

## ORIGINAL ARTICLE

**Frequency of Raised Serum Uric Acid in Patients with Stroke; A Cross-Sectional Study**Rehana Kousar<sup>1</sup>, Mirza Sijeel Ahmad<sup>2\*</sup>, Robina Kousar<sup>3</sup>, Sobia Latif<sup>4</sup>, Anam Zargham<sup>5</sup>, Arif Khan<sup>6</sup>**ABSTRACT****Objective:** To define the rate of raised serum uric acid in patients with Stroke.**Study Design:** Cross-sectional study.**Place and Duration of study:** The study was carried out in the Department of Medicine, Military Hospital, Rawalpindi, Pakistan, from 13<sup>th</sup> July 2017 to 12<sup>th</sup> January 2018.**Materials and Methods:** A total of 96 cases of ischemic Stroke aged 26-74 years were selected. Cases with hemorrhagic Stroke who were consuming anti-hyperuricemia medications, diuretics, and Gout were excluded. Patients who fulfilled the clinical or radiological diagnostic criteria of Stroke underwent laboratory tests which included serum uric acid levels, fasting lipid profile, 24hrs urine for creatinine clearance and proteinuria, blood sugar levels, and renal profile.**Results:** Among 96 patients from 26 to 74 years of age, with a mean of  $54.01 \pm 12.42$  years. Fifty six cases (58.33%) were from 51 to 74 years of age, 48 (50.0%) were male, and 48 (50.0%) were females. Hyperuricemia was found in 55 (57.29%) patients, whereas there was no Hyperuricemia in 41 (42.71%) patients.**Conclusion:** The rate of raised serum uric acid is high in patients with Stroke.**Keywords:** *Hyperuricemia, Serum Uric Acid, Stroke.***How to cite this:** Kousar R, Ahmad MS, Kousar R, Latif S, Zargham A, Khan A. Frequency of Raised Serum Uric Acid in Patients with Stroke; A Descriptive Cross Sectional Study. 2023; 4(3): 319-324. doi: <http://doi.org/10.37185/LnS.1.1.321>This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license. (<https://creativecommons.org/licenses/by-nc/4.0/>). Non-commercial uses of the work are permitted, provided the original work is properly cited.**Introduction**

Stroke is a worldwide health problem resulting in high mortality and morbidity as per the global burden of diseases in 2013. Stroke is a devastating disease, and its prevalence increases death and functional disability.<sup>1</sup> Stroke is becoming 2<sup>nd</sup> primary origin of premature death and 3<sup>rd</sup> principal source of disability globally, as most stroke survivors continue

to live with a disability.<sup>2</sup>

Stroke not merely follows but also deteriorates preexistent dementia and cognitive impairment in most patients, particularly aged patients.<sup>3</sup> Owing to the lack of principal records and insufficient statistics accessibility in Pakistan on this issue, there is inadequate writings on causes of Stroke in Pakistani population. A revision was approved in 2014, indicating a great incidence of adaptable causes containing High blood pressure and high cholesterol levels in Pakistanis. This reading also showed Atherosclerosis as the main reason for this issue. Geriatric individuals showed not merely a greater possibility of death but a mounting percentage of in-hospital complications, slower recovery, and increased periods of hospitalisation.<sup>4</sup>

Pakistan is not known to have high stroke incidence and prevalence, but even then the reported incidence is as high as 48% which means 4 million people in Pakistan are living with Stroke. The estimated Stroke in our country is 250 per 100,000 individuals, which means around 350,000 new stroke cases each year.<sup>5</sup>

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Uric Acid is the outcome of purine breakdown in humans and is produced by the act of xanthine oxidase. Hyperuricemia is demarcated as elevated serum uric acid levels of >420  $\mu\text{mol/l}$  in men and >360  $\mu\text{mol/l}$  in women.<sup>6</sup> Elevated uric acid levels are associated with circulatory risk factors such as higher lipids and cholesterol levels, elevated blood pressure, overweight, insulin resistance, and metabolic abnormalities.<sup>7</sup> Role of hyperuricemia in the causation of ischemic Stroke is not fully established. Evidence linking increased uric acid levels with Stroke has emerged as a subject of great interest and research. The high incidence of disabilities and wide range of complications resulting from Stroke, along with the high magnitude of the cost on long-term treatment, make it a very important subject that needs to be screened thoroughly and intervened. There is hardly any study from Pakistan for the evaluation of the frequency of elevated uric acid levels in patients with Stroke.

A recent investigation of 16 studies showed a rise in serum uric acid levels in individuals is related to an uncertain but statistically substantial increase in the risk of Stroke and death.<sup>8</sup> In a study done by Mehrpour et al. on 55 patients revealed that 47.3% of patients with Stroke had elevated levels of uric acid in their blood.<sup>9</sup>

The purpose of this research was to define the occurrence of hyperuricemia in individuals with Stroke in the Pakistani population. The clinical implication of these findings is that patients with hyperuricemia may benefit from more aggressive surveillance and early therapeutic interventions to decline the possibility of Stroke. If levels are found to be high, further randomized controlled trials can be performed to see the effect of therapeutic interventions to halt the progression of hyperuricemia before it can result in the development of Stroke in these patients.

