Original Article

Relationship between Serum Uric Acid Levels and Cerebrovascular Risk Factors in Acute Stroke

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Abstract

Background: Worldwide, stroke is the commonest cause of chronic adult disability. Hyperuricemia is said to predict first ever stroke. Uric acid has both prooxidant and antioxidant effects. So this study was taken up to find whether high uric acid levels are beneficial or associated with risk in acute stroke.

Aim: This study aims to determine the serum uric acid levels in acute stroke patients and assess its relationship with cerebrovascular risk factors.

Material & Methods: This was a cross sectional study done in stroke patients admitted to the General Medicine department of Government Medical College, Thrissur during the period of January 2017 to December 2017. 82 participants with acute stroke (ischemic stroke or intracranial hemorrhage) were included in this study. Uric acid levels were estimated by uricase method. The serum uric acid levels and its relationship with cerebrovascular risk factors namely hypertension, diabetes mellitus, smoking, history of ischemic heart disease, dyslipidemia, and valvular heart disease were determined. Significance for association between cerebrovascular risk factors and uric acid levels was tested using Chi Square test.

Results: 61% of participants belonged to the age group of 56-75yrs. Out of total 82 participants, 60 had ischemic stroke and 22 had hemorrhagic stroke. Mean uric acid levels were 6.13 $\pm$ 0.46 mg/dl and 36 participants were hyperuricemic. Serum uric acid was found to be significantly higher in men (6.63 $\pm$ 1.32) compared to women (5.57 $\pm$ 1.43). There was a significant positive correlation between serum uric acid concentration and triglyceride levels in patients with acute stroke. No significant association was obtained between serum uric acid levels and cerebrovascular risk factors including diabetes mellitus, hypertension, smoking, history of ischemic heart disease, dyslipidemia, valvular heart disease, previous history of cerebrovascular accident and stroke type ($p > 0.05$) .

Conclusions: Increased serum uric acid levels can be considered as a risk factor for acute stroke due to its high levels and its accompanying increase in triglyceride levels.

Key words: Hyperuricemia, lipid profile, Ischemic stroke, triglyceride

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Introduction

Stroke is the commonest cause of mortality after coronary artery disease and the commonest cause of chronic adult disability. A stroke is defined as an abrupt onset of a neurologic deficit that can be attributable to a focal vascular cause.[1] Stroke also provides a high socioeconomic burden due to increased morbidity and mortality. According to current reports, the incidence of stroke in India is much higher than the Western population.[2] In India, ischemic stroke occurs in about 68- 80% and hemorrhagic stroke in 20-32% of patients.[3] Early identification of individuals at risk could be of help in primary prevention strategies.[4]

Uric acid is the end product of purine catabolism and exists as sodium urate in extracellular compartment.[5] Hyperuricemia is found to be strongly associated with preeclampsia and vascular diseases of peripheral, carotid, and coronary arteries that are involved in the development of stroke.[6] Also, increased levels of uric acid are associated with elevated serum triglyceride and cholesterol concentration, hypertension, obesity, insulin resistance and metabolic syndrome.[7]

According to existing literature, uric acid has dual antagonist properties. Uric acid can function as a pro-oxidant, by generating free radicals during its degradation or by stimulating NADPH oxidase.[8] Previous studies done by Weir CJ et al and Bos MJ et al [9, 10] suggest that increased serum UA levels may predict an increase in risk for cerebrovascular (CV) events like stroke. On the other hand, UA has been known to exert neuroprotective effects by acting as a free radical scavenger (hydroxyl, superoxide and peroxynitrite radicals) and may serve a protective physiological role by preventing lipid peroxidation.[11]

From the above studies it is understood that uric acid has both prooxidant and antioxidant effects. So this study was taken up to find whether high uric acid levels are beneficial or associated with risk in acute stroke. Though some similar studies are already available, this study was done to understand the role of uric acid in patients admitted for acute stroke in our tertiary care hospital. Therefore this study aims to determine the serum uric acid levels in acute stroke patients and assess its relationship with cardiovascular risk factors.

