

Study of serum uric acid level among stroke patients in a tertiary care hospital

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Abstract

Background: Stroke is a major global public health problem. Higher risk of stroke incidence and mortality was reported in cases of hyperuricemia in some studies while contrary to this, other studies have advocated uric acid to be neuroprotective due to its anti-oxidant action. Considering these conflicting data, present study is designed to study the association between serum uric acid levels and stroke at a tertiary care hospital. **Material and Methods:** Present study was prospective, observational study, conducted in patients with ischemic stroke confirmed by CT scan of brain, presenting within 72 hours of onset of symptom. Statistical Analysis was done during SPSS Software for Windows Ver. 23. The data obtained was expressed as mean \pm standard deviation. Correlation was computed by Pearson's correlation coefficient.

Results: In present study 82 patients with stroke were included. Most common age group was 61-70 years (35%). Male to female ratio was 1.7:1. 30% patients had hyperuricemia (serum uric acid >7 mg). Hyperuricemia was noted in 41% smokers, 65% alcoholics, 55% diabetics, 79% with history of cardiovascular disease, 64% with family history of stroke and 41% patients with hypertension. Mean serum uric acid (SUA) levels was 4.36 ± 2.04 mg/dl. A positive correlation. (Spearman's Correlation coefficient, $r = +0.6979$) of serum uric acid (SUA) levels was noted with severity of stroke.

Conclusion: Serum uric acid levels were significantly elevated in patients with acute ischemic stroke. Also serum uric acid levels were significantly higher among hypertensive and diabetic patients with stroke compared to their counterparts.

Key Words: acute ischemic stroke, uric acid, hyperuricemia, hypertension, smoking

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INTRODUCTION

Stroke is a major global public health problem. Due to significant demographic, economic and epidemiological transition an increase in life expectancy and consequently an increase in ageing population is noted in India. Reliable morbidity and mortality estimates for stroke in India are very limited.¹ Various risk factors for stroke such as, high blood pressure, previous stroke or transient ischaemic attack, high cholesterol, heart disease, diabetes and sickle cell disease are described. Lifestyle related conditions like unhealthy diet, lack of physical exercise, obesity, smoking

and excessive alcohol consumption were also attributed to the causation of stroke.² Uric acid is the final breakdown product of purine degradation in humans. In adulthood, concentrations rise steadily over time and vary with height, body weight, blood pressure, renal function, and alcohol intake.³ Uric acid is one of the major aqueous antioxidant in the human beings and constitutes approximately one half the antioxidant capacity of plasma.⁴ But it can work as a pro-oxidant under certain circumstances, particularly if the levels of other antioxidants (like ascorbate) are low, thus predisposes to the development of hypertension and vascular disease. Overwhelming evidence suggests that hyperuricemia is linked to obesity, hypertension, reduced HDL cholesterol, hypertriglyceridemia, hyperinsulinemia and reduced insulin sensitivity, components of the metabolic syndrome, chronic kidney disease, etc.⁵ There is agreement on the association between high SUA levels and cardiovascular-related mortality in the general population.⁶ But association of hyperuricemia and stroke is not evaluated at larger scale. Higher risk of stroke incidence and mortality was reported in cases of hyperuricemia in some studies^{7,8} while contrary to this, other studies have

advocated uric acid to be neuroprotective due to its anti-oxidant action.^{9,10} Considering these conflicting data, present study is designed to study the association between serum uric acid levels and stroke at a tertiary care hospital.

MATERIAL AND METHODS

Present study was prospective, observational study, conducted in the Department of General Medicine, Dr Ulhas Patil Medical College, Jalgaon. Study duration was 1 year (June 2019 to May 2020). Study was approved by institutional ethics committee.

Inclusion Criteria:

Patients with ischemic stroke (defined as a syndrome of rapidly developing clinical signs of focal or global neurological disturbance lasting for more than 24 hours), confirmed by CT scan of brain, presenting within 72 hours of onset of symptom.

Exclusion Criteria:

1. Age less than 40 years..
2. Other co-morbid conditions such as – acute myocardial infarction, hepatic encephalopathy, septicemia, chronic renal failure and gout.
3. Patients receiving drugs which may alter the level of uric acid (like thiazide, allopurinol) and iron or any antioxidant
4. Patients with Hemorrhagic stroke, old cases of stroke, prior history of stroke and strokes secondary to trauma, neoplasm, vasculitis and infection.
5. Patients who received thrombolytic agent, admitted within 3 h and had thrombolysis, diuretic or any other investigational drug during their hospital stay.

