



## ESTIMATION OF SERUM URIC ACID IN ACUTE ISCHEMIC STROKE AND ITS PROGNOSTIC SIGNIFICANCE

### General Medicine

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### ABSTRACT

**Introduction**-stroke is "abrupt onset of a neurologic deficit that is attributable to a focal vascular cause."

**Objective**- To study the prognostic significance of serum uric acid in acute ischemic stroke.

**Method**- the study was carried out on 100 patients of acute ischemic stroke admitted to department of medicine RIMS Ranchi.

**Conclusion**- outcome was poor with rising level of serum uric acid but no statistically significant relationship was found in between outcome of patient and hyperuricemia in patient with acute ischemic stroke.

### KEYWORDS

#### I. INTRODUCTION

Stroke is the second common cause of death in the world after coronary heart disease specially in the elderly. Evidence from epidemiological studies suggest that elevated SUA levels may predict an increased risk for stroke and cardio-vascular events<sup>1</sup>.

Stroke is the second leading cause of death worldwide, causing 6.2 million deaths in 2011 and is double the rate of heart disease in China. causes 200,000 deaths each year in the United States and is a major cause of disability. The crude stroke prevalence in different parts of India ranged from 44.29 to 559/100,000 persons during the past two decades. In general, hyperuricemia is defined as a plasma (or serum) urate concentration >6.8mg/dl. Hyperuricemia can result from increased production or decreased excretion of uric acid or from the combination of the two processes. prevalence of hyperuricemia in Indian population is about 15.8%.<sup>2</sup>

#### MECHANISM OF ACTION OF URIC ACID IN STROKE

##### Uric acid as a risk factor for stroke

Evidence from experimental studies linking , urate to atherothrombosis supports its role in the pathogenesis of stroke<sup>3</sup>. patient with hyperuricemia had great prevalence of documented atherothrombotic disease.<sup>4</sup>

strong positive association was observed between hypertension and hyperuricemia in both male and female.<sup>5</sup> Hyperuricemia has a higher prevalence (25-40%) in individuals with hypertension and has been associated with increased morbidity in these patient. Serum uric acid was associated with 31% increase in risk of stroke in men.<sup>6</sup>

Elevated SUA is an independent Predictor of hypertension and is present in the vast majority of adolescents with new-onset, untreated essential hypertension.<sup>7,8</sup> Hypertension remains the most common modifiable risk factor for stroke in the general population, including the elderly. Experimentally induced hyperuricemia has been shown to precipitate hypertension in rats via a renal mechanism related to the inhibition of nitric oxide, the activation of the renin-angiotensin system and the subsequent development of renal arteriosclerosis.<sup>9</sup> It has been also shown that uric acid promotes macrophage infiltration in atherosclerotic vessels by stimulating the synthesis of monocyte chemoattractant protein-1 in rat vascular smooth muscle cells.<sup>10</sup> Increased SUA levels promote oxygenation of LDL and facilitate lipid peroxidation.<sup>11</sup> In addition, increased SUA levels are associated with increased production of oxygen free radicals. *Li Min et al.* did a systematic review and meta analysis of 15 prospective studies indicate that hyperserum uric acid may modestly increase the risk of both stroke incidence and mortality.<sup>12</sup>

#### II. MATERIALS AND METHODS

**Population** The present study was carried out on 100 patients of acute ischaemic stroke admitted to Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi who satisfy the selection criteria. The study was conducted from June 2017 to September 2018.

**INCLUSION CRITERIA**- cases of acute ischemic stroke admitted in RIMS Ranchi.

#### EXCLUSION CRITERIA

- Patients having disease known to increase serum uric acid or taking drugs which can cause hyperuricemia were excluded from study.
- Hemorrhagic stroke, embolic stroke & Old case of Stroke were excluded from study.
- Taking Drugs which can cause Hyperuricemia.

