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Association between Hyperuricemia and Ischemic Stroke in patients admitted in Medical ward in a tertiary care hospital Multan

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Author`s Contribution

[1,2]Substantial contributions to the conception or design of the work; or the acquisition, [4,6]Active participation in active methodology, [2,3]analysis, or interpretation of data for the work, [5]Drafting the work or revising it critically for important intellectual content

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ABSTRACT

Objective: To assess the association of Hyperuricemia with Ischemic Stroke.

Methodology: This case-control study was carried out at the department of Medicine Nishtar 2 Tertiary Care Hospital in Multan from June 2023 to Dec 2023. At the time of admission, the serum uric acid level was tested in addition to other standard laboratory tests. Patients' information was gathered using a pre-made proforma only after written informed permission was obtained from the individuals, their spouses, or relatives in the case of patients with aphasia or decreased awareness. Version 24 of the statistical program for the social sciences (SPSS) was used to analyze the data. A p-value of less than 0.05 and an OR greater than one were deemed statistically significant.

Results: In the current study, 60 patients were cases and 60 were healthy control. In cases there were 33 (55%) males and 27 (45%) females while in healthy control, the males were 30 (50%) while females were also 30 (50%). In patients with ischemic stroke, the frequency of hyperuricemia was 26 (43.33%), while in controls, it was 15 (25%). Compared to controls, ischemic stroke patients had a 3.11-fold increased incidence of hyperuricemia. Accordingly, hyperuricemia (p=0.002) is a substantial risk factor for ischemic stroke. In individuals aged 30 to 50, ischaemic stroke and hyperuricemia were significantly associated (p = 0.001). Additionally, ischaemic stroke patients had a 4.15-fold increased incidence of hyperuricemia compared to control subjects. On the other hand, there was no significant correlation (p = 0.29) between hyperuricemia and ischaemic stroke in the 51–70 age range. Additionally, there was a 2.1-fold increased incidence of hyperuricemia in ischaemic stroke patients.

Conclusion: Patients with ischemic stroke had a considerably greater prevalence of hyperuricemia (43.33%). Furthermore, those who have had an ischemic stroke are 3.11 times more likely to get hyperuricemia. Hyperuricemia may thus be looked at as an additional ischemic stroke risk factor. However, further study is required before regular uric acid levels may be advised.

Key words: Association; Hyperuricemia; Ischemic Stroke.

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Introduction

Stroke is a condition that may be prevented; however it is a primary cause of morbidity and death for almost half of stroke patients who are over 65 years of age.[1] There are many known risk factors for stroke, including smoking, atrial fibrillation, hypertension, high cholesterol, diabetes mellitus, and carotid artery stenosis.[2] According to available data, the prevalence of non-conventional risk factors for variables is rising. These comprise obesity,

