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Serum Uric Acid Levels in Predicting the Clinical Course and Outcome in Acute Ischemic Stroke Patients

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ABSTRACT

The levels of serum uric acid in ischemic stroke has been has been questioned for decades. Evidence from epidemiological studies suggest that the elevated SUA levels may predict an increased risk for cerebrovascular (CV) events including stroke. SUA can work as pro-oxidant under certain circumstances, particularly if the levels of other antioxidants like ascorbic acid are low. Various studies have shown that uric acid can result in endothelial dysfunction which can lead to vascular disease. An association between SUA and inflammatory marker shaves also been discovered More over therapeutic modalities with a SUA lowering potential have been shown to reduce CV disease morbidity and mortality. The present study was conducted in Adichunchanagiri hospital and research institute, BG Nagara Mandya. 100 patients of first ever on life time acute ischemic stroke were included. the blood samples like complete hemogram, serum uric acid, blood sugar, lipid profile was taken within 24hours of onset of stroke and sent for biochemical analysis. The patients were further evaluated for presence of additional risk factors like hypertension, diabetes, coronary artery disease, adverse lipid profile, smoking and alcoholism. 100 patients participated in the study in which 82 males and 18 females. Majority Were in the age group of >50 yrs, constituted 48%of stroke population mean uricacid levels in males is 6.49% and in females its 5.83%. age wise distribution of uricacid is statistically significant, as age advances uricacid also rises. Diabetes constitutes major risk factor with 49% of the population with 51.2mg/dl and 38.9% females. Hypertension ranks second as risk factors, constitutes 46% of study populations 48.8% males and 33.3% females. CAD is associated in 38% of study populations with 40.2% males and female 27.8% females. 45% stroke population has adverse lipid profile, 53% affected with stroke are smokers and 51% are alcoholics. Our study shows that elevated serum uric acid is strongly associated with an increased risk for development of acute ischemic stroke, also the relation between other risk factors and raised uric acid levels association between elevated serum uric acid and ischemic stroke may need to be considered especially when treating elderly patients, Diabetes, CAD and Hypertension.

INTRODUCTION

The World Health Organization defines a stroke as a clinical syndrome with rapidly manifesting clinical indications indicating a focal (or global, in the case of acoma) disturbance of cerebral function, with symptoms lasting for 24 hours or longer or leading to death, with no apparent other than of vascular origin[1]. Stroke is the second biggest cause of death in the world, accounting for 6.2 million deaths in 2015[2]. Uric acid has been found to be an independent risk factor for hypertension and cerebrovascular disorders, according to numerous investigations, including the THANES study[3]. A major natural antioxidant, serum uric acid has been linked to improved neurological and immunological processes as well as a slowed progression of severeneurodegenerativedisorders[4]. In the acute stage of an ischemic stroke, the function of serum uric acid (SUA) is being studied. In the first few hours following an ischemic stroke, SUA concentrations rise and then return to baseline levels in the following days[5]. Because it prevents lipid per oxidation, uric acid-the most prevalent aqueous antioxidant in humans-may play beneficial physiological effect. Acute stroke patients who have lower plasma antioxidant levels at the time of the stroke have aworseprognosis[6]. Stroke incidence is rising globally, mostly in those with poorer access to healthcare. Due to increased mortality and morbidity, stroke also carries a significant socioeconomic burden[8]. Ischemic stroke accounts for around 80% of strokes. Primary prevention may be ne fit formerly detection of those who area risk[9]. All physicians have a role in the prevention of stroke by encouraging the reduction in risk factors[10]. The most prevalent aqueous antioxidant in humans, uricacid (UA), may play a beneficial physiologic role by reducing lipid per oxidation[11]. Although its antioxidant capabilities had not previously been taken into consideration, uric acid has long been employed in clinical practice as a marker of numerous metabolic disturbances[12]. Compared to some antioxidants like vitamin C and vitamin E, Uricacid's plasma concentration is nearly ten times higher. It is particularly powerful at squelching hydroxyl, super oxide and peroxynitri teradicals[13]. During acute ischemia and acute stress, local UA concentrations rise in a number of vascular beds and organs and the elevated concentrations may be a compensatory mechanism that offers protection from elevated free radical activity[11]. Hence, it might be suggested that having higher SUA levels during a stroke might be advantageous. Acute stroke patients who have lowered plasma anti oxidant sat the time of the stroke have a poor prognosis[7]. Stroke is related with a rapid drop in serum antioxidants. Local UA concentrations maximally rise after acute brain damage animal models[14]. For instance, middle cerebral artery blockage in rats increases cerebral UA concentrations significantly and this effect can last for several days after the injury[15]. Uric acid is a natural antioxidant that has been linked in epidemiological studies to the risk of cere bro vascular or coronary ischemic events[16]. However, it is not completely clear whether this association indicates that uric acid is it represents a marker of a the rosclerotic disease and an independent ischemic risk factor. Whether the concentration of uric acid at the onset of ischemic symptoms in fluence the severity of stroke also remains to bee elucidated. The significance of serum uric acid levels (SUA) as a separate risk factor for vascular disease has been questioned for decades[17]. Evidence from epidemiological studies suggests that the elevated SUA levels may predicate increased risk force rebro vascular (CV) events including stroke[18]. Assuming the relevance of and the antioxidant capacity of uric acid and oxidative stress in patients with brain ischemia we addressed this question in alargeseries of patients with acute ischemic stroke.

