ORIGINAL RESEARCH PAPER

General Medicine

STUDY OF SERUM URIC ACID LEVEL AS A PROGNOSTIC FACTOR IN ACUTE ISCHEMIC STROKE - A HOSPITAL BASED STUDY

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ABSTRACT

Background -SUA level is found to be associated with cardiovascular disease and DM. SUA role is controversial in stroke and need to be elucidated further.

Aim- To determine the importance of SUA as a prognostic factor in AIS patients.

Methods- A prospective study carried out over one year, including 72 cases of AIS. SUA levels were done on Day 1 and Day 4 and were statistically analyzed.

Results- 26.39% of stroke patients had SUA ≥ 7 mg/dl. In AIS, hyperuricemia had statistically significant association with hypertension and CAD with a p value of 0.02 and 0.044 respectively. Difference in mean MRS score at day one and day four in two groups having SUA level <7 and ≥ 7mg/dl was not significant at day one (p=0.119) but it was found significant at day four (p=0.022) indicating poor improvement or prognosis among hyperuricemic group.

Conclusions- SUA can be used for risk stratification and as an indicator of poor prognosis in acute ischemic stroke.

INTRODUCTION

Stroke is the second leading cause of death worldwide and it is also one of the leading causes of adult disability. [1] In India, stroke prevalence is 90-222 per 1 lakh people at all ages [2] and every Year 1.44-1.64 million new cases of acute stroke occur. [3] stroke or cerebrovascular accident is defined as an abrupt onset of a neurological deficit that is attributable to a focal vascular cause. A definition of stroke is clinical and laboratory studies including brain imaging are used to support the diagnosis. The clinical manifestations of stroke are highly variable because of the complex anatomy of the brain and its vasculature. Cerebral is chemia is caused by reduction in blood flow that last longer than several seconds. [4]

Numerous risk factors are involved in the development of stroke such as hypertension, CAD, smoking, dyslipidemia and diabetes mellitus. There is a need to identify these treatable risk factors that are highly prevalent and can be easily measured, in order to identify patients at high risk for stroke. Elevated serum uric acid independently predicts stroke and excess mortality in patients with non–insulin-dependent diabetes mellitus, [2] whereas in the general elderly population, it is independently associated with increased incidence of fatal stroke. [3] In diabetic patients, elevated serum uric acid is thought to play a role, along with obesity, blood pressure, and insulin resistance, in the metabolic syndrome that may be responsible for endothelial dysfunction. Over the last few years, considerable progress has been made in identifying and treating modifiable risk factors for stroke. Serum uric acid has traditionally been thought of as an inert byproduct of the catabolism of ingested and endogenous nucleoproteins and purines. [5] Epidemiological studies have suggested a direct relationship between the levels of the natural antioxidant uric acid and the risk of coronary or cerebrovascular ischemic events. [2–10] However, it is not completely clear whether this association indicates that uric acid is an independent ischemic risk factor or it represents a marker of atherosclerotic disease. If identified as an etiological agent in the pathogenesis of vascular disease, hyperuricemia could be targeted therapeutically in the same way that we now routinely treat other risk factors such as dyslipidemia and blood pressure after stroke. Whether the concentration of uric acid at the onset of ischemic symptoms influence the severity of stroke remains to be elucidated.

MATERIAL AND METHODS-
STUDY POPULATION - The study comprised of 72 patients of either sex and age 18 years or above admitted in the Department of General Medicine, Jhalawar Medical College and SRG Hospital, Jhalawar within 24 hrs of onset of first-ever-in lifetime acute ischemic stroke (with CT Scan evidence of infarction).

STUDY DESIGN- Prospective observational study.

PERIOD OF STUDY- December 2018 to November 2019.

INCLUSION CRITERIA-
Patients of either sex and age of 18 years or above, admitted in our hospital within 24 hrs of onset of first-ever-in life time AIS (with CT Scan evidence of infarction).

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 evidences 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 who were of known cardiac diseases which could be sources of emboli or whose echocardiogram shown sources of emboli.
7. Patients with hematological abnormalities like leukemia or other myeloproliferative disorders.

METHODS
After taking institutional ethical committee clearance prospective data of patients admitted with first ever AIS at Department of General Medicine, JMC, Jhalawar were collected. Thorough physical examination was performed as per proforma made. The severity of neurological deficit was recorded as per Modified Rankin Scale (mRS). NCCT head of every patient was done to confirm the diagnosis of AIS. SUA levels were measured by standard laboratory procedures on day one and day 4 and hyperuricemia was defined as SUA level > 7 mg/dl.

OBSERVATIONS AND RESULTS
Table 1: Distribution of stroke patients according to age and gender.

Age in years	Stroke patients		Total (%)
	Male (%)	Female (%)	
< 40	-	-	-

41-50	07 (17.5)	06 (18.75)	13 (18.05)
51-60	11 (27.5)	07 (21.88)	18 (25)
61-70	14 (35)	12 (37.5)	26 (36.11)
71 - 80	05 (12.5)	06 (18.75)	11 (15.28)
> 80	03 (7.5)	01 (3.13)	04 (5.56)
Total	40 (55.56)	32 (44.44)	72 (100)
Mean age	60.24 ± 6.8	63.46 ± 8.3	61.64 ± 7.4

Study participants constituted 55.56% males and 44.44% females. Mean age of stroke patients was 61.64 ± 7.4 years. Majority of stroke patients were in the age group of 61 to 70 years (36.11%).Mean age of stroke was higher in females (63.46 ± 8.3) than males (60.24 ± 6.8).