Materials and Methods

This was a cross sectional study done in stroke patients admitted to the General Medicine department of Government Medical College, Thrissur. The study was conducted during the period of January 2017 to December 2017, a total duration of 1year. The subjects in the study included all stroke patients satisfying the inclusion and exclusion criteria prescribed for this study. Patients diagnosed with acute stroke on the basis of CT head findings, admitted to the General Medicine department were included in the study. Patients with history of chronic kidney disease, malignancy, trauma, gout and intake of diuretics and alcohol were excluded from the study. A total of 82 patients were included in this study. The sample size was calculated using formula 4 pq / d2 where, $p =$ prevalence of hyperuricemia in acute stroke i.e 54.9% [1], $q =$ (100- p) and $d =$ 20% of p. (Maximum allowed error)

Approval was obtained from the Institutional Ethical Committee before the start of study. Written permission was taken from the Head of the Department of General Medicine to conduct the study. Informed written consent was taken from all patients satisfying inclusion criteria. The following data was collected from each patient included in the study. Demographic data including age, sex, history of diabetes, hypertension, ischemic heart disease (IHD), dyslipidemia, previous cerebrovascular accident (CVA) and smoking history and type of stroke were recorded in a proforma.

Serum uric acid was estimated from the same blood sample that was taken for routine workup, within 24 hours of admission into the medical ward. For estimation of fasting blood sugar (FBS) and lipid profile, a total of 5ml blood sample was drawn after 10-12 hours of fasting. Blood sample for FBS and lipid profile were collected in sodium fluoride anticoagulant and plain vaccutainer with no anticoagulant respectively. The analysis was done using fully automated ERBA XL 640 instrument.

Serum Uric Acid (SUA) was estimated by uricase method. Fasting blood sugar (FBS) was estimated by glucose oxidase peroxidase (GOD-POD) method. A FBS value of less than 110 mg/dL was considered normal.[12] Lipid profile parameters like total cholesterol was estimated by end point enzymatic method, Triglycerides by glycerol phosphate oxidase method, HDL cholesterol by modified poly vinyl sulphonic acid and polyethylene glycol methyl ether coupled classic precipitation method and LDL cholesterol was calculated by using Friedewald's equation. The cutoff values for total cholesterol, triglycerides, LDL cholesterol are less than 200 mg/dL, 150 mg/dL and 130 mg/dL. A value of greater than or equal to 40 to 60 mg/dL was considered

normal for HDL cholesterol.[12] Hyperuricemia was defined as serum uric acid levels more than 7mg/dl in males and that more than 6mg/dl in females based on previously published studies and which is commonly followed in most laboratories.[12]

STATISTICAL ANALYSIS

Parameters with quantitative values are expressed as mean and standard deviation. Significance for association was tested using chi square test between cerebrovascular risk factors and uric acid levels. Correlation was checked between lipid profile parameters and uric acid levels. Statistical significance was considered if p value is less than 0.05.

RESULTS

Table 1 shows the demographic characteristics of stroke subjects participated in this study.

Table 1: Demographic characteristics of study subjects

Parameters	Total Subjects(82)
Males	43
Females	39
Age group (36 – 55 yrs)	22
Age group (56 – 75 yrs)	50
Age group (> 75 yrs)	10
Ischemic Stroke	60
Hemorrhagic Stroke	22

Mean age of the subjects were 61.48 ± 12.46 years. Mean uric acid levels were 6.13 (± 1.46) and 36 participants (43.9%) were hyperuricemic. Serum uric acid levels were found to be significantly higher in men compared to women.

Table 2 shows the mean values of biochemical and physiological parameters of stroke subjects participated in this study.

Table 2: Mean values of serum biochemical and physiological parameters

Parameter	Mean ± SD (mg/dl)
Triglycerides	151 ± 63.8
Total cholesterol	205.10 ± 59.3
LDL cholesterol	122.5 ± 53.5
HDL cholesterol	51.07± 17.84
Fasting Blood Sugar	122.0 ± 157.4
Systolic Blood Pressure	140.80 ± 34.9
Diastolic Blood Pressure	86.59 ± 17.2

The proportion of cerebrovascular risk factors among the participants are shown in [Table/Fig-2]. 41 (50%) participants with acute stroke were hypertensive followed by 31 (37.8%) who were diabetic and 29 (35.4%) were smokers.

Serum uric acid levels were found to be significantly higher in men (6.63 ± 1.32) compared to women (5.57 ± 1.43) and the difference was statistically significant (p value 0.001). No statistically significant (p value 0.146) association was obtained between serum uric acid levels of ischemic (6.27±1.40) and haemorrhagic stroke (5.74 ± 1.61).

