DOI: https://doi.org/10.53350/pjmhs22166702

ORIGINAL ARTICLE

Prevalence of Hyperuricemia in Patients with Ischemic Stroke

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ABSTRACT

Introduction: An attack of stroke is one of the most prevalent but also the deadliest and most disabling conditions in the field of neurology. Stroke development is influenced by many risk factors, including high blood pressure, smoking, hyperlipidemia, and diabetes. Recent research suggeststhat other risk factors, such as elevated levels of blood uric acid, might influencethe onset or progression of the condition.

Objective: To determine the prevalence of hyperuricemia in stroke patients.

Methods: The Department of Medicine, Khyber Teaching Hospital, Peshawar, did this cross-sectional research. Patients of both sexes were included in this trial from October 10th, 2019, through March 31st, 2020. who had ischemic stroke-related symptoms and imaging findings? Each patient who was proven to have had an ischemic stroke was examined for hyperuricemia, which means a blood uric acid level of more than7 mg/dL in men and more than 6 mg/dL in women. All patients received the same level of care in the lab. After that, the prevalence of hyperuricemia in ischemic stroke patients were determined.

Results: The average age of 60.833± 3.70 years was used in this investigation, along with mean serum uric acid concentration of 6.340± 2.06 mg/dl was examined for hyperuricemia, which means a blood uric acid level of more than7 mg/dL in men and more than 6 mg/dL in women and mean period between onset of symptoms and admission of 5.993± 2.94. The vast majority of the patients were male gender (70 percent). Sixty patients were found to have hyperuricemia (40 percent).

Conclusion: According to our research, hyperuricemia was found in a more significant percentage of acute stroke patients than in the general population.

Keywords: Hyperuricemia, Stroke, Frequency

INTRODUCTION

Purine metabolism in humans culminates in the formation of uric acid. After being synonymous for decades, hyperuricemia and gout are now recognized as indicators of various metabolic and hemodynamic abnormalities[1]. The medical literature has debated the clinical relevance of elevated uric acid levels in patients with cardiovascular or cerebrovascular illnesses. Urinary excretion of uric acid has been linked to an increased risk of cardiovascular and brain illness in several studies, including the National Health and Nutrition Examination Survey (NHANES)[2].

According to a recent survey, stroke is on the rise. An estimated 780000 individuals have a new or recurrent stroke every year, with one occurring every 40 seconds. After coronary heart disease and cancer, stroke is the third leading cause of mortality worldwide, particularly among the elderly [3-4]. There is a 20% mortality rate in the acute phase of stroke, which persists for many years following the acute occurrence in stroke patients [4]. Nearly a quarter of stroke survivors acquire dementia, making it the second leading cause of disability and dementia in those aged 65 and older globally[5]. In addition

To short-term handicap, up to 40% of stroke survivors are likely unable to regain their independence via self-care, and 25% will be unable to walk without assistance[6].

An attack of stroke is one of the most prevalent but also the deadliest and most disabling conditions in the field of neurology. Hypertension, smoking, high cholesterol, and diabetes are just a few risk factors that might contribute to a stroke[7]. Recent research suggests that other risk factors, such as elevated levels of blood uric acid, might influence the onset or progression of the condition. A study of acute stroke patientsin the United States found that those with more significant blood uric acid levels were more incapacitated, with more recurrences and cardiovascular accidents[8]. A 3-month follow-up of stroke patients in England showed that individuals with higher uric acid levels were more likely to die than those with lower levels[09]. A Greek study of 163 individuals with non-embolic ischemic stroke found that those with higher uric acid levels had more sequelae and a more significant probability of recurrence. In the United States, the research found that hyperuricemia increased the incidence of both cerebral and cardiovascular accidents[10].

Diet and other environmental factors may impact the occurrence of hyperuricemia in stroke patients. Our town does not have any local data. 47.3 percent of ischemic stroke patients were reported to be hyperuricemic by Mehrpour et al. [11].