metabolic syndrome, chronic inflammation, sleep apnoea syndrome, chronic kidney illness, and nutrition. It is usual to observe elevated blood uric acid, or hyperuricemia, in individuals who have metabolic syndrome, diabetes mellitus, obesity,
hypertension, chronic kidney disease, and cardiovascular diseases.[3] Despite the fact that in plasma serum uric acid is strongest antioxidants and seems to have a neuro-protective effect in animal models, findings of human research are conflicting and of mixed quality. One the one hand, research indicates that a decreased level of blood uric acid is a significant and independent predictor of bad outcomes both during and after an ischaemic stroke. It also shows an independent correlation with stroke severity, an unfavorable course for the stroke, and vascular events that occur after the stroke.[4-6] Conversely, in the multi-center Mexican trial, patients who had ischaemic stroke and had low SUA levels had quite favourable short-term outcomes.[7] MiedemaI et al.'s Dutch investigation revealed no correlation of serum uric acid levels and the short and long term consequences of ischaemic stroke.[8] Another study has observed that hyperuricemia is a reliable indicator of a poor outcome in hospital for diabetic ischaemic stroke patients who are 75 years of age or older .[8] However, they did not find any correlation between hyperuricemia and the prognosis of stroke in patients with or without diabetes. In contrast, hyperuricemia is a major protective feature in men and in a subtype of ischaemic stroke patients with big artery atherosclerosis, according to research by Wang YF, et al. [10] Studies on the frequency of hyperuricemia in ischemic stroke have been conducted globally, with varying degrees of success. According to Mapoure et al., 52.3 percent of Black African patients who suffered from ischemic stroke also had hyperuricemia.[11] In an Indian research,[12], it was shown that 54.9% of ischaemic stroke patients had SUA levels that were considerably higher (>6 mg/dl) than 24.7% of controls ($p<0.05$).[13] Thirty percent of individuals with acute ischaemic stroke in another South Indian research had hyperuricemia.[14]According to an Iranian investigation, 10.7% of controls and 13.0% of ischaemic stroke patients had hyperuricemia; no correlation between ischaemic stroke and increased serum uric acid levels was observed.[14] In another Iranian research, Mehrpour et al. discovered that hyperuricemia affected 47.3% of ischaemic stroke patients.[15] Given these conflicting findings, a study was carried out to ascertain if hyperuricemia and acute ischaemic stroke patients are related, since no previous research from Pakistan has been reported in this area.

Methodology

This case-control study was carried out at the department of Medicine Nishtar 2 Tertiary Care Hospital in Multan from March 2024 to August 2024. Assuming an estimated proportion of hyperuricemia of 54.9% in ischemic stroke individuals and 24.7% in controls, the sample size of 130 participants was computed with an 80% power of test and a 5% threshold of significance.[12] The Institutional Review Board gave its clearance, and then sixty patients with acute ischemic stroke of either gender, ranging in age from forty to seventy-five years, who presented within twelve hours of the stroke's beginning symptoms including Aphasia, weakness of any part of the body or hemiplegia were recruited. Computed Tomography of the brain was done as initial test for stroke recognition in such patients. Additionally, sixty healthy controls who were age and gender matched were also recruited. Following a Senior Registrar examination either in medical emergency or in the medical ward, the American Heart Association/American Stroke Association criteria[16] were used to classify all ischemic stroke patients. There was no clinical indication of any cerebrovascular illness in the controls. Exclusion criteria included those with Haemarrhagic stroke, Brain Abscess or tumor, inflammatory bowel disease, thyroid dysfunction, hepatic or renal illness, and Meningitis. None of the participants had ever used alcohol, nor were they taking any medications that decrease cholesterol (statins, for example) or that alter uric acid levels (corticosteroids, allopurinol). At the time of admission, the serum uric acid level was tested in addition to other standard laboratory tests. A level of serum uric acid of >6 mg per dl was considered hyperuricemia.[9] Patients' information was gathered using a pre-made proforma only after written informed permission was obtained from the individuals, their spouses, or relatives in the case of patients with aphasia or decreased awareness. Version 24 of the statistical program for the social sciences (SPSS) was used to analyze the data. The means and standard deviations of quantitative data, such as age and serum uric acid level, were shown. Frequencies and percentages were used to represent qualitative factors like gender and hyperuricemia. To determine the p-value for blood uric acid levels in patients with ischemic stroke and controls, the student t-test was used. The chi-square test was used to determine the p-value and odds ratio (OR) in order to determine if hyperuricemia and controls were associated

with ischemic stroke. Age and gender stratified the data. Adjusted OR was computed after stratification. A p-value of less than 0.05 and an OR greater than one were deemed statistically significant.