### **Materials and Methods**

It is a cross-sectional study carried out in the Department of Medicine, Military Hospital, Rawalpindi, Pakistan, from 13<sup>th</sup> July 2017 to 12<sup>th</sup> January 2018. Individuals were incorporated in this research after approval from the hospital ethical committee vide letter no EC-28-2022. The WHO calculator calculated sample size with a Confidence

level 95%, Estimated inhabitants 47.3%, Absolute accuracy of 10%, and a sample size of 96 Patients.<sup>9</sup> The sampling method was non-probability, Consecutive sampling. Individuals included had an age range from 25 to 75 years, all ethnicity and gender, and ischemic Stroke confirmed based on NCCT brain or neural dysfunction persisting >24hrs. While Patients with hemorrhagic Stroke, taking anti-hyperuricemia medications, with GFR <35, with Gout, and taking diuretics were excluded from this study.

All the patients referred to the hospital's medical department with ischemic Stroke were deliberated for this research. A comprehensive description was set aside from the patient or the family by the trainee researcher. Demographic features (name, age, sex, residence, and contact number) were documented for all patients. Clinical parameters (symptoms, history of hypertension or diabetes mellitus, hyperlipidemia, IHD, clinical examination findings like focal neurological dysfunction) of all the patients were recorded as well. Non-contrast CT Brain was done to make the diagnosis of Stroke by the trainee researcher. Patients who fulfilled the clinical or radiological diagnostic criteria of Stroke underwent laboratory tests, including serum uric levels, fasting lipid profile, 24 hours' urine for creatinine clearance and proteinuria, blood sugar levels, and renal profile. A printed, well-versed permission form was filled from each individual incorporated in the research. Statistics were entered and evaluated using SPSS version 17. Statistics were designed for both qualitative and quantitative variables. Incidences and proportions were designed for qualitative variables like gender, diabetes mellitus, hypertension, IHD, hyperlipidemia, and hyperuricemic patients were presented by tables. Mean and standard deviation were used for measurable variables like age and number of strokes. Variables like age, gender, diabetes mellitus, elevated blood pressure, ischemic heart disease, and elevated cholesterol were organized by stratification. Outcomes are prepared by using the Chi-square test. *p-value* <0.05 was reserved as the level of significance.

### **Results**

Of 96 patients, aged 26 to 74 years with a mean age

of  $54.01 \pm 12.42$  years, the bulk of the patients, 56 (58.33%) were from 51 to 74 years, 48 (50.0%) were men and 48 (50.0%) were women with men to

women ratio of 1:1. Dissemination of individuals with other confounding variables is displayed in Table 1.

**Table 1: Distribution of patients with other confounding variables (n=96)**

confounding variables		Frequency	%age
Diabetes mellitus	Yes	55	57.29
	No	41	42.71
Hypertension	Yes	54	26.25
	No	42	43.75
Ischemic heart disease	Yes	34	35.42
	No	62	64.58
Hyperlipidemia	Yes	26	27.08
	No	70	72.92

A mean number of strokes was  $2.41 \pm 0.33$ . Hyperuricemia was found in 55 (57.29%) patients, whereas there was no hyperuricemia in 41 (42.71%) patients. When the stratification of hyperuricemia was completed on age groups, no significant difference was established among different age

groups, while the stratification of hyperuricemia with respect to gender also exhibited no major variance between men and women. Tables 2 and 3 have presented the stratification of hyperuricemia concerning diabetes and elevated blood pressure, respectively.

**Table 2: Stratification of hyperuricemia in relation to DM**

Diabetes mellitus	Hyperuricemia		p-value
	Yes (n)	No (n)	
Yes	32	23	0.838
No	23	18	

**Table 3: Stratification of hyperuricemia in relation to hypertension**

Hypertension	Hyperuricemia		p-value
	Yes (n)	No(n)	
Yes	29	25	0.420
No	26	16	

Stratification of hyperlipidemia and ischemic heart

disease is shown in Tables 4 and 5, respectively.

**Table 4: Stratification of hyperuricemia in relation to hyperlipidemia**

Hyperlipidemia	Hyperuricemia		p-value
	Yes (n)	No (n)	
Yes	16	10	0.608
No	39	31	

**Table 5: Stratification of hyperuricemia in relation to IHD**

IHD	Hyperuricemia		p-value
	Yes (n)	No (n)	
Yes	17	17	0.285
No	38	24	

**Discussion**

Stroke incidence is increasing, as proved by the latest studies. About 780000 Americans suffer a fresh or recurring stroke annually, which means, one

individual suffers from a stroke after every forty seconds.<sup>10</sup> It's the common reason for mortality worldwide next to coronary disease and malignancy, particularly in the geriatrics<sup>11</sup> But in few studies, uric

acid role is controversial as it is also considered an antioxidant and neuroprotective agent but in this study we have discussed different aspects of increase uric acid in Stroke.<sup>11,12</sup> The death rate in the critical period is 20% which stays elevated for centuries following the critical episode in stroke cases other than the general inhabitants.<sup>11</sup> Stroke is the 2nd reason for debility and dementia in adults aged  $\geq 65$  years: about 25% of patients survived stroke to dementia. Stroke is likewise a main reason for death and debility: about 40% of cases who survived this disease are not likely to improve their liberation, and 25% are incapable of walking self-reliantly.<sup>11</sup>

