Original Article

Association of Serum Uric Acid Levels in Patients with Acute Ischemic Stroke and Clinical Outcome

Muhatarima Tabassum,[1] Md Kafil Uddin,[2] Md Ahmed Ali,[3] S M Emdadul Haque,[4] Md Raseul Kabir[5]
Md Amjad Hossain Pramanik [6]

Abstract

Background: Stroke is one of the most common, most fatal, and debilitating neurologic diseases. Numerous risk factors are involved in the development of strokes, such as hypertension, cigarette smoking, hyperlipidemia, and diabetes. In addition, other factors may influence the disease's development or course, like uric acid serum level.

Objective: To determine the association between serum uric acid (SUA) levels in patients with acute ischemic stroke and clinical outcomes.

Material and method: This was a longitudinal descriptive study carried out among one hundred and twenty consecutive patients with acute ischemic stroke (AIS) admitted to the Department of Neuromedicine, Rajshahi Medical College Hospital (during a period of two years from July'2015 to July' '2017 were included in the study.

12.11 years. Of 120 patients with AIS, 60.8% were male, and 39.2% were female. The study revealed that AIS patients with high SUA levels have significantly lower Glasgow Coma Scale (GCS) scores in comparison to normal SUA levels (p<0.001). There is also a considerably higher modified Rankin Score (mRS) at discharge (4.02 ± 1.47), at one month (4.03 ± 1.01), and at three months (4.21 ± 1.12) (p< 0.001). Thus in our study, mRS analysis showed a significant clinical deterioration in patients with high SUA levels. A comparison of clinical outcomes of AIS patients by MRS between high and normal SUA levels revealed that at three months of follow-up, there is significant deterioration in patients with high SUA levels (p<0.001). There was significantly less improvement with high SUA levels (p<0.001).In this study, a total of 20 patients died at different intervals; at discharge (11), at one month (3), and three months (6). The study showed that patients with high SUA levels had significantly increased mortality in comparison to patients having normal SUA levels. It was statistically significant at discharge and one month (p<0.01 and p<0.05) but not significant at three months (p>0.05).

Conclusion: A significant association was found between high serum uric acid levels and the clinical outcome of AIS patients. Estimation of serum uric acid offers a simple, inexpensive, quick, and non-invasive method for identifying such high-risk patients.

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Introduction

Stroke is the 2nd leading cause of death worldwide. There are more than 4.5 million survivors of stroke, of whom more than a million have a significant residual disability. After a heart attack and cancer, stroke is the 3rd leading cause of death in the United States. This mirrors causes of death in most Western countries, where approximately 50% of deaths are attributed to vascular disease. Despite advances in the

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[1] Assistant Professor, Department of Neurology, Rajshahi Medical College, Rajshahi.

[2] Professor, Department of Neurology, Rajshahi Medical College, Rajshahi.

[3] Associate Professor, Department of Neurology, Rajshahi Medical College, Rajshahi.

[4] Assistant Professor, Department of Neurology, Rajshahi Medical College, Rajshahi.

[5] Assistant Professor, Department of Neurology, Rajshahi Medical College, Rajshahi.

[6] Assistant Professor, Department of Neurology, Rajshahi Medical College, Rajshahi.

understanding and management of stroke around the world, South Asia still faces many challenges relating to this disease. In a door-to-door survey by Mohammad et al.[1] the overall prevalence rate was 3.00 per1000. Numerous risk factors are involved in the development of strokes, such as hypertension, cigarette smoking, hyperlipidemia, and diabetes. Recent studies indicate that other factors may influence the development or course of the disease, like serum level of uric acid.[2] Uric acid (UA) is the final breakdown product of purine degradation in humans. Hyperuricemia was defined as serum uric acid $\geq$ 7 mg/dl in men or $\geq$6 mg/dl in women.[3,4]

Elevated serum uric acid (SUA) has proved to be a risk factor for ischemic heart disease and other cardiovascular diseases in several epidemiologic studies. Experimental studies have shown a uric acid link to endothelial dysfunction, impaired oxidative metabolism, platelet adhesiveness, and platelet aggregation.[5] The worldwide prevalence of hyperuricemia is high.[6]

Serum uric acid is a strong predictor of stroke, coronary artery disease, and metabolic syndrome. However, the definite role of uric acid in these diseases is still the subject of much discussion and debate because it is always accompanied by other risk factors such as diet, obesity, and dyslipidemia.

