



Role of Life style factors on Serum Uric Acid levels in Acute Ischemic Stroke patients- a Cross sectional study

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Abstract

Background: Serum Uric Acid(SUA) is a powerful antioxidant but in elevated levels it acts as a pro oxidant which is associated with pro inflammatory reactions. The lifestyle factors play an important role in influencing the SUA level which is strongly associated with acute ischemic stroke.

Objective: To assess the role of Lifestyle factors on Serum Uric Acid levels in Acute Ischemic Stroke patients.

Methodology: A cross sectional study was conducted in 50 acute ischemic stroke patients admitted at a Tertiary Care Hospital in Chennai. Samples were selected by simple random sampling method. The patients admitted in the hospital with first episode of acute ischemic stroke were included in the study. The data was collected using a semi structured questionnaire. Within 24 hours of onset of acute ischemic stroke, SUA levels were measured. The data was analysed using SPSS software version 25. Both descriptive and inferential statistical analysis were done.

Results: The majority of the study participants were in the age group 51-70 years 36(72%), predominantly male patients 33(66%). Among the study participants 38(76%) had hemiparesis and 12(24%) had hemiplegia. Elevated SUA levels were seen in 13(26%) patients. Non vegetarian diet intake (p value 0.035*), alcohol intake (p value 0.003*) and increase in BMI (p value 0.000*) had shown a statistically significant association with the elevated SUA levels in acute ischemic stroke patients.

Conclusion: This study revealed that alcohol intake, non-vegetarian diet intake and raise in BMI had increased the SUA levels in acute ischemic stroke patients. Healthy lifestyle factors prevent hyperuricemia.

Keywords: Lifestyle factors; Serum Uric Acid level; Acute Ischemic Stroke

INTRODUCTION

Serum Uric Acid(SUA) being one of the major aqueous antioxidant in human beings should have a protective role in stroke patients. Several large studies have provided conflicting results regarding the clinical significance of elevated serum uric acid levels in cerebrovascular diseases. Many studies including the National Health and Nutrition Examination Survey (NHANES) study concluded that uric acid is an independent risk factor for development of

cardiovascular and cerebrovascular diseases^[1]. Persons with High Serum uric acid level may not be symptomatic in conditions such as obesity, high-fat protein diets, alcohol intake, diuretic consumption, some genetic disorders, hypothyroidism. SUA is one of the important risk factor for developing acute ischemic stroke^[2].

Studies of basic research have shown that increased uric acid might cause hypertension via reducing nitric oxide, activation of renin-angiotensin system and smooth muscle proliferation. Alcohol intake itself is an important and strong risk factor for the development of not only hyperuricemia but also hypertension. Several mechanisms related to the increase in uric acid have been clarified, such as excess purine or alcohol intake, obesity, renal dysfunction, and genetic alterations^[3]. Meat and fish may increase the concentration of uric acid because of the high purine content of these foods^[4].

Cigarette-smoking is a well-known risk factor for atherosclerosis development and its complications including cerebral and cardiovascular diseases (CVD) through vascular endothelial damage that possibly occurs through oxygen free radical's production as superoxide radicals, hydrogen peroxide and hydroxyl radicals. Several enzymes capable of producing oxygen free radicals including xanthine oxidase, NADPH oxidase, myeloperoxidase, and endotoxin. Higher level of SUA behave like an pro oxidant causing endothelial damage by increasing the oxidatitive free radicals^[5].

Alcohol consumption is believed to elevate serum UA through two mechanisms: the accelerated synthesis of UA from adenosine, which is produced after the degradation of adenosine triphosphate to adenosine monophosphate, and reduced urinary excretion due to the elevation of blood lactate caused by the oxidation of ethanol^[6].

Life style factors like Alcohol intake, smoking, fructose rich diet, high protein non vegetarian diet, obesity play an important role in elevation of serum uric acid level in the body. Hence, the above said life style factors are risk factor for development of ischemic stroke. This study focus on the role of life style factors in determining the SUA level.

OBJECTIVE: To assess the role of Life style factors on Serum Uric Acid levels in Acute Ischemic Stroke patients.

