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Original Research Article

A study of serum uric acid levels in patients with ischaemic stroke and its relation with hypertension and diabetes mellitus in a tertiary hospital in Goa: a cross-sectional study

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ABSTRACT

Background: Stroke is second leading cause of mortality worldwide[1] and fifth leading cause of disability-adjusted life years in India. Multiple studies show relationship of serum uric acid levels to prognosis of cardiovascular and cerebrovascular diseases. The present study aims to ascertain relationship of serum uric acid levels with ischaemic stroke and its co-morbidities, hypertension and diabetes mellitus.
Methods: The present cross-sectional study was conducted in a tertiary care hospital in Goa. 100 admitted patients with ischaemic stroke meeting the inclusion criteria were enrolled for the study. Patients were evaluated for hyperuricemia, hypertension and diabetes mellitus. The unpaired student's t test was used for assessing association.
Results: A total of 100 patients were studied during the study period of 18 months. The mean age among males was 60.92±11.49 years and among females was 70.55±12.03 years. The mean serum uric acid levels in the patients with ischaemic stroke was 6.04±1.09 mg/dl which was significantly higher in male patients. There was a significant association between the mean serum uric acid levels and hypertension and diabetes among these patients.
Conclusions: Serum uric acid levels could be of value in identifying patients at risk of ischaemic stroke especially those with comorbidities such as diabetes and hypertension. Judiciously selecting drugs, which could produce a hypouricemic effect may play a role in preventing ischaemic stroke in such patients. Further prospective studies are needed to establish the role of serum uric acid in ischaemic stroke.

Keywords: Cerebrovascular accident, Stroke, Uric acid

INTRODUCTION

Stroke is the second leading cause of mortality worldwide.[1] It is also the fifth leading cause of disability-adjusted life years in India which is expected to increase in the years to come.[2] Like other non-communicable disease, stroke has a multi-factorial causation. The INTERSTOKE study done across 32 countries showed that 90% of the strokes are associated with modifiable risk factors in men and women and in all ages.[3] Early identification of these modifiable risk factors for stroke will help us plan and prescribe primary preventive strategies to those people who are at an increased risk of developing stroke.

One such risk factor under study is hyperuricemia. Multiple studies have shown that the level of serum uric acid is related to the prognosis of cardiovascular and cerebrovascular diseases, affecting the morbidity and mortality of coronary heart disease, stroke, congestive

heart failure, and hypertension. Hyperuricemia is previously shown to be correlated with vascular risk factors such as hypertension, diabetes and other metabolic disease which can significantly increase the risk of ischaemic stroke in younger and older populations.[4–8] Another study demonstrated that increased uric acid levels were predictors of cytotoxic injury and infarct expansion after stroke.[9] The present study is done to ascertain the relationship of serum uric acid levels with ischaemic stroke and its co-morbidities, mainly hypertension and diabetes mellitus.

METHODS

The present cross-sectional study was conducted in a tertiary care hospital in Goa. The admitted patients diagnosed with ischaemic stroke in the general wards of Department of General Medicine of the hospital were included in the study after they were transferred to in-patient wards upon initial stabilisation in the casualty. The study and its purpose were explained to the patient or the relative and written informed consent was taken for participation in the study either from the patient or from a relative when the patient was unable to give consent. A 100 admitted patients with ischaemic stroke over a period of 15 months (October 2018-December 2019) who met the inclusion criteria were enrolled for the study. The study included consenting patients with ischaemic stroke documented by a CT scan done within 48 hours of onset of symptoms of focal neurological deficit. Whereas, those patients diagnosed with ischaemic stroke with chronic renal failure, gout, haematological or myeloproliferative disorders or those on medications which directly alter uric acid levels such as diuretics and anti-gout drugs, as well as those patients with non-ischaemic stroke were excluded from the study.

Data were collected using a predesigned questionnaire following a pilot study to ascertain the feasibility of the study. The questionnaire was administered by face-to-face interview by the interviewer which included socio-demographic details, history of diabetes mellitus and hypertension followed by general physical examination and detailed central nervous system examination findings. This was followed by biochemical investigations which included complete blood count, fasting blood sugar levels, HbA1C levels, serum uric acid levels and renal function tests.

Patients were evaluated for additional risk factors for stroke such as hypertension which was defined according to joint national committee-VII as systolic blood pressure >140mmHg and/or diastolic blood pressure >90mmHg or patients self-reported history of hypertension or use of anti-hypertensive drugs, supported by documents. Patients were also evaluated for diabetes mellitus which was diagnosed if fasting blood sugar level was >126mg/dl, post prandial blood sugar level was >200mg/dl or random blood sugar level was >200mg/dl with symptoms of diabetes or if patients self-reported history of diabetes mellitus with history of taking anti-diabetic medications. In addition, patients were evaluated for hyperuricemia which as per the Goa Medical College biochemistry reference range of uric acid levels in male:(3.5-7.20) and female (2.6-6.0), hyperuricemia was >7.2mg/dl in males and >6.0mg/dl in females, using the chemiluminescent microparticle immunoassay analysis.

The sampling method used was simple random sampling. The collected data were entered and analysed using Statistical Package for the Social Sciences (SPSS) Software Version 22. The unpaired student's t test was used for assessing association. The results are presented using tables and figures.

RESULTS

A total of 100 patients were studied during the study period of 18 months of which 79 were males and 21 were females. The mean age among males was 60.92±11.49 years and the mean age among the females was 70.55±12.03 years. A majority of 73 patients presented with motor complaints of hemiparesis or hemiplegia. Of these 73 patients, 29 patients also had cranial nerve involvement, 4 patients had involvement of higher function. There were 7 patients who presented with cerebellar involvement. There were 16 patients who presented with pure cranial nerve involvement. Only 4 patients presented with pure sensory complaints.