MATERIAL AND METHODS

It was done at the Department of Medicine, Khyber Teaching Hospital in Peshawar, Pakistan. It lasted from October 10th, 2019, through March 30th, 2020. The number of participants in my research was 150. In the literature, 47.3 percent of obese people have metabolic syndrome, which is based on a 95 percent confidence interval. The WHO method for determining the proper sample size for health research was used, with an error margin of no more than 8%. The sampling method Samples were taken sequentially without randomness.

Choice of Samples: Patients between 50 and 70 with clinical and radiographic indications of ischemic stroke are eligible for participation.

Criteria for exclusion: Clinical history and examination, as well as prior medical records, were used to eliminate the following patients:

Patients have a history of gout in the family or have been shown to have urate metabolism enzyme deficits.

Treatment-naive or treatment-refractory patients with cancer of any form.

Patients use drugs such as mercaptopurine hydrate, azathioprine, pyrazinamide, ethambutol, niacin, and anticoagulant.

Hypothyroidism and hyperthyroidism patients

Pregnancy: Past medical history, general and particular physical examination, or laboratory tests were used to discover this problem. Including patients with the diseases mentioned above in the research, the samplecreated a bias in the study's results.

Process of Collecting Information: Our institute's Ethical and Research Committee gave the project the go-light. The research was carried out at the Khyber Teaching Hospital Peshawar's Department of Medicine. Outpatient And emergency departments

were used to identify newly diagnosed ischemic stroke patients. All patients and their guardians were informed of the study's goals and advantages. All patients signed a permission form after receiving full explanations.

Following enrollment in the research, participants had a comprehensive physical and systemic examination, which included the collection of a thorough medical history. All patients had a CBC, LFTs, RFTs, RBS, Chest X-ray, and ECG as a baseline study. According to the operational definition, the patient had an ischemic stroke. Patients suspected of having had an ischemic stroke were hospitalized and given a CT scan of their brains. All individuals enrolled in the trial had their fasting blood sugar and lipid profile tested to determine whether they had diabetes or Dyslipidemia. Additionally, a baseline blood pressure reading was taken into consideration.

Each patient who was proven to have had an ischemic stroke was examined for hyperuricemia, which means a blood uric acid level of more than 7 mg/dL in men and more than 6 mg/dL in women.All patients received the same level of care in the lab. After that, the prevalence of hyperuricemia in ischemic stroke patients was determined. Dislipidemia, Hypertension, and diabetes were discovered and categorized as effect modifiers.

Process for the Analysis of Information: SPSS version 22 was used to store and analyze all of the data. The mean and standard deviation were calculated for each quantitative factor, such as age, serum uric acid level, and the time elapsed between the onset of symptoms and the hospitalization. Qualitative factors like gender and hyperuricemia were analyzed using frequency and percentages. Hyperuricemia was categorized by age, gender, time since symptoms first appeared, and hospitalization to Determine whether there were any differences in the effects. Dyslipidemia, Hypertension, and diabetes were all controlled by the stratification of the population. P-values of less than 0.05 were maintained in post-stratification chi-square tests. Tables and infographics summarized the findings.

RESULTS

Uric acid levels varied from 8.4 mg/dl to 4.28 mg/dl, having a mean of 6.340±2.06 mg/dl, with a mean age of 60.833± 3.70 years, and there was a 5.993+2.94-hour delay between the beginning of symptoms and admission, as shown in Table-I. There were 70% male patients in Table II, which is consistent with past research on the subject. Table III reveals that 40% of the participants had high uric acid concentrations.

Table IV illustrates the prevalence of hyperuricemia by age, gender, time from the beginning of symptoms and hospitalization, dyslipidemia (high cholesterol), Hypertension (hypertension), and diabetes.

