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Ijaz Ali
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Zaid Waqar
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Bushra Khalid
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Maryam Naseem
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Soban Khan
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

See next page for additional authors

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Authors

Ijaz Ali, Zaid Waqar, Bushra Khalid, Maryam Naseem, Soban Khan, Sajid Ali, Muhammad Tariq, Muhammad Adil, Hira Badar Abbasi, and Mazhar Badshah

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ASSOCIATION OF HYPERURICEMIA WITH ISCHEMIC STROKE IN ADULT POPULATION

Ijaz Ali[1], Zaid Waqar[1], Bushra Khalid[1], Maryam Naseem[1], Soban Khan[1], Sajid Ali[1], Muhammad Tariq[1], Muhammad Adil[1], Hira Badar Abbasi[1], Mazhar Badshah[1]
[1]*Department of Neurology, Pakistan Institute of Medical Sciences, Islamabad*

Corresponding author: Zaid Waqar *Department of Neurology, Pakistan Institute of Medical Sciences, Islamabad* ***Email:*** *chikky789@gmail.com*

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ABSTRACT

Background and Objective:

Stroke is the second most prevalent cause of dementia, the third biggest cause of mortality, and the top cause of disability globally. Hyperuricemia is frequently seen in patients with vascular risk factors. The objective of this study was to determine the association of hyperuricemia with ischemic stroke in adult patients presenting to neurology department of a tertiary care hospital.

Methods:

This was a case-control study of 200 patients, 100 patients with stroke and 100 unmatched controls were accessed for vascular risk factors and hyperuricemia. The setting was Pakistan Institute of Medical Sciences, Islamabad and study duration was six months (August 2021 to February 2022). Odds Ratio (OR) was calculated to measure the association of ischemic stroke with hyperuricemia for each group. OR>1 was taken as significant.

Results:

Out of 100 patients in the case group, 25 (25%) had hyperuricemia. Whereas, out of 100 patients in the control group, 07 (7%) had hyperuricemia. The P-value was 0.001. Odds ratio was 4.42. Out of 100 patients in the case group, the median patient age was 35 and the highest patient age was 75. The mean age, symptom duration, and uric acid level were 55.216.24 years, 20.588.97 hours, and 7.212.24 mg/dl, respectively. The control group had 100 patients with an average age of 35 and a maximum age of 75. The median age was 52.48 years old, and the median uric acid level was 2.48 mg/dl.

Conclusion:

Hyperuricemia is linked positively to occurrence of ischemic stroke as evidenced by the positive odds ratio. Further studies need to be done to investigate whether uric acid lowering therapy is useful in preventing stroke or reducing mortality.

Keywords: Hyperuricemia, Stroke, Hypertension, Diabetes

INTRODUCTION

Stroke is the leading cause of disability worldwide, the second most common cause of dementia, and also the second leading cause of mortality.[1] In addition to the risk factors that are generally accepted, such as smoking, diabetes, hypertension, ischemic heart disease, etc. few risk factors for acute ischemic stroke have been discovered by recent research, including blood calcium, hs-CRP, homocysteine, and albumin levels. Without any gout symptoms, hyperuricemia is a common accidental observation in individuals with additional vascular risk factors.[2] There have been conflicting findings about the relationship between hyperuricemia and the prognosis of stroke, and this is made more difficult by the intimate connection between serum uric acid and aberrant glycol metabolism. According to studies, people with ischemic stroke have a statistically significant higher incidence of hyperuricemia.[3,4] Uric acid, which is poorly soluble and largely removed from the body through the urine, is the end product of protein and purine metabolism. Blood uric acid levels in men and women should range from

3.4 to 7.0 mg/dL and 2.4 to 6.0 mg/dL, respectively.

Hyperuricemia increases the risk of obesity, diabetes, non-alcoholic fatty liver disease, renal illness, acute myocardial infarction (AMI), and cardiovascular disease (CVD). The oxidative metabolism, platelet adhesiveness and aggregation, and uric acid-induced endothelial dysfunction are only a few of the hypothesized CV disease mechanisms in hyperuricemia.[5] Additionally, uric acid has both pro- and anti-oxidant properties. Urate functions physiologically by reducing the oxo-heme oxidant produced when haemoglobin and peroxide mix. One of the initial effects of uric acid exposure on cells is the induction of oxidative stress, which causes the production of reactive oxygen species (ROS), which then causes the emergence of local inflammation, a decrease in the production of nitric oxide, and activation of the renin-angiotensin system.[6, 7]

Thrombosis, embolism, or systemic hypoperfusion, which lower the blood flow to the brain, are the causes of ischemic stroke. Usually, vascular dysfunction caused by inflammatory illnesses, atherosclerotic disease, or arterial dissection comes before thrombosis. A complicated chain of biochemical and molecular processes that are brought on by changes in circulation and a lack of blood flow result in ischemic cell death. Neuronal death and irreversible loss of brain function are the results of the ischemic cascade triggered by a stroke. Patients who suffer from ischemic stroke have a variety of prognoses. The prognosis is influenced by the kind and severity of the stroke, the damaged structures and regions, the time between onset and diagnosis, the length and intensity of physical and occupational therapy, and baseline performance.