Table 2: Distribution of SUA levels in study population.

Uric Acid	Males (n=40)		Females (n=32)		Total (n=72)	
	Numbers	%	Numbers	%	Numbers	%
< 5 mg/dl	20	50.00	13	40.63	33	45.83
5 – 6.9 mg/dl	11	27.50	09	28.13	20	27.78
≥ 7 mg/dl	10	25.00	09	28.13	19	26.39
Mean ± SD	5.72 ± 1.68		5.89 ± 1.72			
P value	0.674					

25% male and 28.13% females had SUA level ≥ 7mg/dl. Mean SUA level was 5.72 ± 1.68 mg/dl among males and 5.89 ± 1.72 mg/dl among female patients although this difference is not statistically significant (p=0.674). Statistically significant association was found between age and mean SUA level (p=0.0001) and this association was maintained even when male and female populations are considered separately (p <0.05).With increase in age, mean SUA level is also increasing.

Table 3: Association of SUA level with various risk factors.

Risk factors	Uric acid (mg/dl)				P value
	< 7 mg/dl (n=53)		≥7 mg/dl (n=19)		
	Number	%	Number	%	
Age					
≤60	15	28.30	11	57.89	0.012
>60	38	71.70	8	42.11	
Gender					
Male	31	58.49	10	52.63	0.75
Female	22	41.51	9	47.37	
Hypertension					
Present	29	54.72	15	78.95	0.02
Absent	24	45.28	4	21.05	
DM					
Present	24	45.28	11	57.89	0.35
Absent	29	54.72	8	42.11	
CAD					
Present	11	20.75	9	47.37	0.044
Absent	42	79.25	10	52.63	
Dyslipidemia					
Present	22	41.51	6	31.58	0.305
Absent	31	58.49	13	68.42	
Smoking					
Present	14	26.42	5	26.32	0.744
Absent	39	73.58	14	73.68	
Alcohol					
Present	15	28.30	5	26.32	0.681
Absent	38	71.70	14	73.68	

Hypertension constituted the major risk factor in stroke population, found in 68.06% of the population out of which 70.0% were males and 65.63% were females. The mean SUA level is 5.68 ± 1.71 mg/dl and 5.12 ± 1.24 mg/ dl respectively in hypertensive and normotensive population respectively

and no significant association was seen between hypertension and mean SUA (p=0.164).

51.39% of the study population are diabetics and found in 55.0% of males and 46.88% of females. Mean SUA level was 6.01 ± 1.75 mg/dl and 4.92 ± 1.59 mg/dl among Diabetics and Non-Diabetics respectively and it was found to be statistically significant association (p= 0.007).

CAD was present in 33.33% of the population with 27.50% males and 40.63% females. Patient with CAD and without CAD had mean SUA level 6.42 ± 1.74 mg/dl and 5.14 ± 1.41 mg/dl respectively which establishes a statistically significant relationship (p= 0.001).

34 % of the stroke population had dyslipidemia and both sexes share equal number of dyslipidemic patients (13 each). Mean SUA level was 5.78 ± 1.84 mg/dl and 5.29 ± 1.58 mg/dl among patients with and without dyslipidemia respectively and is statistically not significant r (p= 0.237).

42.50% of males and 12.50% of females were smokers while 37.50% of male and 9.38% of females consumed alcohol. Smoking and alcohol consumption did not show statistically significant association with mean serum uric acid level (p=0.311 and p=0.695 respectively).

Table 4: Distribution of stroke patients according to Modified Rankin's Scale score among two groups of serum uric acid level on Day 1 and Day 4.

MRS Scale	Uric Acid Level at Day 1		Uric Acid Level Day 4	
	< 7 mg/dl	≥7 mg/dl	< 7 mg/dl	≥7 mg/dl
0	0 (00%)	0 (00%)	00 (00%)	0(00%)
1	6 (11.32%)	1 (5.26%)	12(22.64%)	1 (5.26%)
2	7 (13.21%)	2 (10.53%)	19(35.85%)	3 (15.79%)
3	12 (22.64%)	5(26.32%)	17(32.08%)	4 (21.05%)
4	16 (30.19%)	6 (31.58%)	4 (7.55%)	6 (31.58%)
5	12 (22.64%)	5 (26.32%)	1 (1.89%)	4 (21.05%)
6	0 (00%)	0 (00%)	0(00%)	1(5.26%)
Total	53	19	53	19
	P value 0.785		P value 0.045	

Table 5: Comparison of mean Modified Rankin's Scale score at day 1 and day 4.