#### METHOD

On admission in hospital detailed history was taken and thorough physical examination was performed as per Performa made. The severity of neurological deficit was recorded according to the Scandinavian Stroke Scale (SSS).

**Individual found suitable for the study were subjected to the following investigation:**

Hemoglobin, Total leukocyte count, Differential leukocyte count, Platelet count & ESR, blood sugar (fasting and post prandial), blood urea, serum creatinine, serum electrolyte, lipid profile, ECG, echocardiography, CT brain.

hyperuricemia was defined as serum uric acid level >6.8mg/dl.<sup>13</sup>

#### Scandinavian stroke scale

|                                                  |   |
|--------------------------------------------------|---|
| <b>CONSCIOUSNESS</b>                             |   |
| Fully conscious                                  | 6 |
| Somnolent, can be awakened to full consciousness | 4 |
| Reacts to verbal command but not fully conscious | 2 |
| <b>EYE MOVEMENT</b>                              |   |
| No gaze palsy                                    | 4 |
| Gaze palsy present                               | 2 |
| Conjugate eye deviation                          | 0 |
| <b>ARM, MOTOR POWER</b>                          |   |
| Raises arm with normal strength                  | 6 |
| Raises arm with reduced strength                 | 5 |
| Raises arm with flexion in elbow                 | 4 |
| Can move but not against gravity                 | 2 |
| Paralysis                                        | 0 |
| <b>LEG, MOTOR POWER</b>                          |   |
| Normal strength                                  | 6 |
| Raises straight leg with reduced strength        | 5 |
| Raises leg with flexion of knee                  | 4 |
| Can move but not against gravity                 | 2 |
| Paralysis                                        | 0 |
| <b>ORIENTATION</b>                               |   |
| Correct for time place person                    | 6 |
| Two of these                                     | 4 |
| One of these                                     | 2 |
| Completely disoriented                           | 0 |

|                                           |    |
|-------------------------------------------|----|
| <b>SPEECH</b>                             |    |
| No aphasia                                | 10 |
| Limited vocabulary or incoherent speech   | 6  |
| More than yes/no, but no longer sentences | 3  |
| Only yes/no or less                       | 0  |
| <b>FACIAL PALSY</b>                       |    |
| None                                      | 2  |
| present                                   | 0  |
| <b>GAIT</b>                               |    |
| Walks 5 m without aids                    | 12 |
| Walks with aids                           | 9  |
| Walks with help of another person         | 6  |
| Sits without support                      | 3  |
| Bedridden/wheel chair                     | 0  |

Patients were followed up during hospital stay and outcome was graded by using Modified Rankin's Scale.

#### Statistical tests

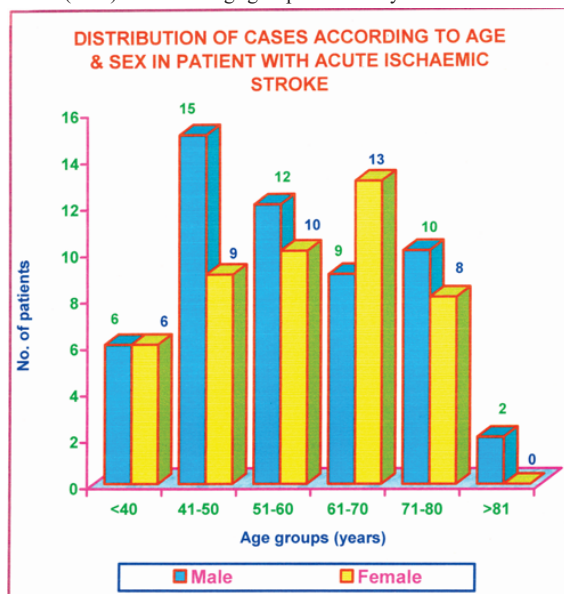
Chi square and student 't' test were applied wherever appropriate, p value < 0.05 was considered significant.

