



SERUM URIC ACID LEVEL AMONG ACUTE CEREBROVASCULAR ACCIDENT PATIENTS IN MANIPUR

Biochemistry

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ABSTRACT

A large number of studies in the past give conflicting results about the role of uric acid as a risk factor in patients with acute cerebrovascular accident (CVA). This study was carried out to measure the level of uric acid among acute cases of CVA and compare it with normal controls and also to find its relationship with cerebrovascular risk factors. It was a cross sectional study, carried out on 60 patients with acute stroke, admitted in Regional Institute of Medical Sciences (RIMS) hospital, Imphal, from Nov 2018 to Oct 2020. Another 60 healthy individuals were taken as controls. Serum uric acid was measured by Enzymatic Colorimetric method. Mean age of the patients was 58.35 ± 11.54 years. 54 patients were hypertensive, 28 (46.67%) had haemorrhagic stroke and 32 (53.33%) had ischemic stroke. Serum uric acid level was significantly higher in CVA cases (7.64 ± 2.01 mg/dL) compared to controls (5.06 ± 0.98 mg/dL). The level of uric acid was found to be significantly higher in males (8.55 ± 1.75 mg/dl) compared to females (7.64 ± 2.00 mg/dL). Maximum number of the patients had uric acid level > 8 mg/dl. The level of uric acid was found to be more among the patients with ischemic stroke (7.97 ± 1.87 mg/dl) compared to haemorrhagic stroke (7.27 ± 2.13 mg/dl). A strong significant positive correlation was observed with all the lipid parameters and a significant negative correlation with HDL cholesterol. Increased serum uric acid may be considered as a risk factor of acute cerebrovascular accident.

KEYWORDS

uric acid, cerebrovascular accident, lipid profile

INTRODUCTION:

Stroke or cerebrovascular accident (CVA) is the rapid loss of brain function due to disturbance in the blood supply to the brain which may be due to ischemia caused by blockage (thrombosis, arterial embolism or haemorrhage).¹ It is the second leading cause of death worldwide after coronary heart disease.² WHO clinically defines cerebrovascular accident as the rapid development of clinical signs and symptoms of focal neurological disturbance lasting more than 24hrs or leading to death with no apparent cause other than vascular origin.³

Uric acid is the ultimate catabolite of purine metabolism in humans.⁴ It has been established that increased levels of uric acid are associated with established cardiovascular risk factors such as elevated serum triglycerides, cholesterol concentration, hypertension, obesity, insulin resistance and metabolic syndrome.⁵ On the other hand uric acid has been known to exert neuroprotective effects by acting as a free radical scavenger.⁶ In humans, half the antioxidant capacity of plasma comes from uric acid.^{7,8}

Several studies have provided conflicting results regarding the clinical significance of elevated serum uric acid levels in CVA. It is also unclear whether serum uric acid promotes or protects against the development of cerebrovascular disease or simply act as a passive marker of increased risk.

AIMS AND OBJECTIVES:

To estimate serum uric acid in patients suffering from CVA and compare these with healthy controls. Also, to find out any difference in serum uric acid levels between hemorrhagic and ischemic stroke cases and to assess its relationship with cardiovascular risk factors.

MATERIALS AND METHODS:

A case control study was carried out in the Department of Biochemistry in collaboration with the Department of Medicine RIMS, Imphal, Manipur for a period of 2 years from Nov 2018 to Oct 2020.

Inclusion Criteria:

Cases of acute stroke of age ≥ 18 years, admitted in Medicine ward, within 24 hours of onset and age & sex matched apparently healthy individuals as controls

Exclusion Criteria:

1. Patients with a known or possible cardiac source of emboli.
2. Past history of vascular disease and receiving drugs affecting serum uric acid levels (diuretics, analgesics, lipid lowering drugs)
3. Active infections and history of gout: taking antigout medicines
4. Malignancies; renal or liver diseases, thyroid dysfunctions, chronic inflammatory bowel diseases.

Detailed history of each individual case was recorded. CVA was confirmed by clinical examination and special investigations (NCCT brain). A written informed consent was taken from all the subjects. About 5ml venous blood was collected before initiation of medical therapy. Serum uric acid was measured by Enzymatic Colorimetric method as described by Barham D et al⁹ by Randox series RX Imola-autoanalyser. Serum lipid profile estimation was done by Enzymatic Colorimetric Test using kits marketed by Human Gesellschaft fur Biochemia und Diagnostica mbH.

Statistical analysis was performed using SPSS version 20. Data were expressed as Mean $\pm$ SD. Statistical tests like χ^2 -test, independent t-test, ANOVA (F-test) and correlation coefficient 'r' were applied whenever found suitable and necessary. The P-value < 0.05 was considered significant.

Study was approved by the institutional ethical committee, RIMS.

RESULTS AND DISCUSSION:

The present study showed that incidence of stroke was maximum in the age group of 51 – 60 years, which comprises of 40% of total stroke patients. It correlates with the findings of Eapen RP et al¹⁰ and Wadhvani J et al.¹¹

Prevalence of CVA was found to be higher among males with 33 (55%) cases than females with 27 (45%) cases. The male to female ratio in the study group is 1.2:1, which was statistically significant. These findings are comparable to the findings of Shrestha A et al¹² and Mehropour M et al.¹³ This may be due to differences in risk factors such as smoking and alcohol drinking which are more prevalent among men in India compared with women.¹⁴

In this study, majority of the patients 37(61.66%) showed Systolic Blood Pressure (SBP) between 161 to 170 mm Hg and 52 (86.67%) showed diastolic blood pressure (DBP) between 91 to 100 mm Hg indicating that majority of patients had blood pressure on higher range.