The present study was done to assess serum uric acid levels in patients with acute ischemic stroke admitted to the Department of Neuromedicine, Rajshahi Medical College Hospital, as prognostic parameters and their relation to clinical outcome.

Materials and Methods

A Longitudinal descriptive study was carried out among One hundred and twenty patients with acute ischemic stroke admitted into the Neuromedicine Department, Rajshahi Medical College Hospital, Rajshahi, for a period of two years **from** July 2015 to July 2017.

Inclusion criteria:

1. First-ever acute ischemic stroke evidenced by clinical evaluation and CT scan or MRI of the brain.
2. The age of the patients is 18 years and above.

3. Both male and female patients.
4. Patient or legal guardians willing to participate.

Exclusion criteria:

1. Patients below 18 years of age.
2. Subjects with a history of the previous stroke.
3. Patients with critical cardiac, renal, hepatic, endocrine, musculoskeletal, malignant diseases, and recent infections.
4. Patients received specific lipid-lowering treatment (i.e., a statin or a fibrate), urate-lowering drugs, alcohol, diuretics, and low-dose aspirin.

With the approval of the Institutional Review Board (IRB) of Rajshahi Medical College, Rajshahi, the data was collected from the respondents according to the questionnaire by face-to-face interview. Every patient and or responsible family member was asked for informed consent. They were informed about the procedure and study goal. All relevant clinical examination findings and laboratory results were recorded in a case record form. Initially, patients were assessed by GCS score. The outcome was evaluated and recorded with the help of the modified Rankin Scale (mRS). The modified Rankin Scale (mRS) is a 7-level ordered categorical scale capturing levels of patient functional independence following a stroke, with scores ranging from 0 (fully independent) to 6 (dead)[7,8]

mRS assessment was performed at discharge, after one month, and after three months. The numerical data were analyzed, and the significance of differences was estimated using computer-based SPSS-16.

Results

Table-1: Socio-demographic profile and baseline characteristics of the study population (n=120)

Baseline characteristics	Frequency (%)	Mean (±SD)
Age distribution		
1. <40 years	8 (6.7)	
2. 40-50 years	27 (22.5)	
3. 50-60 years	22 (18.3)	56.30± 12.11
4. 60-70 years	37 (30.8)	
5. >70 years	26 (21.7)	
Sex		
1. Male	73 (60.8)	
2. Female	47 (39.2)	
HTN		
1. Yes	65 (54.2%)	
2. No	55 (45.8%)	
DM		
1. Yes	47 (39.2%)	
2. No	73 (60.8%)	
Tobacco use		
1. Yes	91(75.8)	
2. No	29(24.2)	
Food habits (beef or other red meat)		
1. Never	15(12.5)	
2. Once a week	105(87.5)	
Dyslipidaemia		
1. Present	111 (92.5)	
2. Absent	9 (7.5)	

Table 1: shows most of the patients were in the age group of 60 to 70 years. The mean age was 56.30 ±12.11. Male was predominant at 60.8%. The majority of the population had a monthly income of <3000 Taka. Among risk factors dyslipidaemia 111 (92.5%), tobacco use was 91(75.8%), hypertension 65 (54.2%) and diabetes mellitus 47 (39.2%).

Table-2: Comparison of male with female AIS patients with SUA level (n=120)

Sex	Serum uric acid		p-Value
	Normal n (%)	High n (%)	
1. Male	41 (56.2)	32 (43.8)	>0.05
2. Female	32 (68.1)	15 (31.9)	

Table 2. 41 male patients and 32 female patients were within normal SUA level.32 male and 15 female patients had high SUA (p-value >0.05). It was statistically insignificant.