### III. OBSERVATION

**TABLE - 1 DISTRIBUTION OF CASES ACCORDING TO AGE & SEX IN PATIENT WITH ACUTE ISCHAEMIC STROKE**

| Sl. No. | Age groups (in years) | Sex      |          | Total (n=100) |
|---------|-----------------------|----------|----------|---------------|
|         |                       | Male     | Female   |               |
| 1       | <40                   | 06 (11%) | 06 (13%) | 12            |
| 2       | 41-50                 | 15 (28%) | 09 (20%) | 24            |
| 3       | 51-60                 | 12 (22%) | 10 (22%) | 22            |
| 4       | 61-70                 | 09 (17%) | 13 (28%) | 22            |
| 5       | 71-80                 | 10 (19%) | 08 (17%) | 18            |
| 6       | >81                   | 02 (04%) | 00 (00%) | 02            |
| 7       | TOTAL                 | 54       | 46       | 100           |

54% Patients were male and 46% patients were female, majority of patients (62%) were in the age group of 50 to 80 years.



**TABLE - 2 DISTRIBUTION OF CASES ACCORDING TO AGE & ITS RELATION WITH URIC ACID IN ACUTE ISCHAEMIC STROKE**

| Sl. No. | Age groups (in years) | No. of cases based on SUA level |                     | Total (n=100) |
|---------|-----------------------|---------------------------------|---------------------|---------------|
|         |                       | SUA <6.8 mg% (n=71)             | SUA >6.8 mg% (n=29) |               |
| 1       | <40                   | 11 (15.5%)                      | 01 (3%)             | 12            |
| 2       | 41-50                 | 21 (30%)                        | 03 (10%)            | 24            |
| 3       | 51-60                 | 13 (18%)                        | 09 (31%)            | 22            |
| 4       | 61-70                 | 13 (18%)                        | 09 (31%)            | 22            |
| 5       | 71-80                 | 11 (15.5%)                      | 07 (24%)            | 18            |
| 6       | >81                   | 02 (3%)                         | 00 (00%)            | 02            |
| 7       | TOTAL                 | 71                              | 29                  | 100           |

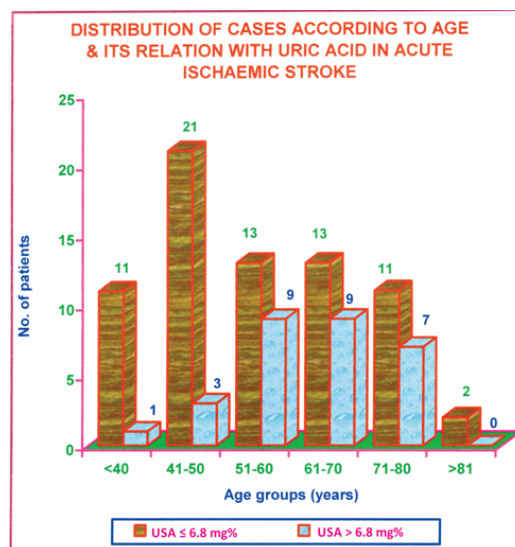
Mean age ( $\pm$ SD) of stroke patients =  $58.73 \pm 13.97$  years Mean serum uric acid ( $\pm$ SD) of hyperuricemic patients =  $9.52 \pm 2.56$  mg/dl

Mean serum uric acid ( $\pm$ SD) in patient below 60 years =  $6.01 \pm 2.93$  mg/dl

Mean serum uric acid ( $\pm$ SD) in patient above 60 years =  $6.59 \pm 2.40$  mg/dl

(<60 years vs. >60 years; chi square = 16.870; p = 0.0002; Significant)

Out of 29 hyperuricemic patient 16(55%) were above the age of 60 years as compared to patient with normal serum uric acid in whom out of 71 only 26 (37%) patients were above 60 years}