MATERIALS AND METHODS: A cross sectional study was conducted in acute ischemic stroke patients admitted at a Tertiary Care Hospital in Chennai. The study was carried out after obtaining permission from the Institutional Ethics Committee and informed

consent. The minimum sample size arrived was 50. Samples were selected by simple random sampling method. The patients admitted in the hospital with first episode of acute ischemic stroke were included in the study. The patients with previous H/o of Transient Ischemic Attacks, malignancies, patients on Thiazide diuretics, patient who are a known case of gout or with clinical evidence of gout, chronic renal failure, patients with hemorrhagic stroke are excluded from the study. The data was collected using a semi structured questionnaire. Within 24 hours of onset of acute ischemic stroke, Serum Uric Acid levels were measured. The upper limit for normal uric acid was taken as 6.5mg/dl. The data is entered using MS Excel and analysed using SPSS software version 25. Both descriptive and inferential statistical analysis were done.

OPERATIONAL DEFINITION:

Lifestyle factors: Lifestyle factors are the adaptable behaviours and ways of life that influence an individual's health and wellbeing. Examples of lifestyle factors include diet, exercise, smoking and alcohol^[7].

Stroke: Rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer with no apparent cause other than vascular origin^[8].

Current smoker: An adult who has smoked 100 cigarettes in his or her lifetime and who currently smokes cigarettes. **Former smoker:** An adult who has smoked at least 100 cigarettes in his or her lifetime but who had quit smoking at the time of interview. **Never smoker:** An adult who has never smoked in his or her lifetime^[9].

Body Mass Index: It is defined as a person's weight in kilograms divided by the square of the person's height in metres (kg/m²). BMI Below 18.5 - underweight; BMI 18.5-24.9 - Normal weight; BMI 25-29.9 - preobesity; BMI ≥ 30 - Obesity^[10].

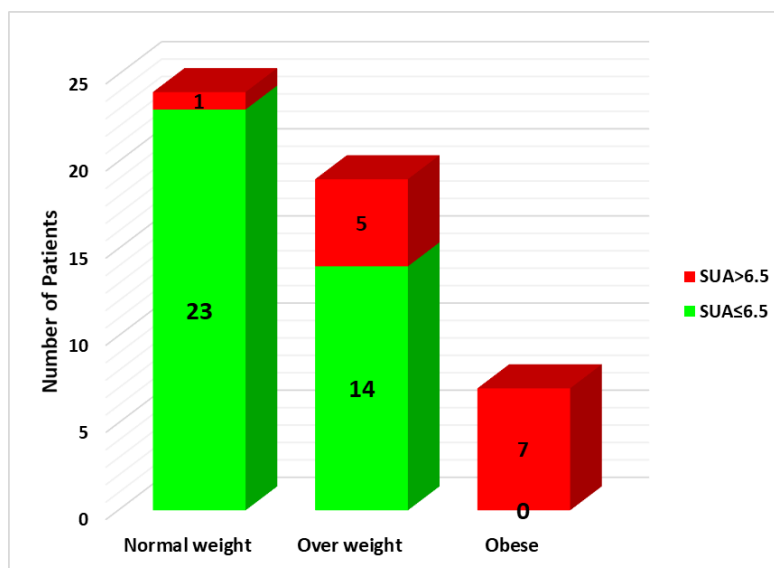
Current Drinker: Those who consumed one or more than one drink of any alcohol in the year preceding the survey. **Former Drinker:** Those who have consumed alcohol but those who did not consume one or more drink during the year preceding the survey. **Lifetime Abstainer:** Those who have never consumed one or more drink of any type of alcohol in lifetime^[11].

RESULTS:**Table 1: Descriptive analysis**

Variables		Frequency(N=50)	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%
Smoking	Yes	17	34%
	No	33	66%
Alcohol	Yes	12	24%
	No	38	76%
Diet	Vegeterian	20	40%
	Non-Vegeterian	30	60%
BMI	Normal	24	48%
	Overweight	19	38%
	Obese	7	14%
SUA	≤6.5mg/dl	37	74%
	>6.5mg/dl	13	26%

As shown in the Table 1, the majority of the study participants were in the age group 51-70 years, 36(72%), predominantly male patients 33(66%). Among the study participants 38(76%) had hemiparesis and 12(24%) had hemiplegia. Out of 17 smokers, 15 were current smokers and 2 were former smokers.

