Research On Serum Uric Acid In Acute Ischemic Cerebrovascular Stroke

Dr. Anokhi Shah*, Dr. Parth Shah*, Dr. Nirmal Patel*, Dr. Nilesh Docter**

*Resident Doctor, **Associate Professor Department Of General Medicine, SMIMER, Surat, Gujarat

Abstract: Background: The role of uric acid as a risk factor for vascular disease and acute stroke is controversial and there is little information about it. In this study, we determined serum uric acid levels in patients with acute ischemic CV stroke and assessed its relationship with cerebrovascular risk factors. Material And Methods: In this cross sectional study, we have assessed patients with acute ischemic CV stroke who were admitted in SMIMER Hospital from September 2018 to March 2019. Clinical records of patients and their serum uric acid level was investigated. Finally, the collected data was analysed using SPSS software Ver.16. Result: 73 patients with acute stroke were evaluated, 26 of these patients were female and 47of those were male. The mean age of patients was 57.57 ± 1.89 years. Mean serum uric acid levels in the patients studied was 6.72 ± 0.43 mg/dL, and about half of the patients (53%) were hyperuricemic. There was a significant negative correlation between age of patients and their serum uric acid level ($p > 0.05$). Uric acid level was significantly higher in men than women ($p < 0.05$). Hyperuricemia was associated with increased amounts of triglycerides and low-density lipoprotein (LDL) cholesterol ($p<0.05$). In patients with acute ischemic stroke, there was no significant association between serum uric acid level and diabetes mellitus, hypertension, smoking. Conclusion: Due to the high prevalence of hyperuricemia in patients with acute ischemic stroke, and its accompanying increase in other modifiable risk factors of atherosclerosis, it can be considered as a risk factor for acute ischemic stroke. [Shah A Natl J Integr Res Med, 2020; 11(5):50-55]

Key Words: Uric acid, acute ischemic CV stroke

Author for correspondence: Dr. Parth Shah, Resident Doctor, A9/ Sachchidanand Society, Adajan, Surat - 395009 E-Mail: tresconium@gmail.com

Introduction: A stroke, or cerebrovascular accident, is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause. Thus, the definition of stroke is clinical, and laboratory studies including brain imaging are used to support the diagnosis[1]. The aetiology of ischemic stroke is multifactorial, and therapeutic actions focused on vascular risk factors, particularly in secondary stroke prevention have been shown to reduce the risk of recurrent stroke, as well as the risk of any other coronary or peripheral vascular episode[2].

The scientific literature shows that elevated serum acid uric level was strongly associated with metabolic syndrome, type 2 diabetes, early stage kidney injury and progressive renal disease, all of which could lead to atherosclerosis progression, acute cardiovascular events and greater mortality[3]. Hyperuricemia is defined as a plasma (or serum) urate concentration >7 mg/dl in male and >6 mg/dL in female. Epidemiological studies have suggested a direct relationship between the levels of the natural antioxidant uric acid and the risk of cerebrovascular and coronary ischemic events. 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. Whether the concentration of uric acid at the onset of ischemic symptoms influences the severity of stroke also remains to be elucidated. Very few studies are done to see the association of serum uric acid in patient of acute ischemic cardiovascular stroke. Our purpose of the study is to see the association of serum uric acid in patient of acute ischemic cardiovascular stroke.

Aims And Objectives: To find out the association of serum uric acid with acute ischemic CV stroke severity. To find out uric acid variation related to gender and age. To study uric acid level in patients of acute ischemic CV stroke with diabetes and hypertension.

Material & Methods: A total of 73 patients aged between 25 to 90 years, who were admitted in SMIMER hospital (Surat, Gujarat) were evaluated in the cross sectional study. The patients recruited from September 2018 to March 2019 satisfying the inclusion criteria after having clearance from ethical committee for study. All patients were informed and the consent was obtained from all patients.

With informed consent of subjects, subjects were enrolled in our study. Confidentiality of subjects were maintained and subjects who had complications were given treatment under guidance of specialist, and whenever surgical interventions were required subjects were referred to a vascular surgeon.

