

A Study of Serum Uric Acid Levels in Acute Ischemic Stroke Patients Admitted in Tertiary Care Hospital At Tirupati

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Abstract: It is unclear whether Serum Uric Acid [SUA] promotes or protects against cerebrovascular disease. Present study was done to estimate uric acid levels and its association in patients of acute ischemic stroke.

Method: Total 100 consecutive patients (50 males and 50 females) with first episode of stroke as evidenced by CT scan within 48 hours were chosen for the study. The serum uric acid was estimated by the Uricase method. The patients were further evaluated for the presence of additional risk factors like hypertension, diabetes mellitus, coronary heart disease [CAD], smoking and alcoholism.

Results: Out of total 100 patients, 50 were males and 50 were females. The age of the patients in the present study were from 40 years to 84 years with mean age of 59.8 years. Mean serum uric acid level in patients were studied 5.58 ± 1.68 mg/dl and about 25% patients were hyperuricemic. As age advances the uric acid level also rised with the 'p' of < 0.001 . Among diabetics the mean uric acid value was 6.12 ± 1.64 mg/dl while among non diabetics it was 5.02 ± 1.54 mg/dl, among in CAD patients it was 6.5 ± 1.9 mg/dl and in those without CAD was 5.1 ± 1.4 mg/dl; Among the patients with large infarct was 7.2 mg/dl compared to those with small infarct was 4.816 mg/dl and thus established a statistically significant relationship (p value of < 0.0001). The present study didn't show any significant association between hypertension, hyperlipidemia, smoking, alcoholism and uric acid.

Conclusions: The prevalence of hyperuricemia in acute ischemic stroke patients in the present study was 25%. There was a statistically significant association between levels of uric acid and age, diabetes mellitus, CAD, larger infarct size. There was no stastically a signicant association between hypertension, hyperlipidemia, smoking, alcoholism and uric acid levels.

Keywords: Serum uric acid, acute ischemic stroke

I. Introduction

Stroke is the second leading cause of death worldwide, causing 6.2 million deaths in 2011¹. Stroke entails a high socio economic burden due to increased morbidity and mortality. Early identification of individuals at risk could be of help in primary prevention strategies.² The role of serum uric acid (SUA) levels as an independent risk factor for vascular disease has been questioned for decades.³ Evidence from epidemiological studies suggests that elevated SUA levels may predict an increased risk for cerebrovascular events including stroke.^{3,4}

In some studies serum uric acid has been linked to prognosis of patient with acute ischemic stroke. Evidence suggests that increased level of uric acid is bad prognostic factor in patients with acute ischemic stroke while some studies suggests increased level of serum uric acid as protective in patient with acute ischemic stroke.^{5,6}

In this respect SUA levels estimation could be used as serum marker in selecting and appropriately caring for subjects at risk. As there are few studies in India on the role of SUA in acute ischemic stroke, hence a study on this aspects likely to be fruitful.

II. Materials And Methods

A cross sectional observational hospital based study was conducted on 100 patients of acute ischemic stroke who presented to the emergency department of medicine, Sri Venkateswara Medical College, Tirupathi, during the period of 10 months from 1st December, 2014 to 31st October, 2015.

2.1. Inclusion criteria

1. Patients with first episode of stroke and stroke are documented with CT scan taken within 48 hours of onset of symptoms of focal neurological deficit.
2. Patients willing to participate in the study by giving written informed consent.

2.2. Exclusion criteria:

1. Patients with previous history of TIA/CVA.
2. Patients who are on thiazide diuretics.
3. Patients who are known cases of gout or show clinical evidence of gout.
4. Patients with chronic renal failure.
5. Patients whose CT scan show haemorrhage or other space occupying lesions other than infarct.
6. Patients with haematological abnormalities like leukemia or other myeloproliferative disorders.

2.3 Methodology:

A total 100 consecutive patients (50 males and 50 females) who met the inclusion and exclusion criteria during the study period with first episode of stroke as evidenced by CT scan within 48 hours were chosen for the study . Blood sample was taken from all patients with acute stroke during 48 hours of admission to check serum uric acid by the Uricase / Phenol/ 4- Amino Phenazone (PAP) method in the Central Laboratory of SVRRGGH, Tirupati. (Normal uric acid levels in females 2.4 -6.0 mg/dl, males 3.4 -7.0 mg/dl).The patients are evaluated for the presence of additional risk factors such as

1. Hypertension:

a) Known case of hypertension b) Blood pressure > 140/90 mm of Hg.

