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### RESEARCH ARTICLE

## ELEVATED SERUM URIC ACID LEVELS- A RISK FACTOR IN ACUTE NON-EMBOLIC ISCHEMIC STROKE.

\*S. Mohd. Ali, M.A Raheem, M.A. Muqith Quadri, S.Mohd. Gufran and Mohd . Siraj.

Department of General Medicine, Deccan College of Medical Sciences, Hyderabad, India.

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### Abstract

Serum uric acid (SUA) levels were estimated in a total of 100 acute non-embolic ischemic stroke cases comprising of 50 males and 50 females having mean age of  $59.10 \pm 10.20$  and  $60.50 \pm 11.10$  years respectively. Mean SUA levels were found to be  $5.41 \pm 1.88$  in males and  $5.47 \pm 1.53$  mg/dL in females. Frequencies of additional risk factors in these patients like hypertension, Diabetes mellitus, smoking, age above 65 years, and coronary artery disease (CAD) were also determined. The cases were divided into those with SUA levels less than and more than 7mg/dL to relate with the risk factors. A statistically significant ( $p < 0.001$ ) relationship was demonstrated between CAD and age  $> 65$  years with increased SUA levels. It is concluded that elevated SUA levels (in the upper normal range) are an important risk factor for acute non-embolic ischemic stroke.

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### Introduction:-

Stroke is defined as a rapid onset of focal neurological deficit, resulting from diseases of cerebral vasculature and its content. Stroke cases constitute nearly 20% of total neurological cases [1]. The mortality rate due to stroke in acute phase is as high as 20% [2]. Stroke is also an important cause of morbidity and long term disability [3]. Consequently early identification of individuals at high risk is likely to help in primary prevention strategies [4]. With this objective most of the epidemiological studies have been carried out to identify high risk factors that predispose to this debilitating condition. One such risk factor is hyperuricemia. Millions et al 2005 reported that the serum uric acid (SUA) levels are independent risk factor for acute non-embolic ischemic stroke [5]. The authors also suggested that treatments with hypouricemic action have a favourable effect on cardio-vascular event prevention. Hence the objective of the present study was to estimate SUA levels in cases with acute non-embolic ischemic stroke as a risk factor.

### Materials and Methods:-

#### Selection of cases:

Patients with first ever in life time acute ischemic non-embolic stroke with computerized tomography scan (CT) evidence of infarction within 24 hours of onset of stroke were selected. These patients were admitted in the Princess Esra Hospital and research centre (Hyderabad).

The following categories of cases were excluded: i) Patients with previous history of Transient ischemic attack (TIA)/ Cerebrovascular accident, ii) those who are on thiazide diuretics, and iii) known cases of gout and patients with chronic renal failure. A total of 100 patients (50 males and 50 females) with acute stroke who met the selection

**Corresponding Author:- S. Mohd. Ali**

Address:- Department of General Medicine, Deccan College of Medical Sciences, Hyderabad, India.

criteria were included in the study. All subjects gave informed consent and the study protocol was approved by institutional ethical committee.

#### Collection of Blood samples and Biochemical analysis:-

Blood samples were collected within 24 hours of onset of stroke and biochemical tests were performed in a standard analyzer. The patients were further evaluated for the presence of additional risk factors using the following mentioned parameters: i) Hypertension: Known cases of hypertension having a systolic blood pressure of >140 mmHg and a diastolic of more than 90 mm Hg, ii) Known cases of diabetes mellitus with a fasting blood sugar of more than 126 mg/dL, and iii) Cases with a history of CAD, smoking and hyperlipidemia.

#### Results:-

Details of mean uric acid levels, and mean age of the patients are shown in Table 1. Out of a total of 100 acute non-embolic ischemic stroke cases 50 each were males and females. The mean age of male patients was  $59.10 \pm 10.20$  while that of females was  $60.50 \pm 11.10$  years. In both males and females the age range was 41 to 84 years. As for the mean serum uric acid levels are concerned, they were  $5.41 \pm 1.88$  and  $5.47 \pm 1.53$  mg/dL respectively in male and female cases respectively.

