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A Study On Serum Uric Acid In Acute Ischemic Stroke.

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ABSTRACT

A stroke or cerebrovascular accident is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause. Stroke is the third common cause of death in the world after coronary heart disease and cancer especially in the elderly. The mortality rate of stroke in the acute phase is as high as 20% and it remains higher for several years after the acute event in stroke patients than in the general population. To identify whether uric acid level among the stroke cases has any association with diabetes and hypertension. This study was conducted in the Department Of General Medicine, Government Thiruvapur Medical College, Thiruvapur, Tamil Nadu, India in the year 2021 august to January 2022. Totally 102 of acute ischaemic stroke were enrolled and were compared with same number of age and sex matched 40 healthy controls. Serum uric acid levels were measured in cases (within 24 hours of stroke evolution). Glasgow coma scale (GCS) score was calculated for cases at time of admission. The results were statistically analysed. Mean serum uric acid level in cases was 6.15 ± 1.91 mg/dl whereas it was 5.1 ± 1.4 mg/dl in controls. The difference of serum uric acid levels between cases and controls was statistically significant ($p = 0.0054$). Patients with poor GCS had higher mean serum uric acid levels as compared to patients with mild or moderate GCS score which was statistically significant ($p = 0.0426$). Serum uric acid can be used as a marker for increased risk of stroke. Furthermore, serum uric acid can also be used for risk stratification after stroke.

Keywords: GCS, Stroke, Serum uric acid

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INTRODUCTION

In clinical practice, uric acid has been used as a marker of severe metabolic disturbances. Its antioxidant property has not been considered much for a longtime [1]. The plasma concentration of uric acid is almost 10-fold higher than other antioxidants such as Vitamin C and Vitamin E [2]. It is considered that uric acid has much higher antioxidant capacity. Uric acid which is formed by catabolism of purine is proposed to neutralize the free radical injury that occurs in ischemic stroke [3]. Epidemiological studies have suggested a direct relationship between the levels of the natural antioxidant uric acid and the risk of cerebrovascular and coronary ischemic events. However, it is not completely clear whether this association indicates that uric acid is an independent ischemic risk factor or it represents a marker of atherosclerotic disease [4]. Whether the concentration of uric acid at the onset of ischemic symptoms influences the severity of stroke also remains to be elucidated [5].

METHODS

This study was conducted in the Department Of General Medicine, Government Thiruvavur Medical College, Thiruvavur, Tamil Nadu, India in the year 2021 August to January 2022. Totally 102 of acute ischemic stroke were enrolled and were compared with same number of age and sex matched 40 healthy controls. Serum uric acid levels were measured in cases (within 24 hours of stroke evolution).

Inclusion Criteria

Patients with stroke as defined by WHO criteria: Rapidly developing clinical signs of focal or global (coma) neurological deficit lasting more than 24 hrs. or leading to death with no apparent cause other than vascular origin. All patients who presented within 48 hours of onset of stroke and who gave informed consent to participate in the study were included.

Exclusion Criteria

- Patients with Sub arachnoid haemorrhage, extradural haemorrhage subdural haemorrhage and intra cerebral haemorrhage were excluded by CT.
- Patients with previous history of TIA/RIND.
- Patients with gout.
- Patients who were alcoholics.
- Patients taking drugs causing hyperuricaemia. eg. With the following drugs like
 - Loop diuretics
 - Anticancer drugs (Cisplatin, cyclosporine, cyclophosphamide)
 - ATT (Pyrazinamide, Ethambutol)
 - Aspirin, Pentamidine, Theophylline, ketoconazole,
 - Levodopa, isotretinoin.
- Patients with previous history of coronary vascular events
- Kidney disease
- Patient on medication to reduce oxidant levels
- Hypothyroidism
- Inflammatory diseases

Data Collection

The socio demographic, clinical, laboratory parameters and outcome data were collected. Socio demographic data included age of the patients, sex, area of residence, income, diet and time of hospitalisation after stroke. Clinical data included recording of vital parameters, fundus examination, the type of stroke, conscious level of the patients assessed by the Glasscow coma scale and complete neurological examination. Laboratory parameters included complete blood count, renal function tests, fasting blood sugar and CT Scan brain. The serum uric acid level was measured in the stroke patients and control by the uricase method.

Glasgow Outcome Scale

1. Indicates death
2. Vegetative state (patient is unable to interact with environment)
3. Severe disability (patients is unable to live independently but can follow commands)
4. Moderate disability (patients is capable of living independently but unable to return to work or school).
5. Mild or No disability Patient can return to work or school.

Scale 4 & 5- Favourable outcome (good outcome) Scale 1,2 & 3- Unfavourable outcome (poor outcome)

The data were entered in Microsoft excel software and analysed using SPSS 2007 statistically.

