DOI: 10.47799/pimr.1101.05

Estimation of serum uric acid level in acute ischemic stroke

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Date of Submission: 25/03/2022 Date of Review: 26/06/2022 Date of Acceptance: 15/08/2022

ABSTRACT

Background: The impact of uric acid as a stand-alone risk factor for non-communicable illness has been debated for decades. Strong free radical scavengers like hydroxyl ions, peroxynitrite, and other antioxidants like ascorbic acid are all scavenged by serum uric acid. Neuroprotective agents include uric acid and its connection to ischemic stroke is still debatable. Therefore, the current study tried to evaluate the serum uric levels in acute ischemic stroke patients.

Methods: Patients with acute stroke were included in the trial, thus if rTPA was given to them, it was noted. The patient's baseline blood pressure was taken (in a supine position). All acute stroke patients had blood drawn within 24 hours of admission to assess their lipid profiles, fasting blood sugar levels, and uric acid levels. A neurologist assessed each patient, and computer tomography (CT) and magnetic resonance imaging were used to distinguish between ischemic stroke and other types of stroke (MRI).

Results: Serum UA levels were found to be significantly higher in stroke patients, with 77.5 percent of patients having high levels (>6 mg/dL) compared to 30.0 percent of controls. When compared to the controls, the mean serum UA level in patients was considerably higher (p=0.0212). Multiple logistic regression analysis was used to determine the relationship between serum UA levels and outcome. Independent of other prognostic criteria, patients with high serum UA levels had a significantly worse outcome.

Conclusion: A significant relationship exists between high serum UA levels and ischemic stroke, stroke subtypes (excluding lacunar stroke), and poor outcomes. Finding and managing modifiable risk factors for stroke has advanced quite a bit. Hyperuricemia could be therapeutically targeted in the same manner that other risk factors, such as dyslipidemia and blood pressure, are regularly treated after stroke.

KEYWORDS: Serum Uric Acid, Acute Ischemic Stroke, Hyperuricemia, Dyslipidemia

INTRODUCTION

Stroke is thought to be the second biggest cause of death after heart disease and is a significant factor in the loss of disability-adjusted life years (DALYs) globally. [1] According to figures from around the world, strokes and ischemic heart disease contributed to approximately 15.2 million deaths in 2015. [1] In 2017, 57.9 million DALYs were lost due to intracerebral hemorrhage, while 47.8 million were lost due to ischemic stroke. [2] Strokes can be avoided. Numerous modifiable risk factors have been widely documented in the prevention and treatment of stroke, including hypertension, diabetes mellitus, atrial fibrillation, dyslipidemia, smoking, obesity, lack of physical exercise, etc. [1] However, worldwide, the number of stroke events, survivors, and deaths from stroke-related causes as well as DALYs is still rising. [3] Because of this, deeper comprehension of extra potential risk variables is required to design new preventive strategies for stroke. In humans and higher primates, uric acid is the final catabolite in the purine metabolism. [4] It exists as sodium urate in the extracellular compartment and is eliminated from the plasma through the kidney. [5] Age and sex have an impact on uric acid levels. Before puberty, both boys and females have an average blood uric acid level of 3.6 mg/dl. The value increases to adult levels after puberty, with women typically having 1 mg/dl less than men. This lower amount in women appears to be due to an increase in renal urate clearance caused by estrogen. [4] It has been shown that higher uric acid levels are linked to well-known cardiovascular risk factors such as metabolic syndrome, hypertension, obesity, and raised blood triglyceride and cholesterol concentrations. [5] Uric acid, on the other hand, has a history of acting as a free radical scavenger and exerting neuroprotective benefits. [5, 6] Uric acid contributes roughly 50% of the antioxidant capacity of plasma in humans. [6, 7] Depositions of uric acid as monosodium urate (MSU) crystals in the first metatarsophalangeal joint and other diverse joints, tendons, and tissues throughout the body have long been recognized as a key cause of gouty arthritis. Only 10% of gout cases are caused by increased uric acid production, while 90% of cases are caused by renal under-excretion of uric acid. [8] It is debatable, though,

