

COMPARISON OF SERUM URIC ACID LEVELS WITH OUTCOMES IN PATIENTS WITH ACUTE ISCHEMIC STROKE

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ABSTRACT

Objective: To determine the link between uric acid levels and outcome in acute ischemic stroke (infarct).

Study Design: Cross-sectional, observational study.

Place and duration of study: Department of Medicine, Pakistan Ordnance Factories (POF) Hospital, Wah Cantt , 06 months (August 2023 to January 2024).

Methodology: We included 100 patients in our study. All patients underwent serum uric acid level during their admission. After 72 hours, following their admission their Modified Rankin score was calculated and recorded.

Results: The analysis reveals a strong positive correlation between uric acid levels and the Modified Rankin Score (mRS) in acute stroke (infarction). The Pearson correlation coefficient is 0.920, indicating a very high degree of association with $p < 0.001$.

Conclusion: Serum uric acid levels are significantly linked with the Modified Rankin Score while considering the disease outcome in acute cerebral infarction.

Keywords: Acute Ischemic stroke, Prognosis, Uric acid

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INTRODUCTION

Stroke, also called Cerebrovascular accident or Acute brain attack is a condition caused by either disruption in the blood flow to the brain or because of rupture of blood vessels leading to a spectrum of various clinical manifestations due to impairment in brain function¹. Ischemic stroke occurs when the blood supply to the brain is impaired due to the occlusion of the blood vessel supplying that part. The Global burden of disease data revealed very high disease prevalence of stroke and is the second highest cause of mortality worldwide among all the non-communicable disorders with approximately more

than 7 million deaths annually². The prognosis of acute stroke is poor with high mortality rates particularly for those requiring intensive care management. Various factors affect the outcomes and the survival rates are poor in those with increase age group and those with severe impairment in their conscious level during the time of admission to the intensive care³. Some of the advanced management interventions like re-perfusion therapy and decompressive craniectomy have been found to improve the survival rates in stroke patients. The in-hospital mortality of stroke patients is dependent on many factors like age, complications, severity on admission and resource limitation while deciding appropriate therapy⁴. Delirium has also been found to negatively affect the stroke outcomes with increased risk of complications and higher mortality⁵. Similarly, those non-diabetic patients with stroke who developed hyperglycemia during admission had a bad prognosis compared with those with normal sugars⁶.

Hyperuricemia has been found to be an important parameter that is linked with the prognosis and survival in stroke patients. Patients with elevated serum acid are at more risk of developing

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acute stroke with increased mortality rates mediated by the inflammatory mechanisms⁷. Elevated uric levels or Hyperuricemia is an independent risk factor linked with disease severity and progression in cerebral small vessel disease⁸. Therefore, serum uric acid levels, although a simple investigation can be a useful marker in assessment of the disease severity and overall prognosis in patients with acute stroke. The major objective of our study was to determine the association between serum uric acid and stroke outcome in our patient population, with the aim of informing and optimizing future management and preventive strategies.

CAPSULE SUMMARY

A link between uric acid levels and outcome in acute ischemic stroke (infarct) was determined. Serum uric acid levels were significantly linked with the Modified Rankin Score. Serum uric acid levels may prove as a useful biomarker for predicting the severity of disability following a stroke.

measured after 72 hours of admission. All the data was collected on the proforma and saved.

SPSS v 26 was used for the data analysis. Descriptive statistics was calculated for all variables. Quantitative variables particularly age, height, weight, BMI, serum uric acid level at admission was measured by mean and standard deviation. The modified Rankin score calculated at 72 hours was calculated as mean and standard deviation. A p-value of ≤ 0.05 was taken as significant. Stratification was also done on the basis of age, gender and BMI, post stratification correlation coefficient was checked.

METHODOLOGY

We conducted this cross-sectional study in the Department of Medicine, POF Hospital, Wah Cantt, from 10-07-2023 to 09-01-2024 after taking the ethical approval from the hospital ethical review board . A total of 100 patients, between age 18 to 80 years, of both genders who suffered from an acute ischemic stroke presenting with 48 hours of onset of symptoms were included. The diagnosis of stroke was confirmed based on clinical evaluation and CT findings in patients with persistent neurological deficit after 24 hours. Sample size was calculated, using parameters of uric acid in predicting the presence of adverse outcomes in patients with acute ischemic stroke as described by Perveen et al using correlation of coefficient calculated as follows: Level significance: 5%, Power of test: 90%, Correlation of coefficient: r 0.511, Expected sample size: n 100⁹. Consecutive non-probability sampling was utilized. Those with a previous history of CVA, gout, taking urate lowering therapy, alcohol consumers, history of malignancy or taking drugs affecting uric acid levels like Aspirin and diuretics were excluded from the study. Informed consent was obtained from the patients or from their attendants. Serum uric acid levels were checked on admission by taking the blood samples and values expressed in mg/dl. and modified Rankin score was

RESULTS

The mean age of the patients was 57.97 ± 11.66 years (Table-1). Out of 100 patients, 66 (66.0%) were male, while 34 (34.0%) were female (Table-1). The distribution of patients by BMI shows that a majority of the study population, 61.0% had BMI of ≥ 30 kg/m². The analysis reveals a strong positive correlation between uric acid levels and the Modified Rankin Score (mRS) in people with acute infarct. The Pearson correlation coefficient is 0.920, indicating a very high degree of association, and the $p < 0.001$. The values of uric acid more than 8 mg/dl generally correlate with mRS scores of 4 or higher, indicating a stronger association with more severe disability.