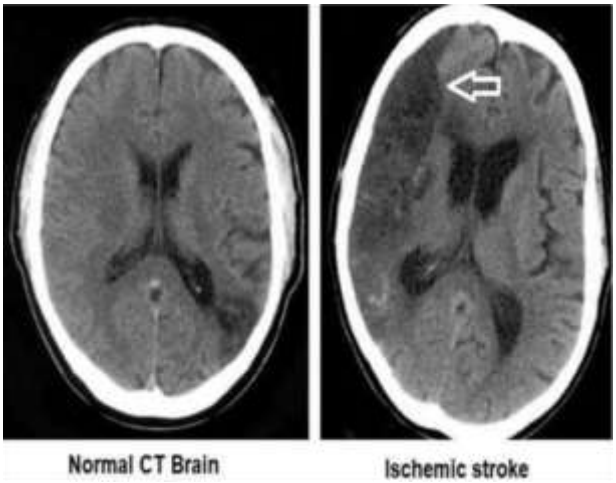

Figure 1: Normal Ct Brain Vs. Ischemic Stroke

Table 1: Mean± SD of like age, Serum uric acid level, and time since symptoms appearance and hospitalization n=150

Demographic variables	Mean ± SD
Age(years)	60.833± 3.70
Serum uric acid level (mg/dl)	6.340± 2.06
Time since symptoms appearance and hospitalization (hours)	5.993± 2.94

Table 2: Frequency and %age of patients according to gender n=150

Gender	No. of Patients	%age
Male	105	70%
Female	45	30%
Total	150	100%

Table 3: Frequency and %age of patients according to Hyperuricemia n=150

Hyperuricemia	No. of Patients	%age
Yes	60	40%
No	90	60%
Total	150	100%

Table 4: Stratification of Hyperuricemia con c e r n i n g age

Age (years)	Hyperuricemia		
	Yes	No	p-value
50-60	29(43.3%)	38(56.7%)	0.461
61-70	31(37.3%)	52(62.7%)	
Total	60(40%)	90(60%)	

Table 05: Stratification of Hyperuricemia con c e r n i n g gender

Gender	Hyperuricemia		
	Yes	No	p-value
Male	41(39%)	64(61%)	0.716
Female	19(42.2%)	26(57.8%)	
Total	60(40%)	90(60%)	

Table 6: Stratification of Hyperuricemia con c e r n i n g time since symptomsappearance and hospitalization

Time since symptoms appearance and hospitalization (hours)	Hyperuricemia		
	Yes	No	p-value
<6	30(44.1%)	38(55.9%)	0.034
6-12	25(32.9%)	51(67.1%)	
>12	5(83.3%)	1(16.7%)	
Total	60(40%)	90(60%)	

Table 7: Stratification of Hyperuricemia con c e r n i n g Dyslipidemia

Dyslipidemia	Hyperuricemia		
	Yes	No	p-value
Yes	16(32%)	34(68%)	0.157
No	44(44%)	56(56%)	
Total	60(40%)	90(60%)	

Table 8: Stratification of Hyperuricemia con c e r n i n g Hypertension

Hypertension	Hyperuricemia		
	Yes	No	p-value
Yes	20(42.6%)	27(57.4%)	0.666
No	40(38.8%)	63(61.2%)	
Total	60(40%)	90(60%)	

Table 9: Stratification of Hyperuricemia concerning diabetes

Diabetes	Hyperuricemia		
	Yes	No	p-value
Yes	32(82.1%)	7(17.9%)	0.000
No	28(25.2%)	83(74.8%)	
Total	60(40%)	90(60%)	

DISCUSSION

Uric acid weights 168.112 g/mol. Urate is the bloodstream's main uric acid type. Purine catabolism's end product, uric acid, is flushed out of the body through urine if renal function is notimpaired. Ideal ranges for women and men are 1.5 to 6.0 mg/dL and 2.5 to 7.0

mg/dL,respectively. Oestrogen inhibits URAT1 in the proximal tubule [141]. Blood urate levels > 6.8 mg/dl may cause monosodium urate crystals [12]. Urate oxidase (UOX) changes early in human and reptile development. The kidneys can't remove uric acid since it's not converted to polar molecules like allantoic acid and ammonia. Humans have higher blood uric acid levels than other animals due to decreased levels of urate oxidase and increased glomerular reabsorption[13].

