

The Study of Serum Uric Acid Levels in Ischemic Stroke Patients

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ABSTRACT

Introduction: Stroke is defined by (WHO) World Health Organization as ‘a clinical syndrome consisting of rapidly developing clinical signs of focal (or global in case of coma) disturbance of cerebral function lasting more than 24 hour or leading to death with no apparent cause other than a vascular origin.’ There are few studies conducted in Indian scenario, which shows the role of serum uric acid in cases of acute ischaemic stroke. So the present study aimed at evaluating role of uric acid in assessing severity of acute ischemic stroke.

Material and methods: It was an Analytical, Non interventional Prospective study conducted among 100 cases of acute ischaemic stroke admitted in medicine ward and ICU at Krishna hospital, Karad over the period of 18 months, who fulfilled inclusion criteria were included in our study.

Results: In the present study, serum uric acid levels and its distribution was carried out. Mean levels of Serum Uric acid was 4.92 ± 1.89 mg/dl. Maximum value being 8.4 mg/dl and minimum value was 1.2 mg/dl.

Conclusion: The severity of acute ischaemic stroke was proved to be directly proportional to the mean serum uric acid levels in the present study.

Keywords: Acute Ischaemic Stroke, TIA, Serum Uric Acid, Hypertension, NIHSS Scale

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MATERIAL AND METHODS

It was an Analytical, Non interventional Prospective study conducted among 100 cases of acute ischaemic stroke admitted in medicine ward and ICU at Krishna hospital, Karad over the period of 18 months, who fulfilled inclusion criteria were included in our study.

Patients with more than 18 years, with CT brain / MRI brain confirmed cases of acute ischaemic stroke were included in the present study.

Whereas, Patients with known case of cardio-embolic stroke, Past history of valvular heart disease, Patients receiving drugs which are likely to alter levels of serum uric acid (diuretics, Losartan, Allopurinol), Malignancy, Renal or liver dysfunction were excluded from the present study.

All the required details about cases such as demographic data (Age, gender, address, registration number, etc), clinical presentations (signs and symptoms), general examination findings, systemic examination findings were carried out.

Investigations like Complete hemogram, Renal profile, Serum uric acid and Lipid profile were performed wherever necessary.

The NIH Stroke Scale (NIHSS) was used as a diagnostic method for quickly assessing the severity of a stroke experienced by a patient.^{3,4} In the present study, NIHSS score for the study subjects was calculated and categorized it into 5 categories:

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

STATISTICAL ANALYSIS

All the data was recorded with the help of standard case record proforma. The data was entered using Microsoft Excel software.

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How to cite this article: Shah Harsh, Patange Aparna. The study of serum uric acid levels in ischemic stroke patients. International Journal of Contemporary Medical Research 2019;6(1):A16-A20.

DOI: <http://dx.doi.org/10.21276/ijcmr.2019.6.1.19>

INTRODUCTION

Globally, stroke is third common cause for mortality and fourth leading cause for disease burden. Stroke is defined by (WHO) World Health Organization as ‘a clinical syndrome consisting of rapidly developing clinical signs of focal (or global in case of coma) disturbance of cerebral function lasting more than 24 hour or leading to death with no apparent cause other than a vascular origin.’ A transient ischaemic attack (TIA) is defined as stroke symptoms and signs that resolve within 24 hours. There are limitations to these definitions. ‘Brain Attack’ is sometimes used to describe any neurovascular event (NICE Clinical Guidelines)¹

Various risk factors are involved for development of stroke, like hyperlipidemia, hypertension, diabetes and smoking etc. Recent studies shows that there may be other factors causing the development of the disease like serum uric acid level. Identification of potential prognostic factors for ischaemic stroke may enable better prediction for outcome and conducting early interventions may improve the prognosis. Uric acid is an end product of purine metabolism in humans, is known to be relation with many systemic risk factors of stroke, such as hypertension, diabetes mellitus, insulin resistance and obesity.²

There are few studies conducted in Indian scenario, which shows the role of serum uric acid in cases of acute ischaemic

The data was analysed with the help of SPSS statistical package trial version 21. Descriptive statistics was compared with the help of tables, graphs and charts. Quantitative variables were analyzed using parametric tests (student's t-test, Z-test), whereas Qualitative variables were analyzed with the help of non-parametric statistical tests (chi-square test). Correlation methods (Spearman and Pearson's) were used to find the correlation between various parameters. The correlation between SUA levels and severity of acute ischaemic stroke was assessed using speaman's correlation methods.