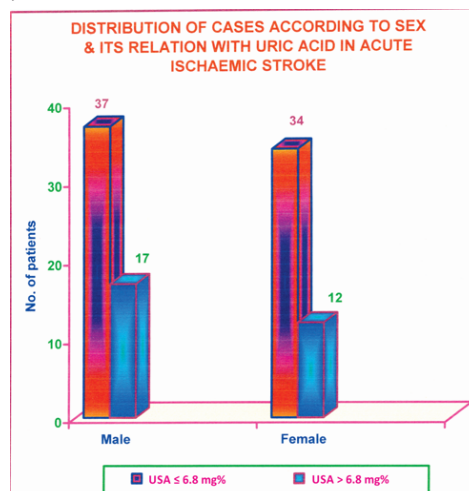


**TABLE-3 DISTRIBUTION OF CASES ACCORDING TO SEX & ITS RELATION WITH URIC ACID IN ACUTE ISCHAEMIC STROKE**

| Sl. No. | Sex    | No. of cases based on SUA level |                     | Total (n=100) |
|---------|--------|---------------------------------|---------------------|---------------|
|         |        | SUA ≤6.8 mg% (n=71)             | SUA >6.8 mg% (n=29) |               |
| 1       | Male   | 37 (52%)                        | 17 (59%)            | 54            |
| 2       | Female | 34 (48%)                        | 12 (41%)            | 46            |
| 3       | Total  | 71                              | 29                  | 100           |

Mean serum uric acid ( $\pm$ SD) hyperuricemic male =  $9.97 \pm 3.02$  mg/dl Mean serum uric acid ( $\pm$ SD) hyperuricemic female =  $8.89 \pm 1.62$  mg/dl (Male vs. female; 't' value = 1.126; p = 0.2702; non significant)

(This study includes 54 males and 46 females, males were having higher Incidence (59%) of hyperuricemia as compared to females (41%).)



**TABLE- 4 CORRELATION OF HYPERTENSION AND SERUM URICACID IN ACUTE ISCHAEMIC STROKE**

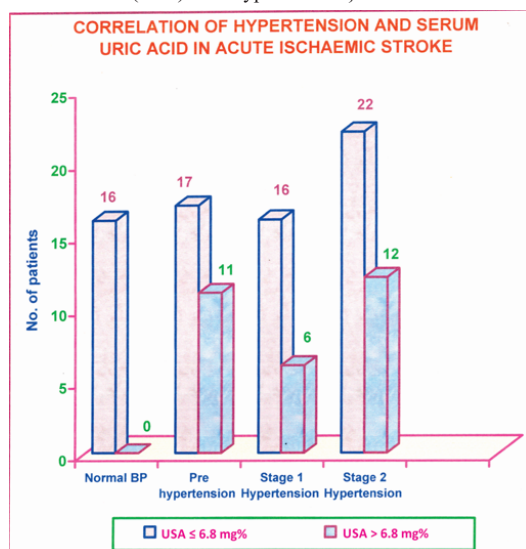
| Sl. No. | Blood pressure       | No. of cases based on SUA level |                     | Total (n=100) |
|---------|----------------------|---------------------------------|---------------------|---------------|
|         |                      | SUA <6.8 mg% (n=71)             | SUA >6.8 mg% (n=29) |               |
| 1       | Normal BP            | 16 (23%)                        | Nil                 | 16            |
| 2       | Pre hypertension     | 17 (24%)                        | 11 (38%)            | 28            |
| 3       | Stage 1 Hypertension | 16 (23%)                        | 6 (21%)             | 22            |
| 4       | Stage 2 Hypertension | 22 (31%)                        | 12 (41%)            | 34            |
| 5       | Total                | 71                              | 29                  | 100           |

Mean serum uric acid ( $\pm$ SD) amongst hypertensive  $6.30 \pm 2.64$  mg/dl

Mean serum uric acid ( $\pm$ SD) amongst non-hypertensive =  $6.19 \pm 2.85$  mg/dl

(Hypertensive vs. Non-hypertensive; chi square = 2.715; p -0.043; Significant)