2. Diabetes Mellitus:

a) Known case of diabetes mellitus b) Random blood sugar > 200 mg/dl and / or Fasting blood sugar > 126 mg/dl and Post prandial blood sugar >200 mg/dl.

3. Coronary Heart Disease:

Patients with ECG (Electrocardiogram) evidence of infarction or Echocardiogram showing regional wall motion abnormalities.

4. Adverse Lipid Profile:

a) Total cholesterol - > 200 mg/dl b) Triglycerides - > 150 mg/dl c) LDL-Cholestrol - > 130 mg/dl d) HDL-cholesterol - < 40mg/dl

5. Smoking And Alcoholism:

History of smoking and alcoholism within the last 5 years has been taken as smokers and alcoholics.

2.4 Statistical analysis:

The study results were analysed using Epi Info 7 Software Version:

- Calculation of frequencies, percentage, mean and standard deviation
- Unpaired Student 't' test was applied wherever appropriate.
- p value calculation for statistical significance (less than 0.05)

III. Results

Table 1: Age distribution of ischemic stroke patients according to sex

AGE IN YEARS	PATIENTS	
	MALE	FEMALE
	NO.	NO.
< 40	-	-
40-49	8 [16%]	11 [22%]
50-59	20 [40%]	6 [12%]
60-69	13 [26%]	22 [44%]
70- 79	7 [14%]	9 [18%]
80&above	2 [4%]	2 [4%]
Total	50 [50%]	50 [50%]

The mean age of the male patients was 59.1±10.2 years and of the female patients was 60.5± 11.1years .

Table 1 showed 50% were males and 50% were females. The majority of the stroke patients were presented between 50 to 69 years accounting to 61% of patients with 33 males and 28 females.

Table 2: Distribution of serum uric acid levels among ischemic stroke patients:

SERUM URIC ACID LEVELS (mg%)	PATIENTS NUMBER (%)
< 7	75 (75%)
≥ 7	25 (25%)
Total	100 (100%)

Mean serum uric acid level in stroke patients was 5.58 ± 1.68 mg/dl. Table 2 showed Hyperuricemia (7 or more than 7 mg/dl) was present in 25% of Stroke patients. 75% Stroke patients had less than 7 mg/dl of serum uric acid.

Out of 25 hyperuricemia in stroke patients, 11 (68.8%) patients were between 70 –79 years old. Hyperuricemia was associated in 25% stroke patients with 24% (12) males and 26% (13) females.

Table 3: Age and mean serum uric acid (mg/dl) levels according to sex among ischemic stroke patients

AGE IN YEARS	MEAN SUA LEVELS \pm SD IN MALES	MEAN SUA LEVELS \pm SD IN FEMALES
40-49	4.4 \pm 1.7	4.5 \pm 0.7
50-59	5.1 \pm 1.5	4.97 \pm 1.3
60-69	5.6 \pm 1.4	5.7 \pm 1.5
70-79	7.3 \pm 1.97	7.2 \pm 1.45
80&above	8.4 \pm 0.0	4.8 \pm 0.85
'p' value	0.001; Significant (unpaired 't' test)	0.001; Significant (unpaired 't' test)

Table 3 showed the mean uric acid value for 40-49 years group was 4.46 mg/dl while the elderly age group of above 70 years had the mean value 7.2 ± 1.45 mg/dl. Age wise distribution of uric acid was found statistically significant. As age advances the uric acid level also rises with the 'p' of < 0.001 . The significance was maintained even when male and female populations were considered separately ('p' of 0.001 for males and 0.001 for females).

In the present study overall 65% patients were hypertensive and 35% patients were non hypertensive. Out of 25 hyperuricemic patients, 20 (80%) patients were hypertensive, whereas in patients with normal level of serum uric acid 45(60%) out of 75 were hypertensive. The mean uric acid level in hypertensive population was 5.78 ± 1.66 mg/dl and in non hypertensive population was 5.18 ± 1.658 mg/dl. This study does not show significant association between hypertension and uric acid.

Among the patients 51% were diabetic and 49 % patients were non diabetic. Out of 25 hyperuricemic patients 17 (68%) were diabetic, whereas in patients with normal level of serum uric acid 34 (45.3%) out of 75 were diabetic.