This study showed higher percentage of ischemic type stroke 32 (53.33%) than the hemorrhagic stroke 28 (46.67%). This is supported by the stroke statistics findings that most strokes (85%) are ischemic stroke.¹⁵

Table 1: Serum uric acid level and lipid parameters among cases and controls

parameter	Controls (n = 60)	CVA cases (n = 60)	t	P-value
Serum Uric Acid (mg/l)	5.06 ± 0.98	7.64 ± 2.01	8.9	<0.001
TC (mg/dl)	168.67 ± 29.49	235.26 ± 49.55	8.9	<0.001
TG (mg/dl)	149.85 ± 23.14	217.11 ± 56.38	8.5	<0.001
LDL (mg/dl)	93.03 ± 25.19	155.09 ± 49.91	8.6	<0.001
VLDL (mg/dl)	29.96 ± 4.63	43.42 ± 11.28	8.5	<0.001
HDL (mg/dl)	54.33 ± 5.18	36.74 ± 9.42	12.7	<0.001

As shown in table-1, stroke patients have significantly higher serum uric acid levels as compared to controls (7.64 ± 2.01 mg/dl vs 5.06 ± 0.98 mg/dl) these findings are in accordance with findings of earlier researches who also found significantly higher serum uric acid levels among cases as compared to controls. On the other hand these findings were in contrast with the study conducted by Goldberg RJ et al¹⁶ who did not find any significant correlation between serum uric acid and thromboembolic stroke. In a Japanese middle-aged population, hyperuricemia was not associated with stroke mortality in 108284 persons as shown by Sakata K et al.¹⁷ Cazzato G et al¹⁸ reported no difference in uric acid level between patients with stroke and control group. Serum uric acid being one of the major aqueous antioxidant should have protective role in stroke patients. However, it works as a prooxidant under certain circumstances, particularly if the level of other antioxidants are low.¹⁹ Studies have shown that uric acid can result in endothelial dysfunction which can lead to vascular damage.²⁰ Another putative mechanism is that serum uric acid levels might reflect an increased activity of xanthine oxidase which leads to generation of superoxide anions and reactive oxygen species in human vasculature.^{21,22}

Table 2: Distribution of uric acid according to sex of patients and different types of CVA

	Cases Uric acid			Controls Uric acid		
	No.	Mean ± SD (mg/l)	Range (mg/l)	No.	Mean (mg/l)	Range (mg/l)
Male	33	8.55 ± 1.75 ^{b***}	3.40 – 11.20	34	5.39 ± 0.86	3.40 – 7.00
female	27	6.54 ± 1.75	3.00 – 10.00	26	4.63 ± 0.97	3.50 – 7.00
total	60	7.64 ± 2.00 ^{***}	3.00 – 11.20	60	5.06 ± 0.98	3.40 – 7.00
parameter	Hemorrhagic stroke (n = 28)		Ischemic stroke (n = 32)	Controls (n = 60)		
SUA (mg/dl)	7.27 ± 2.13 ^{a***}		7.97 ± 1.87 ^{a***b*}	5.06 ± 0.98		

a*** p<0.001, between control and CVA cases; b*** p<0.001, between males and females of CVA cases, b* p>0.05 comparison between Ischemic stroke and hemorrhagic stroke.

There was statistically significant increase of serum uric acid level in males compared to females which is in agreement with the findings of Milionis HJ et al²³ and Bos MJ et al²⁴. There was no significant difference in the level of uric acid in patients having haemorrhagic stroke and ischemic stroke. This was in accordance to the study conducted by Mehrpour M et al.¹³

Table 3: Correlation of TG, TC, LDL, VLDL, HDL at different levels of Serum uric acid (SUA)

uric (mg/dl)	No.	TC	TG	LDL	VLDL	HDL
Mean ± SD (mg/dl)						
<4	3	169.33 ± 8.33	129.00 ± 20.22	96.53 ± 6.38	25.80 ± 4.04	47.00 ± 5.57
>4-6	9	189.79 ± 30.98	181.12 ± 31.47	113.06 ± 20.92	36.22 ± 6.30	40.50 ± 8.50

> 6-8	20	214.90 ± 28.27	199.26 ± 27.53	133.30 ± 26.55	39.85 ± 5.50	41.75 ± 10.00
>8-10	22	266.67 ± 44.10	246.82 ± 57.56	185.74 ± 49.58	49.36 ± 11.51	31.52 ± 5.64
>10	6	289.22 ± 19.70	265.75 ± 63.13	207.65 ± 33.01	531.15 ± 12.63	28.40 ± 3.74
Correlation with uric acid	r	0.750	0.591	0.707	0.591	-0.507
	p	<0.001	<0.001	<0.001	<0.001	<0.001

This table shows that the lipid profile in cases becomes more deranged with increasing level of uric acid. This finding is in accordance with the study conducted by Sarmah D et al²⁵ and Shah H et al²⁶. Moreover, a study conducted by Arora T et al²⁷ concluded that hyperuricemia and its accompanying dyslipidemia can be considered as the risk factor for acute ischemic stroke.

CONCLUSION

This study showed that hyperuricemia in stroke patient was significantly higher compared to controls and the increase was more in male patients. The increase was found to be significantly correlated to the increase in lipid parameters, so it can be considered as an important risk factor for acute stroke. Serum uric acid can cause deleterious effect by promoting atherosclerotic process as pro-oxidant at an elevated level indicating its property of antioxidant-pro-oxidant urate redox shuttle. Further long term prospective studies are needed to establish the role of serum uric acid in acute stroke and also serum uric acid lowering drugs can be considered in stroke patients.

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