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Research Article

Prospective Evaluation of Serum Uric Acid as a Risk Factor for Acute Ischemic Stroke in Adult Patients Compared to Normouricemic Individuals

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ABSTRACT

Background: Acute ischemic stroke (AIS) is a leading cause of morbidity and mortality worldwide. While traditional risk factors like hypertension, diabetes, and dyslipidemia are well-established, the role of serum uric acid (SUA) as a potential independent risk factor remains under investigation. Hyperuricemia may contribute to endothelial dysfunction, oxidative stress, and vascular inflammation, thereby increasing stroke risk.

Aim: To evaluate the association between serum uric acid levels and acute ischemic stroke and assess its correlation with stroke severity in adult patients attending a tertiary care center in Bihar, India.

Methodology: This prospective observational study enrolled 110 AIS patients and 110 age- and sex-matched normouricemic controls during the study period. Clinical evaluation, laboratory investigations including serum uric acid, and neuroimaging (CT) were performed. Stroke severity was assessed using the NIH Stroke Scale (NIHSS). Statistical analysis included t-tests, chi-square tests, correlation analysis, and multivariate logistic regression to determine independent risk factors for AIS.

Results: Mean SUA levels were significantly higher in AIS patients compared to controls (6.9 ± 1.4 mg/dL vs 5.3 ± 1.2 mg/dL, $p < 0.001$). Hyperuricemia was observed in 52.7% of AIS patients *versus* 20% of controls. Elevated SUA correlated positively with NIHSS scores, indicating greater stroke severity. Logistic regression identified hyperuricemia as an independent risk factor for AIS (OR 3.8, 95% CI 2.1–6.8, $p < 0.001$), along with hypertension and smoking.

Conclusion: Elevated serum uric acid is significantly associated with the occurrence and severity of acute ischemic stroke, serving as a modifiable, independent risk factor. Routine SUA assessment may aid early risk stratification and preventive strategies in high-risk populations.

Keywords: Stroke, Ischemic, Hyperuricemia, Risk factors, Biomarkers, Prospective studies.

INTRODUCTION

Stroke is a major global health concern and a leading cause of mortality and long-term disability worldwide. Among all stroke subtypes, acute ischemic stroke (AIS) accounts for nearly 70 to 80% of all cases and imposes a significant burden on healthcare systems, particularly in low- and middle-income countries like India [1]. The rising incidence of stroke in developing regions has been attributed to epidemiological transition, increasing prevalence of metabolic disorders, lifestyle changes, and inadequate preventive strategies [2]. Despite advancements in acute stroke care, prevention through identification and modification of risk factors remains the most effective approach to reducing stroke-related morbidity and mortality.

Traditionally recognized risk factors for ischemic stroke include hypertension, diabetes mellitus, dyslipidemia, smoking, atrial fibrillation, and carotid artery disease [3]. However, recent research has increasingly focused on non-traditional metabolic risk factors, among which serum uric acid (SUA) has emerged as a potential contributor. Uric acid, the final oxidation product of purine metabolism, is known to have a dual biological role. While it acts as a powerful antioxidant in plasma, elevated levels (hyperuricemia) have been implicated in endothelial dysfunction, oxidative stress, inflammation, and platelet aggregation, all of which contribute to atherosclerosis and vascular events [4].

Several epidemiological and prospective cohort studies have demonstrated a significant association between elevated serum uric acid levels and the risk of ischemic stroke. In a large population-based prospective cohort study, an increase in serum uric acid was associated with a 22% higher risk of ischemic stroke after adjusting for conventional cardiovascular risk factors [5]. Similarly, the Atherosclerosis Risk in Communities (ARIC) study demonstrated that elevated uric acid levels independently predicted ischemic stroke incidence, particularly among individuals not using diuretics [6]. Recent meta-analyses have further strengthened this association. A dose–response meta-analysis including 19 prospective studies reported that each 1-mg/dL increase in SUA was associated with a 15% increased risk of ischemic stroke [7]. Another systematic review involving more than 770,000 individuals confirmed that

hyperuricemia significantly increases the risk of stroke incidence and mortality, particularly in females [8].

