

A study on association of serum uric acid levels in acute ischemic stroke patients in a tertiary level care hospital, Chennai

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Abstract

Background: For decades the role of Uric acid as a independent risk factor for non-communicable disease is a subject of discussion. Serum Uric acid is a powerful antioxidant that scavenge many harmful free radicals like hydroxyl ions, peroxynitrite along with other anti-oxidants like ascorbic acid .But elevated serum uric acid can act as pro-oxidant that cause various inflammatory reactions .High Serum uric acid can cause endothelial dysfunction, nitric oxide reduction in cells, platelet dysfunction, vascular smooth muscle cells proliferation and activates Renin Angiotensin Aldosterone System. **Objective:** 1. To study the association between serum uric acid level and acute ischemic stroke patients. 2. To assess the serum uric acid level in the various risk factors of acute ischemic stroke. **Methodology:** This is an cross sectional study done at Government Royapettah Hospital, Chennai. After obtaining the official permission from Institutional Ethics Committee and informed consent from the patients, the study was conducted. The arrived sample size was 50. Simple random sampling done to arrive at the sample size. The Patients admitted in Govt. Royapettah Hospital with first time acute ischemic stroke were included in the study. Those with Previous history of TIA (Transient Ischemic Attack), CVA(Cerebro Vascular Accident),Patients on Thiazide diuretics, Patients with Malignancies, Patients who are a known case of gout or have clinical evidence of gout, Patients with chronic renal failure, Patients with hemorrhagic stroke are excluded from the study. Serum uric acid levels were measured within 24hours of onset of acute ischemic stroke. Cutoff value of Serum uric acid level was taken as 6.5mg/dl. Other risk factors including Diabetes Mellitus, Hypertension, CAD and hyperlipidemia are evaluated with appropriate lab investigations. The data is entered using MS Excel. Analysed using SPSS Version 16. Descriptive and Inferential statistical analysis done by Chi Square Test, Fisher's Exact Test, p value less than 0.05 is taken as statistically significant. **Results:** In the study population 66% were male and 34% were female. 76% were hemiparetic and 24% were hemiplegic. 74% had serum uric acid \leq 6.5mg/dl and 26% had serum uric acid levels $>$ 6.5mg/dl. The study revealed the strong association between the high serum uric acid levels and Cerebro Vascular Accident (p=0.000*), Diabetes Mellitus(p=0.007*), Systemic Hypertension(p=0.042*), Coronary Artery Disease(p=0.029*), elevated LDL(p=0.046*) and Total Cholesterol levels(p=0.002*). **Conclusion:** The study shows that uric acid levels may be considered as an independent predictor for ischemic stroke. SUA has a strong association with DM, SHT, CAD and elevated Cholesterol levels. Lowering of SUA level can be considered as one of the preventive modalities for stroke while treating high risk population.

Key Word: Serum Uric Acid, Acute ischemic stroke, anti-oxidant.

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INTRODUCTION

The Framingham Heart Study was the first one to evaluate an association between elevated Serum Uric Acid(SUA) levels and cardiovascular disease outcome in general population. The study concluded that the association with cardiovascular disease merely reflects the link between SUA levels and other risk factors including hypertension, kidney disease, elevated lipoprotein levels and use of diuretics¹. On the contrary

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several other epidemiological studies have shown elevated SUA levels to predict increased risk of cardiovascular events, hypertension, congestive heart failure and Type II diabetes mellitus. Increased SUA levels were found to be associated with increased risk of ischemic as well as hemorrhagic strokes. Higher SUA levels in stroke patients have also been described in association with improved or worse outcome¹. One of the major sites where the anti-oxidant effects of uric acid have been proposed is in the central nervous system, particularly in conditions such as multiple sclerosis, Parkinson’s disease, and acute stroke. While chronic elevations in uric acid are associated with increased stroke risk, acute elevations in uric acid may provide some anti-oxidant protection. For example, uric acid protects cultured rat hippocampal neuronal cells from oxidative stress, and administration of uric acid 24 hours prior to middle artery occlusion also attenuated brain injury induced by acute ischemia in rats². Therefore, the aim of the present study was to assess the serum UA levels in ischemic stroke and association with risk factors.

