ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Association of uric acid as a risk factor in ischemic stroke – A hospital-based observational study

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Submission: 05-08-2022 Revision: 12-09-2022 Publication: 01-10-2022

ABSTRACT

Background: The second most prevalent cause of mortality globally, next to coronary artery disease, is stroke. In humans, uric acid is the final catabolite in the metabolism of purine. **Aims and Objectives:** The aims of this study were to determine the importance of blood uric acid levels in stroke patients in South Indian population. **Materials and Methods:** In this observational study, we evaluated acute stroke patients who were admitted to Melmaruvathur Adhiparasakthi Institute of Medical Sciences and Research (MAPIMS) Hospital from December 2021 to May 2022. One hundred patients meeting the inclusion standards were enrolled and divided into two groups randomly following acquisition of ethical approval and informed consent. **Results:** In our study consisting of both study and control groups, low-density lipoprotein cholesterol (P = 0.034), non-high-density lipoprotein cholesterol (HDL-C) (P = 0.0127), total cholesterol (P = 0.0196), HDL-C (P = 0.042), and triglyceride (P = 0.0266) were found to be statistically significant. Mean serum uric acid (SUA) level between cases (6.94 ± 1.97 mg/dL) and controls (5.49 ± 1.27 mg/dL) were also statistically significant (P = 0.0306 and P = 0.049). **Conclusion:** Our study showed that stroke patients had a significant occurrence of hyperuricemia. In keeping cardiovascular risk factors such as diabetes, hypertension, triglyceride level, total cholesterol level, coronary heart disease, and tobacco use under control, SUA was observed to be substantially linked with the initial phase of ischemic stroke.

Key words: Ischemic stroke; Body mass index; Smoking; Uric acid

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v13i10.47267

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

The World Health Organization defines stroke as "a clinical syndrome consisting of rapidly developing clinical signs of focal disturbance of cerebral function lasting more than 24 h or leading to death with no apparent cause other than a vascular origin." Transient ischemic attack is when the signs and symptoms of a stroke resolve in <24 h.[1] Stroke is the second most prevalent cause of mortality globally, after coronary artery disease. After age 55, strokes occur in one out of five women and six men in their lifetime.[2] In the US, stroke being the sixth major cause of death, results in 142,000 fatalities annually and 795,000 new or recurrent stroke cases. Stroke is the third major reason for long-term adult-onset physical disability and years of life lost.[3,4] Detailed population-based information on incidence, prevalence, and relevant risk factors, however, have not been thoroughly researched. The mainstay of stroke prevention up to this point has been the discovery of alterable risk factors and application of risk reduction techniques.[5]

Uric acid is present in the extracellular compartments as sodium urate and the kidneys are responsible for removing it from the plasma. In humans, uric acid contributes around 50% of the plasma's antioxidant capability.[6] Increased uric acid levels have been linked to known cardiovascular and cerebrovascular risk factors such as insulin resistance, high blood pressure, obesity, and metabolic syndrome. These risk factors also include

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elevated levels of serum triglycerides and cholesterol. Uric acid, on the other hand, has a history of working as a free radical scavenger and having neuroprotective effects.[7,8]

Concerning the clinical importance of increased uric acid in individuals with cerebrovascular illness of diverse ethnic backgrounds, several investigations have produced contradictory findings. There is no proper study conducted among the South Indians to study the relation between uric acid concentration and acute stroke.

Aims and objectives

The aim of this study was to determine the importance of the level of blood uric acid in stroke patients in South Indian population.

MATERIALS AND METHODS

In this observational study, we evaluated acute stroke patients who were admitted to Melmaruvathur Adhiparasakthi Institute of Medical Sciences and Research (MAPIMS) Hospital, from December 2021 to May 2022. A total of 100 subjects who met the requirements were involved in our study after getting ethical approval and informed consent and divided into case group (50 patients with acute stroke) and control group (50 patients without stroke) using a random number table.

Inclusion criteria

Stroke patients admitted to the MAPIMS hospital within 48 h after the start of symptoms, who expressed a willingness to take part in the study.

Exclusion criteria

The following criteria were excluded from the study:

- All individuals with a history of stroke.
- Strokes brought on by trauma, neoplasms, coagulation issues, or aneurysms.
- Patients with primary intraventricular or subarachnoid hemorrhage.
- Patients using diuretics, antioxidant, or iron supplements.
- Patients with kidney or liver diseases and Cancerous disease.
- Patients who first experienced a stroke more than 48 h before being admitted.