Mean serum uric acid levels in patients with and without additional risk factors are given in Table II. There was no significant difference between mean SUA levels in patients with and without hypertension. Similar observations were recorded for the risk factors hyperlipidemia and smoking. However, a significant ( $p < 0.001$ ) difference was recorded between the mean SUA levels in patients with and without diabetes mellitus and CAD.

Further analysis was carried out to see if a relationship exists between uric acid levels less than and more than 7mg/dL and the risk factors (Table-III). This analysis revealed that age more than 65 years and CAD have statistically significant ( $p < 0.01$ ) relationship with uric acid levels.

#### Discussion:-

Stroke is defined as rapid onset of focal neurological deficit, resulting from disease of cerebral vasculature and its content. Stroke cases constitute about 20% of total neurological cases in hospital admissions (6). Long term disability due to stroke is an important cause of morbidity and warrants further studies on identifying risk factor so that proper preventive measures can be suggested.

SUA is a major anti-oxidant and about 2/3<sup>rd</sup> of total plasma free radical scavenging activity is by SUA and hence thought to have a protective role in stroke. Ironically it has been shown that under certain circumstances like reduced levels of other antioxidants like ascorbic acid, SUA can function as a pro-oxidant [7]. Further evidence for a role of uric acid in the pathogenesis of stroke comes from the observations that elevated SUA levels are an important predictor of hypertension in 25% of patients with recent onset untreated hypertension [8]. Moreover, decreased renal blood flow that generally accompanies the hypertension condition also causes increase in SUA levels. Experimental studies provided additional evidence for a role of increased SUA levels in the pathogenesis of stroke which demonstrated that experimentally induced hyperuricemia also increased blood pressure in rats by a renal mechanism linked to inhibition of nitric oxide (NO), activation of rennin-angiotensin system and development of renal arteriosclerosis [9] It is known that cerebral infarction initiates a series of metabolic events in the surrounding tissues and free radical mediated oxidative damage appears to play an important role in the pathogenesis of cerebral ischemia [10]. The role of SUA in predisposition to non-embolic stroke is further supported by a study carried out in Chinese cohort which demonstrated that SUA levels as an independent risk factor for all cause cardiovascular and ischemic stroke mortality. [10].

**Table I:** Mean uric acid levels and Mean ages in male and female stroke patients

Gender	No	Mean Uric acid levels (mg/dL)	Mean Age (in years)
Males	50	$5.41 \pm 1.88$	$59.1 \pm 10.20$
Females	50	$5.47 \pm 1.53$	$60.50 \pm 11.10$

\*Normal values 2-7mg/dL

**Table II:** Mean Uric acid levels in stroke patients with and without risk factors

Risk Factor		Number	Mean uric Acid mg/DL	P value
Hypertension	Present	65	5.64 ± 1.7	N.S
	Absent	35	5.06 ± 1.68	
Diabetes Mellitus	Present	51	5.98 ± 1.66	P<0.001
	Absent	49	4.88 ± 1.59	
CAD	Present	32	6.46 ± 1.87	P<0.001
	Absent	68	4.96 ± 1.40	
Hyperlipidemia	Present	34	5.75 ± 1.90	NS
	Absent	66	5.28 ± 1.59	
Smoking	Present	34	5.14 ± 1.8	NS
	Absent	16	5.96 ± 1.98	

\*Only in male cases

**Table III:** Risk factors and uric acid levels <7/ or >7mg/dL in stroke patients

Risk Factor		<7mg/dL		>7mg		P value
		No	%	No	%	
Hypertension	Present	45	60	20	80	N.S
	Absent	30	40	5	20	
Diabetes Mellitus	Present	34	45.3	17	68	N.S
	Absent	41	54.7	8	32	
CAD	Present	15	20	17	68	0.001
	Absent	60	80	8	32	
Hyperlipidemia	Present	22	29.3	12	48	N.S
	Absent	53	70.7	13	52	
Alcoholism	Alcoholic	15	39.5	4	33.3	N.S
	Non-alcoholic	23	60.5	8	66.7	
Smoking	Present	27	71.1	7	58.3	N.S
	Absent	11	28.9	5	41.7	
	No risk factor	7	9.3	2	8	N.S
	Atleast one risk factor	8	90.7	23	13.7	
Age	>65 years	11	42.3	15	57.7	<0.01
	<65 years	64	86.5	10	13.7	

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