RESULTS

Current study was conducted among 100 patients of acute ischaemic stroke, admitted in medicine ward and ICU at Krishna hospital, Karad. Out of total 100 study subjects, there were 76 males (76%) and 24 females (24%). The percentages of male and female are also shown in table 1.

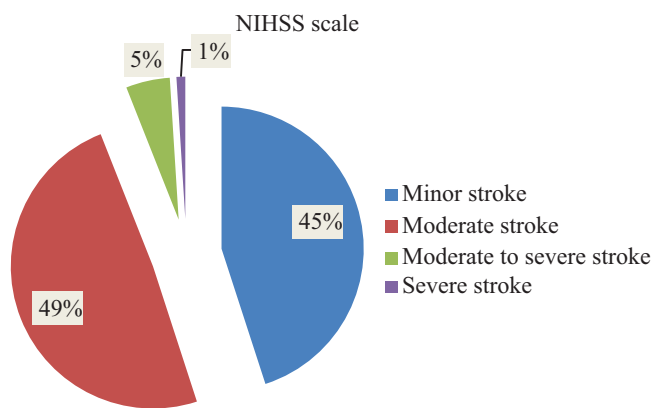


Figure-1: Distribution of cases according to NIHSS scale severity

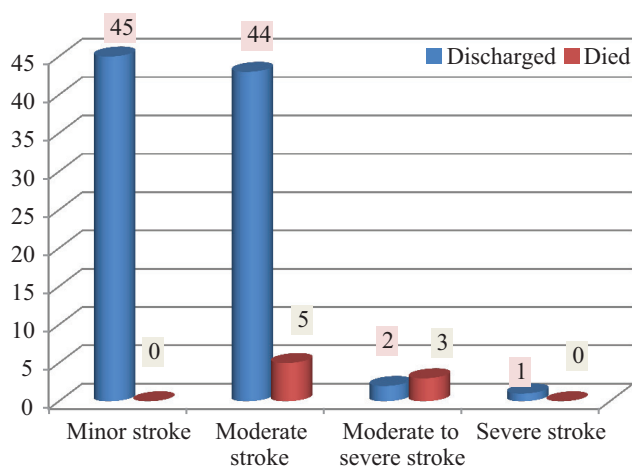


Figure-2: NIHSS Score compared with outcomes

Demographic features	(n=100)	Mean SUA Levels
Gender		
Male	76	4.98±1.95 mg/dl
Female	24	4.87±1.67 mg/dl
Age Group		
<25	1	3.4 ±0 mg/dl
26-35	5	5.38 ±1.13 mg/dl
36-45	3	4.9 ±0.95 mg/dl
46-55	12	4.59 ±1.62 mg/dl
56-65	28	4.42 ±2.10 mg/dl
66-75	32	5.05 ±1.79 mg/dl
76-85	14	5.51 ±2.09 mg/dl
>86	4	6.9 ±1.01 mg/dl
Total	100	4.96 ± 1.88 mg/dl

Table-1: Distribution of cases according to their demographic features

Hypertension on admission	(n=100)	Mean SUA levels
YES	43	5.17±1.83 mg/dl
NO	57	4.63±1.89 mg/dl
Total	100	4.92±1.88 mg/dl
T-value	1.479	
p-Value	0.35 (not significant)	

