



A COMPARATIVE STUDY OF SERUM URIC ACID LEVELS AMONG ISCHEMIC STROKE PATIENTS AND HEALTHY SUBJECTS

Juhi Gupta¹, Abhishek Sharma^{2*}, Hemant Bareth³

¹Assistant Professor, Department of Obstetrics and gynecology, National Institute of Medical Sciences and Research, Nims University Rajasthan, Jaipur

²Associate Professor, Department of General Medicine, National Institute of Medical Sciences and Research, Nims University Rajasthan, Jaipur

³Assistant Professor, Department of Pharmacy Practice, Nims Institute of Pharmacy, Nims University Rajasthan, Jaipur

Corresponding author- Dr. Abhishek Sharma, MBBS,MD

dr.abhisheksharma1987@gmail.com

ABSTRACT

Background: It is unclear whether Serum Uric Acid (SUA) promotes or protects against the cerebrovascular disease. Present study was done to estimate uric acid levels in patients of acute ischemic stroke.

Methods: 40 cases of acute ischemic stroke were studied along with 40 controls. Risk factors for stroke were noted such as hypertension, diabetes mellitus, metabolic syndrome etc. Serum uric acid levels were measured in cases and controls.

Results: Out of 40 patients, 24 were males and 16 were females. Mean SUA level in cases was 6.35 ± 1.74 mg/dl whereas it was 4.88 ± 1.46 mg/dl for controls. SUA values were higher among males than females, but this difference was not statistically significant ($P = 0.95$). The mean SUA in hypertensive subjects (6.18 ± 1.99 mg/dl) was higher than that in normotensive subjects (5.34 ± 1.59 mg/dl). There was a statistically significant difference between SUA levels in diabetic (6.53 ± 2.15 mg/dl) and non-diabetic patients (5.30 ± 1.52 mg/dl) ($P = 0.00$). Mean SUA in obese patients was 5.96 ± 1.74 mg/dl whereas it was 5.47 ± 1.77 in patients who had a normal weight. Using Pearson's correlation coefficient it was found that serum uric acid is positively

correlated with SBP, FBS and serum Triglyceride. On Binary logistic regression, Hypertension, diabetes, obesity and serum uric acid level were independently associated with Acute ischemic stroke.

Conclusions: SUA can be used as a marker for increased risk of stroke. Furthermore, SUA can also be used for risk stratification after stroke.

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INTRODUCTION

Hyperuricemia was first associated with hypertension and cardiovascular disease in 1879.¹ Since that time, many studies including Framingham Heart Study attributed this association to a simple clustering of hyperuricemia with well-established cardiovascular risk factors, and an elevated serum uric acid level by itself has generally been regarded as insignificant or incidental.² On the contrary NHANES study concluded that Uric Acid is an independent risk factor for development of cardiovascular and cerebrovascular disease. So the mystery regarding the role of serum uric acid in causation of cerebrovascular accident is yet unsolved. Amidst this controversy and lack of Indian data, this study was carried out to study serum Uric acid levels in patients of Acute Ischemic Stroke.

MATERIALS & METHODS This case control study was performed from April 2013 to November 2014. A total of 40 cases of acute ischemic stroke were studied. 40 age and sex matched healthy controls were also enrolled in the study. Accepting mean uric acid level among stroke patients and healthy subjects 6.48 ± 1.92 and 5.09 ± 1.07 respectively (as per seed article), the sample size required to find out this difference at 99% confidence interval and 90% power is 36 in each group. This would be rounded off to 40 in each group

Cases of acute ischemic stroke were included in the study. Stroke was defined as per the WHO, 'A syndrome of rapidly developing clinical signs of focal or global neurological disturbance lasting for more than 24 hours.' Only CT brain or MRI brain proven cases of acute ischemic stroke were included in the study.

EXCLUSION CRITERIA

Following patients were excluded from study: 1) Duration of symptoms more than 24 hours; 2) Past history of vascular diseases (previous stroke, angina, myocardial infarction); 3) Liver dysfunction; 4) Renal dysfunction; 5) Known or possible cardiac source of emboli 6) Patient receiving drugs affecting serum uric acid levels (diuretics, levodopa, ethambutol, purinzamide, salicylates, allopurinol, Losartan, fenofibrate, probenacid); 7) Active infections; 8) Malignancy; 9) Excessive alcohol consumption.