Enzymatic deamination and dephosphorylation convert GMP, IMP, and AMP into inosine, xanthosine, and guanosine. PNP transforms nucleosides into purine bases. Hypoxanthine and Guanine deamination is converted to xanthine by two enzymes. Only XOR and XOR can do this.XOR irreversibly oxidizes xanthine to uric acid [14].

Uric acid is a Potent Antioxidant. After a stroke, it provides 60% of free-radical scavenging blood's capability—comparable to or more robust antioxidant activity than ascorbate [144]. When a thrombus obstructs a brain vessel, oxidative stress develops. Infarct cores without blood flow and perfusion destroy neurons and cells permanently. A functionally damaged but still alive ischemia penumbra surrounds the infarct center. Thrombolytic drugs like rtPA are the most effective treatment for stroke[15].

Animal studies demonstrate uric acid reduces infarct size and neurofunctional impairment. Romanos et al. questioned combined urate & recombinant tissue plasminogen activator (rtPA) therapy. Combined therapy decreased neutrophil infiltration, cerebral edema, and infarct size. Neuroprotective uric acid has been tested in humans. Human perceptions reflect positive and negative outcomes. Using uric acid with rtPA is safe and effective [16]. In the phase 2b/3 URICO-ICTUS clinical study, 421 stroke patients received intravenous uric acid plus alteplase or a placebo. Trial participants tolerated uric acid with thrombolytic therapy well tolerated, although the proportion of patients with an excellent three-month follow-up after stroke was not raised. The 2016 meta-analysis of 10 research with 8,131 ischemic stroke patients validated these results [151]. Patients with higher uric acid levels had better clinical results, indicating it may prevent stroke[17].

Uric acid is harmful in several ways. Uric acid increases LDL oxidation, reduces endothelial nitric oxide synthase, and promotes platelet-derived growth factors. These variables may cause thrombosis, arterial obstruction, and cerebral atherosclerosis. Atherosclerotic plaques contain higher uric acid and xanthine oxidase levels than controls, supporting uric acid's function in plaque development [18]. High uric acid is connected to cerebrovascular illness. Hyperuricemia raises IL-6, TNF-a, and CRP [154]. Recent research links uric acid to systemic inflammation through the NF-kB pathway. Two meta-analyses support the link between stroke and urine acid levels.

Ischemic stroke patients' uric acid levels were checked. 40% of research participants had uric acid levels of 6.3402.06 mg/dl. 10-year follow-up research [158] found that 20,1% of Americans had hyperuricemia. 35.2% of men and 8.7% of females in a developing nation had hyperuricemia. Acute stroke patients are more likely to develop hyperuricemia, research show[19].

Research is equivocal on uric acid as a stroke risk factor. Some studies relate uric acid to stroke, whereas others don't. Bansal et al. found 30% hyperuricemia in ischemic thrombotic cerebrovascular patients. Increasing blood uric acid levels may contribute to CVD, especially inindividuals under 40 and [20-21]. In 16 prospective cohort studies, Kim et al. found a link between hyperuricemia and stroke and death. Hyperuricemia increases stroke incidence and death [22]. According to Milionis and colleagues, aged urine acid levels may enhance ischemic stroke risk.

[165] In the Syst-Eur experiment, no significant association was found. A study of 108284 middle-aged Japanese people found no link between stroke and hyperuricemia [23]. After 20 years, Goldberg et al. found no link between uric acid and thromboembolic stroke. Hyperuricemia does not enhance stroke risk based on uric acid levels in patients and controls. [24]. Chen and colleaguesevaluated 226 renal dialysis patients for 18 months and found 43 experienced rapid and severe brain damage associated with high blood sugar. Possible causes include research technique, demographics, or variables[25].

CONCLUSION

According to our research, hyperuricemia was detected in a more significant percentage of acute stroke patients than in the general population. Hyperuricemia might be regarded as a risk factor for acute. Stroke because of its high incidence in individuals with acute stroke and the concomitant rise intriglyceride and LDL cholesterol levels.