whether hyperuricemia poses a significant threat to the development of stroke. Numerous prospective studies have examined the connection between blood uric acid levels and the frequency of strokes during the past few decades, but the findings have been inconsistent. Uric acid is a free radical scavenger and antioxidant that shields the brain from oxidative damage, preventing worse post-stroke neurological outcomes, according to numerous studies. [9, 10] While numerous other research has demonstrated that hyperuricemia is to blame for the rise in the incidence and mortality of stroke. [11–13] This discrepancy is caused by the different sample sizes, and characteristics of the representative population, such as regional disparities, ethnic differences, gender differences, age differences, socioeconomic issues, and the research techniques used. we conducted this study to address this discrepancy, offer an extensive estimation of the potential association between serum uric acid, stroke event, stroke mortality, and confirm if hyperuricemia is a risk factor for stroke.

MATERIAL AND METHODS

This cross-sectional study was conducted in the Department of General Medicine, Prathima Institute of Medical Sciences, Nagunur, Karimnagar, Telangana State. Institutional Ethical committee approval was obtained for the study. Written consent was obtained from all the participants of the study after explaining the nature of the study in the local language.

Sample size: n=4pq/d^2

Where n=sample size, p=prevalence taken as p=5, q= 95, d=absolute error

n=4*5*95/49=38 (A total of n=40 cases were included in the study)

Inclusion criteria were patients with 1^{st} time acute ischemic stroke confirmed from investigations of all age group and gender. Exclusion Criteria were Previous H/o TIA, CVA, Patients on Thiazide diuretics,Patients with Malignancies, Patients who are a known case of gout or have clinical evidence of gout, Patients with chronic renal failure, Patients with hemorrhagic stroke

The patient's demographic information such as age, sex, and history of disorders such as diabetes mellitus, hypertension, and ischemic heart disease was documented. The patients were questioned about their smoking history and duration. Patients with acute stroke were included in the trial, thus if Recombinant Tissue Plasminogen Activator (rTPA) was given to them, it was noted. The patient's baseline blood pressure was taken (in a supine position). All acute stroke patients had blood drawn within 24 hours of admission to assess their lipid profiles, fasting blood sugar levels, and uric acid levels. A neurologist assessed each patient, and computer tomography (CT) and magnetic resonance imaging were used to distinguish between ischemic stroke and other types of stroke (MRI). Every patient had both an MRI and a CT scan. Patients with severe skeletal, endocrinological, cardiac, renal, hepatic, or kidney diseases

Statistical analysis: Utilizing SPSS for Windows version 19 software, statistical analysis was carried out. For every continuous data, the mean and standard deviation (SD) are presented. The independent samples T-test for normally distributed variables and the chi-square test was utilized, to ascertain the relationship between two continuous variables.

RESULTS

Out of the total n=40 cases included in the study n=28(70%) were males and n=12(30%) were females. The most common age group involved was 41 – 50 years with n=16(40%) of the patients in this age group followed by 51 - 60 n=10(25%) of the cases. The mean age of the cases in the study was 51.25 $\pm$ 8.45 years. Similarly, in the control group the mean age of the controls included was 49.83 $\pm$ 5.56 years. The BMI calculation in both groups found most of the cases were overweight and obese and the mean BMI was 27.33 Kg/m^2. In the controls the mean BMI was below 25.0 Kg/m^2 the p values were < 0.05 and significant details are depicted in .Table 1

Variable	Cases (n=40)	Controls (n=40)	P values
Age	51.25 $\pm$ 8.45	49.83 $\pm$ 5.56	0.125
Male	28(70%)	25(62.5%)	0.258
Female	12(30%)	15(37.5%)	0.361
Weight	61.27 $\pm$ 6.27	55.64 $\pm$ 4.71	0.147
BMI (Kg/m^2)	27.33 $\pm$ 3.21	24.15 $\pm$ 2.40	0.042*