Age and sex matched healthy controls were taken for each case

METHODOLOGY

Applying inclusion and exclusion criteria patients were categorised into Group A (patients with Acute ischemic stroke) and Group B (age and sex matched control). Various clinical and demographic parameters were recorded like age, sex, hypertension (known hypertension treated with antihypertensive drugs OR 2 or more blood pressure recordings greater than 140/90 mm Hg), diabetes mellitus (known diabetes treated with diet or drugs or both), central obesity (waist circumference >102cm for male and >88cm for female) BMI, serum uric acid and other

laboratory parameters (Hematological, RFTs LFTs, B. glucose, total lipid profile) were measured in all patients and control participants.

Statistical Analysis

The qualitative data were expressed in proportion and percentages and the quantitative data expressed as mean and standard deviations. The difference in proportion was analysed by using chi square test and the difference in means were analyzed by using student T Test .and Correlation analyses by using Pearson correlation coefficient and linear regression were performed. Multiple logistic regression analysis was performed to find out the significant predictors of Acute ischemic stroke. Significance level for tests were determined as 95% (P< 0.05).

OBSERVATION & DISCUSSION

TABLE-1

Comparison of various clinical & biochemical parameters between cases & controls

Parameter	Mean for Cases	Mean of Controls	P value
Age	62.03 ± 11.03	62.03 ± 11.03	1.00
BMI	24.37 ± 3.406	22.44 ± 3.38	0.013
WC	95.28 ± 14.67	87.90 ± 8.21	0.007
SBP	148.40 ± 29.89	119.75 ± 24.89	<0.001
DBP	91.05 ± 11.69	79.20 ± 9.28	<0.001
FBS	134.68 ± 42.66	102.73 ± 27.36	<0.001

HDL	44.7 ± 4.86	49.4 ± 7.73	0.002
TG	139.88 ± 27.04	128.83 ± 11.63	0.02
Uric Acid	6.35 ± 1.74	4.88 ± 1.46	<0.001

Out of 40 patients we studied, 24 were males and 16 were females. Male:female ratio was 1.5:1. The mean age of cases was 62.05 ± 11.03 years and the range was 45 to 86 years. Mean BMI for cases was 24.37 ± 3.406 kg/m². Mean Waist circumference was 95.28 ± 14.671 cm. Mean SBP and DBP were 148.40 ± 29.89 mmHg and 91.05 ± 11.69 mmHg. Mean FBS, HDL and TG were 134.68 ± 42.66 mg/dl, 44.7 ± 4.86 mg/dl and 139.88 ± 27.04 mg/dl respectively. Mean serum uric acid levels were 6.35 ± 1.74 mg/dl in cases while it was 4.88 ± 1.46 mg/dl in controls.

Table No 2: Distribution of the Conventional Risk Factors of Stroke in Cases and Control Groups

Hypertension	Cases (N=40)		Control (N=40)		Total No	Chi square test	Odds ratio	95% confidence interval
	No	%	No	%		P value LS		
Present	26	65	4	10	30	23.520 with 1 df; p = 0.000	16.71	4.933 to 56.634
Absent	14	35	36	90	50			
DM								
Present	16	40	4	10	20	8.067 with 1 df; p = 0.005	6	1.787 to 20.14
Absent	24	60	36	90	60			
Obesity								
Present	20	50	2	5	22	18.119 with 1 df; p=0.000	19	4.028 to 89.621
Absent	20	50	38	95	58			

Conventional risk factors like Hypertension, Diabetes and obesity were significantly higher in cases as compared to controls.

Table no 3

Uric Acid (mg/dl)				P Value LS
Age	N	Mean	SD	
<50	10	4.81	1.27	0.32 NS
50 To 59	26	5.5	1.69	
60 To 69	28	6	2.04	
≥70	16	5.59	1.57	
Total	80	5.61	1.77	
Hypertension				
No	54	5.34	1.59	0.04S
Yes	26	6.18	1.99	
Diabetes				
No	60	5.30	1.52	0.006S
Yes	20	6.53	2.15	
Obesity				
No	57	5.47	1.77	0.262NS
Yes	23	5.96	1.74	
Smoking				
No	64	5.43	1.65	0.063NS
Yes	16	6.34	2.06	

Diabetics were having significantly higher levels of Uric Acid as compared to nondiabetics. Same was true for patients with Hypertension. Though no significant difference in mean serum uric acid was found in smokers and obese.