MATERIALS AND METHODS

The present study was conducted in the Department of General Medicine, Adichunchanagiri Hospital and Research Institute, BG Nagara, Mandya and included 100 patients experiencing their first-ever acute ischemic stroke. Blood samples, including complete hemogram, serum uric acid, blood sugar and lipid profile, were collected within 24 hours of stroke onset and analyzed biochemically. Patients were assessed for additional risk factors such as hypertension, diabetes, coronary artery disease, adverse lipid profile, smoking and alcoholism. Inclusion criteria encompassed patients above 18 years with CT-confirmed ischemic stroke and informed consent, while exclusion criteria ruled out those on certain medications, with prior strokes, gout, chronic renal failure, hematological abnormalities, hypoparathyroidism, CT evidence of hemorrhage or space-occupying lesions, or embolic cardiac diseases. Ethical committee approval was obtained. The blood samples were drawn with in 24 hours of the stroke's on set and sent for bio chemical investigation. They were examined in our biochemical laboratory using a standard analyzer. Using the metrics listed below, the patients were further assessed to see if any additional risk factors were present.

Statistical Analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software and Epi-info version 7.2.1 (CDC Atlanta) software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test** was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. **Normality of the continuous data, was tested by Kolmogorov-Smirnov test and the**

Shapiro-Wilk test. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. p value <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS AND DISCUSSIONS

Table 1: Age Distribution According to Sex

		Cases			
		Male (n =82)		Female (n = 18)	
		No.	%	No.	%
Age (Years)	50-59yrs	5	6.1%	5	10.0%
	60-69yrs	45	54.9%	10	55.0%
	70-79yrs	31	37.8%	2	33.0%
	>80yrs	1	1.2%	1	2.0%
	Mean Age	67.60 ± 6.32		63.44 ± 8.4	

In the present study, the majority of male subjects (54.9%) were in the age group of 60-69 years, followed by 37.8% in the 70-79 years group. Similarly, the majority of female subjects (55.0%) were also in the 60-69 years age group, followed by 33.0% in the 70-79 years group. The mean age was 67.60±6.32 years for males and 63.44 ± 8.4 years for females. There was no significant difference in the age distribution between the sexes (Table 1).

