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Research Article

"To Study the Role of Serum Uric Acid as a Risk Factor in Acute Ischemic Stroke in Navodaya Medical College Hospital & Research Centre, Raichur"

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Abstract: Among all the neurological diseases, the cerebrovascular clearly rank the first in frequency and importance. At least 50% of the neurological disorders in a general hospital are of this type. Stroke, after heart disease and cancer is the most common cause of death in tertiary health center. Various studies have shown that uric acid can result in endothelial dysfunction which can lead to vascular disease. An association between SUA and inflammatory markers has also been discovered moreover therapeutic modalities with a SUA lowering potential have been shown to reduce CV disease morbidity and mortality.**Aim:** To study the role of Serum Uric Acid (SUA) in acute ischemic stroke and the association between SUA and other risk factors namely hypertension, diabetes mellitus, CAD and adverse lipid profile.**Methods:** The present study was conducted in Navodaya Medical College, Raichur over a period of one year. 100 patients of first ever in life time acute ischemic stroke were included. The blood samples were taken within 24 hrs of onset of stroke and sent for detailed biochemical analysis. The patients were further evaluated for risk factors such as hypertension, diabetes, coronary artery disease, adverse lipid profile, smoking and alcoholism.**Results:** Out of 100 patients of acute ischemic stroke included in our study, 50 were males and 50 were females. The mean serum uric acids level in our study of 100 patients with acute ischemic stroke was 5.51 mg/dl and the overall mean age for stoke in our study was 60.57. The age distribution showed that the majority of our patients i.e. 61% were above 50-69 years of age. Thus our study supports the fact that prevalence of stroke is more in elderly people and it is associated with raised serum uric acid levels with upper limit of normal value. Hypertension constitutes major risk factor with 65% study population being hypertensive. Diabetes Mellitus ranks second as risk factor, constitutes 51% of study population. CAD is associated in 32% of study population. 34% stroke population has adverse lipid profile.

Keywords: Uric acid serum; Diabetes Mellitus; CAD; Hypertension; Stroke.

INTRODUCTION:

Amongst all the neurological diseases of adult life, the cerebro-vascular clearly ranks the first in frequency and importance. At least 50% of the neurological disorders in a general hospital are of this type. (WHO. 1988) Cardiovascular disease including stroke which comprises of 19% of death in India in 2001-2003. And is estimated to rise to 36% by 2030.2Uric acid (UA) is one of the most abundant aqueous antioxidant in humans, and contributes about two-thirds of all free radical scavenging capacity in plasma, plasma concentration of uric acid is about 10-fold higher than that of other antioxidants. The role of serum uric acid (SUA) level as an independent risk factor for stroke has been questioned for many years. (Daskalopoulou, S. S. *et al*., 2004) Evidence from various epidemiological studies suggests that increased SUA levels may be predicted as risk factor for stroke and cardiovascular events. (Milionis, H. J. *et al*., 2005; Verdecchia, P. *et al*., 1991; Freedam, D. S. *et al*., 1995) Evidence also suggests that increased level of uric acid is a bad prognostic factor in patients with acute ischemic stroke.[10,11] Thus in patients with acute stroke the fall in ascorbate level could predispose the SUA to take on pro-oxidant properties. Although presence of high SUA levels has been identified as an important

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risk factor for stroke in a number of epidemiological studies but it is unclear whether high SUA levels promotes or protects against the development of CV disease or simply acts as a passive or circumstantial marker of increased risk. The present study is designed to study the association between serum uric acid and stroke. It is also intended to study the association between serum uric acid and other traditional risk factors for stroke.

AIMS AND OBJECTIVES:

1) To study the role of Serum Uric Acid (SUA) in acute ischemic stroke.

2) To study the association between Serum Uric Acid (SUA) and other traditional risk factors such as hypertension, Diabetes mellitus, CAD and adverse lipid profile.

MATERIALS AND METHODS:

- A total of 100 patients with acute stroke who met the inclusion criteria, admitted in Medicine department in Navodaya Medical College and Research Centre, Raichur were included in this study.
- The informed written valid Consent was obtained.
- The study protocol was approved by the Ethical Committee.
- Detail history of patient along with various risk factors and associated co-morbidities were noted.
- General clinical examination and detailed neurological examination with other systemic findings of the patient were noted at the time of admission.
- The blood samples were taken within 24 hours of onset of stroke and sent for biochemical analysis and were analyzed in Biochemical Laboratory using standard analyzer.
- Patients were investigated with CBC, TLC, Platelet counts, urine (Routine Microscopy), ESR, BSL, LFT, RFT, Serum electrolytes, serum uric acid, lipid profile, CXR , radiological examination CT/MRI [as indicated].
- The patients were further evaluated for the presence of additional risk factors as follows, using the below mentioned parameters.