Table-2: Distribution of cases according to their hypertensive status

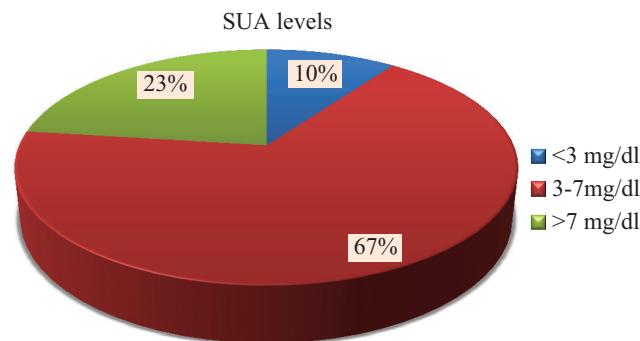


Figure-3: Serum uric acid levels parameters

Score	Stroke severity	Number of cases	Mean SUA levels	Correlation parameters
0	No stroke symptoms	0	0	r=+0.67
1-4	Minor stroke	45	3.69±0.12 mg/dl	
5-15	Moderate stroke	49	5.82±0.4 mg/dl	
16-20	Moderate to severe stroke	5	7.14±0.86 mg/dl	
21-42	Severe stroke	1	8.4±1.2 mg/dl	

Table-3: Distribution of cases according to NIHSS scale severity

Laboratory parameters Vs Clinical outcome	Mild	Mild-Moderate	Moderate	Severe
Total cholesterol	142±34.31	165.56±58.56	170.75±39.20	180.4
Triglycerides	80±53.06	98.2±40.66	116.65±54.35	113.46
HDL	51.6±13.86	48.44±13.62	49.66±13.93	40.12
VLDL	27.44±18.39	25±11.77	32.63±27.16	41.46
LDL	86.82±29.30	72.7±47.08	98.97±53.91	90.18

Table-4: mean lipid profile levels according to stroke severity (NIHSS Scale)

The mean SUA levels among males and females were 4.98 mg/dl and 4.87 mg/dl respectively. In the current study there was no significant difference between the mean SUA levels among males and females. (Table 1)

In the present study assessment of study subjects according to their age distribution carried out. Majority of the cases belonged to age group of 66-75 years (32%), followed by 56-65 years (28%), and 46-55 years (12%). Only 1 patient is in age group <25. Comparison of mean serum uric acid levels according to age distribution was carried out and showed that SUA levels were on lower side for younger age group, as compared to elderly. For the age group less than 40 years, mean SUA levels were observed between 4-5 mg/dl, whereas it was found above 5 mg/dl above age of 60 years. In the cases with age more than 86 years, Mean SUA level was 6.9±1.01 mg/dl. (Table 1)

As Hypertension is one of the important risk factor for development of stroke. Analysis of presence of hypertension among study subjects was carried out. In the present study, we classified the cases which presented with hypertension at the time of admission, as shown in table 3. 43 patients among 100 are hypertensive while 57 are not. We observed relatively higher (5.17 ± 1.83 mg/dl) mean SUA levels among the cases presented with hypertension at the time of admission as compared to non hypertensive (4.63 ± 1.89 mg/dl). The differences were not found to be statistically significant (t-value: 1.479, p value: 0.35). (Table 2)

Serum uric acid levels and its distribution was taken. Mean Serum Uric acid levels was 4.92 ± 1.89 mg/dl. Maximum value being 8.4 mg/dl and minimum value was 1.2 mg/dl. In present study majority of the cases had their serum uric acid levels between the range of 3 to 7 mg/dl (67%), followed by 23% cases with SUA levels more than 7 mg/dl, and 10% cases with SUA levels below 3 mg/dl. (Table 3)

No stroke symptoms 0 cases, Minor stroke with 45 cases, Moderate stroke with 49 cases, Moderate to severe stroke with 5 cases and single case with Severe stroke. In the present study, statistical parameters associated with NIHSS scores assessed and observed that mean NIHSS score of 6, with standard deviation of 4, minimum value of 1 and maximum value of 21. Mean SUA levels are shown in the table and figures mentioned below. Cases presented with Minor stroke had mean SUA levels 3.69 ± 0.12 mg/dl, cases with Moderate stroke had mean SUA levels 5.82 ± 0.4 mg/dl, cases with Moderate to severe stroke had mean SUA levels 7.14 ± 0.86 mg/dl and cases presented with Severe stroke had mean SUA levels 8.4 ± 1.2 mg/dl. (Table 3) (Figure 1)