* Significant

Table 1: Demographic characteristics of the cases and controls included in the study

Of the various parameters recorded in the cases and controls of the study the history of hypertension was reported in 52.5% of the cases and 27.5% of the controls and the p, values were significant. The mean SBP of the cases was also significantly higher as compared to the controls and the p values were significant. Similarly, the diastolic blood pressure was also significantly higher in the cases as compared to controls. A history of diabetes was recorded in 57.5% of the cases as compared to 20% in the control group details of comparison of all parameters are given in Table 2 . The risk factors of smoking were found in 52.5% of the cases as compared to 20% in the controls. Alcohol consumption was found in 42.5% of cases as compared to 27.5% in controls.

The estimation of the lipid profile of the patients was done in cases and controls the values of serum triglycerides; low-

Parameter	Cases (n=40)	Controls (n=40)	P values
Systolic Blood Pressure (mmHg)	139.82 ± 12.63	117.25 ± 8.14	0.0316*
Diastolic Blood Pressure (mmHg)	89.26 ± 6.8	77.21 ± 5.2	0.0442*
Hypertension	52.5%	27.5%	0.020*
Random Blood Glucose (mg/dl)	133.38 ± 15.6	118.36 ± 6.5	0.0391*
Diabetes Mellitus	57.5%	20.0%	0.0112*

Table 2: Parameters recorded in the cases and controls of the study

density lipoproteins were found to be significantly higher in the cases as compared to the controls given in Table 3 . However, the serum total cholesterol values were high in cases but the p values were not found to be significant. The mean high-density lipoprotein parameters were lower in the cases as compared to the control group.

Lipid Parameter	Cases (n=40)	Controls (n=40)	P values
Serum Triglycerides (mg/dl)	185.24 ± 15.36	166.33 ± 10.81	0.0419*
Total Cholesterol (mg/dl)	199.52 ± 10.2	182.36 ± 11.20	0.637
LDL-C (mg/dl)	162.33 ± 7.89	138.66 ± 8.4	0.0317*
HDL-C (mg/dl)	47.88 ± 4.6	55.32 ± 6.5	0.0143*

Table 3: Estimation of lipid profile in cases and controls of the study

Group	Normal levels	High levels	Mean levels	Total	Odds Ratio	P value
Cases	11 (27.5%)	31(77.5%)	7.25 ± 3.2	40	3.59 2.66 – 4.52	0.0212 *
Controls	28 (70.0%)	12 (30.0%)	4.03 ± 1.8	40		

Table 4: Comparison of serum uric acid levels in cases and controls of the study

Serum UA levels were found to be significantly higher in stroke patients, with 77.5 percent of patients having high levels (>6 mg/dL) compared to 30.0 percent of controls (table 4). When compared to the controls, the mean serum UA level in patients was considerably higher (p=0.0212). Multiple logistic regression analysis was used to determine the relationship between serum UA levels and outcome. Independent of other prognostic criteria, patients with high serum UA levels had a significantly worse outcome. In contrast to patients with low blood UA levels, patients with high serum UA levels had a higher probability of death and stroke recurrence. Regarding the different subtypes of stroke, it was discovered that high serum UA levels were substantially linked with all but lacunar stroke. N=3(7.5%) cases with high serum uric acid levels >7.5 mg/dl suffered mortality in two weeks following ischemic stroke.Table 4