In several epidemiological studies, it has been shown that there is a J-shaped relationship between serum uric acid and cardiovascular events, indicating that both low SUA levels (5.6 mg/dL in men and 4.325 mg/dL in women) and high SUA levels (>7.1 mg/dL in men and >5.5 mg/dL in women) increase mortality from CV illness. One proposed method by which CV risk is created is hyperuricemia, which directly contributes to the development of atherosclerosis. By causing arterial endothelial dysfunction, activating the crucial chemokine monocyte chemotactic protein 1, and encouraging the growth of vascular smooth muscle cells, it may also unintentionally contribute to atherosclerosis. It is believed that oxidative stress brought on by decreased nitric oxide bioavailability after urate entrance into endothelial cells is the primary cause of endothelial dysfunction.[8,9]
This study was carried out to investigate the association of hyperuricemia with ischemic stroke among patients presenting to a tertiary care hospital in Pakistan.

METHODS

Study Type: Case-control Study
Place and duration of study: It was conducted at Department of Neurology, Pakistan Institute of Medical Sciences from August 2021 to February 2022.

Sample size: Two hundred patients, 100 patients in each group. Cases were patients with ischemic stroke and controls were family members of patients without ischemic stroke.

Sampling Technique: Non-Probability consecutive sampling.

Inclusion Criteria: All patients presenting with acute ischemic stroke during the study period.

Exclusion Criteria: All patients with clinical or imaging/lab features of stroke mimics such as hypoglycemia, space occupying lesions, and meningitis.

Data collection and analysis: Data was collected on informed consent questionnaires on demographics, comorbid and Serum uric acid levels. Data was entered and analyzed through SPSS version 22. Odds Ratio was calculated to measure the association of ischemic stroke with hyperuricemia for each group. OR>1 was taken as significant.

Ethical considerations: This study was approved by Institutional Review Board of Pakistan Institute of Medical Sciences, Islamabad.

RESULTS

Two hundred patients in total (100 in case and control were included. Out of 100 patients in the case group, the median patient age was 35 and the highest patient age was 75. The mean age, symptom duration, and uric acid level were 55.216.24 years, 20.588.97 hours, and 7.212.24 mg/dl, respectively. Similar to the case group, the control group had 100 patients with an average age of 35 and a maximum age of 75. median age was 52.48 years, and the median uric acid

level was 2.48 mg/dl.

Out of 100 patients in the case group, 36 (36%) and 64 (64%) patients fell into the age groups of 35–55 and 56–75 years, respectively, according to the frequency distribution. Out of 100 patients in the control group, 50 (50%) were between the ages of 35 and 55, and 50 (50%) were between the ages of 56 and 75. Out of 100 patients in the case group, 43 (43%) had type II diabetes mellitus. Out of 100 patients in the control group, 13 (13%) had type-II diabetes mellitus. Out of 100 patients in the case group, the frequency distribution of hypertension revealed that 61 (61%) had hypertension. In contrast, out of 100 patients nine (9%) people in the control group had hypertension. The frequency distribution of smoking status for the case group's 100 patients showed that 59 (59%) of them smoked. While 12 (12%) of patients in control group were smokers.

According to the frequency distribution of hyperuricemia, out of 100 patients in the case group, 25 (or 25%) had hyperuricemia. In contrast, out of 100 patients in the control group, seven (7%) had hyperuricemia while the remaining patients did not. P-value was set at 0.001. The probability was 4.42. According to age stratification in relation to hyperuricemia, among patients in the 35–55 age range, 09 (25%) and 00 (00%) had hyperuricemia in the case and control groups, respectively. P-value was set at 0.01. There was a 34.8 odds ratio. Age stratification in relation to hyperuricemia revealed that, in the case and control groups, respectively, 16 (25%) and 07 (14%) of the patients in the 56–75 years age range had hyperuricemia. P was equal to 0.15. 2.04 was the odds ratio. In patients who were in the male group, stratification for hyperuricemia by gender revealed that in the case and control groups, respectively, 16 (27.6%), and four (8.9%) had hyperuricemia. P-value was at 0.02. The probability was 3.90. In the case and control groups, stratification for gender in relation to hyperuricemia revealed that, among the patients in the female group, nine (21.4%) and three (5.5%) had hyperuricemia, respectively. P was equal to 0.02. The odds ratio was 4.72.

In the case and control groups, stratification for diabetes mellitus type II with regard to hyperuricemia revealed that 16 (37.2%) and 03 (23.1%) of the patients with diabetes had hyperuricemia, respectively. Indicator P was 0.35. It had a 2.42 odds ratio. With regards to hyperuricemia, stratification for diabetes mellitus type II revealed that, in the patients who did not have diabetes, 09 (15.8%) and 04 (4.6%) in the case and control groups, respectively, had hyperuricemia. P-value was at 0.03. The probability was 3.89.