In our study, assessment of serum uric acid levels according to NIHSS scale, and categorized cases according to mild to severe. When we correlated these levels using Spearman's correlation methods with severity of stroke, reflects positive correlation. (Correlation coefficient, $r = +0.6979$). (Table 3)

In order to further evaluate the cases of acute stroke, necessary investigation like Serum Uric acid, Total cholesterol, Triglycerides, HDL, VLDL, LDL were done. (Table 4). Mean total cholesterol level was 168.48 ± 48 , mean triglycerides level was 113.93 ± 53 mg/dl, Mean HDL

level was 49.1 ± 13.6 , mean VLDL level was 26.01 ± 16.1 and LDL level was 89.07 ± 40 mg/dl. (Table 4)

Lipid profile parameters of study subjects were compared with severity of the stroke (NIHSS scale). Patients presenting with moderate and severe stroke have comparatively higher levels of total cholesterol, triglycerides, VLDL and LDL than cases presenting with mild stroke. HDL levels are lower among cases of severe strokes as compared to mild stroke, which shows inverse correlation between HDL levels and severity of the stroke. (Table 4)

In the present study, outcomes among the patients were compared with serum uric acid levels. 8 cases in the present study died, while 92% cases were discharged. Comparison between mean serum uric acid levels among the cases who died and the cases discharged shown that mean SUA levels among the cases died is 7.67 mg/dl while it in cases discharged were 4.66 mg/dl. The difference was found to be statistically significant (p-value <0.005). Majority of the cases with minor stroke were discharged, whereas among the cases died, more cases belonged to moderate to severe stroke scale. (Figure 2)

DISCUSSION

The objectives for the present study was to correlate between levels of serum uric acid and severity of ischaemic stroke. 100 patients of acute ischaemic stroke admitted in medicine ward and ICU at Krishna hospital, Karad, who fulfilled inclusion criteria were included in the study.

In present study, assessment of demographic characteristics of the study population was carried out. Out of total 100 study subjects, there were 76 males (76%) and 24 females (24%). The ratio of male:females in the present study was 3.16:1. There were no significant statistical difference, when serum uric acid levels between males (4.98 ± 1.95 mg/dl) and females (4.87 ± 1.67 mg/dl) were compared.

Majority of the cases belonged to age group of 66-75 years (32%), followed by 56-65 years (28%), and 46-55 years (12%). In present study comparison of mean serum uric acid levels according to age distribution showed that SUA levels were on lower side for younger age group, as compared to elderly. For the age group less than 40 years, mean SUA levels were observed between 4-5 mg/dl, whereas it was found above 5 mg/dl above age of 60 years. In the cases with age more than 86 years, mean SUA level was 6.9 ± 1.01 mg/dl.

Tushar Patil et al cited that out of 100 patient, 63 were males and 37 were females. Male: female ratio was 1.7: 1. The controls were appropriately matched for age and sex. The mean age of cases was 60.05 ± 9.98 . Mean SUA level in cases was 6.48 ± 1.92 mg. The mean SUA was 5.94 ± 1.72 (Range 2.1 - 12 mg/ dl) for males and 5.51 ± 1.64 (Range 2.1 - 10) mg/dl for females. SUA values were higher among males as compared to females, but this difference was not statistically significant ($P = 0.085$).⁵

Study by Millinois et al quoted 163 patients above 70 years, found that serum uric acid levels are associated with increasing risk for acute ischemic/non embolic stroke

in elderly patients independently of concurrent metabolic derangement.⁶

Yu-Fang Wang et al retrospectively analysed the outcomes of 1166 patients with ischaemic stroke who were hospitalized during August 2008 to November 2012. In their study correlations of prognostic outcomes with serum uric acid were analysed. In their study mean age was 64.48 ± 13.35 year, and in male cases it was 62.65 ± 13.10 years, while for female cases it was 67.54 ± 13.22 years.⁷