Table 1: Sex-wise mean serum uric acid levels (mg/dl) in patients with ischaemic stroke.

Sex	Mean serum uric acid±SD
Male	6.18±1.08
Female	5.49±0.93

The mean serum uric acid levels in the patients with ischaemic stroke was 6.04±1.09 mg/dl. The mean serum uric acid levels were higher in male patients with ischaemic stroke, which ranged from 4-10.2 mg/dl. Whereas, in females it ranged from 3-6.6 mg/dl. The mean serum uric acid levels in male patients was 6.18±1.08 mg/dl. The mean serum uric acid level in female patients was 5.49±0.93 mg/dl (Table 1). This difference was statistically significant with a t statistic of 2.67 and a p value of 0.008. Of the total patients, 14 had hyperuricemia of which 10 were males and 4 were females (Table 2).

Table 2: Sex-wise proportion of patients with ischaemic stroke and hyperuricemia.

Sex	Se uric acid levels	
	Normal	**High**
Male	69	10
Female	17	4
Total	86	14

A majority of 82 patients in the study had hypertension as a comorbidity. The mean serum uric acid level in patients with hypertension was 6.28±0.98 mg/dl which was higher in comparison to those without hypertension. The mean serum uric acid level in non-hypertensive patients was 4.88±0.77 mg/dl. There was a significant difference in the mean serum uric acid levels across these groups with a t statistic of 5.68 and a *p* value of <0.001, which is statistically significant (Table 3).

Table 3: Mean serum uric acid levels (mg/dl) among patients with hypertension and diabetes.

Comorbidity	Number of patients	Mean serum uric acid ± SD	t statistic	*p* value
Hypertension				
Present	82	6.28±0.98	5.68	<0.001
Absent	18	4.88±0.77		
Diabetes				
Present	53	5.82±0.83	2.1	0.04
Absent	47	6.27±1.28		

Among all the patients with ischaemic stroke, 53 patients had diabetes mellitus. The mean serum uric acid level in these patients with diabetes was 5.82±0.83 mg/dl that is lower than that observed in patients without diabetes. The mean serum uric acid level in the patients without diabetes was 6.27±1.28 mg/dl. This difference in the mean serum uric acid levels was statistically significant with a t statistic of 2.1 and a *p* value of 0.04 (Table 3).

DISCUSSION

In the current study, we found that the mean serum uric acid levels were statistically higher in male patients with ischaemic stroke as compared to female patients. Similarly, higher mean serum uric acid levels were reported by studies done by Freedman et al, Nicholls et al and Matsubara et al.[10–12] In contrast, a similar study done by Shah et al in Karad, Maharashtra reported that there was no significant difference in the mean serum uric acid levels in male and female patients with acute ischaemic stroke.[13] Physiologically, men have higher circulating levels of uric acid than women which may be a result of suppressive effects of estradiol on uric acid.[14]

Age is a non-modifiable risk factor for the development of stroke. In our study, 44% of the patients are between 60 to 79 years with 37 males (84%) and 7 females (16%). Millinois et al in their study of 163 patients above 70 years for association of serum uric acid and stroke found that serum uric acid is associated with an increased risk for acute ischaemic/non embolic stroke in elderly patients independently of concurrent metabolic derangements.[15] In the German dataset, a maximum male preponderance was found for patients aged between 55 and 64 years, whereas patients older than 84 years revealed a strong overbalance of females.[16] These results are analogous to the findings in our study with majority of patients belonging to age group between 60-79 years with male preponderance and a younger age of onset in males than females.

Amongst the cases of acute ischaemic stroke in our study, mean serum uric acid level was 6.04±1.09 mg/dl. In a study done by Kaur et al in Punjab, it was seen that the mean serum uric acid levels among cases of acute ischaemic stroke was 6.15±1.9 mg/dl.[17] Another study done by Mehrpour et al in Iran among patients with acute stroke showed that 47.3% of the patients had hyperuricemia.[18] However in our study, hyperuricemia was found only in 14% of the study population.

In this study, 82 patients had hypertension as a comorbidity. The mean serum uric acid level in patients with hypertension was 6.28±0.98 mg/dl that was significantly higher in comparison to those patients without hypertension. Numerous recent studies in medical literature support the possibility that an elevated uric acid level can increase the risk for development of hypertension within 5 years.[19–21] The strength of the relationship between uric acid level and hypertension decreases with increasing patient age and duration of hypertension, suggesting that uric acid may be most important in younger subjects with early-onset hypertension.[6]

Among all the patients with ischaemic stroke, 53 patients had diabetes mellitus. The mean serum uric acid level in these patients with diabetes was 5.82±0.82 mg/dl that was significantly lower than that observed in patients without diabetes. Increasing evidence suggests that uric acid may play a role in the metabolic syndrome and development of hyperinsulinemia. As reported by multiple studies, hyperuricemia often precedes the development of hyperinsulinemia and diabetes.[7,8,22]

The study had a few limitations. Since the sample size of the study was small, the study participants may not be true representatives of the general population. Also, there was no follow up to collect information on patient outcome. Thus, it does not evaluate the prognostic value

of serum uric acid levels in patients with ischaemic stroke.

CONCLUSION

Serum uric acid levels could be of value in identifying patients at risk of ischaemic stroke especially those with comorbidities such as diabetes and hypertension. Judiciously selecting drugs (alone or in combination), which could produce a hypouricemic effect may play a role in preventing ischaemic stroke in such patients. Further long-term prospective studies are needed to establish the role of serum uric acid in ischaemic stroke.

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