collection. Serum uric acid levels and National Institutes of Health Stroke Scale scores were calculated to assess stroke severity. Statistical Package for Social Sciences version 25.0 was used for analysis. Descriptive statistics were used to present the data. The association between serum uric acid levels and stroke severity was assessed using Pearson's correlation coefficient and p value <0.05 was considered significant.

Results: Out of 95 patients, 53 (55.79%) were males and 42 (44.21%) females. The mean serum uric acid was 5.18 ± 1.48 mg/dl. Among them, 82 (86.31%) patients had serum uric acid level <6.8 mg/dl. Pearson correlation coefficient was used to assess the association between serum uric acid level and NIHSS score. There was no statistically significant correlation between the two variables ($r = 0.066$, $p = 0.525$, $n = 95$).

Conclusions: This study found no statistically significant association between serum uric acid levels and ischemic stroke severity.

Keywords: ischemic stroke; national institutes of health stroke scale; serum uric acid; stroke severity.

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Introduction

Acute ischemic stroke (AIS) is defined as the sudden onset of neurological deficits due to insufficient blood flow to the brain, leading to significant morbidity and mortality world-wide.^{1,2} While established risk factors such as hypertension, diabetes, and hyperlipidemia play a critical role in stroke pathogenesis, emerging research has proposed an association between serum uric acid (SUA) levels and stroke risk.³

SUA, end product of purine metabolism, traditionally considered a waste product, is a clinical indicator of various metabolic disorders such as metabolic syndrome, hypertension, gout, cardiovascular disease and its role as an antioxidant has only recently gained recognition.^{4,5} Some studies indicate that SUA may have pro-oxidant or antioxidant properties and may exert neuroprotective effects.⁶ In contrast, some studies showed high prevalence of hyperuricemia in ischemic stroke patients, indicating possible role of uric acid as a risk factor of ischemic stroke.⁷

Although some research supports the notion that high SUA levels may predispose individuals to stroke, others suggest a protective effect.^{8,9} Given this conflicting evidence, this study aimed to evaluate the association between serum uric acid levels and severity of acute ischemic stroke.

Methods

This cross-sectional study was performed in Bir Hospital, National Academy of Medical Sciences (NAMS) for a period of 1 year (November 2020 to October 2021) after IRB approval of the institution (Reference no:1317/2078/79). The study population

were the patients diagnosed with Acute Ischemic Stroke (AIS) admitted in the medicine unit. The sample size was calculated as follows:

$n = (Z^2 \times p \times q) / e^2$ where,

n= Required sample size

Z= Statistics for level of confidence (for 95% level of significance, Z= 1.96)

p= Prevalence of increased SUA in stroke cases (47.3%)¹⁰

e= Precision or maximum tolerable error

$n = 1.96^2 \times 0.473 \times (1 - 0.473) / 0.12^2 = 95.76$

Purposive sampling technique was used. The inclusion criteria were patients of either sex above the age of 18 years with acute ischemic stroke within 7 days of presentation (gait abnormalities, speech abnormalities, facial deviation, paralysis etc) and confirmed by neuroimaging (CT, CT Angiography, MRI). The study excluded patients with hemorrhagic stroke, known malignancies, chemotherapy, recent surgery, trauma, or drugs affecting SUA level. The data were collected using structured proforma and informed written consent was taken from all the patients. The data collection tool comprised socio-demographic variables, co-morbidities like hypertension, diabetes mellitus etc. as well as serum uric acid level and NIHSS score at the time of admission. For all the patients modified National Institutes of Health stroke scale were calculated to access the severity of stroke and severity categorization; there are altogether 11 variables and total score of 42 and according to the score it is categorized as minor, moderate and severe stroke.¹¹

Table 1: National Institute of Health Stroke Scale (NIHSS).

SN	Definition	
1.	1a. Level of consciousness	0= Alert, keenly responsive 1= Not alert, but arousable by minor stimulation 2= Not alert, arousable by repeated stimulation 4= Unresponsive or responds only with reflex
	1b. LOC questions (Ask patients the month and her/his name)	0= Answers two questions correctly 1= Answers one question correctly 2= Answers neither question correctly
	1c. LOC commands (Ask patient to open/close eyes and form and release fist)	0= Performs both tasks correctly 1= Performs one task correctly 2= Performs neither task correctly
2	Best gaze (only horizontal eye movements)	0= Normal 1= Partial gaze palsy 2= Forced deviation
3	Visual field testing	0= No visual loss 1= Partial hemianopia 2= Complete hemianopia 3= Bilateral hemianopia