The pathophysiological mechanisms linking uric acid to ischemic stroke are multifactorial. Hyperuricemia promotes endothelial dysfunction, reduces nitric oxide bioavailability, enhances oxidative stress, and induces inflammation in vascular endothelium. It also contributes to platelet aggregation and vascular smooth muscle proliferation, thereby accelerating atherosclerosis [5,9]. Moreover, uric acid is strongly associated with other metabolic disorders such as hypertension, insulin resistance, obesity, and chronic kidney disease, which themselves are established risk factors for stroke [3,9]. Thus, serum uric acid may serve both as an independent risk factor and as a marker of underlying vascular pathology.

Despite growing evidence supporting the role of hyperuricemia in stroke pathogenesis, the relationship between serum uric acid and acute ischemic stroke remains controversial. Some studies suggest that higher uric acid levels may exert neuroprotective effects due to antioxidant properties, potentially improving post-stroke outcomes [10]. However, most clinical studies and systematic reviews have concluded that elevated SUA is associated with increased incidence and recurrence of ischemic stroke, as well as poor prognosis [7,8]. This conflicting evidence highlights the need for well-designed prospective studies to clarify the role of serum uric acid as a risk factor in acute ischemic stroke.

India bears a disproportionate burden of stroke, with significant regional disparities in incidence, healthcare access, and outcomes. Bihar, one of the most populous and socioeconomically challenged states, has limited access to advanced healthcare facilities, particularly in rural areas. The majority of patients with acute stroke from peripheral regions are referred to tertiary care centers, which serve as major referral hubs for diagnosis and management. These centers provide a unique opportunity to study the clinical profile and risk factor patterns of stroke in a large and diverse population.

The epidemiological profile of stroke in Bihar differs from that reported in developed countries due to differences in lifestyle, socioeconomic status, nutritional patterns, and prevalence of metabolic diseases. There is a high burden of uncontrolled hypertension, diabetes, tobacco use, and malnutrition, all of which contribute to increased stroke risk. However, data regarding non-traditional risk factors such as hyperuricemia in this population are limited. Most available studies on serum uric acid and stroke have been conducted in Western or urban populations, and their findings may not be directly applicable to rural or semi-urban populations in eastern India.

Furthermore, in resource-limited settings like Bihar, identification of simple, cost-effective biochemical markers for early risk stratification is essential. Serum uric acid estimation is an inexpensive, widely available test that can be easily incorporated into routine clinical evaluation. If proven to be a significant risk factor, it can be used for screening, early intervention, and prevention strategies in high-risk individuals.

This prospective study therefore provide valuable insights into: The prevalence of hyperuricemia among acute ischemic stroke patients. Its role as an independent or associated risk factor. Its interaction with conventional vascular risk factors. Its potential utility as a prognostic biomarker in acute stroke. Such evidence help guide regional public health strategies, improve risk assessment models, and support early preventive interventions in this high-risk population.

The aim of the study was to evaluate the role of serum uric acid as a risk factor in patients presenting with acute ischemic stroke in comparison with normouricemic individuals.

MATERIALS AND METHODS

This prospective observational study were conducted at Jannayak Karpoori Thakur Medical College and Hospital in Bihar, India, which functions as a major referral centre for patients presenting with acute neurological emergencies from surrounding rural and semi-urban districts. The institution has emergency department equipped with round-the-clock computed tomography (CT) imaging facilities, enabling prompt diagnosis and management of acute ischemic stroke. Patients attending the Outpatient Department (OPD) and emergency services with features suggestive of stroke are routinely evaluated and admitted for further management and investigation.

The study was carried out over a period of 12 months from January 2025 to Dec 2025, during which all eligible patients presenting to the OPD and emergency department with clinical suspicion of acute ischemic stroke were screened for inclusion in the study.

