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Original Article

Hyperuricemia as a Prognostic Marker in Acute Ischemic Stroke

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Abstract

Serum uric acid has also been linked to prognosis of patient with acute ischaemic stroke. Evidence suggests that increased level of uric acid is protective in patients with acute ischaemic stroke although this issue has been debated, the neuroprotective role of uric acid in patient with acute ischaemic stroke is now established . So it could be marker of value in prognosis of patient with acute ischaemic stroke.

Key words: Risk factor, Stroke, Uric acid

INTRODUCTION

Stroke entails a high socioeconomic burden due to increased mortality and morbidity. Early identification of individual at risk could be of help in stroke entails a high socioeconomic burden due to increased mortality and morbidity. Early identification of individual at risk could be of help in designing primary prevention strategies.[1]

The role of serum uric acid (SUA) level as an independent risk factor for stroke has been questioned for many years. Evidence from epidemiological studies suggest that elevated SUA levels may predict an increased risk for stroke and cardiovascular events.[2,3] Moreover, therapeutic modalities with an SUA-lowering potential have been shown to reduce cardiovascular disease morbidity and mortality. In this respect, SUA levels could be as an "easy to measure" serum marker in selecting and appropriately treating subjects at risk.

SUA has also been linked to prognosis of patient with acute ischemic stroke. Evidence suggests that increased level of uric acid is protective in patients with acute ischemic stroke.[4] Although this issue has been debated, the neuro-protective role of uric acid in patient with acute ischaemic stroke is now established.[5] Hence, it could be marker of value in prognosis of patient with acute ischemic stroke.

Despite the widely held view that elevated SUA concentrations confer increased risk of atherosclerotic disease, there is no compelling biological evidence of a causal link. Free radical activity is characteristically increased in patients with any one of several major cardiovascular risk factors and is thought to play a key role in the early development of atherosclerosis. As an antioxidant, uric acid could be expected to confer protection against free radicals. In the context of acute ischemic stroke, there is growing evidence to support a protective role for uric acid. This shows the importance of oxidative stress in the pathogenesis of acute stroke and strengthens the rationale for further investigation of antioxidant treatments in this condition. The feasibility of uric acid administration to temporarily increase circulating concentrations has recently been established and might allow its potential therapeutic impact to be examined in a clinical setting. Ongoing basic research is likely to shed new light on the cardiovascular effects of uric acid and will hopefully allow the significance of serum concentrations to be interpreted more clearly.

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The present study is designed to study the association between SUA and stroke. This study also intends to study the association between major and minor risk factors for stroke and SUA level in patients of acute ischemic stroke.

Aims and Objectives

The objectives of this study were as follows:

To study the clinical profile of acute ischemic stroke patients with normal and elevated uric acid.

To study the incidence of ischemic stroke with uric acid levels and its correlation with major and minor risk factors (i.e., hypertension, diabetes, smoking, alcohol, and hyperlipidemia).

MATERIALS AND METHODS

Population

The present study was carried out on 100 patients of acute ischemic stroke admitted at Mahatma Gandhi Memorial Hospital, Warangal.

Study

This was a prospective observational study.

Period of Study

The study duration was from January 2016 to August 2017.

Inclusion Criteria

Patients with stroke as defined by the World Health Organization (WHO) criteria

Stroke or cerebrovascular accident was defined as rapidly developing clinical symptoms and signs of focal or global loss of cerebral function with symptoms lasting more than 24 h or leading to death with no apparent cause other than that of vascular origin (WHO, 1980).[6] In each case, the diagnosis of recent ischemic stroke was confirmed by computed tomography (CT) scan of brain.

Exclusion Criteria

Patients having disease known to increase SUA or taking drugs which can cause hyperuricemia were excluded from the study.

Hemorrhagic stroke, old cases of stroke, was excluded from the study.

Patient admitted within 3 h and had thrombolysis.

Secondary causes of hyperuricemia as mentioned.