1 Hypertension:

Known case of hypertension with blood pressure more than 140 mm of Hg systolic and / or more than 90 mm of Hg diastolic.

2 Diabetes Mellitus:

Known case of diabetes mellitus with random or postprandial blood sugar more than 200 mgs /dl and / or fasting blood sugar more than 126 mgs /dl. The patients with blood sugar values of impaired fasting glucose or impaired glucose tolerance were not included as diabetics in this study.

3. Coronary Artery Diseases:

Patients with ECG evidence of old infarction or echocardiogram showing regional wall motion abnormalities**.**

4. Adverse Lipid Profile:

Total cholesterol - > 200 mgs/dl
Triglycerides - > 150 mgs/dl
LDL-C - > 130 mgs/dl
HDL-C - < 40 mgs/dl

5. Smoking and Alcoholism:

History of smoking and alcoholism within the last 5 years has been taken as smokers and alcoholics. Person who smoked at least 10 cigarettes per day for 6 months/more or the one who has smoked daily for more than 1 year or more regardless of the number of cigarettes smoked per day was considered as smoker.

6. OUTCOME VARIABLES:

Serum Uric Acid Levels Were Interpreted As Below:

- Males: 3.5 - 7.2 mg/dl (Normal)
- Females: 2.6 – 6.0 mg/dl (Normal)

INCLUSION CRITERIA

- Patients attending OPD and IPD of General Medicine at Navodaya Medical College Hospital & Research Centre, Raichur.
- Patients diagnosed with non haemorrhagic ischemic stroke within 24 hrs of onset with no previous history of stroke.

EXCLUSION CRITERIA

- Patients with previous history of TIA / CVA
- Patients who are on thiazide diuretics
- Patients who are known cases of gout or show clinical evidences of gout.
- Patients with acute or chronic renal failure.
- Patients whose CT scan showing hemorrhage or any other space occupying lesions other than infarct.
- Patients with conditions which alter serum uric acid levels such as
- Lymphoproliferative disease
- Polycythemia vera
- Myeloproliferative disorders
- Diabetic ketoacidosis and Lactic acidosis

STATISTICAL TOOLS:

The information collected regarding all the selected cases were recorded in a Master Chart. Frequencies, percentage, mean standard deviation, x2 and 'p' values were calculated. A 'p' value less than 0.05 is taken to denote significant relationship.

DISCUSSION

Stroke is defined as rapid onset of focal neurological deficit, resulting from diseases of cerebral vasculature and its content. In India, community survey have shown prevalence rate for hemiplegia is in the range of 200 per 100,000 persons accounting nearly 1.5% of all urban hospital admissions, 4.5% of all medical and around 20% of Neurologic cases. Mortality rate of stroke in acute phase is as high as 20% and it remains higher for several years after the acute event in stroke population than the general population. SUA is one of the major aqueous antioxidant in human beings and constitutes about 2/3rd of plasma free radical scavenging ability. It is therefore prudent to expect that SUA should have protective role in stroke. But only one study has found that higher levels of SUA being neuro protective in patients with stroke. An explanation to this comes from study which showed that SUA can work as prooxidant under certain circumstances, particularly if the levels of othermantioxidants 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 markers has also been discovered. According to Hayden *et al*., SUA acts like an antioxidant in the early stages of atherosclerotic process, being one of the most powerful determinant of plasma antioxidant capacity. Later, in the evolution of atherosclerotic process when SUA reaches 4-6mg/dl it becomes prooxidant. The antioxidant prooxidant urate shuttle relies on its surrounding environment. Cerebral ischemia initiates a complex cascade of metabolic events, generating nitric oxide and free oxygen radicals. Those free radicals and ROS mediate a great part of injuries appearing after a transitory ischaemic attack or during permanent ischemia, modifying macromolecules especially DNA , initiating apoptosis and necrosis. Our study was conducted on 100 stroke patients of which males and females were equal in number and hence there is no sex bias. Mean age in males is 59.1years and females 60.1 years. Mean uric acid levels in males 5.41mg/dl and 5.47mg/dl in females. Distribution of risk factors also is more or less in similar pattern (Hypertension: males-34, females-31; Diabetes mellitus: males-23, females-28; CAD: males-15 females-17 ; dyslipidemia ; males-17, females- 17). Millinois *et al*., and waring *et al*., found high levels of SUA in males, which is not seen in our study. However, in elderly population both sexes show high levels of SUA which has statistical significance. Our study is consistent with Milinois *et al*., who found elevated SUA in individuals older than 70 years. Regarding the association between risk factors. CAD is significantly associated with high uric acid levels in both sexes whereas DM is associated only with males and not with females.

