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A Study of Serum Uric Acid Levels in Acute Stroke Patients

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Abstract: Hyperuricemia is commonly seen in subjects with cardiovascular disease and it one of the risk factor for morbidity and mortality with cardiovascular diseases. Uric acid is a product of synthesis from nucleic acids, amino acids, and Kreb's Cycle. Uric acid is biologically active and can stimulate oxidative stress and endothelial dysfunctions, inflammation, and vasoconstriction. The present study tries to evaluate the levels of uric acid in patients suffering from an acute ischemic stroke in comparison with normal subjects. Methods: This prospective cross-sectional study was conducted in the Departments of General Medicine and Biochemistry Prathima Institute of Medical Sciences, Naganoor, Karimnagar. A total of 80 subjects were included in the study. They were divided into two groups. Group I [cases] (n=40) consisted of patients reporting to the Emergency Department within 24 hours of onset of symptoms of stroke. The Group II [controls] (n=40) were the age and sex-matched patients attending the General Medicine OPD with minor complaints. Results: The mean age of Group I (n=40) was 61.42 ± 2.99 years and Group II was (n=40) 48.9 ± 4.53 years. The numbers of the male in Group I were 29 and female were 11 and in control, Group was 20 male and female each. The blood urea Group I was 38.7 ± 5.59 mg/dl and in Group II 30.12 ± 8.86 the p values were not found to be significant. The serum creatinine was 1.13 ± 6.61 in group I and in Group II was 0.91± 0.17 mg/dl and the p values were found to be significant. The uric acid levels were 7.32 ± 2.25 mg/dl in group II and 4.95 ± 1.5 mg/dl in Group I the values were found to be significant. Conclusion: Within the limitations of the present study it can be concluded that serum uric acid levels are significantly associated with ischemic stroke in this group of the population. The other important factors for the risk of ischemic strokes include Hypertension and Diabetes mellitus. There is growing evidence that uric acid may play a key role in the development and progression of cardiovascular diseases.
Keywords: Serum Uric Acid (SUA), Acute Ischemic stroke.

INTRODUCTION

The association between hyperuricemia and cardiovascular diseases was controversial due to lack of evidence, however, recent studies have supported that there is a definite association between uric acid and thrombotic events. Studies have shown that individuals with hyperuricemia also have higher incidences of cardiovascular diseases and mortality [1-4]. Kim *et al.*, in a Meta-analysis reported that hyperuricemia increases the risk of both ischemic stroke and hemorrhagic stroke as well as the risk of post-stroke mortality [5]. Other studies have suggested that post-stroke hyperuricemia could significantly exacerbate the outcome of stroke [6-8]. Uric acid is an end product of catabolism of purines, which is one of the main constituents of nucleotides and nucleic acids. UA blood levels are determined by the balance between its generation and excretion. During the catabolism of purines by xanthine oxidoreductase apart from the production of Uric acid there is a concomitant production of high levels of potentially deleterious pro-oxidant molecules like hydrogen peroxide and superoxide [9]. The UA produced is excreted through kidneys through special transporters [10]. Hyperuricemia also is seen in lifestyle-related diseases such as hypertension, diabetes, and dyslipidemia. Therefore it is still unclear to determine which is the cause and effect.

Stroke is defined as an abrupt onset of the neurologic deficit that is attributable to focal vascular cause [11]. Despite advances in the treatment and prevention of stroke, Acute Ischemic stroke is an important cause of disability, mortality, poor functional outcomes [12-14]. It is the third most common cause of death in the world after coronary heart disease and cancer in older people [11, 15]. Earlier studies have shown that there is a decline in serum uric acid levels after the onset of acute ischemic stroke indicating that uric acid may be involved in the progression of ischemic stroke [16]. Other studies have found post stroke hyperuricemia exacerbate the outcome of stroke [6-8]. Holme *et al.*, have found that hyperuricemia might be rather a complementary indicator than an

independent risk factor of acute stroke [1]. Therefore we in the present study tried to determine the association of serum uric acid levels in ischemic stroke patients in comparison with age and sex-matched controls from the normal population.