Serum uric acid (SUA) levels below 6.5 mg/dL and 7 mg/dL for women and men, respectively, are considered hyperuricemia.[9] We investigated the patients' clinical histories and SUA levels. All analysis were done with SPSS version 22.0, and P-value of significance is deemed to be <0.05.

RESULTS

Mean age of study and control groups was 57.92±9.1 years and 55.17±7.42, respectively. The number of patients who smoked were 15 and 32 and who consumed alcohol were 10 and 28, in case and control groups, respectively. Mean duration of diabetes for control group was 7.17±1.21 years and study group was 8.49±1.92 years. Mean hemoglobin A1C for control group 7.9±0.82 and study group was 8.6±0.72 (Table 1).

The body mass index (BMI) of the majority of patients in control group (42 patients), in our study, was within normal ranges. The study group had only 10% patients within normal range. The study group had 70% overweight patients (25–29.9 kg/m^2) and only eight patients (16%) in control group. About 20% of study group were obese (≥30 kg/m^2). The case and control groups' respective mean BMIs were found to be 26.78 3.47 and 22.13 2.15 (Table 2).

The mean uric acid level was 6.94±1.97 for the study group and 5.49±1.27 for control group (Table 3).

In our study consisting of both study and control groups, low-density lipoprotein cholesterol (P=0.034),

Table 1: Demographic data

Demographic data	Study (n=50)	Control (n=50)
Age	57.92±9.1	55.17±7.42
Sex		
Male	37	31
Female	13	19
Duration of DM (years)	8.39±1.92	7.17±1.21
HbA1c	8.6±0.72	7.9±0.82
Smokers	32	15
Alcohol consumers	28	10
Hypertension	27	40

DM: Diabetes mellitus, HbA1c: Hemoglobin A1C

Table 2: BMI

BMI (kg/m^2)	Study group (n=50)		Control group (n=50)	
	n	%	n	%
18.5–24.9	5	10	42	84
25–29.9	35	70	8	16
≥30	10	20	0	0
Total	50	100	50	100

BMI: Body mass index

Table 3: Uric acid

Uric acid (mg/dl)	Study group (n=50)	Control group (n=50)
3.5–5.0	14 (28%)	25 (50%)
5.1–7.5	27 (54%)	25 (50%)
>7.5 (high)	9 (18%)	-
Total	50 (100%)	50 (100%)

non-high-density lipoprotein cholesterol (HDL-C) (P=0.0127), total cholesterol (P=0.0196), HDL-C (P=0.042), and triglyceride (P=0.0266) were found to be statistically significant (Table 4).

In our study, mean SUA level between cases and controls is found to be statistically significant (P=0.000, P=0.0306 and P=0.049) and nine patients (18%) had hyperuricemia in the study group (Table 5).

DISCUSSION

One of the primary clinical manifestations of cardiovascular disease is stroke, and research looking into the connection between uric acid and stroke have 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.[10]

In humans and higher primates, uric acid is the final catabolite in the purine metabolism.[11] It resides as sodium urate in the extracellular space and is eliminated from the plasma by the kidney.[7] 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. 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 oestrogen.[11]

Increased uric acid levels have been linked to known cardiovascular risk factors as high blood pressure, obesity, insulin resistance, metabolic syndrome, and elevated serum triglyceride and cholesterol levels.[7] The free radical scavenger property of uric acid, on the other hand, has been shown to have neuroprotective effects. Uric acid in humans is responsible for around half of the antioxidant power of plasma.[8,12]

Table 4: Statistical analysis of lipid parameters

Lipid parameters (mg/dl)	Study group (with stroke)	Control group	P-value
Total cholesterol	157.42±42.14	166.10±23.46	0.0196*
HDL-C	40.50±4.761	33.82±3.42	0.042*
LDL-C	111.84±39.52	99.56±37.89	0.034*
Triglyceride	131.56±32.57	125.49±27.58	0.0266*
Non-HDL-C	138.41±51.25	116.16±35.89	0.0127*

*P<0.05=Statistically significant. HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol

Table 5: Correlation between uric acid and stroke in cases

Uric acid (mg/dl)	Study group	Control group	P value
3.5–5.0	14	25	0.049*
5.1–7.5	27	25	0.0306*
>7.5 (high)	9	-	-