Inclusion Criteria: All patients who presented within 48 hours of onset of stroke whose CT scan or MRI evidence of acute ischemic CV stroke and who gave informed consent to participate in the study. Patients with stroke as defined by WHO criteria "Rapidly developing clinical signs of focal or global (coma) neurological deficit lasting more than 24 hrs. or leading to death with no apparent cause other than vascular origin and CT scan or MRI evidence of acute ischemic CV stroke. "

Exclusion Criteria: Patients with Sub arachnoid hemorrhage, extradural hemorrhage subdural haemorrhage and intra cerebral hemorrhage were excluded by CT, Patients with previous history of TIA/RIND, Patients with gout or show clinical evidences of gout, Alcoholics, Patients taking drugs causing hyperuricaemia. like Loop diuretics, Anticancer drugs (Cisplatin, Cyclosporine, Cyclophosphamide), AKT (Pyrazinamide, Ethambutol), Aspirin, Pentamidine, Theophylline, Ketoconazole, Levodopa, Isotretinoin, Patients who were of known cardiac diseases which could be sources of emboli or whose echocardiogram shown sources of emboli , Kidney disease, Patient on medication to reduce oxidant levels, Hypothyroidism, Inflammatory diseases, Steroid therapy, Patients with hematological abnormalities like leukemia or other myeloproliferative disorders, Selected patients who had no history of any cardiovascular events and were not on lipid lowering drugs.

The socio demographic, clinical, laboratory parameters and outcome data are collected. This included age of the patients, sex, and time of hospitalization after stroke.

Clinical data included recording of vital parameters, the type of stroke, conscious level of the patients assessed by the NIHSS score and complete neurological examination.

Laboratory parameters, as mentioned in the patient's proforma included complete blood count, renal function tests, serum uric acid, fasting blood sugar, lipid profile and CT scan or MRI of brain carried out on admission.

The serum uric acid level is measured in the stroke patients within 24 hours of admission. All study participants had blood samples taken the first day of admission and uric acid test is done by the uri case method. Neurological impairment disability and severity was measured at baseline with the use of NIHSS stroke scale.

The NIHSS is composed of 11 items, each of which scores a specific ability between a 0 and 4. For each item, a score of 0 typically indicates normal function in that specific ability, while a higher score is indicative of some level of impairment. The individual scores from each item are summed in order to calculate a patient's total NIHSS score.

The maximum possible score is 42, with the minimum score being a 0 – 1. NIHSS is known to be useful for both clinical prognosis and investigative research of stroke.[4]

Score And Stroke Severity:

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

Statistical Analysis: Collected data were analyzed through SPSS version 20.0 (IBM Corp., NY). Descriptive variables were reported through mean with standard deviation and proportion. The association of the continuous variables was estimated by Student's t-test while that of the categorical variables was computed through Chi-square test. Pearson's correlation coefficient was used to find the correlation. $P < 0.05$ was considered significant.

Results: 73 acute ischemic CV stroke patients were studied, of whom 47 were males and 26 females. The mean serum uric acid level in males was 7.1 ± 0.41 mg/dL and in females was 5.92 ± 1.15 mg/dL which was significantly higher in male than female. Mean age of the study group was 57.57 ± 1.89 years.

Out of 73 subjects who were enrolled in the study, 23 (31%) patients were known case of diabetes, 38 (52%) were hypertensive, 32 (43%) were smokers.

In my study, 73 patients have acute ischemic stroke, 50 patient had hyperuricemia and prevalence is 53%. Mean serum uric acid levels in the patients studied was 6.72 ±0.43 mg/dl, and about half of the patients (53%) were hyperuricemic.