METHODOLOGY

This is an cross sectional study done at Government Royapettah Hospital, Chennai. After obtaining the official permission from Institutional Ethics Committee and informed consent from the patients, the study was conducted. The arrived sample size was 50. Simple random sampling done to arrive at the sample size. The Patients admitted in Govt. Royapettah Hospital with first time acute ischemic stroke TIA were included in the study. Those with Previous H/o TIA, CVA, Patients on Thiazide diuretics, Patients with Malignancies, Patients who are a known case of gout or have clinical evidence of gout, Patients with chronic renal failure, Patients with hemorrhagic stroke are excluded from the study. Serum uric acid levels were measured within 24hrs of onset of acute ischemic stroke. Cutoff value of Serum uric acid level was taken as 6.5mg/dl. Other risk factors including DM, Hypertension, CAD and hyperlipidemia will be evaluated with appropriate lab investigations. The data is entered using MS Excel. Analysed using SPSS Version 16. Descriptive and Inferential statistical analysis done by Chi Square Test, Fisher’s Exact Test and p value less than 0.05 is taken as statistically significant.

RESULTS

Table 1: Descriptive Statistics of the Acute Ischemic Stroke Patients

Variables	Frequency	Percentage
Age group in years	40-50	4 8%
	51-60	15 30%
	61-70	21 42%
	71-80	9 18%
	>81	1 2%
Gender	Male	33 66%
	Female	17 34%
DM	Yes	18 36%
	No	32 64%
CAD	Yes	15 30%
	No	35 70%
HT	Yes	19 38%
	No	31 62%
CVA	Hemiparesis	38 76%
	Hemiplegia	12 24%
Total Cholesterol	≤200mg/dl	43 86%
	>200mg/dl	7 14%
LDL Cholesterol	≤100mg/dl	10 20%
	>100mg/dl	40 80%
TGL	≤150mg/dl	45 90%
	>150mg/dl	5 10%

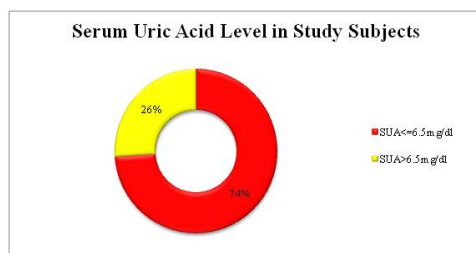


Figure 1: Serum Uric acid Levels in Acute Ischemic Stroke Patients

Table 2: Association Between SUA level and CVA

Diseases	Serum Uric Acid Level		Statistical Test, Value	P Value
	≤6.5mg/dl	>6.5mg/dl		
CVA	Hemiparesis(38)	37(97.4%)	Fisher Exact Test, 44.047	0.000*
	Hemiplegia(12)	0		

*P value <0.05 is taken as statistically significant

Table 3: Association of Serum Uric Acid levels with risk factors of Acute Ischemic Stroke

Risk factors of CVA	Serum Uric Acid Level		Statistical Test, Value	P Value
	≤6.5mg/dl	>6.5mg/dl		
CAD	Yes(15)	8(53.3%)	Chi Square Test, 4.757	0.029*
	No(35)	29(82.9%)		
DM	Yes(18)	9(50%)	Fisher's Exact Test, 8.252	0.007*
	No(32)	28(87.5%)		
HT	Yes(19)	11(57.9%)	Chi Square Test, 4.131	0.042*
	No(31)	26(83.9%)		
Total CHO	≤200mg/dl (42)	35(83.3%)	Fisher's Exact Test, 11.647	0.002*
	>200mg/dl (8)	2(25%)		
LDL CHO	≤100mg/dl (10)	10(100%)	Fisher's Exact Test, 4.304	0.046*
	>100mg/dl (40)	27(67.5%)		
TGL CHO	≤150mg/dl (45)	34(75.6%)	Fisher's Exact Test, 0.555	0.595
	>150mg/dl (5)	3(60%)		

*P value <0.05 is taken as statistically significant

The study revealed the strong association between the high serum uric acid levels and Cerebro Vascular Accident (p=0.000*), and various risk factors like Diabetes Mellitus(p=0.007*), Systemic Hypertension(p=0.042*), Coronary Artery Disease(p=0.029*), elevated LDL(p=0.046*) and Total Cholesterol levels(p=0.002*).