*P<0.05=Significant

The high morbidity and death associated with strokes place a significant socioeconomic strain on society. It is therefore of highest importance to practice primary prevention by identifying at-risk individuals early on and halting the development of risk factors.[13] Stroke ranks first among causes of disability and is the second major reason for mortality worldwide. The aging of the population is increasing its incidence (number of new cases). Although ischemic stroke is more frequent, hemorrhagic stroke is more severe and causes more fatalities and years of lost productivity due to disability. Stroke incidence and death vary between nations, regions of the world, and ethnic groupings.[14] SUA, one of the primary aqueous antioxidants in humans, offers protection to stroke sufferers. Concerning the clinical importance of increased SUA levels in cerebrovascular disorders, several sizable research have produced conflicting findings.[15] Several cardiovascular diseases and SUA have been linked in certain epidemiologic research, although these relationships have not been found in others.[16] Even though there are two recent meta-analytical studies revealing a strong correlation, the connection between hyperuricemia and AIS is still up for debate.[17,18] In a case-cohort study conducted in 2020, blood pressure and other variables were quantified and the association between ischemic stroke and hyperuricemia was examined in a sizable demographic that had participated in the national Reasons for Geographic and Racial Differences in Stroke (REGARDS) study.[19,20]

Numerous investigations revealed a higher connection between hyperuricemia and stroke in females.[21] After accounting for numerous risk factors (HR 1.32; 95% CI: 1.00–1.73), a Taiwanese study found that females with hyperuricemia have an increased risk of ischemic stroke than males.[22]

Blood uric acid levels and the lipid profile parameters (cholesterol, triglycerides, and LDL) were found to be positively correlated with the intensity of acute ischemic stroke, while HDL levels were found to be inversely associated, according to a study by Patange and Kapale[23] The relationship between uric acid levels and triglyceride levels has been studied in the past, and patients from various patient populations, including gout sufferers, have been included.[24,25] In their study of 957 young males, Bonora et al.,[26] found a substantial positive relation between the levels of blood uric acid, total cholesterol, LDL cholesterol, and triglyceride.

According to Khalil et al.,[27] there was a substantial difference between the mean SUA levels for cases (6.03 1.84 mg/dL or 358.58 109.31 mol/L) and controls (4.34 1.60 mg/dL or 258.27 95.36 mol/L). In a study by Mehrpour et al.,[6] the mean SUA was 5.94 (SD=1.70) mg/dL. Twenty-six (47.3%) individuals had hyperuricemia, which was defined as having a high amount of uric acid (>6 and 7 mg/dL for women and men, respectively).

An observational study by Kaspa and Govindu[28] on the prognostic indicators for acute ischemic stroke using SUA revealed that it serves as a signal for a higher chance of stroke and that an increased serum urate concentration may elevate the chances of death following an acute stroke. Retrospective analysis by Tutar et al.,[29] of the association between SUA levels and ischemic stroke and its subtypes revealed that high uric acid levels were regarded as a separate risk factor for stroke. On the contrary, Wang et al.,[30] conducted a retrospective analysis on the topic and found that unfavorable results in terms of neurological function are protected by high SUA levels in subjects who have experienced an ischemic stroke. They also found a strong negative correlation between these two variables. Among the five subtypes of patients in the ORG 10172 acute stroke therapy trial, only those with the large-artery atherosclerosis subtype demonstrated a substantial protective effect of blood uric acid levels on neurological prognosis.

Limitations of the study

The small sample size could be considered a limitation to this study.

CONCLUSION

This study demonstrated that acute stroke patients had a significantly increased frequency of hyperuricemia. In keeping cardiovascular risk factors such as diabetes, hypertension, triglyceride level, total cholesterol level, coronary heart disease, and tobacco use under control, SUA was observed to be substantially linked with the initial phase of ischemic stroke.

ACKNOWLEDGMENT

We would like to acknowledge the Department of General Medicine, Melmaruvathur Adhiparasakthi Institute of Medical Sciences and Research and all the individuals who have extended their help and assistance throughout all aspects of our study.

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https://doi.org/10.1177/0300060517752996

Authors Contribution:
JMY- Concept and design of study, Acquisition of data, Original draft preparation, Review of data, Revision of final manuscript; **SG-** Concept of study, Review of literature, Preparation of manuscript, Revision of final manuscript; **SE-** Review and editing, Statistical analysis, Interpretation of results.

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Source of Support: Nil, **Conflict of Interest:** None declared.