Figure 1: BMI and SUA levels of acute ischemic stroke patients



As shown in the Figure 1, increase in Body Mass Index was associated with elevated levels of Serum Uric Acid levels

Table 2: Life style factors Vs Serum uric acid levels of acute ischemic stroke patients

Life style Factors		Serum Uric Acid Level		Statistical Test, Value	pValue
		≤6.5mg/dl	>6.5mg/dl		
Diet	Vegeterian(20)	18(90%)	2(10%)	Fisher Exact Test 4.435 df = 1	0.035*
	Non-Vegeterian(30)	19(63.3%)	11(36.7%)		
Alcohol	Yes(12)	5(41.7%)	7(58.3%)	Chi Square Test, 8.580 df = 1	0.003*
	No(38)	32(84.2%)	6(15.8%)		
Smoking	Yes(17)	10(58.82%)	7(41.12%)	Chi Square test, 3.08 df = 1	0.07
	No(33)	27(81.82%)	6(18.18%)		
BMI	Normal(24)	23(95.8%)	1(4.2%)	Fisher Exact Test, 23.576	0.000
	Overweight(19)	14(73.7%)	5(26.3%)		
	Obese(7)	0(0%)	7(100%)		

As shown in the Table 2, Non vegetarian diet intake, alcohol intake and increase in BMI had shown statistically significant association with the elevated SUA levels in acute ischemic stroke patients. In this study 30 were non-vegetarian, majority of them consume animal products like meat, poultry and sea foods frequently.

DISCUSSION:

In present study, out of 50 participants, 31(62%) were more than 60 years and 19 (38%) were ≤ 60 years. The SUA levels were found to be elevated in the age group >60 years were 10(32.3%) compared to the age group ≤ 60 years were 3 (15.8%). This findings was found to be similar to the studies by Kaur et al^[11], Milionis et al^[12] and Foerch et al^[13].

In this study, the SUA levels were found to be higher in males 9(27.3%) compared to females 4(23.5%). Though the results were higher in males but this difference were not statistically significant. Similar findings were seen in the following studies by Pearce and Aziz et al^[14], Longo M benza et al^[15], Culleton et al^[16] and Bos et al^[17].

In our study, out of 20 patients who followed vegetarian diet, only 2(10%) had elevated SUA when compared to 30 patients who were on non-vegetarian diet, 11(36.7%) had elevated SUA levels. These findings were very similar to the study by Aihemaitijiang et al^[18]. The animal based food like meat, sea food, beef, pork, lamb, poultry, soft drinks, sweetened drinks, high calorie carbohydrate food and western diet like processed and refined food materials contain high amount of purines causing hyperuricemia. Similar findings are found in the study by Zykova et al^[19]. Increased intake of purine-rich foods, such as meat and seafood, raise the level of uric acid in serum, whereas dairy products, especially low-fat types, are associated with a lower level of serum uric acid. Sweet fruits and soft drinks containing fructose may raise uric acid through uric acid production and/or decreased excretion. The Mediterranean diet reduce hyperuricemia Kakutani Hatayama et al^[20] and also plant based diet has less purine and doesnot elevate serum uric acid levels.

Plant based diets are typically based on the consumption of grains, legumes, vegetables, fruits, and nuts. Lacto-ovo-vegetarian diets include dairy and/or egg products were associated with lower levels

of serum uric acid similar to the Mediterranean diet by Jakse et al^[21] and The DASH diet (Dietary Approach to Stop Hypertension) by Juraschek et al^[22]. One of the modifiable risk factor for hyperuricemia is diet thereby dietary intervention can reduce the risk of Cardiovascular and cerebrovascular diseases like acute ischemic stroke patients by Vedder et al^[23].

According to this study, out of 50 participants 19(38%) were overweight and 7(14%) had obesity. In those with normal weight 95.8% had normal levels of SUA and only 4.2% had elevated SUA compared to overweight individuals 26.3% had elevated SUA levels and in obese individuals 100% had elevated SUA levels. A study done by Seki et al^[3] clearly shows that the BMI plays a very significant role in elevation of serum uric acid levels. Patients with increased BMI had secondary hyperinsulinemia which can induce hyperuricemia by decreasing the urinary excretion of uric acid.

In a study done by Yamashita et al^[24] clearly states that hyperuricemia in obese people is mainly attributed to an impaired renal clearance of uric acid rather than overproduction. SUA level is positively correlated with obesity indicators like BMI was found by Oyama et al^[25]. In Bangladesh study done by Ali et al^[26], in the BMI categories, the prevalence of hyperuricemia was 1.9% in normal weight, 1.6% in overweight and 5.8 in the obesity group. Similar results were found in a study by Zhu et al^[27].