REFERENCES

1. Aditya S, Ghosh S, Banerjee J, Saha SP,Sengupta S, Ganguly SB. Prognostic importance ofserum uric acid in acute ischaemic stroke. Int JBus Man Adv Res. 2016;5:278.
2. Behera BK, Hui PK, Simethy R. Serum uric acid level in acute ischemic stroke in easternIndia. Int J Res Med Sci. 2017;5(6):2353.
3. Katan M, Luft A, Global burden of stroke.Semin Neurol. 2018;38(2):208.
4. Feigin LV, Norrving B, Mensah GA. Global burden of stroke.Circ Res. 2017;120:439.
5. Feigin VL, Lawes CM, Bennett DA. A systematic review is a worldwide stroke incidence and early case fatality reported in 56 population-based studies. Lancet Neurol. 2010;12:20.
6. Guerra LJC, Cepero VA, Concepción FO, Guerra LJJ, Gutiérrez RF, Rodriguez LJJ, et al. Stroke incidence and risk factors in Havana and Matanzas, Cuba.Neurologia. 2015;30(8):488.
7. Adam's and Victor's principles of neurology, 8th ed. New York. McGraw-Hill Company,2005;958.
8. Kanellis J, Johonson RJ. Elevated uric acid and ischemic stroke. Stroke. 2003; 34:1956.
9. Weir CJ, Muir SW, Walters MR. Serum urate is an independent predictor of poor outcomesand future vascular events after acute stroke. Stroke. 2003;34:1951.
10. Milionis HJ, Kalantzi KJ, Goudevenos JA. Serum uric acid levels and risk for acuteischaemic non-embolic stroke in elderly subjects. J Intern Med. 2005;258:435.
11. Muir S, Harrow C, Dawson J. Allopurinol use yields potentially beneficial effects on inflammatory indices in those with recent ischemic stroke; a randomized, double-blind placebo-controlled trial. Stroke. 2008;39:3303.
12. Kaur I, Khurana A, Sachdev JK, Mohan G. Evaluation of serum uric acid in acute ischaemicstroke. Int J Adv Med. 2017;4(1):60.
13. Mehrpour M, Khuzan M, Najimi N, Motamed MR, Fereshtehnejad S-M. Serum uric acid levelin acute stroke patients. Med J Islam Repub Iran. 2012;26(2):66.
14. Raichle ME, Mintun MA. Brain work and brain imaging. Annu Rev Neurosci 2006; 29: 449–476.
15. Magistretti PJ, Chatton JY. Relationship between L-glutamate-regulated intracellular Na+dynamics and ATP hydrolysis in astrocytes. J Neural Transm 2005; 112: 77–85.
16. Fünfschilling U, Supplier LM, Mahad D, et al. Glycolytic oligodendrocytes maintain myelin and long-term axonal integrity. Nature 2012; 485: 517–521.
17. Marder E, Goaillard J-M. Variability, compensation, and homeostasis in neuron and network function. Nat Rev 2006; 7: 563–574. 34 Ischemic Stroke - Updates
18. Locasale JW, Cantley LC. Metabolic flux and the regulation of mammalian cell growth. CellMetabol 2011; 14: 443–451.
19. Lo EH. A new penumbra: transitioning from injury into repair after stroke. Nat Med 2008; 14:497–500.
20. Nicotera P, Leist M, Manzo L. Neuronal cell death: a demise with different shapes. TrendsPharmacol Sci 1999; 20: 46–51.
21. Ünal-Çevik I, Kilinç M, Can A et al. Apoptotic and necrotic death mechanisms are activated in the same cell after cerebral ischemia. Stroke 2004; 35: 2189– 2194.
22. Rossi DJ, Oshima T, Attwell D. Glutamate release in severe brain ischemia is mainly byreversed uptake. Nature 2000; 403: 316–321.
23. Camacho A, Massieu L. Role of glutamate transporters in the clearance and release of glutamate during ischemia and its relation to neuronal death. Archives Med Res 2006; 37: 11–18.
24. Olney JW. Brain lesions, obesity, and other disturbances in mice treated with monosodiumglutamate. Science 1969; 164: 719–721.
25. Choi DW. Glutamate neurotoxicity and diseases of the nervous system. Neuron 1988; 1:623–634.