Table 4: Ischemic stroke patients with diabetes mellitus and mean serum uric acid levels

PATIENTS WITH DIABETES MELLITUS	SERUM URIC ACID (mg/dl) LEVEL
	MEAN \pm S.D
Present	6.12 \pm 1.64
Absent	5.02 \pm 1.54
'p' value	0.001; Significant (Unpaired 't' test)

Table 4 showed a statistically significant association ('p' value of 0.001) found between the level of uric acid and Diabetes mellitus. Among diabetic the mean uric acid value was 6.12 ± 1.64 mg/dl while among non diabetic was 5.02 ± 1.54 mg/dl.

This association was more significant among males (p value of 0.008) among whom the diabetics have 6.3 ± 1.84 mg/dl as mean uric acid level compared to non diabetics, 4.9 ± 1.55 mg/dl as mean value. But, this association was not found significant in female patients.

Out of 100 patients 32% of them had CAD and 68 % patients were without CAD. Out of 25 hyperuricemic patients, 17 (68%) patients were CAD, whereas in patients with normal level of serum uric acid 15 (20%) out of 75 were without CAD.

Table 5: Ischemic stroke patients with coronary artery disease and mean serum uric acid levels

PATIENTS WITH CAD	SERUM URIC ACID (mg/dl) LEVEL
	MEAN ± S.D
Present	6.5 ± 1.9
Absent	5.1 ± 1.4
'p' value	0.0001; Significant (Unpaired 't' test)

Table 5 showed mean uric acid level in the stroke patients with Coronary artery disease was 6.5± 1.9 mg/dl and in those without Coronary artery disease was 5.1 ± 1.4 mg/dl and thus established a statistically significant relationship (p value of < 0.0001). When males and females were considered, males have a significant association with a p value of <0.0001. Female population didn't show such association.

Out of 100 patients 34% of them had adverse lipid profile and 66 % patients had normal lipid profile. Out of 25 hyperuricemic patients 12 (48%) had adverse lipid profile, whereas in patients with normal level of serum uric acid 22 (29.3%) out of 75 had normal lipid profile.

Mean uric acid level in hyperlipidemic stroke population was 5.8± 1.87 mg/dl and compared to 5.5± 1.57 mg/dl mean uric acid level in patients without hyperlipidemia didn't show any statistically significant relationship. There was no statistically significant relationship even when males and females were analysed separately.

In the present study among 50 male patients, 34 (68%) were smokers and 16(32%) were non smokers. Out of 12 hyperuricemic patients 7(20.6%) patients were smoker. 27 (79.4%) patients were smokers had normal serum uric acid levels out of 38 patients.

Mean uric acid level in smokers was 5.25± 1.74 mg/dl and among non smokers were 5.75± 1.63 mg/dl. Thus in this study there was no statistically significant relationship between smoking and uric acid.

In the present study among 50 male patients, 19 (38%) were alcoholic and 31(62%) were non alcoholic. Out of 12 hyperuricemic patients, 4 (33.3%) patients were alcoholic. 15 (39.5%) patients were non alcoholic have normal serum uric acid levels out of 38 patients.

Mean uric acid level in alcoholic patients was 5.4± 1.83mg/dl and among non alcoholic patients was 5.6 ± 1.65 mg/dl. Thus in this study there was no statistically significant relationship between alcoholism and uric acid.

Table 6: Serum uric acid levels (in mg/dl) and size of lesion in ischemic stroke patients

SIZE OF LESION	SERUM URIC ACID (mg/dl) LEVEL	
	< 7	≥ 7
Small (< 3 cm)	63 (92.6%)	5 (7.4%)
Large (> 3 cm)	12 (37.5%)	20 (62.5%)
Total	75	25

Table 6 showed 32% of the patients have large infarct and 68% have small infarct. Out of 25 hyperuricemic (≥ 7 mg/dl) patients, 20 (62.5%) patients have large infarct in CT scan brain. 12 (37.5%) patients with large infarct have normal serum uric acid levels (< 7 mg/dl) out of 75 patients.

Table 7 : Mean serum uric acid levels and size of infarct in ischemic stroke patients

SIZE OF INFARCT	SERUM URIC ACID (mg/dl) LEVEL
	MEAN ± S.D
Small (< 3 cm)	4.816 ± 1.258
Large (> 3 cm)	7.20 ± 1.251
'p' value	0.0001; Significant (Unpaired 't' test)

Table 7 showed mean serum uric acid level in small infarct was 4.816 ± 1.258 mg/dl and in patients with large infarct mean serum uric acid level was 7.2 ± 1.251 mg/dl. The 'p' value was < 0.0001 and the results were statistically significant.