In the younger age group (≤ 50 years), the Pearson correlation coefficient was 0.954 ($p = 0.000$), suggestive of positive correlation (Table 5). The stratification by gender revealed significant positive correlations between levels of uric acid and the Modified Rankin Score (mRS) in both males and females which revealed that elevated uric acid is linked with increased disability across genders. In males, the Pearson correlation coefficient was 0.914 ($p = 0.000$), showing a very strong positive correlation between serum uric acid levels and mRS scores. In females, the correlation was even stronger, with a Pearson

Table 1: Age and Gender distribution

| AGE (Years) | Number | Percentage(%) |
|---------------|--------|---------------|
| 50 | 27 | 27 |
| 51-80 | 73 | 73 |
| | 100 | 100 |
| GENDER | | |
| Male | 66 | 66 |
| Female | 34 | 34 |
| | 100 | 100 |

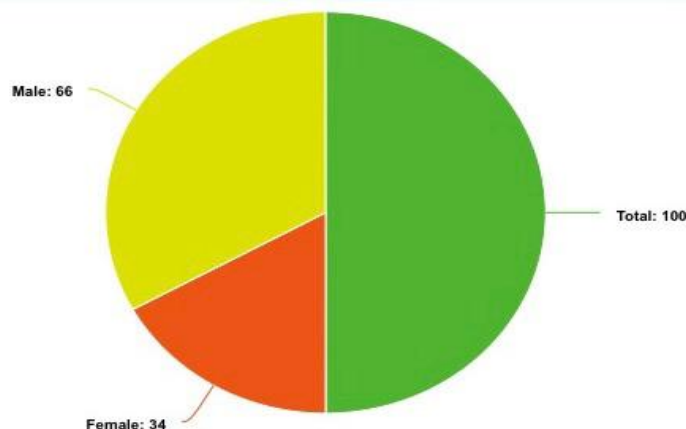


Figure 1: Gender distribution

Table 2: Mean and Standard Deviations of different variables

| Variables | Mean | SD |
|--------------------------|-------|-------|
| Age (Years) | 57.96 | 11.66 |
| Weight (Kg) | 70.2 | 9.17 |
| Height (cm) | 165 | 7.0 |
| BMI (kg/m ²) | 36.68 | 4.92 |
| Uric acid mg/dl | 7.71 | 2.35 |
| mRS | 3.48 | 1.64 |

Table 3: Stratification for BMI

| | | BMI < 30 (kg/m ²) Uric acid (mg/dl) | Modified Rankin Score (mRS) | BMI ≥30 (kg/m ²) Uric acid (mg/dl) | Modified Rankin Score (mRS) |
|-----------|---------------------|----------------------------------------------------|-----------------------------|---------------------------------------------------|-----------------------------|
| Uric acid | Pearson Correlation | 1 | 0.943 | 1 | 0.905 |
| | Sig. (2-tailed) | 0.000 | 0.000 | | 0.000 |
| | N | | 39 | 61 | 61 |
| mRS | Pearson Correlation | 0.943 | 1 | 0.905 | 1 |
| | Sig. (2-tailed) | 0.000 | | 0.000 | |
| | N | 39 | 39 | 61 | 61 |

Table 4: Stratification for Gender

| | | Male Uric acid (mg/dl) | Modified Rankin Score (mRS) | Female Uric acid (mg/dl) | Modified Rankin Score (mRS) |
|-----------|---------------------|---------------------------|-----------------------------|-----------------------------|-----------------------------|
| Uric acid | Pearson Correlation | 1 | 0.914 | 1 | 0.943 |
| | Sig.(2-tailed) | 66 | 0.000 | | 0.000 |
| | N | | 66 | 34 | 34 |
| mRS | Pearson Correlation | 0.914 | 1 | 0.943 | 1 |
| | Sig.(2-tailed) | 0.000 | | 0.000 | |
| | N | 66 | 66 | 34 | 34 |

Table 5: Stratification for Age

| | | Age ≤50 (Years) Uric acid (mg/dl) | Modified Rankin Score (mRS) | (Age51-80) (Years) Uric acid (mg/dl) | Modified Rankin Score (mRS) |
|-----------|---------------------|-----------------------------------------|-----------------------------------|--------------------------------------------|-----------------------------------|
| Uric acid | Pearson Correlation | 1 | 0.954 | 1 | 0.893 |
| | Sig. (2-tailed) | | 0.000 | | 0.000 |
| | N | 27 | 27 | 73 | 73 |
| mRS | Pearson Correlation | 0.954 | 1 | 0.893 | 1 |
| | Sig. (2-tailed) | 0.000 | | 0.000 | |
| | N | 27 | 27 | 73 | 73 |

correlation coefficient of 0.943 (p = 0.000) as highlighted in the Table 4. The average weight of the patients was 70.20 kg, with a standard deviation of 9.17 kg, indicating moderate variability in body weight. The mean BMI was calculated to be 36.68 kg/m², with a standard deviation of 4.92, 62 indicating that the majority of the population was in the obese category. At admission, the mean serum uric acid level was 7.71 mg/dl with a SD of 2.35 mg/dl suggesting notable variability in uric acid levels among patients. The mean Modified Rankin Score (mRS) was 3.48, with a S.D of 1.64, reflecting a moderate degree of functional impairment in the study population.