TABLE NO.4 : Predictor of Acute ischemic stroke status with binary logistic regression

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for	
								EXP(B)	
								Lower	Upper
Step 1 ^a	HTN	3.30	.956	11.90	1	.001	27.02	4.151	175.84
	DM	-2.22	1.364	2.65	1	.104	0.11	.008	1.58
	Obesity	3.23	1.106	8.52	1	.004	25.28	2.890	221.04
	Smoking	-0.07	1.296	0.00	1	.955	0.93	.073	11.78
	Uric Acid	0.77	.245	9.82	1	.002	2.15	1.333	3.48
	Constant	-5.52	1.912	8.34	1	.004	.004		

A logistic regression analysis was done to predict for presence of Acute Ischemic Stroke using HTN, DM, Obesity, smoking and uric acid as predictors. The Wald criteria demonstrated that hypertension, smoking, and obesity were found to be independently associated with ischemic stroke. It was also found that serum Uric acid was also independently associated with ischemic stroke.

DISCUSSION:

The well recognized risk factors for stroke like age, smoking, diabetes, hypertension & metabolic syndrome explain only a part of the cases. Hence a search for other risk factors is the need of the hour. This study was conducted to study the role of serum uric acid in acute ischemic stroke and its effect on stroke outcome.

Out of 40 patients studied, 24 were males and 16 were females. Male: female ratio was 1.5: 1.

The mean age of cases was 62.053 ± 11.03 .

Mean BMI of patients with stroke was $24.37 \pm 3.40 \text{ kg/m}^2$ which was significantly higher as compared to controls ($p=0.013$). Mean Waist circumference of cases was also statistically higher than that of controls (Mean for cases 95.28 ± 14.67 , mean for control 87.9 ± 8.21 , $p=0.007$). In a similar study done by Patil et al³ both BMI and Waist circumference were significantly higher in cases as compared to controls ($p =0.00$). Thus our study supports the result of study done by Seung et al⁴ which concluded that obesity increases risk of stroke.

We found that mean SBP and DBP in cases was significantly higher than that of controls ($p<0.001$). In similar study done by Patil et al³ hypertension emerged as one of the most powerful predictor of Ischemic stroke.

We found that stroke patients were having significantly higher FBS, TG and HDL levels as compared to controls ($p<0.001$).

After studying demographic profile of cases and control we tried to establish relationship of Serum Uric Acid with various conventional risk factors for stroke.

We found that SUA levels among hypertensive patients were significantly higher as compared to normotensive patients (6.18 ± 1.88 vs. $5.34 \pm 1.59 \text{ mg/dl}$, $p <0.04$). Milionis et al⁵ observed that

SUA levels were higher in hypertensive subjects. A Significant positive fair correlation was observed between the Systolic blood pressure and S .uric acid using pearson's correlation coefficient ($r=0.272$, $p<0.05$).

We found that SUA levels in patients suffering from diabetes mellitus were also significantly higher as compared to those in non diabetic subjects (6.53 ± 2.15 vs. 5.30 ± 1.52 mg/dl, $p<0.006$) and our findings are in accordance with the findings of study done by Longo-Mbenza et al⁶ . A Significant positive fair correlation was observed between the fasting blood sugar and S .uric acid ($r=0.333$, $p<0.05$) in our study.

In our study, we found a significant moderately strong inverse correlation between SUA levels and HDL cholesterol, and a significant moderately strong positive correlation between SUA and serum triglyceride levels ($r= - 0.724$, $p <0.001$ for HDL and $r= 0.581$, $p <0.001$ for triglycerides). Lehto et al⁷ concluded that SUA was significantly associated with HDL cholesterol ($r = -0.25$, $p < 0.01$) and triglyceride levels ($r=0.14$, $p <0.01$).

Mean SUA level in cases was 6.35 ± 1.74 mg/dl whereas it was 4.88 ± 1.46 mg/dl for controls. Mean SUA level was significantly higher in cases as compared to controls ($p <0.001$). On multiple regression analysis, correlation of SUA with ischemic stroke was found to be independent of other major risk factors for stroke. These findings are in accordance with most of the data published worldwide. Milionis et al⁵ observed that the SUA levels were significantly higher in stroke patients compared with controls. Srikrishna R and Suresh DR⁸ similarly found that serum uric acid levels were significantly higher in cases as compared to controls. In The Rotterdam study¹⁷⁸, high serum uric acid levels were associated with the risk of stroke.

In conclusion, in our study, high serum UA levels were observed to be associated significantly with ischemic stroke. Considerable progress has been made in identifying and treating modifiable risk factors for stroke. If identified as an etiological agent in the pathogenesis of vascular disease including stroke, hyperurecemia could be targeted therapeutically in the same way as other risk factors like dyslipidemia and blood pressure are routinely treated after stroke. However, more research is needed at scientific and clinical levels before routine treatment of serum urate can be recommended.

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