Uric acid is the end product of purine breakdown in anthropoid and advanced prelates.<sup>13</sup> It occurs in the outer cellular partition as sodium urate, and it is filtered via nephrons.<sup>14</sup> Uric acid is affected by age and gender. Before adolescence, its level is 3.6 mg/dl for both genders. After adolescence, it increases to mature levels, with females characteristically 1 mg/dl fewer than males. Increased levels in females is due to estrogens augmenting urate clearance from nephrons.<sup>14</sup>

It's been stated that elevated uric acid levels are related to conventional coronary risks like raised blood lipids, raised blood pressure, overweight, diabetes, and other endocrine disorders. Besides that, these acids apply central nervous system defensive effects. In homosapiens, about half the antioxidant effect of blood is due to uric acid.<sup>15</sup>

In this research, from 96 patients age 26 to 74 years with mean age of  $54.01 \pm 12.42$  years, bulk of the cases 56 (58.33%) were from 51 to 74 years, 48 (50.0%) were men and 48 (50.0%) were women with men to women proportion of 1:1. Hyperuricemia was found in 55 (57.29%) patients, whereas there was no hyperuricemia in 41 (42.71%) patients. An increase in serum uric acids in adults is related to a slight but statistically noteworthy increase in possibility of stroke occurrence and death.<sup>8</sup>

Bansal et al. 1975 conducted a study on 50 cases with neurovascular syndromes: 30% exhibited elevated uric acids and they established that this might be a key factor in the etiology of neurovascular syndromes in individuals specifically under 40 years of age. Kim et al., 2008 studied a logical analysis of 16

researches comprising 238449 cases to evaluate the relationship of elevated uric acids and possibility of stroke occurrence and death. They demonstrated the same conclusion as Bansal et al. 1975 and his colleagues proved in their studies.<sup>10</sup>

Conferring the results of Millions et al. 2005 research, raised serum uric acids linked with enhanced possibility of severe ischemic Stroke in geriatrics.<sup>16</sup> Besides that in the Syst-Eur literature, which comprised individuals having elevated blood pressure, no substantial correlation was noticed between uric acid levels and lethal and non-lethal strokes.<sup>17</sup> Furthermore, in Japanese average-aged residents, elevated uric acids was not related to deaths due to Stroke in 108284 cases-centuries of monitoring. Goldberg et al. 1995 observed average aged males and monitored them for 2 decades, signifying no relation between serum uric acid and ischemic strokes. Cazzato et al. 1982 described no dissimilarity in uric acid levels in cases with Stroke and the control group. The outcomes confirmed that elevated uric acids could not lead to neurovascular syndromes.

The occurrence of high uric acid levels in the individuals, appearing Nobel Medical College was 28.33% (men 30.06%, women 26.61%).<sup>18</sup> Same literature in Bangkok residents exhibited the predominance of 24.4% elevation in uric acid levels.<sup>19</sup> A research by Folsom HA et al, 2006. also exhibited augmented uric acid levels in individuals undergoing Stroke.<sup>20</sup> Longo Mbenza et al. 1994 in a research amongst Africans established that uric acid levels were raised in stroke cases. In a research by Iribarren, Folsom et al. they observed the relation among uric acid levels and asymptomatic neurovascular diseases.

The effect of urate on ischemic stroke is ill-defined. Another study of 2495 cases in Glasgow proposed that elevated serum urate on admittance anticipated reduced consequence (mortality) and greater vascular incident proportion after ischemic Stroke.<sup>21</sup> On the other hand another literature involving 881 cases established that elevated level of serum urate anticipated improved consequences after Stroke, signifying that serum urate might be advantageous and shield against unfortunate consequences.<sup>22</sup> Additionally an investigational research ing mice

brain suffering from ischemic stroke revealed that high uric acid effect on ischemic Stroke is neuro-protective and outspreads the advantages of recombinant tissue plasminogen activator (rTPA).<sup>23</sup>

### Conclusion

This study concluded that the incidence of raised serum uric acid levels in individuals with Stroke is extraordinary. So, we recommend that timely detection and management of hyperuricemia in order to decrease the death rate and morbidity of patients. Also considering this research, community attentiveness programmes on domestic and local levels can be organized for initial screening and management of hyperuricemia in order to decrease cerebrovascular accidents (CVA) and their impediments.

### Limitation of study

Collection of laboratory investigation and radiological investigation were the major limitation in my study.

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