DISCUSSION

The study molecule Serum uric acid(SUA) cause stimulation of renin-angiotensin-aldosterone system and may contribute to the development of CAD apart from development of renal vascular constriction. In this study, there was a significant increase in the serum uric acid levels in acute ischemic stroke patients and the elevated SUA levels are strongly associated with the risk factor Coronary Artery Disease which was similar to the findings of the study done by Zhang *et al* in 2014³. In Diabetes Mellitus patients, SUA cause mitochondrial oxidative stress leads to fatty liver. This results in insulin resistance (IR) - Hepatic Effect; SUA in adipocytes promotes NADPH oxidase that cause lipid oxidation and release super oxide radicals, MCP1 and also reduces

adiponectin. This results in increased IR and leptin overexpression in visceral fat-Adipose Effect. SUA cause reduced nitric oxide by blocking L-arginine results in IR and endothelial cell dysfunction- Vascular Effect SUA promote macrophage induced hyalinosis cause islet cell destruction by pro-inflammatory substances and results in type 2 DM- Islet Cell Effects. SUA block the ability of insulin to deliver glucose to skeletal muscle -Muscle effect. In this study the risk factor Diabetes Mellitus also has significant association with elevated SUA levels which was very similar to the study done by Bhole *et al* 2010⁴ The increase in the prevalence of hyperuricemia cases and the accumulated evidence that hyperuricemia increases the risk for hypertension (HT) onset and lack of optimal blood pressure (BP) control. Hyperuricemia leads to the increase in BP values by stimulating oxidative stress and inflammatory mechanisms through endothelial dysfunction and proliferation of smooth muscle cells in the blood vessels and stimulation of the Renin-Angiotensin-Aldosterone-System. SUA also cause Arteriolar wall thickening leading to Hypertension. In this study, there is a significant association between the Hypertension status and the Elevated SUA levels which

was very identical to the study done by Roxana *et al* 2018.⁵ This study shows similar results of study done by Devajit *et al* 2013⁶ of significant association of elevated SUA levels with high Total Cholesterol. Due to the high prevalence of hyperuricemia in patients with acute stroke, and its accompanying increase in triglyceride and LDL cholesterol levels, it can be considered as a risk factor for acute stroke. In this study there was a strong association between Elevated LDL levels and elevated SUA levels and this study finding is similar to the study done by Masoud *et al* 2012⁷. Serum uric acid, the strong anti oxidant, under certain circumstances like absence of other anti-oxidants may act as pro-oxidant. Thus serum uric acid may be taken as a marker of elevated risk of cerebrovascular accident. The NHANES study concluded that uric acid is an independent risk factor for development of cardiovascular and cerebrovascular diseases⁸. Weir *et al* 2003 who studied 3731 patients and measured serum urate in 2498 reported that elevated urate level predict a lower chance of good 90-day outcome independent of stroke severity and other prognostic factor⁹. Serum uric acid may have a direct role in the atherosclerotic process, because human atherosclerotic plaque contains more uric acid than do control arteries. Inflammation is one of the features of atherosclerosis, and uric acid crystals may induce inflammatory responses that are reduced by lipoproteins which have an ability to bind uric acid crystals. Hyperuricemia may also promote thrombus formation.¹⁰

CONCLUSION

This study shows that elevated SUA is strongly associated with an increased risk for the development of acute ischemic/ non-embolic stroke in this study population. SUA is the substance with both anti inflammatory and pro-inflammatory activity. Elevated SUA can be considered as one of the risk factors for acute ischemic non-embolic stroke and also it is found to be strongly associated with various risk factors of non-communicable diseases. Lowering of SUA level can be considered as one of the preventive modalities for stroke while treating high risk population. It is also suggested that further studies are required to assess whether lowering of SUA level with drugs can actually reduce the risk of ischemic stroke. SUA is associated with all the risk factors of cerebrovascular disease, this study could be used to support the evidence that serum uric acid may be used as a early marker for development of cerebrovascular disease

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