None of the hyperuricemic patient was Normotensive. In 29 patient with hyperuricemia 11 (38%) were having pre-hypertension and 18 (62%) were hypertensive as compared to patient with normal serum uric acid where 38 (54%) were hypertensive.}

**TABLE-5 CORRELATION OF SERUM URIC ACID AND SSS IN ACUTE ISCHAEMIC STROKE**

| S. No. | SSS   | No. of cases based on SUA level |                     | Total (n=100) |
|--------|-------|---------------------------------|---------------------|---------------|
|        |       | SUA ≤6.8 mg% (n=71)             | SUA >6.8 mg% (n=29) |               |
| 1      | <20   | 18(25%)                         | 03(10%)             | 21            |
| 2      | 21-30 | 18(25%)                         | 06(21%)             | 21            |
| 3      | 31-40 | 19(27%)                         | 07(24%)             | 27            |
| 4      | 41-50 | 14(20%)                         | 09(31%)             | 26            |
| 5      | >51   | 02(3%)                          | 04(14%)             | 05            |

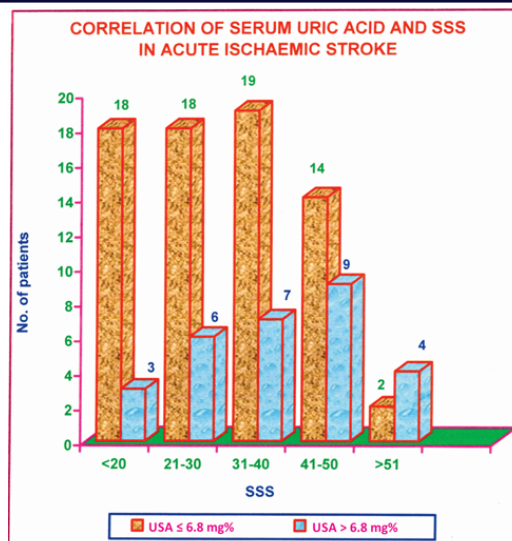
Mean SSS Score in hyperuricemic patients =  $38.31 \pm 11.31$

Mean SSS Score in normal patients =  $31.35 \pm 12.64$

(SSS <30 Vs >30;  $t^{14}$  value = 2.573 ; p = 0.0116; significant)

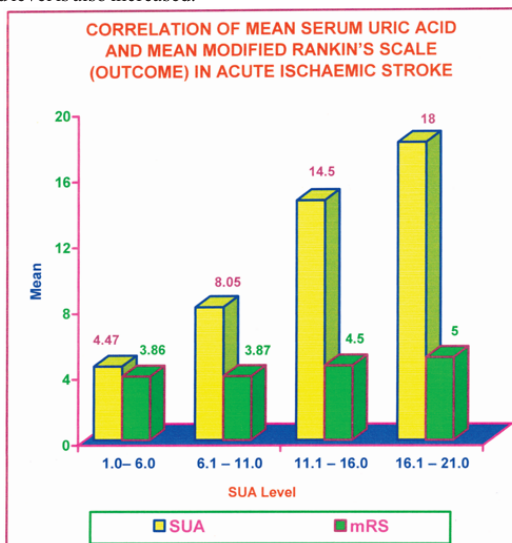
Mean SSS Score in patient with elevated serum uric acid was  $38.31 \pm 11.31$  vs.  $31.35 \pm 12.64$  in patient with normal serum uric acid p value equals 0.0116, which is statistically significant.

(Majority of patients 20 (69%) with elevated serum uric acid) were having SSS score >30 as compared to patients with normal serum uric acid who in whom only 35 (49%) were having SSS score >30}.