4	Facial paresis (Ask patient to show teeth, raise eyebrows and close eyes tightly)	0= Normal symmetric movement 1= Minor Paralysis 2= Partial paralysis 3= Complete paralysis of one or both sides
5	5a. Motor Function Arm (Right) 5b. Motor Function Arm (Left)	0= No drift 1= Drift 2= Some efforts against gravity 3= No efforts against gravity; limbs fall 4= No movement
6	6a. Motor Function Leg (Right) 6b. Motor Function Leg (Left)	0= No drift 1= Drift 2= Some efforts against gravity 3= No efforts against gravity; limbs fall 4= No movement
7	Limb Ataxia	0= Absent 1= Present in one limb 2= Present in both limbs
8	Sensory (Use pinprick to test arms, legs, trunk and face- compare side to side)	0= Normal, no sensory loss 1= Mild to moderate sensory loss 2= Severe to total sensory loss
9	Best Language (Ask patient to describe Picture, name items, read sentences)	0= No aphasia, normal 1= Mild to moderate aphasia 2= Severe aphasia 3= Mute, global aphasia
10	Dysarthria (Ask patients to read several words)	0= Normal 1= Mild to moderate dysarthria 2= Severe dysarthria
11	Extinction and inattention (Formerly neglect) (Use Visual or sensory double stimulation)	0= No abnormality 1= Visual, tactile, auditory, spatial or personal inattention 2= Profound hemi-inattention or extinction
Total score= 0-42		
National Institute of Health (NIH) Stroke Score		Stroke severity
0		No stroke symptoms
1-4		Minor stroke
5-15		Moderate stroke
16-20		Moderate to severe stroke
21-42		Severe stroke

Though the purposive sampling technique made sure that clinically relevant cases were included, selection bias could be introduced because the sample might not accurately reflect the larger stroke population. This may limit the findings' generalizability and compromise their external validity.

Collected data were entered and analyzed using Statistical Package for Social Sciences version 25.0. Analyzed data were presented in the form of tables as mean $\pm$ standard deviation for continuous variables and as numbers and percentages for categorical variables. The relationship between uric acid levels and stroke severity, as measured by the National Institutes of Health Stroke Scale (NIHSS), were assessed using Pearson's correlation coefficient. The p-value of less than 0.05 was considered significant.

Results

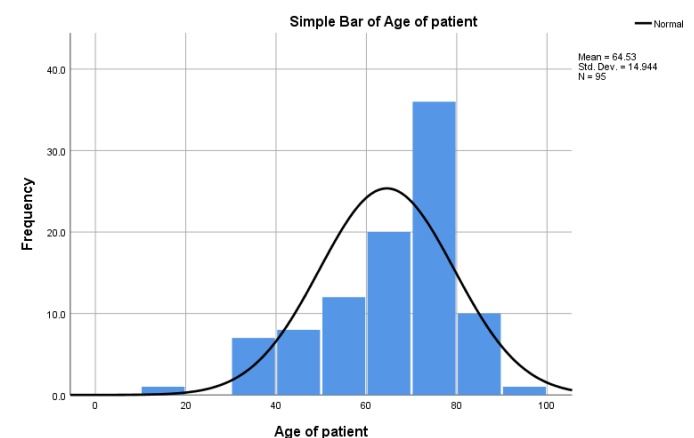


Figure 1: Age Distribution of the Patients with Ischemic Stroke

In this study, the ages range broadly, with most patients clustered between 50 and 80 years old. The mean age of patients with ischemic stroke was found 64.53 years; suggesting the majority of patients in this study are older adults.

Table 2: Characteristics of Patients with Ischemic Stroke (n=95).

Characteristics of Patients		n (%)
Sex	Male	53 (55.79)
	Female	42 (44.21)
Smoking	No	34 (35.79)
	Yes	61 (64.21)
Alcohol intake	No	61 (64.21)
	Yes	34 (35.79)
Diabetes	No	67 (70.52)
	Yes	28 (29.48)
Hypertension	No	43 (45.26)
	Yes	52 (54.74)
Past history of CVD	No	90 (94.74)
	Yes	5 (5.26)
Past history of CAD	No	88 (92.63)
	Yes	7 (7.37)

Out of 95 patients, 53 (55.79%) were males and 42 (44.21%) females. The risk factors of ischemic stroke, smoking 61 (64.21%) ranked the highest followed hypertension 52 (54.74%).

Table 3: Serum uric acid level in patients of Ischemic stroke (n=95).

Uric acid level	Sex	n(%)
<6.8	Male	46(48.42)
	Female	36(37.89)
≥6.8	Male	7(7.37)
	Female	6(6.32)

The mean serum uric acid was 5.18±1.48 mg/dL. Among the total patients, 82 (86.31%) patients had serum uric acid level <6.8 mg/dL. Similarly, 13 (3.69%) patients had serum uric acid level ≥6.8 mg/dL.

Table 4: Serum Uric Acid Level and Severity of Stroke (n=95).