Results

In the current study, 60 patients were cases and 60 were healthy control. In cases there were 33 (55%) males and 27 (45%) females while in healthy control, the males were 30 (50%) while females were also 30 (50%). The mean age (SD) of the patients in the case group was 58 (±6.12) years, with a minimum age of 38 years and a maximum age of 70 years; conversely, the mean age (SD) of the control group was 57 (±5.15) years, with a minimum age of 40 years and a maximum age of 70 years. (Figure 1)

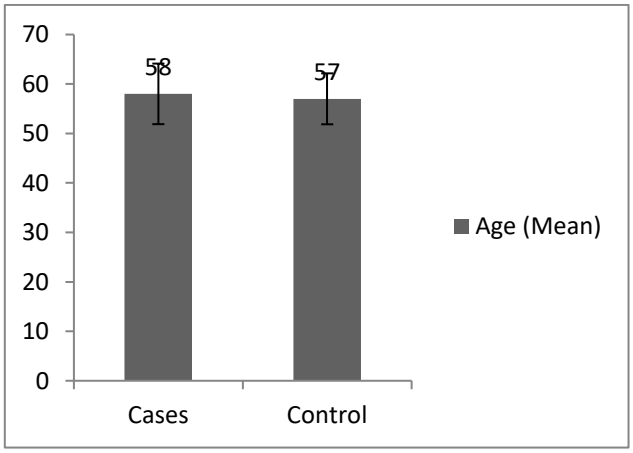

Figure 2: Mean age in both cases and control

It was observed that the mean (SD) serum uric acid level in patients who had suffered an ischemic stroke was 5.62 (±2.0) mg/dl, whereas the mean (SD) serum uric acid level in controls was 5.16 (±0.89) mg/dl, indicating statistical significance (p=0.001).

In patients with ischemic stroke, the frequency of hyperuricemia was 26 (43.33%), while in controls, it was 15 (25%). Compared to controls, ischemic stroke patients had a 3.11-fold increased incidence of hyperuricemia. Accordingly, hyperuricemia (p=0.002) is a substantial risk factor for ischemic stroke. (Table I)

Table 1: hyperuracemia associated with the ischemic stroke

Hyperuracemia	Cases	Control	Chi-square value	Odd ratio	P value
Yes	26 (43.33%)	15(25%)	7.51	3.11-	0.002
No	34 (56.67%)	45 (75%)			

In individuals aged 30 to 50, ischaemic stroke and hyperuricemia were significantly associated (p = 0.001). Additionally, ischaemic stroke patients had a 4.15-fold increased incidence of hyperuricemia compared to control subjects. On the other hand, there was no significant correlation (p = 0.29) between hyperuricemia and ischaemic stroke in the 51–70 age range. Additionally, there was a 2.1-fold increased incidence of hyperuricemia in ischaemic stroke patients. Males did not show a significant correlation of hyperuricemia with ischaemic stroke, and the probability of acquiring hyperuricemia were 2.41 times higher in comparison to controls; however, females did show a significant correlation (p = 0.001) of hyperuricemia and ischaemic stroke and the probability of getting hyperuricemia were 5.11 times higher in females with ischaemic stroke in comparison to controls. (Table II)

Table II: Stratification of age and gender for Association between hyperuricemia and ischemic stroke.

Parameter	Sub-category	Cases	Control	Chi-square value	Odd ratio	P value
Age	30-50 years	14 (53.84%)	8(53.33%)	5.81	4.15	0.001
	51-70 years	12 (46.15%)	7 (46.66%)	1.15	2.1	0.29
Gender	Male	12 (46.15%)	9 (60%)	2.41	2.41	0.21
	Female	14 (53.84%)	6 (40%)	5.01	5.11	0.001

Discussion

This research revealed that acute ischemic stroke patients had considerably higher blood uric acid levels than controls, and that these patients also had a 3.11-fold higher risk of hyperuricemia. Numerous experimental investigations have shown that uric acid is a strong neuroprotectant and antioxidant, and they have also described hyperuricemia as a defense against free radical damage. For every mg/dl rise in serum uric acid among individuals suffering from ischemic stroke, Chamorro et al. observed a twelve percent rise in the likelihood of a favorable functional result.[17] Hyperuricemia, on the other hand, has been connected to a number of pro-atherogenic mechanisms, including elevated oxidative stress or damage, vascular smooth muscle growth, and a cascade of leukocytic activation. In recent years, Arévalo-Lorido et al. observed that individuals with ischemic stroke who had the higher levels of serum uric acid had worse atherosclerotic carotid artery disease ($p < 0.005$).[18] In patients with ischemic stroke, the frequency of hyperuricemia was 26 (43.33%), while in controls, it was 15 (25%). Compared to controls, ischemic stroke patients had a 3.11-fold increased incidence of hyperuricemia.