Table 2: Risk Factors According to Sex

Risk Factor		Cases			
		Males		Females	
		No.	%	No.	%
Hypertension	Present	40	48.8	6	33.3
	Absent	42	51.2	12	66.7
DM	Present	42	51.2	7	38.9
	Absent	40	48.2	11	61.1
Smoking	Present	53	64.6	0	0
	Absent	29	35.4	18	100
CAD	Present	33	40.2	5	27.8
	Absent	49	59.8	13	72.2
Hyperlipidemia	Present	42	51.2	3	16.7
	Absent	40	48.8	15	83.3
Alcoholism	Alcoholic	49	59.8	2	11.1
	Non-Alcoholic	33	40.2	16	88.9

In the present study, 48.8% of males and 33.3% of females had hypertension. Diabetes mellitus (DM) was observed in 51.2% of males and 38.9% of females. Smoking was exclusively present in males, with 64.6% smokers and no smokers among females. Coronary artery disease (CAD) was noted in 40.2% of males and 27.8% of females. Hyperlipidemia was present in 51.2% of males compared to 16.7% of females. Alcoholism was observed in 59.8% of males, whereas only 11.1% of females reported alcohol consumption. These findings indicate significant sex differences in the distribution of risk factors (Table 2).

Table 3: Comparison of UricAcid(mg/dl) Levels Between Males and Females

		Cases				
		Male (n =82)		Female (n = 18)		
		No.	%	No.	%	P-value
UricAcid (mg/dl)	<5	9	11.0%	5	27.8%	0.1601
	5-6.9	34	41.5%	7	38.9%	
	≥7	39	47.6%	6	33.3%	
	Mean±SD	6.49±1.66		5.83±1.58		

In the present study, uric acid levels of <5 mg/dl were observed in 11.0% of males and 27.8% of females, while levels of 5-6.9 mg/dl were seen in 41.5% of males and 38.9% of females. Elevated levels (≥7 mg/dl) were found in 47.6% of males and 33.3% of females. The mean uric acid level was 6.49±1.66 mg/dl for males and 5.83±1.58 mg/dl for females. There was no significant difference in uric acid levels between the sexes (P=0.1601) (Table 3).

Table 4: Uricacid Levels with Respect to CAD

		UricAcid (mg/dl)		
		Mean	SD	P-value
CAD	Present	6.71	6.16	<0.001*
	Absent	1.72	1.6	

In the present study, the mean uric acid level was significantly higher in subjects with CAD (6.71±6.16 mg/dl) compared to those without CAD (1.72±1.6 mg/dl). This difference was statistically significant (P<0.001), suggesting a strong association between elevated uric acid levels and the presence of CAD (Table 4).

Table 5: Association Between Risk Factors and Uricacid Levels

Risk Factor		Uricacid				
		<7mg/dl		>7mg/dl		
		No.	%	No.	%	P-value
Hypertension	Present	25	54.3	21	45.7	0.904
	Absent	30	55.6	24	44.4	
DM	Present	26	53.1	23	46.9	0.005*
	Absent	29	56.9	22	43.1	
Smoking	Present	30	56.6	23	43.4	0.732
	Absent	25	53.2	22	46.8	
CAD	Present	20	52.6	18	47.4	<0.001*
	Absent	35	56.5	27	43.5	
Hyperlipidemia	Present	19	42.2	26	57.8	0.02*
	Absent	36	65.5	19	34.5	
Alcoholism	Alcoholic	28	54.9	23	45.1	0.984
	Non-Alcoholic	27	55.1	22	44.9	

In the present study, hypertension was observed in 54.3% of subjects with uric acid levels <7 mg/dl and 45.7% with levels >7 mg/dl, with no significant difference (P=0.904). DM was significantly associated with elevated uric acid levels, with 46.9% of diabetic subjects having uric acid >7 mg/dl compared to 43.1% of non-diabetic subjects (P=0.005). CAD was also significantly associated with higher uric acid levels (47.4% with >7 mg/dl., P<0.001). Hyperlipidemia showed a significant association, with 57.8% of subjects with uric acid >7 mg/dl having hyperlipidemia (P=0.02). Smoking and alcoholism were not significantly associated with uric acid levels (P=0.732 and P=0.984, respectively). These results highlight specific risk factors that are significantly linked to elevated uric acid levels (Table 5). In present study, the majority of subjects were in the age group of 60-69 years. The mean age of the subjects is 65.52± years. The mean age of the subjects in the present study is compared too the similar studies. The mean age in other studies are 61.17±14.1 in Lokkanahallip[19].