Table 1. Uric Acid Concentration On Admission In Relation To Demographics And Risk Factors

	Yes	No	P value
Age ≤50 years	6.55 ± 1.09	6.74 ± 0.086	0.4172
Male	7.1 ± 0.41	5.92 ± 1.15	0.0001
Diabetes	6.75 ± 0.72	6.64 ± 1.03	0.6465
Hypertension	6.86 ± 0.64	6.48 ± 1.16	0.7813
Smokers	6.68 ± 1.02	6.68 ± 0.89	0.999
Cholesterol >200	7.21 ± 0.34	6.07 ± 1.04	0.0001
TG >150	7.24 ± 0.34	6.07 ± 1.04	0.0001
HDL >40	6.54 ± 0.97	7.2 ± 0.57	0.001
LDL > 120	7.16 ± 0.42	6.1 ± 1.07	0.0001
Dyslipidemic (Triglyceride>150 mg/dl & LDL > 120 mg/dL)	7.25 ± 0.35	6.82 ± 0.41	0.016

Table 2. Relationship Between Risk Factors And Stroke Severity And Disability At Presentation Using NIHSS In Acute Ischemic CV Stroke Cases

	Mean NIHSS Scores At Presentation		P value
	Yes	No	
Age ≤50 years	17.44 ± 10.28	25.64 ± 8.5	0.005
Male	22.29 ± 9.83	23.80 ± 10.13	0.5361
Diabetes	28.56 ± 6.97	18.48 ± 9.61	0.0002
Hypertension	27.10 ± 7.31	15.74 ± 9.19	0.0001
Smokers	26.65 ± 9.0	17.75 ± 9.04	0.0081
Dyslipidemic (Triglyceride >150 mg/dL and LDL > 120 mg/dL)	22.77 ± 10.02	20.30 ± 9.96	0.2969
Hyperuricaemia	23.87 ± 9.75	19.11 ± 9.81	0.041

Table 3. Prevalence Of Hyperuricemia In Acute Ischemic CV Stroke Case

Case	No Of Case	No of case with Hyperuricemia (Male >7mg/dL , Female>6mg/dL)	Prevalence
Total Number Of Acute Ischemic CV Stroke Case	73	39	53%
Total Number Of Acute Ischemic CV Stroke Case in male	47	28	59%
Total Number Of Acute Ischemic CV Stroke Case in female	26	11	42%
Total Number Of Acute Ischemic CV Stroke Case With Hypertension	38	23	60%
Total Number Of Acute Ischemic CV Stroke Case With Diabetes	23	15	65%
Total Number Of Acute Ischemic CV Stroke Case With DM + HTN	16	10	62%
Total Number Of Acute Ischemic CV Stroke Case Smoking	32	19	60%

Statistically significant association was found between gender and uric acid level (P <0.05) and dyslipidemia and uric acid (p<0.05). Though the serum uric acid level was higher in subjects who were > 50 years of age, Hypertensive, diabetic, smokers but the difference was not statistically significant.

Discussion: In this study, we determined the serum uric acid levels in patients with acute

ischemic CV stroke. Mean serum uric acid level was 6.72 ± 0.43 mg/dL and about half of the patients were hyperuricemic. According to a large 10 years follow up study the prevalence of hyperuricemia in the United States is 20.1%[5]. Another large study in Bangkok population showed that prevalence of hyperuricemia is 24.4% and a study in a developing country reported the prevalence of hyperuricemia is 35.2% in men and 8.7% in women[7]. According to these studies prevalence of hyperuricemia is significantly higher in patients with acute stroke than normal population.

Stroke is the one of the main clinical manifestation of CVD and studies investigating the relationship between the uric acid and stroke have been inconsistent. Some studies reported a positive independent relationship between uric acid and stroke whereas others demonstrated that uric acid did not relate significantly to stroke occurrence.

Bansal et al studied 50 patients with ischemic thrombotic cerebrovascular disease: 30% of the cases showed hyperuricemia and they concluded that elevated serum uric acid level may be playing a role in the causation of ischemic thrombotic cerebrovascular disease in general and especially in patients below 40 years of age[8].

Kim et al conducted a systematic review and meta-analysis of 16 prospective cohort studies including 238449 adults to assess the association between hyperuricemia and risk of stroke incidence and mortality. They found that hyperuricemia may modestly but statically significantly increase the risk of both stroke incidence and mortality[8]. According to results of Milionis et al study, elevated serum uric acid levels associated with increased risk of acute ischemic stroke in the elderly[9] ,there is some explanations for discrepancies; there are several limitations including the study design, the population studied (different ethnicities with different CVD risk) and the confounders measured[8].