Table-3: Comparison of death of AIS patients with high and normal SUA levels (n=20)

Death	Serum uric acid		p-Value
	Normal (%)	High (%)	
Before discharge	1 (9.1)	10 (90.9)	<0.001
After 1 month	0 (0)	3 (100)	<0.05
After 3 months	3 (50.0)	3 (50.0)	>0.05

Table 3 shows patients with high SUA levels had significantly increased mortality (10 at discharge, three at one month, three at three months) in comparison to patients having normal SUA levels (1 at discharge, 0 at one month, three at three months) It was statistically significant at discharge and one month (p<0.01 and p<0.05) but not significant at three months (p>0.05)

Table-4: Comparison of clinical outcomes at three months follows up by mRS between AIS patients with high and normal SUA levels (n=120)

At three months, follow up by mRS	Serum uric acid		p-value
	Normal (%)	High (%)	
1. Deteriorates	15 (28.3)	38 (71.7)	
2. Static	14 (60.9)	9 (39.1)	<0.001
3. Improved	44 (100.0)	0 (0.0)	

Table 6 show the deterioration of patients with high SUA level (p<0.001).

Less improvement with high SUA level (p<0.001)

Table-5: Comparison of mortality (death) by GCS and mRS of AIS patients with high and normal SUA levels (n=120)

Death	Serum uric acid		p-value
	Normal	High	
	Mean (±SD)	Mean (±SD)	
GCS score	14.12 (1.45)	10.64 (2.43)	<0.001
mRS (at discharge)	2.97 (1.05)	4.02 (1.47)	<0.001
mRS (at 1 month)	2.51 (1.34)	4.03 (1.01)	<0.001
mRS (at 3 month)	2.43 (1.62)	4.21 (1.12)	<0.001

Table 5 shows high SUA levels have significantly lower GCS scores (p<0.001) and substantially higher mRS at discharge (4.02 ± 1.47), at one month (4.03 ± 1.01), and three months (4.21 ± 1.12) (p< 0.001).

Patients with normal SUA had a GCS score of 14.12 (1.45), and high SUA scored 10.64(2.43). It was statistically significant (p<0.001).

During discharge, patients with normal SUA had a mRS of 2.97 (1.05), and those with high SUA had a mRS of 4.02 (1.47). It was statistically significant (p<0.001).

At one month, patients with normal SUA had mRS of2.43 (1.62), and those with high SUA had mRS4.21 (1.12). It was statistically significant (p<0.001).

After three months, patients with normal SUA had MRS of 2.51 (1.34), and those with high SUA had mRS of 4.03 (1.01). It was statistically significant (p<0.001).

Discussion

Stroke is among the most common, fatal, and debilitating neurologic diseases. This longitudinal descriptive study was conducted in the neurology department, Rajshahi Medical College Hospital (RMCH), to find out the association between serum uric acid (SUA) and outcomes in patients with acute ischemic stroke (AIS). One hundred and twenty consecutive patients with AIS were included in the study. The study population was between 35 to 75 years. The mean age was 56.30 ± 12.11 years. This finding is consistent with the data published by Behera et al. (2017) and Imarhiagbe (2012).[9,10] Higher mean age (65.84 ± 13.37 and 67 ± 13.6) was observed by Kotwal et al.[11] and Mehrpour et al.[12] Most of the patients were in the age group of 60 to 70 years (30.80%). Of 120 patients with AIS, 60.8% were male, and 39.2% were female. Male predominance was found by Behera et al. (2017),[9] Kotwal et al. (2015),[11] Mehrpour et al. (2012)[12] Similar male predominance was also found in our country by Khalil et al. (2013)[13] and Mohammad (2011).[1]On the other hand, female predominance was found by Moghaddam et al. (2015)[14] (53% vs. 47%) and Karragiannis et al. (2007)[15] (51.7% vs. 48.3%).