RESULTS

In the 102 stroke patients, 66 were males and 36 females. The mean serum uric acid level in males (5.76 mg/dL) was higher than in females (5.47 mg/dL). No significant association was found between gender and uric acid level (P = 0.370) as shown in Table No. 1.

Table 1: Serum Uric Acid Level Between Males & Females In The Stroke Cases

S. No.	Gender	No.	Serum Uric Acid Level			P value
			Mean	SD	C.I.	
1.	Males	66	5.76	1.62	-0.347	0.370
2.	Females	36	5.47	1.40	0.923	

Age

The age of stroke patients varied from 30 to 70 years. Mean age of the study group was 56.72 ± 1.89. The serum uric acid level was compared between age groups of > 50 and ≤ 50 years in the control and stroke cases.

Control Group

In the control above 50 years had uric acid level more than people ≤ 50 years. But statistically it was not significant (P = 0.055) as shown in Table No. 2.

Table 2: Serum Uric Acid Between The Age Groups ≤ 50 Years And > 50 Years Among Control

S. No.	Age	No.	Serum Uric Acid Level			P value
			Mean	SD	C.I.	
1.	≤ 50 years	19	4.050	0.7557	-0.3771	0.055
2.	> 50 years	21	4.105	0.5862	0.4871	

Stroke Cases

Similarly within the stroke cases, uric acid level was compared between the age groups > 50 years and ≤ 50 years.

In the stroke patients > 50 years had mean uric acid level of 5.788 mg/dL while patients ≤ 50 years had mean serum uric acid level 5.238 mg/dL. Statistical no association seen (P = 0.125), as shown in Table No. 3.

Table 3: Serum Uric Acid Between Age Groups \leq 50 Years & $>$ 50 Years Among Stroke Cases

S. No.	Age	No.	Serum Uric Acid Level			P value
			Mean	SD	C.I.	
1.	\leq 50 Years	34	5.238	1.578	-1.260	0.127
2.	$>$ 50 years	68	5.788	1.518	0.1588	

Table 4: Serum Uric Acid Level Between Stroke Cases And Controls

S. No.	Group	No.	Serum Uric Acid Level			P value
			Mean	SD	C.I.	
1.	Stroke Cases	102	5.66	1.54	-1.214	0.000
2.	Control	40	4.08	0.67	-1.949	

The study group consisted of 102 stroke patients. The mean serum uric acid level in the stroke cases was 5.66 mg/dL with range 4.12 to 7.2 mg/dL. The control group had 40 members. The mean serum uric acid level in the control group was 4.08 mg/dL with range 3.41 to 4.75 mg/dL.

The serum uric acid level of the stroke cases was compared with control group. The stroke cases had increased uric acid level than control with statistically significant association ($P < 0.001$) as shown in Table No. 4.

Table 5: Serum Uric Acid Among Diabetic Stroke Cases And Control

S. No.	Group	No.	Serum Uric Acid Level			P value
			Mean	SD	C.I.	
1.	Stroke Cases	33	5.50	1.59	-0.353	0.009
2.	Control	11	4.15	0.63	-2.350	

In the study group 33 patients had diabetes and in the control group 11 were diabetics. The serum uric acid level was compared between them.

Diabetics with stroke had elevated uric acid than diabetics without stroke ($P < 0.001$). Statistical association was present as shown in Table No. 5.

Table 6: Serum Uric Acid Among Diabetic And NonDiabetic Stroke Cases

S. No.	Risk Factor	No.	Serum Uric Acid Level			P value
			Mean	SD	C.I.	
1.	Diabetics	33	5.74	1.526	0.889	0.467
2.	Non-Diabetics	69	5.4970	1.588	0.410	

Similarly, serum uric acid level in diabetics and non-diabetics within the stroke cases were compared. The mean uric acid level in diabetics with stroke was 5.74 mg/dL while that of non-diabetic stroke patients were 5.49 mg/dL. There is no statistical significance between them ($P = 0.467$) as shown in Table No. 6.

Table 7: Outcome In Diabetic And Non-diabetic Stroke Cases

Cases	Outcome		Total
	Good	Poor	
Diabetes	15 (45.5%)	18 (54.5%)	33 (32.4%)
Non-Diabetics	45 (65.2%)	24 (34.8%)	69 (67.6%)
Total	42 (41.2%)	60 (58.8%)	102 (100%)

The outcome was compared between the diabetics and non diabetics in the stroke patients.

In the diabetic poor outcome (54.5%) was more common than good outcome (45.5%) but not statistically significant (P = 0.057) as shown in Table No. 7.