Hypertension is one of the major risk factor for development of stroke. In present study analysis of study subjects presented with hypertension at the time of admission carried out. 43 patients (43%) among 100 are hypertensive while 57 are not. It observed relatively higher (5.17 ± 1.83 mg/dl) mean SUA levels among the patients presented with hypertension on admission as compared to non hypertensives (4.63 ± 1.89 mg/dl). The differences were not found to be statistically significant (t-value: 1.479, p value: 0.35).

Tushar Patil et al in their similar study cited that the mean SUA in hypertensive subjects was (6.42 ± 1.85 mg/dl) and in normotensive subjects was (5.49 ± 1.55 mg/dl) which is comparatively higher in hypertensive subjects compared to non-hypertensive subjects. This difference was statistically significant ($P = 0.00$).⁵

Milionis et al quoted SUA levels were higher in hypertensive subjects compared to non-hypertensives (5.4 ± 1.6 mg/dl vs. 5.0 ± 1.6 mg/dl, $P = 0.04$).⁶

In the present study assessment of serum uric acid levels and its distribution revealed mean serum Uric acid levels 4.95 ± 1.89 mg/dl. Maximum value being 8.4 mg/dl and minimum value was 1.2 mg/dl.

Study by Vannorsdall et al cited that a mild elevation of SUA was associated with cerebral ischemia among adults. It showed that impaired vascular tone and endothelial dysfunction may cause ischemic changes because it permits cerebrospinal fluid to cross the blood-brain barrier, which may causes areas of edema.

Khalil MI et al cited association between serum uric acid and ischemic stroke. Mean serum uric acid level was 4.94 ± 1.76 . Among them 76.7% had normal and 23.3% had abnormal serum uric acid levels. An increase in serum uric acid for 1mg/dl has a 47.0% increase in odds ratio of having ischemic stroke.⁸

In the present study, calculation of NIHSS score of the study subjects carried out and categorized it into 5 categories- No stroke symptoms 0 cases, Minor stroke with 45%, Moderate stroke with 49%, Moderate to severe stroke with 5% cases and single case with Severe stroke.

In the present study, assessment of statistical parameters with NIHSS scores carried out and observed that mean NIHSS score of 6, with standard deviation of 4, minimum value of 1 and maximum value of 21.

In the present study, assessment of serum uric acid levels according to NIHSS scale carried out, and categorized cases according to mild to severe. When correlated these levels using Spearman's correlation methods with severity of stroke, it observed positive correlation. (Correlation

coefficient, $r = +0.6979$). Patients presented with Minor stroke had mean SUA levels 3.69 ± 0.12 mg/dl, patients with Moderate stroke had mean SUA levels 5.82 ± 0.4 mg/dl, patients with Moderate to severe stroke had mean SUA levels 7.14 ± 0.86 mg/dl and patients presented with Severe stroke had mean SUA levels 8.4 ± 1.2 mg/dl

In order to further evaluate the cases of acute stroke, patients were subjected to all the necessary investigation like; Serum Uric acid, Total cholesterol, Triglycerides, HDL, VLDL, LDL Mean total cholesterol level was 168.48 ± 48 , mean triglycerides level was 113.93 ± 53 mg/dl, mean HDL level was 49.07 ± 13.6 , mean VLDL level was 34.49 ± 77 and LDL level was 92.07 ± 40 mg/dl.

In present study, lipid profile parameters of study subjects were compared with severity of the stroke (NIHSS scale). Patients presenting with moderate and severe stroke have comparatively higher levels of total cholesterol, triglycerides, VLDL and LDL than patients presenting with mild stroke. HDL levels are lower among patients of severe strokes as compared to mild stroke, which shows negative correlation between HDL levels and severity of the stroke.