In this study, most of the patients belong to anterior circulation territory, especially of middle cerebral artery region with commonest presentation being hemiplegia. As most of the posterior circulation strokes have masquerading clinical presentations and often lack CT scan evidence infarction, they are not included in this study to avoid inclusion bias. Age is the most common non-modifiable risk factor for the development of stroke. In this study, 25 % of the patients are above 65 yrs with 12 males and 13 females. Millinois *et al*., studied about 13163 patients 94 above 70 yrs studied for association of SUA and stroke concludes that SUA is associated with an increased risk for acute ischaemic / nonembolic stroke in elderly patients. This study also shows evidences for a significant association between SUA and elderly stroke population, and their association was maintained even when both sexes are considered separately. These findings are consistent with those in this study. Hypertension is the most common modifiable risk factor for stroke. SUA is also commonly associated with hypertension.Elevated SUA level is an independent predictor of hypertension in 25 % of patients with new onset untreated primary hypertension. In this study, Hypertension constitutes the major risk factor as 65 % of the stroke population is hypertensive. The mean uric acid level of hypertensive patients is 5.74 mgs / dl and of nonhypertensive is 5.08 mgs / dl and thus this study does not show any statistically significant relationship between SUA and hypertension. Diabetes mellitus ranks second as a risk factor in this study, constitute 51 % of the study population. Lehto S *et al*., conducted study involving 1017 persons with NIDDM, concludes that hyperuricemia is a strong predictor of stroke events in middle aged persons with NIDDM, independently of other CV risk factors. SUA levels are often increased in subjects with Met S. In this study, with the mean SUA level of 6.03 mgs / dl among diabetics and 4.97 mgs / dl among nondiabetics there is a strong association between SUA and DM. Further analysis shows this association is more stronger among males (mean SUA in male diabetics -6.18 mgs / dl vs non-diabetic males- 4.89 mgs /dl) than females. Thus this study strongly favours for an association between SUA and acute ischaemic /nonembolic stroke in diabetic population. SUA is significantly associated with cardiovascular mortality in certain epidemiological studies. According to study conducted by Rotterdam on 4385 participants came for follow up for 8.4 years showed that SUA is a strong risk factor for myocardial infarction and stroke. In this study CAD is found in 32 % of the patients. The mean SUA level in this CAD population is 6.53 mgs / dl comparing this to the patients without CAD is 5.03 mgs / dl which shows a strong statistical significance. Among those 32 stroke patients with CAD 17 have SUA > 7 mgs / dl. This also shows a strong statistical significance with a ‘p’ value of 0.000 <0.05. Hence this study strongly favours Rotterdam study and suggests SUA is a strong risk factor for myocardial infarction and stroke. Several prospective studies have shown that higher levels of total cholesterol increase the risk of ischaemic stroke. Amerenco p *et al*., conducted a metaanalysis of 90000

patients170 showed that administration of statins reduces the risk of 67 stroke among patients with CAD and that this risk reduction is primarily related to the extent to which LDL-C levels are lowered. In some studies relating metabolic syndrome and SUA, increased SUA levels correlated with low HDL-C levels. In our study, dyslipidemia is considered separately and not as a part of metabolic syndrome. Moreover, most of our patients in this study population are from low socioeconomic group and are not found to be obese. In this study, the mean uric acid level in dyslipidemia patients is 5.88 mgs / dl and in patients without dyslipidemia is 5.32 mgs / dl and does not show any significant association between these variables. Out of 34 patients with dyslipidemia in this study, only 12 are found to have SUA > 7 mgs / dl.Among the other risk factors like smoking and alcoholism, they are not considered to be separate risk factors in many pilot studies of this kind. This study also fails to show any statistically significant relationship between SUA and risk factors such as smoking and alcoholism when considered separately. Further analysis between < 7mgs/dl and> 7 mgs / dl SUA groups also maintain the association between high SUA and the risk factors namely age, diabetes and CAD.

CONCLUSION

- In the present study more than fifty percent of the patients with acute ischemic stroke had serum uric acid levels above the mean value.
- The mean serum uric acids levels in our study of 100 patients with acute ischemic stroke were 5.51 mg/dl which is on the higher side.
- Our study supports the fact that prevalence of stroke is more in elderly people and it is associated with raised serum uric acid levels.
- The uric acid levels association with gender in our study population suggests that significant percentage of females with stroke had raised serum uric acid levels as compared to males but the mean serum uric acid was higher in males as that of females.
- Association of raised serum uric acid with known risk factors of stroke like age, hypertension, DM, adverse lipid profile, CAD, smokers and alcohol was studied. Statistically significant association was found between raised serum uric acid and age, gender, diabetes and adverse lipid profile. Thus, it requires further detailed study to conclude that serum uric acid is a risk factor for stroke.

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