Methods

The prospective observational study conducted in MGM Hospital, Warangal. On admission in hospital, detailed history was taken and thorough physical examination was performed as per pro forma made. The severity of neurological deficit was recorded according to the Scandinavian stroke scale (SSS).

Individual found suitable for the study was subjected to the following investigation:

- Hemoglobin, total leukocyte count, differential leukocyte count, platelet count, and erythrocyte sedimentation rate.
- Blood sugar (fasting and postprandial). Patient was diagnosed as having diabetes based on the Americans with disabilities act 2004 criteria.
- Blood urea, serum creatinine, and serum electrolytes.
- Lipid profile was obtained after 12 h of fasting.
- Electrocardiography was done in every case to detect atrial fibrillation, ischemic heart disease, and left ventricular hypertrophy.
- Echocardiography was done as and when indicated.
- Echocardiography was done as and when indicated Table 1.

CT scan of the brain was done in every patient to confirm the diagnosis of acute ischemic stroke.

SUA - hyperuricemia was defined as SUA level >7 mg/dl Table 2.

Table 1: Distribution of cases according to age and sex in patients with acute ischaemic stroke

S. No.	Age groups (in years)	Sex		Total (100)
		Male (%)	Female (%)	
1	<40	05 (09)	01 (2)	06
2	41–50	08 (15)	08 (17)	16
3	51–60	12 (22)	11 (24)	23
4	61–70	17 (31)	17 (37)	34
5	71–80	10 (19)	09 (20)	19
6	>81	02 (04)	00 (00)	02
7	Total	54	46	100

Table 2: Distribution of cases according to age and its relation with uric acid in acute ischaemic stroke

S. No.	Age groups (in years)	Level of SUA		Total (100)
		SUA ≤7 mg% *n*=71 (%)		SUA >7 mg% *n*=29
1	<40	05 (07)	01 (3.5)	06
2	41–50	15 (21)	01 (3.5)	16
3	51–60	16 (23)	07 (24)	23
4	61–70	22 (28)	12 (41)	34
5	71–80	11 (18)	8 (28)	19
6	>81	02 (03)	00 (00)	02
7	Total	71	29	100

≤60 years versus >60 years; Chi-square; $P<0.05$; significant. SUA: Serum uric acid

OBSERVATION AND RESULTS

About 54% of patients were male and 46% of patients were female, majority of patients (34%) were in the age group of 61–70 years.

Of 29 hyperuricemic patients, 20 (69%) were above the age of 60 years as compared to patient with normal SUA in whom out of 71 only 35 (49%) patients were above 60 years.

This study includes 54 males and 46 females, males were having higher incidence (31%) of hyperuricemia as compared to females (26%) Table 3.

Association of uric acid with smoking in acute ischemic stroke patients was not significant Table 4.

The prevalence of alcoholism in the present study was 33% Table 5. Of which, 13 (39%) patients are hyperuricemic. All alcoholics were male. Although overall there was no significant correlation in between SUA and alcoholism. Statistically significant positive correlation $P < 0.05$ was present among male alcoholics.

None of the hyperuricemic patient was normotensive Table 6. In 29 patients with hyperuricemia, 11 (38%) were having prehypertension and 18 (62%) were hypertensive as compared to patient with normal SUA where 54% were hypertensive.

About 34% of patients with hyperuricemia were diabetic as compared to patient with normal SUA in which only 20% of patients were diabetic Table 7.

The incidence of dyslipidemia was almost equal among patient with hyperuricemia and without hyperuricemia Table 8.

Majority (83%) of patients were having infarct in MCA artery territory Table 9. In 7% of patients, MCA and ACA both were involved. In 10% of patients, PCA artery was involved.

Mean SSS score in patient with elevated SUA was 38.90 versus 30.27 in patient with normal SUA $P = 0.0076$ which is statically significant. Majority of patients 20 (69%) with elevated SUA were having SSS score >30 as compared to patients with normal SUA in whom only 35 (50%) were having SSS score >30 Table 10.