Table 8: Serum Uric Acid Among Hypertensive Stroke Cases & Control

S. No.	Group	No.	Serum Uric Acid Level			P value
			Mean	SD	C.I.	
1.	Cases	54	5.71	1.53	-0.751	0.001
2.	Control	12	4.06	0.59	-2.551	

Among the stroke cases, 54 were hypertensive, while in the control 12 were hypertensive. The serum uric acid level was compared between them.

The hypertensive in control had mean uric acid of 4.06 mg/dL while the hypertensive in cases had mean uric acid of 5.71 mg/dL. There is significant association between stroke patients with hypertension and elevated uric acid (P = 0.001) as shown in Table No.8.

When the serum uric acid level was compared between the hypertensive and non hypertensive within the stroke cases there was no significant association (P = 0.728) as shown in Table No.9.

Table 9: Serum Uric Acid Among Hypertensives And Non-Hypertensives Within Stroke Cases

S. No.	Risk Factor	No.	Serum Uric Acid Level			P value
			Mean	SD	C.I.	
1.	Hypertensive	54	5.71	1.53	-0.503	0.728
2.	Non-Hypertensive	48	5.60	1.57	0.717	

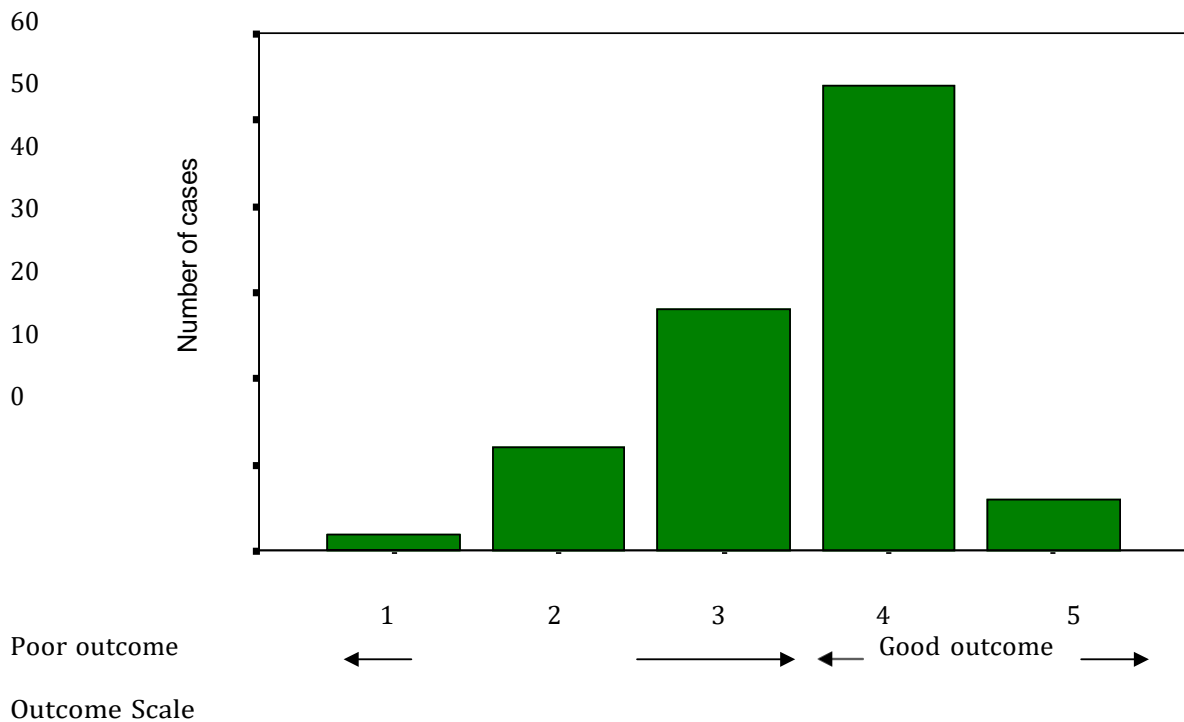
Table 10: Serum Uric Acid Among Smokers And NonSmokers In The Stroke Cases

S. No.	Risk factor	No.	Serum Uric Acid Level			P value
			Mean	SD	C.I.	
1.	Smokers	44	5.63	1.58	-0.633	0.879
2.	Nonsmokers	58	5.68	1.52	0.568	

Stroke Outcome And Uric Acid

Of the 102 cases, 91 had middle cerebral artery territory infarct, while 11 had posterior circulation stroke. The outcome was analysed in the stroke patients using glassgow outcome scale. 60 of them had good outcome while 42 had poor outcome as shown in the Figure - 2.

Figure 1: Outcome Scale In The Stroke Patients



The serum uric acid level was compared between stroke cases with good outcome and poor outcome.

Mean serum uric acid in the stroke patients with poor outcome (6.41 mg/dL) was higher than that in the stroke patients with good outcome (5.13 mg/dL).