DISCUSSION

Our study results revealed a significant link between the high uric acid levels and the stroke outcomes using modified Rankin scale (mRS). We observed that those patients who had high uric acid levels on admission had poor outcomes compared with those having normal levels. A recent study conducted in India also showed that high uric acid levels are linked to more disability risk in acute stroke patients¹⁰ similar to our observations. Hyperuricemia is well recognized entity in chronic inflammatory conditions including the Metabolic syndrome. S Khanna et al reported that the critically ill patients admitted with acute stroke who had high uric acid levels had a high mortality rate with a bad prognosis, both in males and females¹¹. These observations were quite similar to our study findings and we found a significant association of hyperuricemia with poor outcome in stroke, both in males as well as female patients. Interestingly, a study that was done to find out the link of stroke severity using NIHSS scale with common biomarkers found no significant link between hyperuricemia and stroke severity¹². The link of elevated uric acid with stroke prognosis has been remained controversial however majority of the studies showed its detrimental effects on cerebral blood flow via pro-inflammatory mechanisms and some data showing its potential good effects as well¹³. Majority of the patients in our study were obese and hyperuricemia was more frequent in those people,

which also suggests hyperuricemia, obesity and bad prognosis of acute ischemic stroke triggered by the inflammation.

Hyperuricemia has been shown to cause various pro inflammatory effects like impairment in endothelial function and insulin resistance¹⁴. These effects caused by high uric acid leads to increased cell apoptosis and oxidative stress. This in turn causes increased propensity towards development of atherosclerosis. The association of hyperuricemia with stroke prognosis is more in ischemic stroke while most of the studies have shown that the risk of hemorrhagic stroke is not significant¹⁵. The risk of stroke with hyperuricemia was more in females in one study, however we didn't find any gender related differences in our study¹⁵. The clinical evidence suggests that urate lowering therapy has a potential role in reducing the cardiovascular risk including stroke and ischemic heart disease¹⁶. It has also been found that elevated NLR i.e Neutrophil to Lymphocyte ratio in stroke patients has additive effects on uric acid-stroke prognosis association¹⁷. The risk of cognitive impairment is also high in those patients with acute stroke who have elevated uric acid levels¹⁷. Recently some studies have also shown the prognostic association of raised serum uric acid in patients with hemorrhagic stroke¹⁸. A study conducted in Peshawar Pakistan found that elevated serum uric acid levels can be used as predictor of stroke risk highlighting the importance of this useful laboratory test¹⁹. A longitudinal descriptive study from Bangladesh also revealed uric acid levels as a simple, cheap and convenient method to determine the prognosis in acute stroke patients²⁰.

Stroke is among the important causes of mortality and affects quality of life both nationally and worldwide therefore our study highlighted the use of an important and simple biomarker, uric acid therefore showing its good potential in improving the prognosis in these patients by timely diagnosis and management of hyperuricemia prior to the development of complications. Serum uric acid is a cost effective and widely available investigation that should be done in patients with

acute cerebral infarct to assess the overall prognosis. The role of elevated uric acid levels has always remained a controversial issue with some studies showing its neuroprotective benefits while majority showing its deleterious effects, that's why we conducted this study to see the effects particularly in our population.

Our study had a few limitations as well. First of all, it was a single centered study with a relatively smaller sample size so results could not be generalized. There may be some confounding effects of obesity as well as majority of our patients were obese. Lack of a control group also makes the validity of results not very high.

CONCLUSION

Elevated uric acid levels are strongly linked to greater disability at 72 hours post admission in patients with stroke. These findings suggest that serum uric acid levels may prove as a useful biomarker for predicting the severity of disability following a stroke. We recommend further larger prospective studies to further strengthen our findings.

ETHICAL APPROVAL: IRB/POFH/022023/MED/12.

CONSENT FOR PUBLICATION: Written, informed consent was obtained from the study participants.

AVAILABILITY OF DATA: Data is available from the corresponding author on a justified request.

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CONFLICT OF INTEREST: None

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AUTHORS' CONTRIBUTION

- **Danial Mateen:** Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article.
- **Muzamil Jamil:** Conception and design, Analysis and interpretation of data, Drafting the article, Critical revision.
- **Syed Asim Ali Shah:** Conception and design, Analysis and interpretation of data, Drafting the article, Critical revision.
- **Wajahat Sultan Baig:** Conception and design, Drafting the article, Critical revision.
- **Izza Sohail:** Acquisition of data.
- **Junaid ur Rehman:** Acquisition of data, Analysis and interpretation of data.

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