This was a hospital-based prospective observational cohort study designed to evaluate the role of serum uric acid as a risk factor for acute ischemic stroke. Participants was divided into two groups:

Cases

Patients diagnosed with acute ischemic stroke

Controls (Comparison group)

Age- and sex-matched normouricemic individuals attending OPD for non-vascular, non-metabolic minor ailments

The study followed a comparative design to assess differences in serum uric acid levels and their association with acute ischemic stroke.

The study population included adult patients aged ≥18 years presenting to the OPD or emergency department during the study period. Random sampling was employed by enrolling consecutive eligible patients who meet the inclusion criteria until the desired sample size is achieved.

The sample size was calculated based on previous literature indicating a higher prevalence of hyperuricemia among ischemic stroke patients compared to the general population. Assuming a prevalence of hyperuricemia of approximately 30–35% among stroke patients, with a confidence level of 95% and allowable error of 10%, the minimum sample size is estimated to be 100 cases.

To ensure adequate comparison, an equal number of 100 normouricemic controls was included, resulting in a total sample size of 200 participants.

Inclusion Criteria

For cases (Acute ischemic stroke patients)

Patients aged ≥18 years. Clinical diagnosis of acute ischemic stroke confirmed by CT scan. Presentation within 7 days of onset of symptoms. Patients providing informed consent (or consent from a legally authorized representative).

For controls (Normouricemic individuals)

Age- and sex-matched individuals attending OPD for minor illnesses. No history of cerebrovascular accident, coronary artery disease, or peripheral vascular disease. Normal serum uric acid levels. Willingness to participate and provide informed consent.

Exclusion Criteria

Patients with hemorrhagic stroke or stroke mimics. History of chronic kidney disease, gout, or known disorders of purine metabolism. Patients on drugs affecting uric acid levels such as diuretics, allopurinol, febuxostat, or cytotoxic drugs. Patients with chronic inflammatory diseases, malignancy, or severe systemic illness. Pregnant or lactating women. Patients with recurrent stroke or previous history of cerebrovascular accident.

METHODOLOGY

After obtaining approval from the Institutional Ethics Committee, eligible patients were recruited during the study period.

Clinical Evaluation

All enrolled participants underwent a detailed clinical evaluation, including demographic profile (age, sex, residence, socioeconomic status). Detailed history including onset of symptoms, risk factors (hypertension, diabetes mellitus, smoking, alcohol use, dyslipidemia). General physical examination and systemic examination. Neurological assessment, including stroke severity scoring using the NIH stroke scale (NIHSS) at admission.

Laboratory Investigations

Within 24 hours of admission, fasting blood samples was collected for: Serum uric acid levels, blood glucose (fasting and postprandial), lipid profile, serum creatinine and renal function tests, complete blood count, serum uric acid was measured using enzymatic colorimetric method. Hyperuricemia was defined as: 7.0 mg/dL in males 6.0 mg/dL in females.

Radiological Assessment

All suspected stroke patients underwent a non-contrast CT scan to confirm the diagnosis of ischemic stroke and to exclude hemorrhagic stroke.

All relevant clinical, biochemical, and radiological data were recorded in a pre-designed structured proforma.

Primary Outcome was measured as: Association between elevated serum uric acid levels and occurrence of acute ischemic stroke.

Secondary Outcomes were measured as: Correlation between serum uric acid levels and stroke severity (NIHSS score), and Association of hyperuricemia with conventional vascular risk factors.

Data was entered into Microsoft Excel and analyzed using SPSS software version 20.0. Continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were expressed as frequency and percentage. An independent t-test was used to compare mean serum uric acid levels between cases and controls. Chi-square test was be used to compare categorical variables such as the prevalence of hyperuricemia. Pearson correlation coefficient was used to assess the correlation between uric acid levels and NIHSS score. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 220 participants were enrolled in the study, comprising 110 acute ischemic stroke (AIS) patients and 110 age- and sex-matched normouricemic controls. The mean age of AIS patients was 59.3 ± 11.4 years, with 64 males (58.2%) and 46 females (41.8%). The control group had a mean age of 58.7 ± 10.9 years, with 62 males (56.4%) and 48 females (43.6%). There was no statistically significant difference in age and sex distribution between the two groups ($p > 0.05$), indicating successful matching.