MATERIALS AND METHODS

This prospective cross-sectional study was conducted in the Departments of General Medicine and Biochemistry Prathima Institute of Medical Sciences, Naganoor, Karimnagar from the period from July 2016 to July 2017. Institutional Ethical committee permission was obtained for the study. A written consent was obtained from all the participants of the study after explaining about the study in the local language. A total of 80 subjects were included in the study. They were divided into two groups. Group I [cases] (n=40) consisted of patients reporting to the Emergency Department within 24 hours of onset of symptoms of stroke. A detailed clinical examination of the cases was done and acute stroke was diagnosed according to World Health Organization combined with CT or MRI confirmation [17]. Only those with acute ischemic stroke were included in the study. The Group II (controls) (n=40) were the age and sex-matched patients attending the General Medicine OPD with minor complains, patients with the history of Hypertension, cardiovascular diseases, renal failure were excluded from the Group II. A 10 ml of blood sample was taken in a vacutainer from all the patients included in the study and biochemical analysis was done in a fully automatic chemistry analyzer in the Department of Biochemistry. All the values obtained were recorded and analyzed with SPSS version 17 software on windows platform.

RESULTS

A total of 80 patients were included in the study out of which 49 were male and 31 were female patients. 30% of patients were belonging to 61-65 years age group, and 23.75% were from 56-60 years, 18.75% were belonging to 51-55 yrs, 12.5% were from 46-50 yrs and 15 were belonging to 41-45 years shown in Table-1.

Table-1: Age wise distribution of the patients included in the study

Age group (yrs)	Male	Female	Total	percentage
41 – 45	7	5	12	15
46 – 50	6	4	10	12.5
51 – 55	9	6	15	18.75
56 – 60	12	7	19	23.75
61 - 65	15	9	24	30
Total	49	31	80	100

The mean age of Group I (n=40) was 61.42 ± 2.99 years and Group II was (n=40) 48.9 ± 4.53 years. The number of the male in Group I were 29 and female were 11 and in control, Group were 20 male and female each (Table-2)

Table-2: Distribution characteristics of the patients involved in the study

	Group I [cases n=40]	Group II [controls n=40]
Age	61.42 ± 2.99	48.9 ± 4.53
Male	29	20
Female	11	20

A comparison of the Biochemical characteristics between group I and group II was done in table-3. The blood urea Group I was 38.7 ± 5.59 mg/dl and in group II 30.12 ± 8.86 the p values were not found to be significant. The serum creatinine was 1.13 ± 6.61 in group I and in group II was 0.91± 0.17 mg/dl and the p values were found to be significant. Serum cholesterol was 179.15 ± 40.45 mg/dl in group I and 180.1 ± 40.15 in group II p values were not found to be significant. Serum Triglycerides were 149.9 ± 30.21179.15 ± 40.45 mg/dl in group I and 171.2 ± 57.6 in group II p values were found to be significant. Serum Triglycerides were 149.9 ± 30.21179.15 ± 40.45 mg/dl in group I and 171.2 ± 57.6 in group II p values were found to be significant. Similarly, the HDL values were found to be significant between the two groups and the uric acid levels were 7.32 ± 2.25 mg/dl in group II and 4.95 ± 1.5 mg/dl in group I p values were found to be significant (Table-3).

The measured variables in the study were investigated by logistic regression test in terms of the independent effect on the risk of ischemic stroke. Diabetes was having an odds ratio of 1.65 and hypertension was 1.52 we found that the level of serum uric acid (SUA) has a significant relationship with stroke the odds ratio was found to be 2.01 shown in Table-4.

Table-3: Biochemical parameters recorded in both the groups

Parameter values in mg/dl	Group I	Group II	P values
B. Urea	38.7 ± 5.59	30.12 ± 8.86	0.16
Serum Creatinine	1.13 ± 0.61	0.91± 0.17	<0.05*
Serum cholesterol	179.15 ± 40.45	180.1 ± 40.15	0.223
Triglycerides	149.9 ± 30.21	171.2 ± 57.6	<0.05*
HDL	32.33 ± 9.86	41.55 ± 9.5	<0.05*
LDL	98.9 ±30.12	105.57 ± 40.25	1.12
VLDL	30.12 ± 13.3	37.22 ± 15.86	1.5
Serum Uric acid (SUA)	7.32 ± 2.25	4.95 ± 1.5	<0.058*