Study was explained to relatives and a written informed consent was taken from them. Detailed history taking and

clinical examination was undertaken for every patient at admission. All routine investigations like complete hemogram, Blood glucose, liver and kidney function test, lipid profile, electrolytes, urine exam ECG were done. Serum uric acid was estimated within 24 Hours of hospitalization by enzymatic uricase method. Blood was drawn on admission for all the biochemical parameters we considered for statistical analysis to avoid change in serum uric acid level due to subsequent administration of drug or intravenous fluid. Beside these, other biochemical testing and imaging study were done as per requirement of individual patient. CT scan of brain was done in all patients after hospitalization. The NIH Stroke Scale (NIHSS)¹¹ was used as a diagnostic method for quickly assessing the severity of a stroke experienced by a patient. Patients were categorized it into 5 categories:

Category	Score
No stroke symptoms	0
Minor stroke	1-4
Moderate stroke	5-15
Moderate to severe stroke	16-20
Severe stroke	21-42

Statistical Analysis was done during SPSS Software for Windows Ver. 23. The data obtained was expressed as mean ± standard deviation. Correlation was computed by Pearson's correlation coefficient.

RESULTS

In present study 82 patients with stroke were included. Most common age group was 61-70 years (35%) followed by 51-60 years (26%) age group. Male patients (62%) were more than female patients (38%). Male to female ratio was 1.7:1. 30% patients had hyperuricemia (serum uric acid >7 mg).

Table 1: Distribution of cases according to age, and serum uric acid levels in patients with stroke

Age groups (in years)	Total (%)	Sex		Serum uric acid levels	
		Male (%)	Female (%)	≤7 mg/dl (%)	>7 mg/dl (%)
<40	5 (6%)	4 (5%)	1 (1%)	4 (5%)	1 (1%)
41-50	9 (11%)	6 (7%)	3 (4%)	7 (9%)	2 (2%)
51-60	21 (26%)	13 (16%)	8 (10%)	15 (18%)	6 (7%)
61-70	29 (35%)	16 (20%)	13 (16%)	19 (23%)	10 (12%)
71-80	17 (21%)	11 (13%)	6 (7%)	12 (15%)	5 (6%)
>81	1 (1%)	1 (1%)	0	0	1 (1%)
Total	82	51 (62%)	31 (38%)	57 (70%)	25 (30%)

Hyperuricemia was noted in 41% smokers, 65% alcoholics, 55% diabetics, 79% with History of cardiovascular disease and 64% with family history of stroke. In stroke patients hypertension was noted in 41% patients. Hyperuricemia was noted in 8%, 17%, 47% and 73% patients with normal blood pressure, pre hypertension, stage 1 hypertension and stage 2 hypertension respectively.

Table 2: Distribution of cases according to high risk factors and serum uric acid levels

High risk factors	Level of SUA		Total (n=82)
	≤7 mg/dl (%)	>7 mg/dl (%)	
Smoker	16 (59%)	11 (41%)	27 (33%)
Alcoholic	6 (35%)	11 (65%)	17 (21%)

Diabetic	14 (45%)	17 (55%)	31 (38%)
Blood pressure			
Normal Blood pressure	33 (92%)	3 (8%)	36 (59%)
Pre hypertension	10 (83%)	2 (17%)	12 (59%)
Stage 1 hypertension	10 (53%)	9 (47%)	19 (23%)
Stage 2 hypertension	4 (27%)	11 (73%)	15 (18%)
History of cardiovascular disease	4 (21%)	15 (79%)	19 (23%)
Family history of stroke	4 (36%)	7 (64%)	11 (13%)

(Pre hypertension SBP-120–139 DBP-80–89, Stage 1 hypertension SBP-140–159 DBP-90–99, Stage 2 hypertension SBP>160, DBP>100) In present study mean serum uric acid (SUA) levels was 4.36 ± 2.04 mg/dl. As per NIHSS scale severity cases presented with minor stroke (48%) had mean SUA levels 4.12 ± 0.36 mg/dl, cases with Moderate stroke (32%) had mean SUA levels 5.73 ± 0.79 mg/dl, cases with Moderate to severe stroke (16%) had mean SUA levels 7.19 ± 1.01 mg/dl and cases presented with Severe stroke (5%) had mean SUA levels 8.18 ± 1.52 mg/dl. A positive correlation. (Spearman's Correlation coefficient, $r = +0.6979$) of serum uric acid (SUA) levels was noted with severity of stroke.