**TABLE - 6 CORRELATION OF MEAN SERUM URIC ACID AND MEAN MODIFIED RANKIN'S SCALE (OUTCOME) IN ACUTE ISCHAEMIC STROKE**

| SUA Level   | No. of cases | SUA (Mean $\pm$ SD) | mRS (Mean $\pm$ SD) |
|-------------|--------------|---------------------|---------------------|
| 1.0-6.0     | 57           | 4.47 $\pm$ 1.01     | 3.86 $\pm$ 1.31     |
| 6.1 - 11.0  | 40           | 8.05 $\pm$ 1.39     | 3.87 $\pm$ 1.24     |
| 11.1 - 16.0 | 2            | 14.5 $\pm$ 2.12     | 4.5 $\pm$ 0.70      |
| 16.1 -21.0  | 1            | 18.0 $\pm$ 0.00     | 5.0 $\pm$ 0.00      |
| Total       | 100          |                     |                     |

Above table shows that as mean mRS is increased, mean serum uric acid level is also increased.



## I. DISCUSSION

The study was conducted in 100 patients of acute ischaemic stroke admitted to Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi. A Detailed history and systemic examination was carried out in every patient. In each case the diagnosis was confirmed by CT scan brain. On admission patients neurological status was assessed by the Scandinavian stroke scale (SSS) and outcome was graded by using modified Rankin's scale. Serum uric acid was measured within 24 hours of onset of stroke and value >6.8mg/dl was considered hyperuricemia.

In our study the mean age of population was  $58.73 \pm 13.97$  years and majority were males 54% patients. Average serum uric acid in patient above 60 years was  $6.59 \pm 2.40$  mg/dl as compared to patient under the age of 60 years in whom mean serum uric acid level was  $6.01 \pm 2.93$  mg/dl same as study done by Tripathi V D et al<sup>15</sup>. Mean serum uric acid amongst hypertensive was  $6.30 \pm 2.64$  mg/dl and in non hypertensive it was  $6.19 \pm 2.85$  mg/dl. There was significant positive relationship was found in between hypertension and hyperuricemia ( $P < 0.05$ ) same as

*Junnn-Hong Chen et al 2009<sup>6</sup>* study. We didn't found any significant relation in diabetic Vs non-diabetics with serum normal and elevated serum uric acid level ( $p>0.05$ ).

*Chien KI et al 2008<sup>17</sup>* though found a modest relationship. Majority of hyperuricemic patients (20 patient; 69%) were having SSS score  $>30$  as compared to patients with normal serum uric acid who in whom only (35; 49%) were having SSS score  $>30$  same results were obtained in *Tripathi VD et al 2017<sup>15</sup>* study. At present study as mean serum uric acid level increased, mean modified Rankin Scale (mRS) also increased that indicating poor outcome with rise in serum uric acid.

## II. CONCLUSION

Out of all the Traditional risk factors for stroke analyzed, age, hypertension and alcoholism amongst male showed statistically significant positive correlation with hyperuricemia in patient with acute ischaemic stroke. Outcome was also poor with rising level of serum uric acid but no statistically significant relationship was found in between outcome of patient and hyperuricemia in patient with acute ischaemic stroke.

Further studies in this region are required to corroborate with the findings of this study.

## ABBREVIATIONS

|     |                                |
|-----|--------------------------------|
| A   | :Active                        |
| ACA | :Anterior cerebral artery      |
| ADA | :American diabetes association |
| CVA | :Cerebrovascular accident      |
| DM  | :Diabetes mellitus             |
| F   | :Female                        |
| HTN | :Hypertension                  |
| IHD | :Ischemic heart disease        |
| NV  | :Non-vegetarian                |
| M   | :Male                          |
| MCA | :Middle cerebral artery        |
| Mrs | : Modified Rankin's scale      |
| N   | No                             |
| PCA | :Posterior cerebral artery     |
| S   | Sedentary                      |
| Sss | :Scandinavian stroke scale     |
| SUA | :Serum uric acid               |
| UA  | :Uric acid                     |
| V   | :Vegetarian                    |
| W   | :Woman                         |
| Y   | :Yes                           |

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