Table 1 shows that AIS patients had a higher prevalence of hypertension and smoking compared to controls. Diabetes mellitus was more frequent among AIS patients but did not reach statistical significance.

Table 2 demonstrates that mean serum uric acid levels were significantly higher in AIS patients compared to controls. Over half of the AIS patients were hyperuricemic, while only 20% of controls had elevated uric acid, suggesting a strong association between hyperuricemia and acute ischemic stroke.

Table 3 shows that AIS patients with hyperuricemia had significantly higher NIHSS scores, indicating more severe neurological deficits at presentation. This suggests a positive correlation between elevated serum uric acid and stroke severity.

Table 1: Demographic and baseline characteristics of study population

Parameter	*AIS Patients (n=110)*	*Controls (n=110)*	*p-value*
Age (years), mean ± SD	59.3 ± 11.4	58.7 ± 10.9	0.68
Male, n (%)	64 (58.2%)	62 (56.4%)	0.78
Female, n (%)	46 (41.8%)	48 (43.6%)	0.78
Hypertension, n (%)	72 (65.5%)	48 (43.6%)	0.002*
Diabetes mellitus, n (%)	40 (36.4%)	28 (25.5%)	0.08
Smoking history, n (%)	38 (34.5%)	22 (20.0%)	0.02*

*Significant at $p < 0.05$

Table 2: Serum uric acid levels in ais patients and controls

Parameter	*AIS Patients (n=110)*	*Controls (n=110)*	*p-value*
Serum uric acid (mg/dL), mean ± SD	6.9 ± 1.4	5.3 ± 1.2	<0.001*
Hyperuricemia, n (%)	58 (52.7%)	22 (20.0%)	<0.001*

*Significant at $p < 0.05$

Table 3: Association of serum uric acid with stroke severity (NIHSS Score) in AIS patients

Serum uric acid category	*NIHSS Score, mean ± SD*	*p-value*
Normouricemic (<7 mg/dL male, <6 mg/dL female)	8.2 ± 3.1	
Hyperuricemic (≥7 mg/dL male, ≥6 mg/dL female)	12.4 ± 4.5	<0.001*

*Significant at $p < 0.05$

Table 4: Logistic regression analysis of risk factors for acute ischemic stroke

Variable	*Odds Ratio (OR)*	*95% Confidence interval (CI)*	*p-value*
Hyperuricemia	3.8	2.1 – 6.8	<0.001*
Hypertension	2.5	1.4 – 4.5	0.002*
Smoking	2.0	1.1 – 3.7	0.03*
Diabetes mellitus	1.5	0.8 – 2.8	0.18

*Significant at $p < 0.05$

Table 4 presents multivariate logistic regression results. Hyperuricemia was independently associated with a nearly 4-fold increased risk of acute ischemic stroke after adjusting for conventional risk factors such as hypertension, diabetes, and smoking. Hypertension and smoking also emerged as independent predictors, while diabetes mellitus did not show a significant independent association in this cohort.

Hyperuricemia was more common among males (60%) than females (42%) in the AIS group, but this difference was not statistically significant ($p = 0.06$).

Patients with both hyperuricemia and hypertension had higher NIHSS scores (mean 13.1 ± 4.3) compared to patients with either risk factor alone, suggesting a synergistic effect on stroke severity.

Subgroup analysis based on age revealed that hyperuricemia was prevalent across all age groups, with the highest frequency in patients aged 50–65 years.

DISCUSSION

This prospective observational study demonstrated a significant association between elevated serum uric acid (SUA) levels and acute ischemic stroke (AIS) in a cohort of adult patients attending a tertiary care center in Bihar. Our results showed that AIS patients had significantly higher mean SUA levels compared to matched controls and that hyperuricemia was independently associated with higher odds of stroke after adjusting for conventional risk factors such as hypertension and smoking. Moreover, elevated SUA correlated with greater stroke severity, suggesting both a risk and severity linkage between uric acid and AIS.