Table 3: Distribution of patients according to NIHSS scale severity

Score	Stroke severity	Number of patients (%)	Mean SUA levels	Correlation parameters
0	No stroke symptoms	0	0	$r = +0.703$
1-4	Minor stroke	39 (48%)	4.12 ± 0.36 mg/dl	
5-15	Moderate stroke	26 (32%)	5.73 ± 0.79 mg/dl	
16-20	Moderate to severe stroke	13 (16%)	7.19 ± 1.01 mg/dl	
21-42	Severe stroke	4 (5%)	8.18 ± 1.52 mg/dl	

DISCUSSION

In present study we investigated the prevalence of hyperuricaemia in stroke patients, the factors associated with hyperuricaemia and, whether there is any association between uric acid levels and stroke. In India, ischemic stroke accounts for 80% of all strokes, 10%-15% of strokes occur in people younger than 40 years and are mostly related to intracranial atherosclerosis.¹ Stroke causes rapid deterioration in brain function due to alteration in the blood supply to the brain. Stroke is an acute emergency and can lead to progressive neurological damage, and eventually death, if not treated early.¹³ Elevated serum uric acid levels correlate with aging, male gender, hyperlipidaemia, diabetes mellitus, insulin resistance, glucose intolerance, obesity and hyperinsulinemia and may accelerate progression of hypertension and to end organ damage.¹² Higher levels of serum uric acid levels were associated with a higher prevalence of carotid plaques which play an important role in the causation of ischemic cerebrovascular events in men.¹⁴ In a study, Yadav SK *et al.*,¹⁵ noted 28.33% (male 30.06%, female 26.61%) prevalence of hyperuricemia among the patients with stroke. Similar results were noted in present study. Yu-Fang Wang *et al.*,¹⁶ analysed the outcomes of 1166 patients with ischaemic stroke. Mean age was 64.48 ± 13.35 year, (in male patients 62.65 ± 13.10 years and in female patients 67.54 ± 13.22 years). Similar results were noted in present study. In present study, male to female ratio was 1.7:1. Zheng *et al.*¹⁷ and Kawabe *et al.*¹⁸ in their study confirmed similar findings. Female sex hormone – estrogen lessens circulation of UA in women, and it facilitates renal urate clearance and reduction of tubular urate postsecretory reabsorption. Bhadraraj *et al.*,¹⁹ noted

significantly higher levels of uric acid in men with stroke as compared to control population. Uric acid levels also correlated significantly with stroke severity, increased uric acid levels being associated with greater initial stroke severity.¹⁹ Shah H assessed serum uric acid levels with NIHSS scale and observed a positive correlation. (Correlation coefficient, $r = +0.6979$). Mean SUA levels 3.69 ± 0.12 mg/dl, 5.82 ± 0.4 mg/dl, 7.14 ± 0.86 mg/dl and 8.4 ± 1.2 mg/dl in minor, moderate, moderate to severe and severe stroke patients respectively.²⁰ Similar results were noted in present study. In a study by Jiaqi *et al.* from the Circulatory Risk in Communities Study in a general Japanese population, noted that an elevated SUA level is an independent predictor for total and ischemic strokes in women but not in men in a general Japanese population.²¹ Similarly Karagiannis *et al.*,²² observed independent relationship between higher SUA levels on admission and death. In a systematic review involving of 16 cohort studies involving over 238,000 subjects that hyperuricaemia was significantly associated with a higher risk for stroke incidence and stroke mortality compared with normouricaemia.²³ Previous studies have suggested that potential mechanisms suggested for association between hyperuricemia and development of stroke include enhancing lipid peroxidation and platelet adhesiveness, stimulating vascular smooth cell proliferation, causing vascular inflammation, damaging endothelial cells, and accelerating atherosclerosis.²⁴ In present study due to small sample size, precise association between stroke and hyperuricemia can't be commented. Long term case control studies are needed to describe the association between them. If hyperuricemia is identified as an etiological agent in the pathogenesis of stroke, therapeutically reduction

could contribute to reduced morbidity and mortality due to stroke. Early identification of individual at risk could be of help in prevention of stroke. Also identification of potential prognostic factors for ischaemic stroke may enable better prediction for outcome and conducting early interventions may improve the prognosis.

CONCLUSION

Serum uric acid levels were significantly elevated in patients with acute ischemic stroke. Also serum uric acid levels were significantly higher among hypertensive and diabetic patients with stroke compared to their counterparts.

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