Accordingly, hyperuricemia (p=0.002) is a substantial risk factor for ischemic stroke. In individuals aged 30 to 50, ischaemic stroke and hyperuricemia were significantly associated (p = 0.001). Additionally, ischaemic stroke patients had a 4.15-fold increased incidence of hyperuricemia compared to control subjects. On the other hand, there was no significant correlation (p = 0.29) between hyperuricemia and ischaemic stroke in the 51–70 age range. Additionally, there was a 2.1-fold increased incidence of hyperuricemia in ischaemic stroke patients. These results are somewhat similar to those of a South Indian research[12], which showed that stroke patients had considerably higher SUA levels (54.9% compared to 24.7% in controls). In contrast, another research conducted in South India[13] reported that 30% of patients with acute ischemic stroke had hyperuricemia and that the mean blood uric acid level in these individuals was 5.5 (±1.7) mg/dl. Additionally, SUA levels have been shown to be more prevalent in the 56–70 age group and to be substantially greater in females in comparison to male. Their conclusions agreed with the current findings as well. They came to the conclusion that hyperuricemia and concurrent dyslipidemia may be regarded as acute ischemic stroke risk factors. A cross-sectional research conducted in Iran found that 47.3% of patients with hyperuricemia had a mean level of serum uric acid of 5.94 ±1.70 mg/dl in patients with ischemic stroke.[15] Contrary to the current results, another Iranian research showed that hyperuricemia was present in 13.0% of patients with ischemic stroke compared to 10.7% of controls. Additionally, there was no significant correlation between ischemic stroke and increased blood uric acid levels (p>0.05). The mean (SD) levels of serum uric acid of cases and controls were 4.94 (±1.76) and 3.72 (±1.09), accordingly, in a case-control study conducted in Bangladesh[19]; (p<0.05). In contrast to 6.7% of controls, 23.3% of the participants had abnormal levels of serum uric acid. More over half (52.3%) of Black African individuals suffering from ischemic stroke had hyperuricemia, according to Mapoure et al.[11]—a greater percentage than the study group. This conclusion is remarkably similar to that of Sarfo et al.'s research from Ghana, which found that 46.3% of ischemic stroke patients had hyperuricemia.[20] However, their study did not indicate that the incidence of hyperuricemia rose with age in stroke patients. These variations may result from variations in nutrition, location, ethnicity, or way of life. A few drawbacks of this research include its single-center, hospital-based design. Second, these findings cannot be generalized to the general population since the study was limited to ischemic stroke patients with diverse risk factor profiles and poor socioeconomic level.

Conclusion

Patients with ischemic stroke had a considerably greater prevalence of hyperuricemia (43.33%). Furthermore, those who have had an ischemic stroke are 3.11 times more likely to get hyperuricemia. Hyperuricemia may thus be looked at as an additional ischemic stroke risk factor. However, further study is required before regular uric acid levels may be advised.