Tushar Patil et al, cited a significant negative correlation between SUA levels and HDL cholesterol, and a positive correlation between SUA and serum triglyceride levels ($r = -0.334$, $P = 0.001$ for HDL and $r = 0.294$, $P = 0.001$ for triglycerides). Lehto et al. quoted that SUA level was associated with serum HDL cholesterol ($r = -0.25$, $P < 0.01$) and triglyceride levels ($r = 0.14$, $P < 0.01$). Bansal et al. cited significant correlation between SUA and triglyceride ($P < 0.05$).⁵

Hilde M Storhaug et al conducted prospective cohort study among 2696 men and 3004 women, to study uric acid as risk factor for stroke. Mean serum uric acid level in study was 357 ± 84 $\mu\text{mol/L}$ for men and 276 ± 70 $\mu\text{mol/L}$ for women. Which cited increase serum uric acid was significantly associated with increased risk of 31% for ischemic stroke in men and increased mortality risk in both genders, with 11% in men, and 16% in women, after multivariable adjustments. Gender-adjusted, multivariable analyses of pooled data from both men and women showed, for each 1 SD increase level of serum uric acid, causes 22% increased risk for ischemic stroke and increased risk for all-cause mortality up to 13%.⁹ In the present study, the outcomes among the patients were assessed and compared with serum uric acid levels and observed that 8 cases in the present study died, while 92% cases discharged. Comparison of mean serum uric acid levels among the patients who died and the patients who discharged observed that mean SUA levels among the patients who died is 7.67 mg/dl, while it in patients discharged were 4.66 mg/dl. Assessment of clinical stroke severity with outcomes in the present study observed majority of the cases with minor stroke were discharged, whereas among the cases died, more cases belonged to moderate to severe stroke scale.

Tushar Patil et al stated out of 100 patients, 13 patients died and remaining 87 patients were discharged from the hospital. The mean SUA levels were significantly higher in the patients who succumbed as compared to the patients who

were alive at discharge (8.60 ± 2.16 vs. 6.16 ± 1.68 mg/dl, $P < 0.05$).⁵ Karagiannis et al cited an independent relationship between higher SUA levels on admission and death (OR = 1.37, 95% C.I. = 1.13 - 1.67, $P = 0.001$).¹⁰

Mozos et al also cited that the patients who died had a significantly higher SUA values as compared to those who were discharged home (9.5 ± 3 mg/ dl vs. 6.9 ± 4 mg/dl, $P = 0.003$).¹¹ Only one study that was done by Chammoro et al cited that higher levels of SUA at admission were associated with better outcome after ischemic strokes. Rajeshwar K et al cited that SUA levels were significantly elevated in 54% stroke patients (> 6 mg/dL) and also high SUA levels were associated with poor outcome [adjusted odds ratio=3.86 (95% CI; 1.501-5.317) and $p < 0.001$]. The recurrence of stroke and death rate was also reported greater among the cases with elevated SUA levels.¹²

Thus present study concludes that SUA can be used as a marker for increased risk of stroke. Furthermore, SUA can also be used for risk stratification after stroke. Further long term prospective studies are needed to establish the role of SUA in ischemic stroke. Also, trial of SUA lowering drugs in stroke patients as well as in those at increased risk of stroke can be worth considering.

CONCLUSION

In present study, majority of the cases of acute ischaemic stroke were found among males, 65 being the mean age. Mean serum uric acid levels tend to increase with the age. Higher serum uric acid values were noted among the cases of higher age groups. Almost half of the patients of acute ischaemic stroke presented with hypertension, at the time of presentation. The levels of serum uric acid among hypertensive patients were not found statistically different than non hypertensive patients. The severity of acute ischaemic stroke was proved to be directly proportional to the mean serum uric acid levels in the present study. The severity of acute ischaemic stroke was proved to be directly proportional to the mean levels of lipid profile parameters (cholesterol, triglycerides, LDL) and inversely proportional to HDL levels.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 20-12-2018; **Accepted:** 02-01-2019; **Published:** 27-01-2019