Mean mRS score in patients with elevated serum uric acid 3.82 mg/dl Vs 3.41mg/dl in patient with normal uric acid; student t test $P>0.05$ statistically insignificant Table 11.

Table 3: Distribution of cases according to sex and its relation with uric acid in acute ischaemic stroke

S. No.	Sex	Level of SUA		
		SUA ≤7 mg% *n*=71 (%)		SUA >7 mg% *n*=29
1	Male	37 (52)	17 (59)	54
2	Female	34 (48)	12 (41)	46
3	Total	71	29	100

Male versus female, Chi-square, $P>0.05$, insignificant. SUA: Serum uric acid

Table 4: Correlation of SUA and smoking in acute ischaemic stroke

S. No.	Status	Level of SUA		Total (100)
		SUA ≤7 mg (%)	SUA >7 mg (%)	
1	Smoker	28 (39)	10 (34)	38
2	Nonsmoker	43 (61)	19 (66)	62
3	Total	71	29	100

Smoker versus nonsmokers, Chi-square test, $P>0.05$, insignificant.
SUA: Serum uric acid

Table 5: Correlation of SUA and alcoholism in acute ischaemic stroke

S.No.	Status	Level of SUA		Total
		SUA <7 mg *n*=71 (%)	SUA >7 mg *n*=29 (%)	
1	Alcoholic	20 (28)	13 (45)	33
2	Nonalcoholic	51 (72)	16 (55)	67
3	Total	71	29	100

Alcoholic versus nonalcoholic, $P>0.05$, insignificant. SUA: Serum uric acid

Table 6: Correlation of hypertension and SUA in acute ischaemic stroke

S. No.	BP	Level of SUA		Total
		SUA ≤7 mg% *n*=71		SUA >7 mg% *n*=29
1	Normal BP	16 (23)	Nil	16
2	Pre hypertension SBP-120–139 DBP-80–89	17 (24)	11 (38)	28
3	Stage 1 hypertension SBP-140–159 DBP-90–99	16 (23)	6 (21)	22
4	Stage 2 hypertension SBP>160, DBP>100	22 (31)	12 (41)	34
5	Total	71	29	100

Hypertensive versus nonhypertensive; Chi-square; $P<0.05$; Significant.
SUA: Serum uric acid, BP: Blood pressure, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 7: Correlation of diabetes and SUA in acute ischaemic stroke

S. No.	Status	Level of SUA		Total
		SUA ≤7 mg% *n*=71	SUA >7 mg% *n*=29	
1	Diabetic	14 (20)	10 (34)	24
2	Non diabetic	57 (80)	19 (66)	76
3	Total	71	29	100

Diabetics versus nondiabetics; Chi-square test; $P>0.05$: Insignificant.
SUA: Serum uric acid

Table 8: Correlation of lipid profile and SUA in acute ischaemic stroke

S. No.	Lipid profile (mg %)	Level of SUA		Total
		SUA ≤7 mg% *n*=71	SUA >7 mg% *n*=29	
1	No dyslipidemia (S. cholesterol<200 mg%) S. triglyceride<160 mg%	32 (45)	07 (24)	39
2	Hypercholesterolemia (S. cholesterol>200)	10 (14)	05 (17)	15
3	Hypertriglyceridaemia S. triglyceride>160 mg%	19 (27)	10 (35)	29
4	Combineddyslipidemia	10 (14)	07 (24)	17
5	Total	71	29	100

No dyslipidemia versus dyslipidemia; Chi-square P>0.05, insignificant. SUA: Serum uric acid

Table 9: CT scan arterial territory involved

S. No.	Arterial territory involved	Level of SUA		Total
		SUA≤7 mg% *n*=71	SUA>7 mg% *n*=29	
1	MCA	60 (85)	23 (79)	83
2	MCA, ACA	06 (8)	01 (3)	07
3	PCA	05 (7)	05 (18)	10
4	Total	71	29	100