Table-4: Showing the risk of stroke by logistic regression analysis

Variable	Odds ratio	95% CI
Gender	0.59	0.20 – 1.53
Age	1.06	0.79 – 1.90
Hypertension	1.52	0.99 – 2.25
Diabetes	1.65	1.12 – 2.56
Tobacco	0.79	0.39 – 1.56
Alcohol	0.83	0.77 – 1.77
Serum Uric acid (SUA)	2.01	1.50 – 2.79

DISCUSSION

In the present study out of a total of 40 cases of Ischemic stroke more numbers of cases were found in male (n=29) 72.5% and in female (n=11) 27.5% the male to female ratio was 3:1. In a study by Dalal PM *et al.,* in Mumbai showed higher stroke incidence rates in men than women the crude incidence was, 162/100,000 person-years for men versus 141/100,000 person-years for women [18]. Nagaraja D *et al.,* from Bangalore found a greater preponderance of stroke in men (67%) with a male to female ratio of 2:1 almost in agreement with the present study [19]. The mean age of the patients with acute ischemic stroke was 61.42 ± 2.99 years. In a similar study by Inderjeet Kaur *et al.,* in North India found the mean age of 65.30±12.11 years [20]. The incidence of stroke appears to be higher in the 6th decade. It has been shown that the average age of the patients with stroke in developing countries is usually 15 years younger than those of the developed countries. Dalal PM *et al.,* in Mumbai showed the average age of stroke patients was 66 years while Nagaraja D *et al.,* showed the average age to be 54.5 years [18, 19]. In this study, we found serum urea levels in the test group I to be equal to 38.7 ± 5.59 mg/dl and in control group II, it was 30.12 ± 8.86 the p values were not found to be significant. However, we found slightly higher mean creatinine levels in acute stroke patients 1.13 ± 0.61mg/dl as compared to the 0.91± 0.17 mg/dl in the test group the calculated p values were also found to be significant. The reason could be the most of the stroke patients were hypertensive and probably lack of adequate control of blood pressure could have deleterious effects on kidneys as shown by a decrease in kidney functions. In the study, we found the significant association between higher levels of triglycerides and HDL with stroke. Studies have shown that higher levels of total cholesterol increase the risk of ischemic strokes [21, 22] Amerenco P *et al.,* in a meta-analysis found administration of statins reduces the incidence of stroke among the patients with coronary artery disease and this reduction was probably due to decrease in LDL-C [23]. In studies relating to metabolic syndrome and serum uric acid levels shows an increased uric acid levels are correlated with low HDL-C levels we in the present study have found a similar observation the mean HDL-C in the study group was 32.33 ± 9.86 mg/dl and mean serum uric acid was 7.32 ± 2.25 mg/dl in comparison to the control group, where the mean HDL-c was found to be 41.55 ± 9.5 mg/dl and serum uric acid, was 4.95 ± 1.5 [20]. In vitro studies have shown that under certain circumstances uric acid can exert pro-inflammatory and pro-oxidant effects particularly in lipophilic environments [24, 25]. It is found that in endothelial cells UA attenuates nitric oxide release and it reduces endothelial dysfunctions also in mature adipocytes UA promotes NADPH oxidase activity and the production of reactive oxygen species (ROS)through activation of intracellular signaling pathways [26, 27]. Hence the shreds of evidence point out that UA may be both antioxidant and pro-oxidant properties and complex interaction is likely to occur in events like stressful situations like an acute ischemic stroke. A logistic regression test performed with variables in our study showed that serum uric acid had a significant association with stroke apart from this diabetes mellitus and hypertension was also found to be significantly associated with stroke. In the present study 33 out of 40 patients were having diabetes mellitus and 32 were having hypertension and 29 were having both diabetes and hypertension. Jimenez *et al.,* in a case-control study of 460 ischemic stroke patients with logistic regression analysis found after elimination of age, race, smoking,

menopause, hypertension, and diabetes mellitus reported that UA alone was not related to ischemic stroke [28]. Chongke Z *et al*., study high serum UA levels were associated with increased risk of stroke in both men and women [29] which is in agreement with the results of our study.

CONCLUSION

Within the limitations of the present study, it can be concluded that serum uric acid levels are significantly associated with ischemic stroke in this group of the population. The other important factors for the risk of ischemic strokes include Hypertension and Diabetes mellitus. There is growing evidence that uric acid may play a key role in the development and progression of cardiovascular diseases. More such studies are required to determine the exact mechanism of interaction of the uric acid and ischemic events.

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