NIHSS grade	Serum Uric Acid Level	
	<6.8	≥6.8
	n(%)	n(%)
mild	1(33.30)	2(66.70)
moderate	77(90.60)	8(9.40)
moderate to severe	-	2(100)
severe	4(80)	1(20)

Among patients with serum uric acid value < 6.8 mg/dL, 1 (33.30%) patient had mild stroke, 77 (90.60%) patients had moderate stroke followed by 4 (80%) severe stroke (Table 4).

Pearson correlation coefficient was used to assess the association between serum uric acid level and NIHSS score. There was no statistically significant correlation between the two variables ($r = 0.066$, $p = 0.525$, $n = 95$).

Discussion

The findings of this study provide insightful perspectives on the demographic and clinical characteristics of patients who presented with ischemic stroke, particularly focusing on age, gender distribution, risk factors and serum uric acid levels.

In this study, the mean age of patients with ischemic stroke was 64.53 years which is similar to the study done in China by Zhang et al. and Yang et al. that showed mean age, 64.6 years, 65.6 years respectively.^{12,13} However, this value is lesser than that resulted in the study conducted by Arevalo Lorigo et al. and Chamorro et al., which showed mean age as 72.4 years and 72.7 years respectively. Such variation may be due to geographical and environmental variation.^{14,15} The predominance of elderly patients, specifically those aged 71-80 years aligns with existing literature that highlights age as a significant risk factor for stroke.¹⁶ Aging is the most robust non-modifiable risk factor for incident stroke, which doubles every 10 years after age 55 years.¹⁷

The study found that males (53) were more affected with ischemic stroke than females (42). Similar male preponderance (52-59%) was seen in other studies.^{3,18,19} In contrast, females (54%) were seen more affected than males (45%) in another study.²⁰ Furthermore the higher incidence of ischemic stroke in males compared to females is corroborated by previous studies, which have inconsistently shown that men are at a greater risk for stroke at younger ages, although this risk converges as both genders age.^{21,22} Likewise, in the study there were found the patients with ischemic stroke had smoking behavior

(64%), hypertension (55%), excessive alcohol consumption pattern (36%), diabetes (30%), past Coronary Artery Disease (CAD) history (7.4%), and past Cerebrovascular Disease (CVD) (5.3%). Similar results were found in other studies done in Kohalpur Teaching Hospital and Nepal Medical College Teaching Hospital.^{23,24} The predominance of moderate-grade ischemic stroke (85 patients) in our cohort reflects similar trends observed in clinical settings where the severity of stroke correlates with modifiable risks factors such as hypertension, smoking, diabetes.²⁵ Similarly, the high prevalence of hypertension (54%) in our cohort underscores its well-documented role in the pathophysiology of ischemic strokes.²⁶

The study found a mean serum uric acid of 5.18 ± 1.48 mg/dl, similar to previous studies done in 2017 and 2013 with 4.98 ± 1.54 mg/dl and 5.30 ± 1.64 mg/dl respectively but lower with the study (12.36 ± 3.86 mg/dl) done in 2006.^{3,27,28}

This study revealed a statistically non significant association between serum uric acid level and NIHSS ($p = 0.525$) which is similar to one of the previous studies (0.69). However, the study result is contrary to some previous studies that suggested a link between uric acid levels and stroke severity.²⁹ Likewise, another study found that appropriate uric acid levels in ischemic stroke patients improve outcomes, but can be harmful when too high or low.³⁰

This finding indicates that in our samples, serum uric acid may not have a direct impact on stroke severity, which is a noteworthy conclusion. This discrepancy may stem from differences in study populations, sample sizes or methodological variations across research.

In summary, the study sheds light on the demographics and prevalent risk factors associated with ischemic stroke in our cohort, highlighting the importance of tailored intervention strategies for at risk populations. Further research, ideally involving larger samples and diverse populations is warranted to deepen our understanding of the relationship between nature of stroke risk factors.

As this was a single-center study, the findings should be interpreted with caution and may not be generalizable to the broader population. The sample size was calculated using a prevalence formula rather than a formula for assessing the association between serum uric acid levels and stroke severity. Therefore, the study may have been underpowered or overpowered for detecting the observed association, and the findings should be interpreted with caution.

Conclusions

This study found no statistically significant association between serum uric acid levels and ischemic stroke severity as assessed by the National Institutes of Health Stroke Scale (NIHSS) in this cohort of 95 ischemic stroke patients. The predominance of moderate-severity strokes and the low proportion of patients with elevated serum uric acid levels limits the analytic capacity. Though serum uric acid has been proposed as a potential biomarker of oxidative stress in ischemic stroke, definitive conclusions regarding the prognostic utility of serum uric acid in ischemic stroke cannot be drawn from this study alone.

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Conflict of Interest:

The author declares no competing interest. Dr. Himani Poudyal is currently serving as Editor in MJAPFN. She was not involved in the editorial review or decision making for this manuscript.

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