There is statistical association (P value < 0.001) between increased uric acid level and poor outcome as shown in Table No.11.

Table 11: Serum Uric Acid Among Stroke Cases InRelation To Outcome

S. No.	Stroke Cases	No.	Mean	SD	C.I.	P value
1.	Good outcome	60	5.13	1.45	0.716	0.001
2.	Poor outcome	42	6.41	1.37	1.845	

The stroke patients without selected risk factors (hypertension, diabetes, smoking) were 38 in the study. Among them, the uric acid level was compared between those with good outcome and poor outcome.

Mean serum uric acid in the stroke patients without risk factors and poor outcome (4.92 mg/dL) was higher than those with good outcome (6.32 mg/dL).

There is a significant association between elevated uric acid level and poor outcome in stroke patients without risk factors (P < 0.001) shown in Table No.12.

Table 12: Serum Uric Acid In Stroke Patients WithoutRisk Factors With Outcome

S. No.	StrokeCases	No.	Serum Uric Acid Level			P value
			Mean	SD	C.I.	
1.	Good outcome	15	4.92	1.61	4.03 to5.8	< 0.001
2.	Poor outcome	23	6.32	0.69	5.8 to6.8	

DISCUSSION

Uric acid which is an end product of purine metabolism has long been considered only in the pathogenesis of gout and uric acid stones. Its anti-oxidant functions and its various role in the pathogenesis of hypertension, cardiovascular and cerebrovascular events are been considered of late. Various studies conducted during recent years on serum uric acid levels in vascular events have proven its prognostic significance [6]. Uric acid is also been considered as a marker for atherosclerosis. But the exact pathogenesis and whether it is the cause or effect of atherosclerosis remains to be elucidated. Stroke occurs predominantly in the middle and late years of life. When serum uric acid level was compared between age groups of \leq 50 years and $>$ 50 years in control and cases, there was no significant association. Age group of the patients has been found to have no correlation with serum uric acid levels in the present study [7]. Uric acid levels were found to be significantly higher among patients with stroke than the control in this study. In the present study diabetic patients who developed stroke had higher uric acid level than the diabetics in the control group with significant association. Among the stroke patients no significant difference in uric acid levels was found between diabetics and non-diabetics [8]. Among the stroke patients, outcome in diabetic and non-diabetic was analysed, diabetics had higher percentage of poor outcome (54.5%) than good outcome (45.5%), but statistically no significant association ($P = 0.057$) was seen. In the present study only 33% of stroke patients were diabetics. So, this correlation was probably not possible [9]. We may need a large multicentered study. Hypertensive patients who developed stroke had increased uric acid level than the hypertensive in the control group with statistically significant association ($P < 0.001$). Among the stroke patients, no significant difference in uric acid level was found between the hypertensive and non-hypertensives [10]. Elevated uric acid was found to be significantly associated with poor outcome among the stroke patients in the present study [11]. To eliminate the potential bias created by risk factors (diabetes, hypertension, smoking), the uric acid level was analysed among stroke patients without these selected risk factors and compared with outcome. It was found that uric acid was still an independent indicator of poor outcome. Uric acid being an anti-oxidant, it is increased as a compensatory mechanism to protect the ischemic tissues of the brain from free radical injury. Present observation concurs with the above statement [12]. Recent evidence suggests that acute ischemic stroke results in generation of local oxidants that augment local injury and increase infarct size. Acute stroke is associated with a rapid decrease in serum antioxidants that recover slowly over subsequent weeks [13]. Though uric acid is considered an antioxidant, it being an aqueous antioxidant, it can become a pro-oxidant under certain circumstances, particularly if other antioxidants such as ascorbate are low. Thus fall in ascorbate (Vitamin C) levels with acute stroke could predispose the serum uric acid to take on pro-oxidant properties. However, it has been evident by experiments that uric acid is synthesised locally from infarcted tissues, particularly during reperfusion and its level in serum rises often in proportion to the size of the infarcted tissue, reperfusion status and the extent of the free radical injury [14]. So elevated uric acid though not, an abnormality and only a response to physiological stress, and to some extent is a biochemical marker of oxidative stress [15]. As definite correlation between oxidative stress and serum uric acid level was not made earlier, therapeutic intervention for elevated uric acid should not be undertaken. However, it still can be used a surrogate biochemical marker for the oxidative stress in acute ischemic stroke. The elevated uric acid may indirectly reflect high amount of oxidative stress and therefore poor outcome in stroke patients [16,17].

CONCLUSION

Serum uric acid level was increased in stroke patients and was independent of age and gender. Uric acid level among stroke cases was independent of their diabetic and hypertensive status. All the stroke cases who had poor outcome were found to have elevated uric acid level which may be a response to oxidative stress and hence it can be considered as biochemical marker in stroke patients.

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