IV. Discussion

Most epidemiological studies have reported significant association between elevated SUA and increased cerebrovascular disease.^{3,4} UA is one of most important antioxidants in serum and appears to be neuroprotective in animal models, the results from human studies are controversial.⁷ Serum UA levels would change noticeably in association with degree of oxidative stress in acute ischemic stroke.

Present study was conducted on a total of 100 (50 males and 50 females) patients who were diagnosed to have acute ischemic stroke based on clinical features and CT scan of brain.

In the present study, patients were in the age group of 40- 84 years. Commonest age group observed was 50 - 69 years (61%) and the mean age was 59.8 ± 10.6 . Mean SUA in acute ischemic stroke patients was 5.58 ± 1.68 mg/dl and about 25% patients were hyperuricemic. Mean SUA value for 40-49 years age group was 4.4 mg/dl while elderly age group of above 70 years has the mean value was 7.2 mg/dl. Age wise distribution of uric acid was found statistically significant ($p < 0.001$) and the association was maintained even when both sexes were considered separately. Among diabetics the mean uric acid value was 6.12 ± 1.64 mg/dl while among non diabetics it was 5.02 ± 1.54 mg/dl, among in CAD patients it was 6.5 ± 1.9 mg/dl and in those without CAD was 5.1 ± 1.4 mg/dl; Among the patients with large infarct was 7.2 mg/dl compared to those with small infarct was 4.816 mg/dl and thus established a statistically significant relationship (p value of < 0.0001). When males and females were considered, males have a significant association with CAD ($p < 0.0001$) and diabetic ($p < 0.008$) patients. Female population didn't show such association. There was no statistically significant association between hypertension, hyperlipidemia, smoking, alcoholism and uric acid levels.

The Results Of Present Study Were Correlated With The Results Of Available Studies In Literature:

Mangal et al,⁸ Bansal et al,⁹ Masoud et al¹⁰ has reported the prevalence of hyperuricemia of 29%, 30%, 47.3% respectively in patients with acute ischemic stroke.

Milionis et al,⁴ Masoud et al,¹⁰ Patil et al,¹¹ Bansal et al⁹ has reported that mean SUA of 5.6 ± 1.7 mg/dl, 5.94 ± 1.7 mg/dl, 6.48 ± 1.92 mg/dl, 8.94 ± 2.37 mg/dl respectively in study population.

Milionis et al⁴ studied 163 patients above 70 years studied for association of SUA and stroke concludes that SUA was associated with an increased risk for acute ischemic/ non embolic stroke in elderly patients independently concludes metabolic derangements. In Patil et al¹¹ study, mean SUA value for < 50 years age group was 5.43 ± 1.98 mg/dl while elderly age group of ≥ 70 years had the mean value was 5.88 ± 1.56 . The SUA levels increased with increasing age but this correlation was not statistically significant.

Patil et al,¹¹ Longo- Mbenza et al,¹² Singh et al¹³ has reported that the serum uric acid levels were higher in diabetic patients as compared to nondiabetic stroke patients and a significant association was found between diabetic status of ischemic stroke patients and elevated uric acid levels ($p < 0.05$).

Rotterdam¹⁴ study which had 4385 participants with follow up of 8.4 years showed that SUA is a strong risk factor for myocardial infarction and stroke. A study by Freedman et al¹⁵ reported that hyperuricemia often exists in patients with ischemic heart disease and it can be a risk factor for these diseases.

Masoud et al¹⁰ has reported there was no significant association between hypertension, smoking and serum uric acid level ($p > 0.05$).

Mangal et al,⁸ Chamorro et al⁵ has reported insignificant relationship between dyslipidemia and serum uric acid in patient with acute ischemic stroke.

Patil et al¹¹ study reported that SUA levels were also higher in patients with large artery stroke as compared to those with lacunar stroke but this difference was not found to be statistically significant (6.73 ± 2.07 vs. 6.16 ± 1.68 mg/dl, $P = 0.145$).

V. Conclusions

The prevalence of hyperuricemia in acute ischemic stroke patients in present study was 25%. Age wise distribution of uric acid was found statistically significant. As age advances uric acid also rises. There was a statistically significant association between levels of uric acid and diabetes mellitus, CAD, larger infarct size patient. There was no statistically significant association among the hypertension, hyperlipidemia, smoking, alcoholism patients and uric acid levels.

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