In our study, mean age of acute ischemic CV stroke patient was 57.57 ± 6 years. Though Sheik et al study[14] found positive correlation with age and hyperuricaemia, our study couldn't find statistically significant association due to less number of subjects above 70 years. Similar to the previous studies, our study showed that the significant differences in uric acid level between men and women. In the other word, uric acid level was significantly higher in men than women [11, 12, 13] and difference was statistically significant.

In our study mean serum uric acid in female, which was lower than in men, was thought to be related to a higher renal clearance of uric acid in women, possibly due to their higher plasma estrogen levels. The higher prevalence of stroke among males may be due to more smoking and more stressful situations in males than females. Conen et al demonstrated that prevalence of hyperuricemia is higher in men than women and higher alcohol consumption in men may be the cause of this difference[7].

In this study, there was no significant association between serum uric acid level and diabetes mellitus, hypertension and smoking. In contrast some previous studies reported significant association between insulin resistant, systolic and diastolic blood pressure and serum uric acid levels. A study by Bonora et al showed that there is no significant association between smoking and uric acid level[13].

In this study, there was significant association between serum uric acid level and serum triglyceride, total cholesterol, HDL cholesterol and LDL cholesterol and hyperuricemia was associated with them. Bonora et al[13] studied 957 young men and demonstrated that there was a significant positive correlation between serum uric acid levels and levels of serum triglyceride, total cholesterol and LDL cholesterol. Moreover, Chammaro et al reported the association between serum uric acid level and amount of serum triglyceride[10].

The mechanism of this strong association between serum uric acid levels and triglyceride levels is still poorly understood. Most of the researchers believe that hyperuricemia and hypertriglyceridemia may reflect the patient's life style as a part of metabolic syndrome[7].

In our study, prevalence of hyperuricemia in patients with acute ischemic CV stroke was 53% while in Tripathi et al study[15] prevalence of hyperuricemia was 29%, whereas In Bansal et al study [8] the prevalence of hyperuricemia was 30% in patient with acute ischemic stroke. Similar to

our study, prevalence of hyperuricemia significantly higher in males than females, was also seen in Tripathi et al study[15] and Arora et al study[16].

Prevalence of hyperuricemia was higher in diabetic and hypertensive in our study but similar results were not found in studies conducted by Tripathi et al study[15] and Bansal et al study.[8] Though higher prevalence of hyperuricemic in dyslipidemia cases were found in all studies.

In our study, mean NIHSS score was higher in age > 50 years compare to age ≤ 50 years and was statistically significant. Similarly results were also found in Soliman et al[18] study. In our study, mean NIHSS score was higher in female compare to male but difference was not statistically significant, which was also seen in Soliman et al [18] study.

In above table, our study shows mean NIHSS score in diabetic (26.56) cases was higher compared to non-diabetics and was statistically significant, while in Soliman et al[18] did not find same association. This may be due to small sample size and variable age distribution. In our study, mean NIHSS score was higher in smokers and in patinets with dyslipidemia and difference was not statistically significant like that seen in Soliman et al[18] study.

Our study has some limitations. First, this study was cross-sectional descriptive, we can assess the association between uric acid level and incidence of stroke if we used cohort study.

In addition, we didn't consider a control group; if we used the control group we can assess the risk factor of stroke incidence and their association with serum uric acid levels. Therefore, further studies will be a cohort prospective and will include use the control group beside case group.

Conclusion: Our study showed that prevalence of hyperuricemia in patients with acuteischemic stroke was higher. Uric acid level was significantly higher in men than women. As age advanced, chances of acute ischemic CV stroke increased.

Serum uric acid level was high in diabetic and hypertensive patients. Patients, who had higher serum uric acid levels, had more severe acute ischemic CV stroke. Patients, who had dyslipidaemia, had higher serum uric acid level. Acute ischemic CV stroke patients with elevated uric acid had more severity and it was statistically significant.

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