DISCUSSION

The majority of epidemiological research has indicated a strong correlation between increasing cerebrovascular disease with raised serum UA. [14] Although UA appears to be neuroprotective in animal models and is one of the most significant antioxidants in plasma/serum, the results from human studies are debatable. [15] In acute ischemic stroke, serum UA levels would alter significantly in relation to the level of oxidative stress. In the current study, we measured the amounts of serum uric acid in people who had just suffered a stroke. About half of the patients had hyperuricemia, and the mean serum uric acid level was 6.0 mg/dl. A significant 10-year follow-up research found that 20.1 percent of Americans have hyperuricemia. [16] Another significant study in Bangkok's population revealed a prevalence of hyperuricemia of 24.4% [17] and a study in a developing nation revealed a prevalence of 35.2% in men and 8.7% in women. [18] These studies show that patients with acute stroke had a much greater rate of hyperuricemia than the general population. One of the primary clinical manifestations of CVD is stroke, and research looking into the connection between uric acid and stroke has shown mixed results. While other investigations showed that uric acid did not substantially correlate with the occurrence of stroke, some studies found a positive independent connection between uric acid and stroke. [19] In a study of 50 patients with ischemic thrombotic cerebrovascular disease, Bansal et al., [20] found that 30% of the cases had hyperuricemia, and they hypothesized that elevated serum uric acid levels may contribute to the development of the condition generally and particularly in patients under the age of 40. A meta-analysis of 16 prospective cohort studies with 230,000 individuals revealed a slight but statistically significant increased risk of stroke incidence and mortality in adults with elevated serum UA levels. [21] Increased blood UA levels were discovered by Holme et al.9 to be a risk factor for acute myocardial infarctions, congestive heart failure, and stroke in the Apolipoprotein Mortality Risk Study (AMORIS). The question of whether UA is neuro-toxic as a pro-oxidant or neuro-protective as an antioxidant has generated a lot of discussions. [22, 23] The scientific controversy dates back ten years. [24] It has long been understood that urate has antioxidant effects. The problem was first raised by

two related papers that suggested urate was a prooxidant as well as an evolutionary replacement for ascorbate in primates. [21–23] To determine the relationship between hyperuricemia and the risk of stroke incidence and mortality, Kim et al. conducted a systematic review and meta-analysis of 16 prospective cohort studies involving 238449 people. They discovered that hyperuricemia may statically significantly but only mildly raise the risk of stroke incidence and death. [25] According to the findings of the Milionis et al study, older people who have elevated serum uric acid levels are at an increased risk of having an acute ischemic stroke. [26] On the other hand, there was no connection found between blood uric acid levels and both fatal and non-fatal strokes in the Syst Eur study, which included individuals with isolated systolic hypertension. [27] In the current investigation, we discovered that within 24 hours of the onset of symptoms, patients with ischemic stroke had considerably higher serum levels of UA. Even after taking into account potential confounders, the results remained unchanged. The fact that this study was prospective and blinded those who evaluated the follow-up events was its main strength. The study's sample size was sizable, and its outcome measures were reliable. The relevance of our findings was improved by early assessments of serum UA within 24 hours of the start of the stroke. Additionally, we excluded due to the correlation between hyperuricemia and these illnesses, the individuals with gout and renal disorders. Studies on the relationship between serum UA levels and stroke risk and subtypes are scarce. In previous studies looking towards a potential clinical and serum UA correlation mixed findings were obtained.10,11 However, there could be a significant flaw in these studies which include a longer window of time for serum UA readings (For instance, up to 48 or 72 hours). Similar research was done by Weir et al. [28] found that serum UA level forecasts a poor result following an ischemic stroke. Our current research demonstrates elevated serum levels. UA (>6mg/dL) is substantially linked to poor outcomes.

Limitations of the current study: This study was conducted in a single center which is a tertiary care referral Hospital. The sample size was taken as 40 which may not be the true representation of the population since some cases may have been referred to this center following initial treatments at the other point of contact. Therefore, these limitations must be kept in mind before generalizing the results to the population.

CONCLUSION

This study under its limitations concludes that a significant relationship exists between high serum UA levels and ischemic stroke, stroke subtypes (excluding lacunar stroke), and poor outcomes. Finding and managing modifiable risk factors for stroke has advanced quite a bit. Hyperuricemia could be therapeutically targeted in the same manner that other risk factors, such as dyslipidemia and blood pressure, are regularly treated after stroke.

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How to cite this article: Prashanthi K, G KA. Estimation of serum uric acid level in acute ischemic stroke. Perspectives in Medical Research. 2023;11(1):30-34
DOI: 10.47799/pimr.1101.05