References

1. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart disease and stroke statistics—2017 update: A report from the American Heart Association. Circulation 2017; 135(10): 229-445.
2. Aquil N, Begum I, Ahmed A, Vohra EA, Soomro BA. Risk factors in various subtypes of ischemic stroke according to TOAST criteria. J Coll Physicians Surg Pak 2011; 21(5): 280-3.
3. Soltani Z, Rasheed K, Kapusta DR, Reisin E. Potential role of uric acid in metabolic syndrome, hypertension, kidney injury, and cardiovascular diseases: Is it time for reappraisal? Curr Hypertens Rep 2013; 15(3):175-81.
4. Wu H, Jia Q, Liu G, Liu L, Pu Y, Zhao X, et al. Decreased uric acid levels correlate with poor outcomes in acute ischemic stroke patients, but not in cerebral hemorrhage patients. J Stroke Cerebrovasc Dis 2014; 23(3):469-75.
5. Brouns R, Wauters A, Van De Vijver G, De Surgeloose D, Sheorajpanday R, De Deyn PP. Decrease in uric acid in acute ischemic stroke correlates with stroke severity, evolution and outcome. Clin Chem Lab Med 2010; 48(3):383-90.
6. Wu S, Pan Y, Zhang N, Jun WY, Wang C. Lower serum uric acid level strongly predict short-term poor functional outcome in acute stroke with normoglycaemia: A cohort study in China. BMC Neurol 2017; 17(1):21.
7. Chiquete E, Ruiz-Sandoval JL, Murillo-Bonilla LM, Arauz A, Orozco-Valera, Ochoa-Guzmán A, et al. Serum uric acid and outcome after acute ischemic stroke: Premier study. Cerebrovasc Dis 2013; 35(2):168-74.
8. Miedema I, Uyttenboogaart M, Koch M, Kremer B, de Keyser J, Luijckx GJ. Lack of association between serum uric acid levels and outcome in acute ischemic stroke. J Neurol Sci 2012; 319(1-2):51-5.
9. Wang P, Li X, He C, Zhai Y, Sun H, Zhang Y, et al. Hyperuricemia and prognosis of acute ischemic

stroke in diabetic patients. Neurological Research 2019; 41(3): 250-6.
10. Wang YF, Li JX, Sun XS, Lai R, Sheng WL. High serum uric acid levels are a protective factor against unfavourable neurological functional outcome in patients with ischemic stroke. J Int Med Res 2018; 46(5):1826-38.
11. Mapoure YN, Ayeah CM, Ba H, Hentchoya R, Luma HN. The prognostic value of serum uric acid in the acute phase of ischemic stroke in Black Africans. J Stroke Cerebrovasc Dis 2018; 27(3):783-92.
12. Koppula R, Kaul S, Venkateswar Rao A, Jyothy A, Munshi A. Association of serum uric acid level with ischemic stroke, stroke subtypes and clinical outcome. Neurology Asia 2013; 18(4):349-53.
13. Arora T, Mantur PG, Bidri RC, Mulimani MS. Serum uric acid levels and serum lipid levels in patients with ischemic cerebrovascular accident. J Assoc Physicians India 2018; 66:349-54.
14. Iranmanesh F, Sheykholeslami NZ, Gadari F, Ahmady J. Acute ischemic non-embolic stroke and serum level of uric acid. Iran J Neurol 2012; 11(1):1-5.
15. Mehrpour M, Khuzan M, Najimi N, Motamed MR, Fereshtehnejad SM. Serum uric acid level in acute stroke patients. Med J Islam Repub Iran 2012; 26(2):66-72.
16. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, et al. An updated definition of stroke for the 21st Century. A statement for healthcare professionals from the american heart association/american stroke association. Stroke 2013; 44 (7): 2064-89.
17. Chamorro Á, Obach V, Cervera Á, Revilla M, Deulofeu R, Aponte JH. Prognostic significance of uric acid serum concentration in patients with acute ischemic stroke. Stroke 2002; 33(4):1048-52.
18. Arévalo-Lorido JC, Carretero-Gómez J, Robles Pérez-Monteoliva NR. Association between serum uric acid and carotid disease in patients with atherosclerotic acute ischemic stroke. Vascular 2019; 27(1):19-26.
19. Khalil MI, Islam MJ, Ullah MA, Khan RK, Munira S, Haque MA, et al. Association of serum uric acid with ischemic stroke. Mymensingh Med J 2013; 22(2):325-30.
20. Sarfo F, Akassi J, Antwi N, Obese V, Adamu S, Akpalu A, et al. Highly prevalent hyperuricaemia is associated with adverse clinical outcomes among Ghanaian stroke patients: An observational prospective study. Ghana Med J 2015; 49(3):165-72.