Table 3 shows the relationship of serum uric acid levels with presence of risk factors. No significant association was found between history of dyslipidemia, diabetes mellitus, hypertension, ischemic heart disease, valvular heart disease, previous history of cerebrovacular accident (CVA), smoking and serum uric acid levels.

Table 3: Relationship of serum uric acid levels with presence of risk factors

	Uric acid (Mean ± SD)		Mean difference	p value
Risk Factor	**Yes**	**No**		
Dyslipidemia	6.6 ± 1.28	6.01 ±1.49	0.581	0.128
Diabetes Mellitus	6.22±1.46	6.07±1.48	0.156	0.643
Hypertension	5.93 ± 1.48	6.33 ±1.44	0.40	0.22
Ischemic Heart Disease	6.31 ± 1.39	6.09 ± 1.49	0.22	0.613
Valvular Heart disease	6.7 ±1.73	6.1 ± 1.46	0.597	0.431
Previous History of CVA	5.88 ± 1.44	6.21±1.48	0.330	0.377
Smoking	6.30 ± 1.34	6.09 ±1.45	0.21	0.612

There was a significant correlation between serum uric acid and triglyceride levels. (R^2 =0.182). Serum uric acid was significantly higher in those with high triglyceride values. No significant correlation was obtained between total cholesterol (R^2 =0.038), LDL cholesterol levels (R^2 =0.024), HDL cholesterol levels (R^2 =0.008) and serum uric acid levels.

Discussion

Uric acid levels were raised in 46.3% of stroke subjects in this study. A systematic review was done by Kim et al to find the association between increased uric acid levels and stroke incidence and mortality. It was found that increase in uric acid levels increase the risk for both stroke incidence and mortality.[13] In the present study majority of the patients were between 60-77 years with male preponderance. This was similar to the study done by Kaur J et al.[14] where there was no significant association between age of patients and their UA levels in this study.

SUA was significantly higher in men than women in our study. This is similar to the study done by Conen et al[15] that showed a higher prevalence of hyperuricemia in men than women for which the cause may be attributed to higher alcohol consumption in men.There was no significant association between SUA and risk factors like hypertension, diabetes mellitus. This was the same case in the study done by Mehrpour et al.[16] In few other studies,[17,18] there was a significantly higher frequency of hyperuricemia among those with diabetes.In the study by Kaur J et al[14], SUA levels were found to be significantly higher in hypertensive patients compared to the normotensive patients.

According to the present study, there was no association between SUA and history of ischemic heart disease, valvular heart disease and history of CVA. This was in accordance with previous study done by Mehrpour et al.[16] In our study there was no association of SUA levels with stroke type. Here we assessed ischemic and haemorrhagic stroke patients. In the study by Rajeshwar K et al, 54.9 percent of patients with acute stroke were found to have hyperuricemia with a poor outcome. They concluded that serum uric acid level is an independent risk factor for poor outcomes.[19] The study by Wier CJ et al concluded that higher serum urate levels predicted poor outcome and higher vascular event rates.[9] The role of uric acid in pathophysiology of stroke is not clear, but interventions to decrease uric acid levels may be considered.[1]

There was significant association between SUA levels and TG levels in our study. Increased SUA levels were observed in stroke patients with high TG levels. No significant association was found between SUA and total cholesterol, HDL, LDL levels. Study by Chammaro et al[20] showed positive association between SUA and TG levels. A study by Bonora et al[21] showed significant positive correlation between SUA and TG, total cholesterol, HDL and LDL levels. Another study showed that administration of statins reduces SUA levels significantly and preserves the renal function, although the exact mechanism of this strong association between SUA levels and TG levels are still not known.[22] It may also be a part of patient's lifestyle as hyperuricemia and hypertriglyceridemia are part of metabolic syndrome.[16]

Conclusion

Serum uric acid levels were significantly higher in males when compared to females. There was a significant positive correlation between serum uric acid concentrations and triglyceride levels in patients with acute stroke. No significant association was obtained between serum uric acid levels and cerebrovascular risk factors including diabetes mellitus, hypertension, smoking, history of ischemic heart disease, dyslipidemia and valvular heart disease, previous history of CVA and stroke type. Increased serum uric acid levels can be considered as a risk factor for acute stroke due to the high prevalence of hyperuricemia and its accompanying increase in triglyceride levels.

Conflict of Interest: Nil

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Ethical Approval: The study was approved by the Institutional Ethics Committee, Government Medical College, Thrissur. (dated 21/2/2017)

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