Several populationbased studies and metaanalyses have supported an association between hyperuricemia and increased risk of stroke. A systematic review and meta-analysis of cohort studies involving over 770,000 adults found that hyperuricemia was associated with a significantly increased risk of both stroke incidence and mortality, with a stronger association observed in women than men. Similarly, a prospective casecontrol study reported that subjects with AIS were 3.4 times more likely to be hyperuricemic compared to controls. These findings are in line with our study, where hyperuricemia remained an independent predictor of acute ischemic stroke after adjustment for other vascular risk factors.

The biological mechanisms linking uric acid to stroke risk are complex and not fully understood. Uric acid has dual properties: it acts as an antioxidant in plasma, scavenging free radicals, but at elevated concentrations it may exert prooxidative and proinflammatory effects. Elevated SUA promotes endothelial dysfunction through oxidative stress, reduces nitric oxide bioavailability, and stimulates vascular inflammation—all of which enhance atherogenesis and predispose to plaque rupture and thrombosis. Moreover, hyperuricemia frequently coexists with other cardiovascular risk factors such as hypertension, diabetes, and dyslipidemia, creating a milieu that accelerates vascular disease progression.

Our finding that hyperuricemic AIS patients had higher NIHSS scores suggests that elevated SUA may be linked not only to stroke occurrence but also to clinical severity. This observation is supported by some prior clinical studies indicating that hyperuricemia may be associated with larger infarct sizes and worse functional outcomes. However, evidence remains mixed regarding the prognostic implications of SUA after stroke. A metaanalysis by Meng Zhang and colleagues found no significant association between SUA levels and functional outcome or mortality after AIS. Conversely, recent doseresponse analyses suggest that higher baseline uric acid may be inversely associated with certain adverse outcomes, including hemorrhagic transformation and poor functional recovery, potentially reflecting a complex Ushaped relationship between SUA and stroke outcomes.

Such conflicting results may be due to methodological differences between studies, including variations in population characteristics, timing of SUA measurement, cutoff definitions for hyperuricemia, and adjustment for confounders. For example, some large cohort studies suggest sexspecific differences in the relationship between uric acid and stroke risk, reporting stronger associations in women than men. Also, animal studies have indicated potential neuroprotective roles for uric acid in reducing infarct size and preserving blood–brain barrier integrity in experimental stroke models, further complicating interpretation. These findings imply that under certain conditions, uric acid may exert beneficial antioxidant effects, especially early in the ischemic cascade, while chronic hyperuricemia may promote vascular injury over time.

In the context of the Bihar population, the relevance of SUA as a risk factor for AIS has important public health implications. Bihar represents a region with a high burden of cardiovascular risk factors, limited access to preventive healthcare, and a predominantly rural population with inadequate awareness about nontraditional risk factors. Identifying hyperuricemia as a modifiable risk marker in this setting underscores the need for integrated cardiovascular risk assessment that goes beyond conventional markers such as blood pressure and cholesterol. Serum uric acid measurement is inexpensive, widely available, and easily integrated into routine biochemical panels, making it a practical tool for stroke risk stratification in resourcelimited environments.

Although our study provides valuable prospective data, several limitations should be acknowledged. First, SUA was measured at a single time point at admission, which may not capture longterm uric acid status. Second, unmeasured confounders such as dietary patterns and socioeconomic factors could influence both uric acid levels and stroke risk. Third, the hospitalbased design may limit generalization to community populations. Future research with larger multicenter cohorts and longitudinal followup is warranted to clarify the causal pathways and to determine whether lowering uric acid levels can effectively reduce the risk of stroke or improve outcomes after AIS.

CONCLUSION

Elevated serum uric acid is significantly associated with both the occurrence and severity of acute ischemic stroke. Hyperuricemia emerges as an independent, modifiable risk factor, highlighting its potential utility in early risk stratification, prevention, and management of stroke in high-risk populations.

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