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IS SERUM URIC ACID A RISK FACTOR FOR ISCHEMIC STROKE ?

General Medicine

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ABSTRACT

BACKGROUND: It was initially considered to be an inert substance which crystallizes at high concentrations and results in conditions such as gout. However, studies underlined its anti-oxidant activity and importance in scavenging oxidant radicals. It accounts for as much as half of the anti-oxidant properties of the human plasma. It prevents lipid peroxidation and is an especially effective scavenger of hydroxyl, peroxynitrite and superoxide free radicals.However, a pro-oxidant role of uric acid has also been suggested especially in reduction of bioavailability of Nitric Oxide, increasing Insulin resistance, adipogenic differentiation and inflammation in the vascular smooth muscle cells. **METHODOLOGY:** The present study comprised of 144 subjects with acute ischemic stroke who were admitted to G S L General Hospital was conducted with an aim of studying serum uric acid levels in patients with acute ischemic stroke and to study its association with the risk factors for stroke.

CONCLUSION: It is observed from the study that serum uric acid level is significantly associated with the various risk factors for stroke – increasing age, hypertension, diabetes mellitus, CAD and previous stroke and smoking.

KEYWORDS

Ischemic stroke, uric acid, risk factors.

INTRODUCTION

Stroke is a global health problem. It is the second commonest cause of death and fourth leading cause of disability worldwide. Approximately 20 million people suffer from stroke each year and of these 5 million do not survive. In developed countries, stroke is the first leading cause for disability, second leading cause of dementia and third leading cause of death. Stroke was the second-leading global cause of death behind heart disease in 2013, accounting for 11.8 percent of total deaths worldwide[1].

Stroke is also a predisposing factor for epilepsy, falls and depression in developed countries and is a leading cause of functional impairments, with 20% of survivors requiring institutional care after 3 months and 15% - 30% being permanently disabled. Stroke is no longer a disease of the developed world. Low and middle-income countries account for 85.5% of total stroke deaths worldwide and the number of disability-adjusted life years in these countries was approximately seven times that in high-income countries[1].

Morbidity and Mortality associated with Stroke[1]
Global Stroke estimates
400-800 strokes per 100,000.
6.2 million Deaths.
16 million new acute strokes every year.
28,500,000 DALYs (disability adjusted life-year).
28-30 day case fatality ranges from 17%-35%.

Stroke Morbidity and Mortality in India
Prevalence 90-222 per 100,000.
102, 620 million deaths.
1.44-1.64 million cases of new acute strokes every year.
6,398,000 DALYs.
12% of strokes occur in the population aged <40 years.
28-30 day case fatality ranges from 18-41%.

Uric acid is an end product of the metabolism of purines which are the building blocks of the nuclear material and also components of high-energy molecules. It was initially considered to be an inert substance which crystallizes at high concentrations and results in conditions such as gout. However, studies underlined its anti-oxidant activity and importance in scavenging oxidant radicals. It accounts for as much as half of the anti-oxidant properties of the human plasma. It prevents lipid peroxidation and is an especially effective scavenger of hydroxyl, peroxynitrite and superoxide free radicals.However, a pro-oxidant role of uric acid has also been suggested especially in reduction of bioavailability of Nitric Oxide, increasing Insulin resistance, adipogenic differentiation and inflammation in the vascular smooth muscle cells[2].

A number of studies demonstrated that high uric acid is an independent risk factor for hypertension, diabetes, CVD. Even after controlling for associated risk factors, high uric acid is an independent risk factor for cardiovascular events in patients affected by hypertension, diabetes, pre-existing cerebrovascular and cardiovascular disease.

Elevated serum uric acid correlate with aging, male gender, hyperlipidemia, diabetes mellitus, insulin resistance, glucose intolerance, obesity and hyperinsulinemia and accelerate progression of hypertension and end organ damage[3]. Higher levels of serum uric acid were associated with a higher prevalence of carotid plaques which play an important role in the causation of ischemic cerebrovascular events in men[4]. The role of uric acid as an independent risk factor for vascular disease has remained debatable despite enough evidence to suggest that an elevated serum uric acid may predict an increased risk of cardiovascular events including strokes. We aimed at studying the serum uric acid levels in patients with acute ischemic stroke and the association of uric acid level with the various risk factors of stroke.

MATERIALAND METHODS

The present study, A STUDY OF SERUM URIC ACID LEVELS IN ACUTE ISCHEMIC STROKE was done in the department of General Medicine, GSL General Hospital, Rajamahendravaram between 1st November 2015 and 30th April 2017.

Study setting: Department of General Medicine, G S L General Hospital, Rajamahendravaram.
Study period: 1st November 2015 to 30th April 2017.
Study design: Cross – sectional study.

Study subjects:
Patients who presented to G S L General Hospital with features suggestive of stroke were subjected to imaging with CT/MRI brain after thorough history and examination. A total of 144 patients who were diagnosed with acute ischemic stroke between 1st November 2015 and 30th April 2017 were included in the study.

Exclusion criteria:
Patients who were
- Known cases of renal failure,

- Known to be suffering from malignancies and receiving anti-neoplastic drugs,
- Known to have had a renal transplant and receiving immunosuppressive therapy
- Known cases of gout or already on urate lowering drugs were excluded from the study.

Study tools:
An elaborate history was obtained from all the study subjects or from a reliable informant wherever required. A detailed neurological examination was performed. Information regarding the risk factors for stroke was obtained and recorded, such as Hypertension, Diabetes Mellitus, Dyslipidemia,Coronary Artery Disease, Smoking and alcoholism.