CT: Computed tomography, SUA: Serum uric acid

Table 10: Correlation of SUA and SSS in acute ischaemic stroke

S. No.	SSS	Level of SUA		Total
		SUA≤7 mg%	SUA>7 mg%	
1	<20	18 (25)	03 (10)	21
2	21–30	18 (25)	06 (21)	24
3	31–40	19 (27)	07 (24)	26
4	41–50	14 (20)	09 (31)	23
5	>51	02 (3)	04 (14)	06
6	Total	71	29	100

SSS ≤30 versus >30; Chi-square test; *P*<0.05; significant. SSS: Scandinavian stroke scale. SUA: Serum uric acid

Table 11: Correlation of SUA and outcome by mRS in acute ischaemic stroke

S. No.	mRS	Level of SUA		Total
		SUA<7 mg (%) *n*=71	SUA>7 mg (%) *n*=29	
1	1	04 (06)	00 (00)	04
2	2	08 (11)	09 (31)	17
3	3	16 (23)	08 (28)	24
4	4	20 (28)	06 (21)	26
5	5	15 (21)	03 (10)	18
6	6	08 (11)	03 (10)	11
7	Total	71	29	100

mRS <3 versus mRS ≥3, Chi-square test, *P*>0.05, insignificant. SUA: Serum uric acid. mRS: Modified Rankin's scale

DISCUSSION

The study was conducted in 100 patients of acute ischemic stroke admitted to MGM Hospital, Warangal. A detailed history and systemic examination were carried out in every patient. In each case, the diagnosis was confirmed by CT scan brain. On admission, patients' neurological status was assessed by the SSS and outcome was graded using mR's. SUA was measured within 24 h of onset of stroke and value >7 mg/dl was considered hyperuricemia.

The present study included a total of 100 patients with new onset of acute ischemic stroke. Of 100 patients, 54% of patients were male and 46% of patients were female. Majority of patients (57%) were in the age group of 50–70 years. Six patients were below the age of 40 years and two patients were above the age of 80 years.

In the present study, old age appears to be a big risk factor for both stroke and hyperuricemia Table 12. In the present study, the prevalence of hyperuricemia in stroke patient was 29%. Mean SUA was 6.25 ± 2.72 mg/dl. Of 29 hyperuricemic patients, 20 (69%) were above the age of 60 years as compared to patients with normal SUA in whom 35 (49%) patients were above60 years ($P < 0.05$, significant). Overall, 55% of patients were above the age of 60 years. Mean age of stroke in our study was 61.18 ± 13.43 years. Average SUA in patient above60 years was 6.58 ± 2.75 mg/dl as compared to patient under the age of 60 years in whom mean SUA level was 5.84 ± 2.72 mg/dl.

Bansal *et al.* reported the prevalence of hyperuricemia of 30% in patient with acute ischemic stroke, with mean SUA of 6.5 ± 1.19 mg/dl. They reported the mean age of 59.40 ± 12.15 years.

The present study finding is consistent with the finding of Bansal *et al.*

The prevalence of hyperuricaemia was higher in male (59%) out of 29 were male Table 13. In the present study, mean SUA among male was 6.39 ± 2.74 mg/dl, and in female, mean SUA level was 6.07 ± 2.68 mg/dl. However, the difference in SUA level and the gender is not statistically significant (Student's *t*-test $t > 0.05$). Males usually have higher prevalence of hyperuricemia as compared to female. This difference is maintained till menopause, after that this difference normalized. The difference is due to uricosuric effect of estrogen in premenopausal woman.

Table 12: Distribution of cases according to age and its relation with uric acid in acute ischaemic stroke and comparison with other studies

Study	Prevalence of hyperuricaemia (%)	Mean SUA	Mean age
Present series (*n*=100)	29	6.25±2.72 mg/dl	59.40±12.15 years
Bansal *et al*. 2000 (*n*=50)	30	6.5±1.19 mg/dl	59.40±12.15 years

Table 13: Distribution of cases according to sex and its relation with uric acid in acute ischaemic stroke and comparison with other studies

Study	Present study	Chamorro *et al*. 2002 (*n*=881)	Milionis *et al*. 2005 (*n*=100)
Prevalence of hyperuricaemiain males	59%	52%	53.5%
Significance of male gender	<0.05	0.0001	0.01

Chamorro *et al*., 2002, showed a significant relationship between SUA and male gender of patient with acute ischemic stroke ($P = 0.0001$).