Uric Acid Level	Mean of MRS score at day one	Mean of MRS score at day four
< 7 mg/dl	3.42 ± 1.04	2.63 ± 1.08
≥7 mg/dl	3.82 ± 1.10	3.21 ± 1.12
P value	0.119	0.022

At day one, Patients with serum uric acid level ≥7 mg/dl presented with higher MRS score (mean MRS score=3.82 ± 1.10) compared to patients with serum uric acid level below 7 mg/dl (mean MRS score=3.42 ± 1.04), although this difference was found to be statistically insignificant (p=0.785). At day four, 57.89% (11) stroke patient in group of serum uric acid level ≥7 mg/dl had MRS score 4 and above, which indicate poor prognosis in comparison to group who had serum uric acid level <7 mg/dl (05, 09.43%) and this difference in MRS score in both groups was found statistically significant at day four (p=0.045).

DISCUSSION-
Present study was carried out in the Department of General Medicine, SRG Hospital attached with JMC, Jhalawar in Rajasthan. Total 72 patients of more than 18 years of age admitted in Medicine department during December 2018 to November 2019 with first-ever-in life time acute ischemic non-embolic stroke were enrolled in study.

Out of 72 patients 55.56% were males and 44.44% were females. Similar results were observed by **Xia Zhang et. al [11]**. Mean age of stroke patients was 61.64 ± 7.4 years and

majority of stroke patients were in the age group of 61 to 70 years (36.11%). Mean age of stroke was higher in females (63.46 ± 8.3) than in males (60.24 ± 6.8). **Xia Zhang et. al [11]** and **Tavish Arora et. al [12]** observed that the mean age of the patients was 64.6 ± 12.8 years and 63.2 ±14 years respectively (uric acid level ≥ 7mg/dl). Overall prevalence of hyperuricemia was 26.39% among stroke patients. In concordance to this **Bansal et al.[** 13] reported 30% prevalence of hyperuricemia patient with acute ischemic stroke, with mean SUA of 6.5 ± 1.19 mg/dl and mean age of presentation as 59.40 ± 12.15 years.

Prevalence of hyperuricemia (uric acid level ≥ 7mg/dl) was higher among females and seen in 25% and 28.13% of male and females respectively. Mean SUA level was 5.72 ± 1.68 mg/dl and 5.89 ± 1.72 mg/dl among male and female patients respectively although this difference was not statistically significant (p=0.674). In concordance to our study, **Tavish Arora et. al [12]** observed that SUA levels were significantly higher among females (6.2 ± 1.9) compared to the males (5.2 ±1.6) while **Millinois et. al [14]**, **Xia Zhang et. al [11]** and **Waring et al** [15] found high levels of SUA in males as compared to females which is in contrary to present study results. Statistical significant association was found between age and mean SUA level (p=0.0001) and this association was maintained even when male and female populations were considered separately (p <0.05). With increase in age, mean SUA level is also increasing. This finding is match with **B Balaji et. al [16] and Millinois et al** [14].

Hypertension constituted the major risk factor (68.06%) in stroke population with 70.0% males and 65.63% females being hypertensive but no significant association was found between hypertension and mean SUA (p=0.164). Same was observed in study by **Xia Zhang et. al [11].**

Diabetics had mean SUA level of 6.01 ± 1.75 mg/dl while among non-diabetics it was 4.92 ± 1.59 mg/dl and this association is statistically significant (p= 0.007). Our results are in concordance with results of **Tushar et. al [17]** and **Newman et. al [18].** Also **Lehto s et al** [19] in his study concluded that hyperuricemia is a strong predictor of stroke events in middle aged persons with NIDDM, independently of other CV risk factors.

CAD was seen in 33.33% of the population with mean SUA level of 6.42 ± 1.74 mg/dl and 5.14 ± 1.41 mg/dl among those with CAD and those without CAD respectively which establishes statistically significant relationship (p= 0.001). Same was observed in Rotterdam study by **Michiel J. Bos. Et. al** [20]

Mean SUA level was 5.78 ± 1.84 mg/dl and 5.29 ± 1.58 mg/dl among patients with and without dyslipidemia respectively and is statistically not significant r (p= 0.237). **Astrios Kargiannis et al** and **Horestein RB et at** [21,22] in their studies concluded that increased SUA levels correlated with low HDL-C levels.

Smoking and alcohol consumption did not show statistically significant association with mean uric acid level with p=0.311 and p=0.695 respectively. Similar results were observed by **B Balaji et. al** [16]

In our study, Difference in mean MRS score at day one in two groups having SUA level <7 and ≥ 7mg/dl was not significant at day one (p=0.119). This is in concordance with results of **B Balaji et. al [16]** who observed that mean mRS score in patients with elevated serum uric acid was 3.82 mg/dl Vs 3.41mg/dl in patient with normal uric acid (*P*>0.05 & statistically insignificant) but difference in mean MRS score was found to be statistically significant at day four (p=0.022) indicating poor improvement or prognosis among hyperuricemic group (serum uric acid level ≥7 mg/dl).

CONCLUSION: -

Hyperuricemia had significant association with age >60 years, hypertension and CAD. Considering higher mRS score (poor prognosis) among hyperuricemic patients and significant association between both elevated SUA can be considered as one of the prognostic indicator for acute ischemic non-embolic stroke.

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