NCCT/MRI brain was used in the diagnosis of acute ischemic stroke. Serum uric acid levels were obtained within the first 24 hours of hospital admission. Serum uric acid was estimated using photometric analysis of the products obtained by the reaction of the patient's serum with the reagent containing 4-Aminoantipyrine giving rise to a Quinoneimine dye,the absorbance of which is maximum at 546nm. The absorbance of this dye at 546nm is directly proportional to the concentration of urc acid in the sample.

Statistical Analysis:
The details of the study subjects and the risk factors of stroke under study were recorded in a master chart. Statistical analysis was performed using SPSS version 21 and MS-Excel 2007. Descriptive data were expressed as Mean±standard deviation. Unpaired t- test was used to compare the differences between means of quantitative variables. Chi square test was used wherever necessary. 'p' value less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

AGE : In the present study, an increase in the mean serum uric acid level has been observed with advancing age. The mean serum uric acid level in the study subjects below 40 years of age was found to be 3.24mg/dl whereas that in individuals between 70 and 79 years of age was 7.03mg/dl. Out of the 34 patients with hyperuricemia, 22 (64.7%) are above 65 years of age as compared to 12 (35.3%) younger than 65 years of age. This difference is statistically significant.

The average serum uric acid in patient above 60 years was 6.58±2.75 mg/dl as compared to patient under the age of 60 years in whom the mean serum uric acid level was 5.84±2.72 mg/d.

GENDER: In the present study, 86 (59.7%) are male and 58 (40.3%) are female.The mean age of the males is 58.67 (± 14.3) years and that of females is 56.74 (± 12.5) years. The mean serum uric acid level in the males of the study population is 5.59 (± 1.76) mg/dl and of the females is 5.05 (± 1.78) mg/dl. This difference in mean serum uric acid level between males and females has not been found to be statistically significant.

HYPERTENSION: Hypertension is the most common modifiable risk factor for stroke. Hypertension was present in 72% (102) of the study subjects in the present study. The mean serum uric acid level in the hypertensive subjects among the study population (5.96mg/dl) was found to be higher than that in the subjects without hypertension (3.94mg/dl). This difference was found to be statistically significant.

DIABETES MELLITUS: Diabetes mellitus is a risk factor for stroke [53,54,55] and is a highly prevalent condition. It is found in as many 33% of patients with ischaemic stroke [56]. The mean serum uric acid level among subjects with diabetes in the present study was found to be 6.30mg/dl, which is significantly higher than that of the subjects without diabetes mellitus (4.49mg/dl). This statistically significant difference was found even on considering males and females separately.

DYSLIPIDEMIA: In the present study, the mean serum uric acid level in stroke patients with dyslipidemia was found to be 6.27 (± 1.27) mg/dl as against in those without dyslipidemia, which was 4.57 (± 1.37) mg/dl and this difference was found to be statistically significant. This association between serum uric acid level and dyslipidemia was observed even when males and females were studied separately.

CORONARY ARTERY DISEASE: The prevalence of coronary artery disease in stroke patients is substantial. In the present study, 32 out of the 144 study subjects with ischemic stroke (22.2%) had CAD. The mean Serum Uric Acid level in study subjects with CAD among the study population is 6.58 mg/dl, and among those without CAD it is 4.49 mg/dl. This difference in the mean serum uric acid level was found to be statistically significant.

SMOKING: In the present study, the mean serum uric acid level in study subjects who are smokers is 5.80mg/dl and in non-smokers is 4.96 mg/dl. The serum uric acid level was found to be significantly elevated in smokers.

ALCOHOL: A statistically significant association found between the level of uric acid and alcoholism on performing unpaired T-test. The mean uric acid value is 5.67 mg/dl, and among non-alcoholics it is 5.08 mg/dl.

DISTRIBUTION OF STROKE RISK FACTORS ACCORDING TO GENDER

RISK FACTOR	CASES			
	MALES		FEMALES	
	NO.	%	NO.	%
a) Hypertension	60	69.8	42	72.4
Present	26	30.2	16	27.6
Absent				
b) Diabetes Mellitus	39	45.3	31	53.4
Present	47	54.7	27	46.6
Absent				
c) Smoking	64	74.4	6	10.3
Present	22	25.6	52	89.7
Absent				
d) CAD	15	17.4	17	29.3
Present	71	82.6	41	70.7
Absent				
e) Dyslipidemia	39	45.3	29	50.0
Present	47	54.7	29	50.0
Absent				
f) Alcoholism	66	76.7	5	8.6
Present	20	23.3	53	91.4
Absent				
g) Old CVA	4	4.7	2	3.4
Present	82	95.3	56	96.6
Absent				

CONCLUSION

- Elevated serum uric acid level is significantly associated with the risk factors for stroke – hypertension, diabetes mellitus, dyslipidemia, previous stroke, cardio vascular disease and smoking.
- Elevated serum uric acid may be considered as a risk factor for ischemic stroke.
- Elevated serum uric acid level need to be interpreted carefully in patients with risk factors for vascular events like hypertension, diabetes mellitus, dyslipidemia and a history of prior vascular events.
- The elevation of serum uric acid level has to be considered with caution in patients of elderly age group.
- Large prospective study is needed to assess the risk of ischemic stroke in population with elevated uric acid level.
- Urate lowering therapies may be considered as a part of stroke prevention strategies. However, large randomized trials are needed to form an evidence to support such a practice.

LIMITATIONS: The limitations of the present study are that the small sample size percludes generalization of the observations. The study design, being a cross sectional study, doesn't facilitate comparison of the serum uric acid levels in patients with similar risk factors who didn't have a stroke. So, an independent causal relationship of elevated serum uric acid in stroke could not be established. The present study also did not evaluate the impact of elevated serum uric acid level on the outcome of acute stroke.

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