Milionis *et al*., 2005, also showed significant relation between SUA level and male gender in patient with acute ischemic stroke ($P = 0.01$).

In the present study, possible reason for getting insignificant relationship in between sex and SUA level may be due to the fact that majority of woman in the present study were postmenopausal, as after menopause uric acid difference tends to equalize in between male and female.

Summary

The study was conducted in 100 patients of acute ischemic stroke admitted to MGM Hospital, Warangal. A detailed history and systemic examination were carried out in every patient. In each case, the diagnosis was confirmed by CT scan brain. On admission, patients neurological status was assessed by the SSS and outcome was graded using mRS. SUA was measured within 24 h of onset of the stroke and value >7 mg/dl was considered hyperuricemia. Patients with conditions which can cause hyperuricemia were excluded from the study.

About 54% of patients were male and 46% of patients were female. Majority of patients (57%) were in the age group of 50–70 years. The prevalence of hyperuricemia in stroke patients was 29%. Mean SUA was 6.25 ± 2.72 mg/dl.

Of 29 hyperuricemic patients, 20 (69%) were above the age of 60 years as compared to patient with normal serum uric acid in whom 35 (49%) of 71 patients were above 60 years, and there was significant relationship in between age and uric acid in acute ischemic stroke patient ($P < 0.05$, significant).

In the present study, mean serum uric acid among male was 6.39 ± 2.74 mg/dl, and in female, mean serum uric acid level was 6.07 ± 2.68 mg/dl. However, this difference in serum uric acid and gender is not statistically significant ($P > 0.05$).

Total 56% of patients were hypertensive and there was a significant correlation in between hyperuricemia and hypertension in patient with acute ischemic stroke ($P < 0.05$).

Total 24% of patients were diabetic and there was no significant correlation in between diabetes and SUA level in patient with acute ischemic stroke ($P > 0.05$).

Of total 29 hyperuricemic, 22 (76%) of patients were dyslipidemic as compared to patient with normal serum acid in which only 39 (55%) of 71 patients were dyslipidemic. There was also no statistically significant relationship was found in between hyperuricemia and dyslipidemia ($P > 0.05$).

The prevalence of smoking was less 10 (34%) in patient with hyperuricemia as compared to patient with normal SUA level 28 (39%). There was no significant relationship in between smoking and SUA level ($P > 0.05$).

Mean SUA among alcoholic was 6.75 ± 2.76 mg/dl as compared to non-alcoholic in which it was 6.02 ± 2. 72 mg/dl. Significant positive correlation was present among male alcoholics ($P > 0.05$).

Majority (83%) of patients were having in fraction MCA territory. In 7% of patients, MCA and ACA both were involved. In 10% of patients, PCA was involved.

There was a modest but significant positive association in between SSS and hyperuricemia (mean SSS score in hyperuricemic patients was 38.90 vs. 30.27 in patient with normal SUA) ($P < 0.05$).

At the time of outcome, mean mRS in hyperuricemic patient was 3.82 mg/dl versus 3.41 mg/dl in patient with

normal level of SUA. There was no significant difference between these two groups ($P > 0.05$).

CONCLUSION

The prevalence of hyperuricemia in acute ischemic stroke patients in the present study was 29%.

Of all the risk factors for stroke analyzed age, hypertension and alcoholism among male showed statistically significant positive correlation with hyperuricemia in patient with acute ischemic stroke.

Patients with hyperuricemia were having better neurological status as compared to patients without hyperuricemia when assessed at the time of admission.

After 1 week, there is no statistically significant relationship was found in between outcome of patient and hyperuricemia in patients with acute ischemic stroke.

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