Significant association is observed with Tutar[20] and Lokkanahalli[19] studies. In the present study, the male to female ratiois4.5:1,witha significant Male pre ponderance which is comparable with the studies conducted by Mohsin[21] where the ratio is 3.7:1, where the ratio is 3.2:1, Tutar[20] where the ratio is 1.17:1. Significant association is observed with the study conducted by Mohsin[21]. Hypertension in the current study is present in 46% of study subjects of which 48.8%are males and 33.3% are females. It is comparable to the study conducted by Harsh[25], where hypertension is seen in 43% of study subjects of which 45% are males and 33% are females and to the study conducted by Tutar[20], with 57% hypertensive of which 51% are males and 08% are females. Diabetes mellitus in the current study is present in 49% of study subjects of which 51.2% are males and 38.9% are females. It is comparable to the study conducted by Altemimi[22], where diabetes mellitus is seen in 50% of study subjects of which 52.4% are males and 47.6% are females and to the study conducted by Tutar[20], with 36% diabetics of which 36% are males and 28% are females. CAD in the current study is present in 38% of study subjects of which 40.2% are males and 27.8% are females. It is comparable to the study conducted by Zafar[23], where CAD is seen in 40% of study subjects of which 38% are males and 18% are females and to the study conducted by Tutar[20], with 23% with CAD of which 20% are males and 09% are females. Hyperlipidemia in the current study is present in 45% of study subjects of which51.2% are males and 16.7% are females. It is comparable to the study conducted by Garg[24], where hyperlipidemia is seen in 40% of study subjects of which 35% are males and 10% are females and to the study conducted by Tutar[20], 49% with hyperlipidemia of which 44% are males and 05% are females. In the current study the mean serum uric acid levels showed a male pre ponderance i.e., 6.4±1.7 in males and 5.83±1.58 in females. It is comparable to the study conducted by Harsh[25], where Mean SUA in males is 4.98±1.95and in females is4.87±1.67 and to the study conducted by Tutar[20], where Mean SUA in males is 7.2±2.2 in females is 5.7±1.69. Both the latter mentioned studies have shown higher serum uric acid levels in males when compared to females, which is similar to the present study. In the present study as age advanced the serum uric acid levels is also found to rise i.e., 6±1.41mg/dL mean SUA above 80 years which is comparable to the studies conducted by Patil[26]. In both the studies the mean SUA levels above 80 years was 5.88±1.56 and 6.9±1.01 respectively. In the present study the Mean serum uric acid levels in diabetes mellitus is6.49±1.75mg/dL which is having significant association with the studies conducted by Kaurl[27] i.e., 6.85±1.86 and 6.3±26 respectively. In the present study the Mean serum uric acid levels in CAD is6.71±6.1 mg/dL which is having significant association with the studies conducted by Fatime[28] i.e., 6.46±1.5 and 6.95±1.8 respectively. In the current study No, significant association is obtained in ischemic stroke subjects and hypertension, hyperlipidemia. This is comparable to the studies conducted by Kaurl[27], which have shown similar results. In the current study No, significant association is obtained in ischemic stroke subjects and Smoking, Alcohol. This is comparable to the study conducted by Fatime[28,29] which has shown similar result.

CONCLUSION

This study demonstrates a strong association between elevated serum uric acid (SUA) levels and an increased risk of acute ischemic stroke, particularly in elderly patients, individuals with diabetes and those with coronary artery disease. Elevated SUA can be recognized as a significant risk factor for acute ischemic stroke, highlighting the potential benefit of incorporating SUA-lowering interventions as a preventive strategy in high-risk populations. However, further research is warranted to determine whether pharmacological reduction of SUA levels can effectively decrease the risk of ischemic stroke.

Recommendations and Limitations: Based on the study findings, it is recommended to incorporate serum uric acid (SUA) level monitoring as part of the routine risk assessment for acute ischemic stroke, especially in high-risk populations such as the elderly, diabetics and those with coronary artery disease. Preventive strategies, including lifestyle modifications and potential SUA-lowering therapies, should be considered. However, limitations include the small sample size and single-center nature of the study, which may restrict generalizability. The observational design precludes establishing causality and confounding factors may influence outcomes. Further large-scale, multicenter and interventional studies are needed to validate these findings and explore causal relationships.

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