The results from the study done by Niu et al^[28] shows that uric acid in obese children and adolescents was not only positively related to BMI, Fat Mass, and Free Fat Mass, but also to the decrease with the Fat Mass during weight loss. In Thailand study by Suttikomin et al^[29], it was found that serum uric acid levels in obese boys based on BMI and excess body fat were statistically significantly higher than those in normal weight and normal body fat boys. In obese by BMI and excess body fat, participants had highest mean serum uric acid levels. Body weight has a direct influence on the serum uric acid level and by maintaining normal BMI can prevent the occurrence of stroke.

In this study, out of 50 study participants, 17(34%) were smokers and 33(66%) were non-smokers. Among the non-smokers, 27(81.82%) were having SUA level ≤ 6.5 mg/dl when compared to smokers only 10(58.82%) had SUA ≤ 6.5 mg/dl. This

clearly shows that the protective antioxidant property of SUA is lost among the smokers who had low SUA levels compared to normal SUA level. A decrease in SUA level among the smokers can be explained by the inactivation of Xanthine oxidase by cyanide which is eliminated as thiocyanate was revealed in the studies done by Massey and Edmondson et al^[30] and Puig et al^[31].

Low serum uric acid level in smokers was attributed to a reduction of endogenous production as a result of the chronic exposure to cigarette smoke that is a significant source of oxidative stress. Therefore, cigarette smoking may influence oxidative stress by affecting the levels of plasma antioxidants, which may be involved in the mechanisms underlying various cerebro vascular diseases and cardio vascular diseases which was found by the study done by Haj Mohammed et al^[32]. It is recommended for smokers to stop or reduce smoking and introduce serum uric acid estimation as routine test since its cheap and simple to reflect their antioxidant level.

In present study, 12(24%) were alcoholics of which 7(58.3%) had SUA levels >6.5mg/dl, when compared to nonalcoholic with SUA level >6.5mg/dl were 6(15.8%) and 32(84.2%) had SUA levels ≤6.5mg/dl among non-alcoholics which was similar to the findings of study done by Yamamoto et al^[33] which revealed ethanol enhances adenine nucleotide degradation and increases lactic acid level in blood, leading to hyperuricemia. In beer, purines also contribute to an increase in plasma uric acid. Although rare, dehydration and ketoacidosis (due to ethanol ingestion) are associated with the ethanol-induced increase in serum uric acid levels. Ethanol also increases the plasma concentrations and urinary excretion of hypoxanthine and xanthine via the acceleration of adenine nucleotide degradation and a possible weak inhibition of xanthine dehydrogenase activity.

Rapid consumption of ATP produces uric acid via purine nucleotide degradation. Since individuals with ALDH2*1 can catalyze ethanol readily, they consume large amount of ATP, and thus produce more hypoxanthine than those with ALDH2*2. Thus, daily drinker and heavy drinker tend to readily induce hyperuricemia after alcohol ingestion. A high purine content in beer may contribute to the increasing

frequency of hyperuricemia which was quoted by the Yamanaka et al^[34].

In a study done by Seki et al^[3] shows that the uric acid level was significantly higher in drinkers than in non-drinkers. The main mechanisms of alcohol-related hyperuricemia are the increase in intake of purine and the synthesis of its final product, uric acid. The effect of individual alcoholic beverages on serum uric acid levels varies. Substantially, beer confers a larger increase than liquor, whereas moderate wine drinking does not increase serum uric acid levels because it has less alcoholic content and more antioxidative substances as mentioned by Choi et al^[35]. In a study done by Gibson et al^[36], the purine content of various alcoholic beverages especially beer is relatively high and readily absorbed resulting in hyperuricemia. Also, heavy alcohol drinking raises the uric acid level and increases the risk of gout through adenine nucleotide degradation and lactate production^[20].

CONCLUSION: This study reveals that alcohol intake, non-vegetarian diet and raise in BMI had increased the serum uric acid levels. Healthy Life style factors helps to maintain the SUA levels with in normal limits thereby preventing cardiovascular and cerebrovascular diseases.

LIMITATION: Physical activity was not assessed.

RECOMMENDATIONS: Periodical screening of SUA levels helps to identify the persons with increased risk of ischemic stroke. Healthy Life style modification will maintain the SUA levels within normal limits.

ETHICAL CONSIDERATION: Ethical Committee Permission obtained

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