In our study, SUA was higher among males compared with females, with a mean of 6.01±2.19 versus 5.03±2.32 mg/dl, respectively (P<0.05). Higher mean SUA in men was also found by Wasserman (2010)[16] (6.5±2.5 vs. 5.7±2.8 mg/dl, P<0.001). Behara et al. (2017)[9] showed statistically significant higher mean SUA levels among males (6.42±1.42) than females (5.52±1.40) (P-value = 0.003). Longo et al. (1999) found significantly higher SUA levels in males (6.6±7 versus 5.8±6 mg/dl, P < 0.01). Similar results were obtained in the Rotterdam study (Boss et al. 2006)[17] (348 versus 302 μmol/L). Framingham heart study also showed higher SUA levels in males. (Culleton et al. 1999).[18] Hyperuricemia was seen by Chen et al. (2009)

with a male predominance (39.7% men, 11.3% women) (6.8 ±1.6 vs. 5.4 ±1.4, P<0.05)

Glasgow Coma Scale (GCS) and mRS are the reflections of stroke severity that correlate reliably with well-known stroke severity scales like the National Institutes of Health Stroke Scale (NIHSS), and this suggests a tendency of SUA to indirectly reflect stroke severity. We used GCS and mRS to quantify stroke severity and prognosis. In our study, AIS patients with high SUA levels have significantly lower GCS scores in comparison to normal SUA levels (p<0.001). There is also significantly higher MRS at discharge (4.02 ± 1.47), at one month (4.03 ± 1.01), and at three months (4.21 ± 1.12) (p< 0.001). Thus in our study, mRS score analysis showed that there was a significant clinical deterioration in a patient with high SUA levels. A similar study was carried out by Koppula et al. (2013)[19] among the South Indian population in which follow-up of patients was done by Mrs and GCS. The author observed high SUA levels to be associated significantly with AIS and poor outcomes, including death at three months. Imarhiagbe (2012)[10], in his study, showed that in-hospital mortality had a lower mean GCS score (P < 0.001) compared to the group that was discharged or still in care.SUA correlated significantly with GCS in his study.

A study comparing the clinical outcomes of AIS patients by mRS between high and normal SUA levels revealed that at three months follow up, there is significant deterioration in patients with high SUA levels (P<0.001). There was significantly less improvement with high SUA levels as well (P<0.001)

In this study, a total of 20 patients died at different intervals; at discharge (11), at one month (3), and at three months (6). The study showed that patients with high SUA levels had significantly high mortality in comparison to patients having normal SUA levels. It was statistically significant

at discharge and one month (P<0.01 and P<0.05) but not significant at three months (P>0.05). Behera et al. (2017) [9] also, in their study, found a significant correlation between SUA level and clinical outcome. The mean SUA level was significantly higher in the patients who expired than those who were alive at discharge (P=0.014). Karagiannis et al. (2007) [15] found an independent relationship between higher SUA levels on admission and death (OR = 1.37, 95% C.I. = 1.13 - 1.67, P = 0.001). Weir et al. (2003) noted that higher serum urate value was significantly associated with bad outcome (OR = 0.78 per additional 0.1 mmol/L; 95% C.I. = 0.67 - 0.91). Mozos et al. (2007) [20] also found that the patients who died had a significantly higher SUA value as compared to those who were discharged home (9.5±3 mg/dl versus 6.9±4 mg/dl, P = 0.003). A study conducted by Chen et al. (2009) showed high SUA levels affect AIS mortality. In the study done by Longo et al. (1999), hyperuricemia was significantly related to a double risk of all mortality and stroke onset. Wasserman (2010) [16] showed SUA was significantly associated with mortality (7.7±4.9 vs. 6.0±2.5 mg/dl in patients who died versus patients who were alive, P<0.025). The findings of our study were in accordance with the studies mentioned above.

Conclusion

In our study, a significant association was found between high serum uric acid levels and the clinical outcome of AIS patients. Estimating serum uric acid offers a simple, inexpensive, quick, and non-invasive method for identifying high-risk patients. As high serum uric acid could be a modifiable and preventable risk factor of AIS, it may be a potential clinical investigation for evaluating the patients for AIS with elevated serum uric acid in the early stage and prevention of morbidity and mortality of AIS.

Conflict of interest: None declared

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All correspondence to
Dr Muhatarima Tabassum
Assistant Professor
Department of Neurology
Rajshahi Medical College, Rajshahi
Email:tabassummuhatarima@gmail.com