According to stratification for hypertension status in relation to hyperuricemia, in the case and control groups, respectively, 20 (32.8%) and three (33.3%) of the patients with hypertension had hyperuricemia. Indicator P was 0.97. The probability was 0.97. In the case and control groups, respectively, five (12.8%) and four (4.4%) of the patients who did not have hypertension had hyperuricemia, according to the stratification for hypertension with regard to hyperuricemia. P-value was at 0.09. The probability was 3.19. In the case and control groups, stratification for smoking status in relation to hyperuricemia revealed that among the patients who smoked, 19 (32.2%) and 00 (00%) had hyperuricemia, respectively. P-value was at 0.09. The odds were 12.03 to 1. In the case and control groups, respectively, six (14.6%) and seven (8%) of the patients who did not smoke had hyperuricemia, according to stratification for smoking status in relation to hyperuricemia. A 0.24 P-value was used. The probability was 1.98.

DISCUSSION

Stroke is thought to be the second most common killer globally and a substantial contributor to lost disability-adjusted life years (DALYs) that can be prevented. The prevention and treatment of stroke have been widely associated with a number of modifiable risk factors, including hypertension, diabetes mellitus, atrial fibrillation, dyslipidemia, smoking, obesity, lack of physical exercise, etc. However, the number of stroke incidents, survivors, deaths related to stroke, and DALYs are all still rising on a global scale. Therefore, in order to create new preventative measures for stroke, a greater understanding of more possible risk factors is required.

Out of 100 patients in case group, 25 had hyperuricemia. There were 1433 fatalities, 659 MIs, and 430 ischemic strokes during follow-up in a research by Storhaug HM et al. The risk of all-cause mortality rose in both genders with 1 SD (87 mol/L) increase in blood uric acid level, according to fully adjusted Cox regression models (Hazard ratios, HR males; 1.11, 95% CI1.02-1.20; women; 1.16,

1.05-1.29). The stroke HRs and 95% CI for males were 1.31, 1.14-1.50, women were 1.13, 0.94-1.36, and the general population was 1.22 (1.09, 1.35). There were no identifiable independent connections with MI.[11]

Fifty individuals with ischemic thrombotic cerebrovascular illness were investigated by Bansal et al. A 30% prevalence of hyperuricemia led researchers to the conclusion that increased blood uric acid levels may contribute to the development of ischemic thrombotic cerebrovascular illness in general, particularly in individuals under the age of 40. Kim et al. performed a comprehensive review and meta-analysis of 16 prospective cohort studies with 238,449 participants to ascertain the association between hyperuricemia and risk of stroke incidence and mortality. They found that hyperuricemia might slightly but significantly increase the risk of having a stroke and dying from one.[12]

The findings of Milionis et al. showed that older people who had greater blood uric acid levels had a higher chance of having an acute ischemic stroke. The Syst-Eur trial, which included people with isolated systolic hypertension, found no link between blood uric acid levels and fatal and non-fatal strokes. Hyperuricemia was also not linked to stroke mortality in 108,284 person-years of follow-up data in a Japanese population of middle-aged persons. Goldberg et al. found no association between serum uric acid and thromboembolic stroke in middle-aged males who were followed for 20 years beginning in 1994. When Chamorro et al. evaluated the prognostic significance of serum uric acid concentration in patients with acute ischemic stroke, they discovered that patients with type 2 diabetes had lower serum uric acid concentrations than other patients and that uric acid concentration was negatively correlated with fasting blood glucose. [12-16]

Sixteen studies, totaling 238,449 people, were examined in a meta-analysis. The incidence of stroke and death were both substantially increased by hyperuricemia [N=6 studies, RR 1.41, 95% confidence interval (CI): 1.05-1.76], which was also the case for stroke incidence [N=6 studies, RR 1.36, 95% CI: 1.03-1.69]. Despite accounting for known risk factors like age, hypertension, diabetes, and cholesterol in subgroup analyses of studies, hyperuricemia was still significantly linked to stroke incidence (N=4 studies; RR: 1.47; 95% CI: 1.19-1.76; and mortality (N=6 studies; RR: 1.26; 95% CI: 1.12-1.39) and mortality (N=6 studies; RR: 1.26; 95% CI: 1.12-1.39).[17]

CONCLUSION

This study indicates that ischemic stroke and hyperuricemia are related. Hyperuricemia was observed to coexist far more frequently in those who have had AIS than it does in the general population. More research is still required to prove a link between urate-lowering drugs' ability to reduce mortality in people with hyperuricemia and ischemic stroke.

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Ijaz Ali; Concept, data analysis, manuscript writing, manuscript revision
Zaid Waqar; Concept, data collection, data analysis, manuscript writing,
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Maryam Naseem; Data collection, data analysis, manuscript writing
Soban Khan; Data collection, data analysis, manuscript writing
Sajid Ali; Data collection, data analysis, manuscript writing
Muhammad Tariq; Data collection, data analysis, manuscript writing
Muhammad Adil; Data collection, data analysis, manuscript writing
Hira Badar Abbasi; Data collection, data analysis, manuscript writing
Mazhar Badshah; Concept and design, manuscript revision
All the authors have approved the final version of the article, and agree to be accountable for all aspects of the work