

A Study to find out the Association of Serum Concentrations of Uric Acid and Lipid Profile in Stroke Patients with Diabetes Mellitus

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Abstract

Background: Stroke is one of the most common causes of death in the developed as well as developing nations. India is also suffering huge social and economic burden in the rehabilitation of stroke patients.

Aims and Objectives: Our present study is to determine serum uric acid and lipid profile level as risk factors of stroke with diabetes mellitus.

Materials and Methods: This is a Cross-sectional observational study conducted in a tertiary care centre, Burdwan Medical College and Hospital, from February 2017 to July 2018. 50 patients of stroke with diabetes mellitus, 50 patients of stroke without diabetes mellitus and 50 patients of diabetes mellitus without stroke were taken according to inclusion and exclusion criteria. Serum Uric acid and Lipid profile were measured by standard biochemical method in all patients. Age, sex distribution and duration of diabetes mellitus are also studied.

Results: Stroke is more common in older population with male predominance. The differences of mean uric acid level in between CVA+DM group (8.172 ± 1.366 mg/dl) and Only CVA group (6.235 ± 1.247 mg/dl); & CVA+DM group and Only DM group (5.911 ± 1.528 mg/dl) are statistically significant (p value <0.05). In Lipid profile there is variable result, the mean difference of TG level, VLDL level and reduced HDL level among the three groups (CVA+DM, Only CVA, Only DM) are statistically significant (p value <0.05). The mean difference of Cholesterol level and LDL level between CVA+DM group and Only CVA group is statistically not significant (p value >0.05) but between CVA+DM group and Only DM group is statistically significant (p value <0.05).

Conclusion: Hyperuricemia is a probable risk factor of stroke, in patients with Diabetes mellitus. Total cholesterol and LDL cholesterol levels are almost similarly elevated in diabetic stroke patients and non-diabetic stroke patients. High Triglyceride, high VLDL and reduced HDL Cholesterol are probable risk factors of stroke in patients with Diabetes mellitus. Chance of developing stroke is more in diabetic patients having greater HbA1C level.

Keywords: Uric acid; Lipid profile; Stroke; Diabetes Mellitus

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Introduction

WHO defines the clinical syndrome of stroke as rapidly developing clinical signs of focal (or global) disturbance of cerebral function with symptoms lasting 24 hours or longer or leading to death having no apparent cause other than vascular origin. The Stroke

is one of the leading causes of death in the developed nations accounting for nearly 4.5 million deaths each year. Stroke is also a leading cause of functional impairments, with 20% of survivors requiring institutional care after 3 months and 15%-30% being permanently disabled [1-4]. Crude prevalence rate of stroke is 147/100,000 and annual incidence rate is 36/100,000. Stroke is

an event that can change the life of the affected person and their family and caregivers. Stroke is divided into two broad categories according to its pathophysiology:

Ischemic strokes: It is caused by either cerebral thrombosis or embolism and it account for 50%–85% of all strokes worldwide.

Haemorrhagic strokes: These are caused by subarachnoid haemorrhage or intracerebral haemorrhage and account for 1%-7% and 7%-27% respectively of all strokes worldwide.

The effects of a stroke are determined by the extent and site of brain injury, but the clinical symptoms of stroke do not accurately predict its underlying cause or causes. Classic stroke symptoms include the acute onset of unilateral paralysis, loss of vision, speech impairment, memory loss, impaired reasoning ability, coma, or death. Thus, early identification of those at increased risk of stroke should represent a significant contribution to health improvement so that interventions can be targeted to those most likely to benefit. Because stroke risk prediction based Only on conventional risk factors such as blood pressure (BP) is still not completely reliable, a continued search for predictive markers is of interest [5].

Diabetes mellitus plays an important role in cerebrovascular accident. The worldwide prevalence of DM has risen dramatically over the past two decades more so in India. With an increasing incidence worldwide, DM will be a leading cause of morbidity & mortality for the foreseeable future [6,7]. Uric acid is the ultimate catabolite of purine metabolism in human and higher primates. It exists in the extracellular compartment as sodium urate, and it is cleared from the plasma through the kidney.

Age and sex influence serum Uric acid level. Before puberty, the average serum uric acid level is 3.6 mg/dl for males and females. Following puberty, value rises to adult levels in women typically 1 mg/dl less than men. This lower level in women apparently reflects oestrogen related enhancement of renal urate clearance [8].

However, serum uric acid has been recently associated with insulin resistance. Serum uric acid is a soluble antioxidant scavenger, and oxidative stress is a hallmark of tissues' hyperglycaemic milieu. Furthermore, serum uric acid may be considered as a marker of acute endothelial dysfunction, since Hyperuricemia has been observed to be associated with raised endothelin levels, and there is evidence that involvement of uric acid, via purine metabolism, in the process of thrombus formation. Some studies have linked serum uric acid with stroke in diabetes mellitus. But it is debated. Therefore, we decide to evaluate Hyperuricemia as a risk factor for stroke in patients with diabetes mellitus. In our present study we aimed to find out association of uric acid level in diabetic stroke patients.

Materials and Methods

Patients admitted in the Neurology indoor and patients attending medicine outdoor in Burdwan Medical College and Hospital. Cross-sectional observational study was done from February 2017 to July 2018 with 50 patients of stroke with diabetes mellitus, 50 patients of stroke without diabetes mellitus and 50 patients of diabetes mellitus without stroke were taken.

Inclusion criteria

- Focal neurological deficit of sudden onset that persisted beyond 24 hours.
- Cerebral infarction or haemorrhage documented by computed tomography or magnetic resonance imaging scan.
- A case of Diabetes mellitus should have
 - Fasting blood glucose 126 mg/dl Or more,
 - In oral glucose tolerance test, 2 hours plasma glucose 200 mg/dl Or more OR,
 - Symptoms of diabetes (polyuria, polyphagia, polydipsia) with random blood glucose 200 mg/dl Or more
 - HbA1c (Glycosylated haemoglobin) > = 6.5%.

Exclusion criteria

- Focal neurological deficit of sudden onset that lasted less than 24 hrs,
- Concurrent major renal, hepatic and cancerous diseases
- History of recent clinical infection
- Major trauma in previous month
- Patients is on antiuricosuric drugs
- Patients is on hypolipidemic drugs
- Alcoholic patients.

Parameters to be studied

Pulse, blood pressure, neurological profile, serum uric acid, lipid profile, blood for fasting blood sugar, post prandial blood sugar, random blood sugar, HbA1c, Urea, creatinine, computed tomography or magnetic resonance imaging scan of brain.

Study tools

- Computed Tomography machine/Magnetic Resonance Imaging machine
- Auto analyser
- Semi auto analyser
- Centrifuge machine
- Routine laboratory glass wares and PVC wares
- Clot activator vials, oxalo-fluride vials, disposable syringes
- Rubber tourniquet, spirit, cotton swab
- Computer for data analysis.

Study techniques

- History of hypertension, diabetes, heart disease, dyslipidemia, renal disease, malignancy, gout, past history of similar episodes, smoking, drinking, family history.
- General Survey (Pulse, Blood Pressure)
- Clinical assessment
- Imaging Evaluation
- Estimation of serum uric acid by auto analyser

- Estimation of serum lipid profile by auto and semi auto analyser.
- Estimation of plasma glucose by standard biochemical method
- Record Analysis.

Results

Demographic profile of the study population

A total number of 150 patients were taken according to inclusion and exclusion criteria mentioned earlier and divided in 3 groups

Group 1 (CVA+DM): 50 patients having stroke (CVA) with diabetes mellitus (DM)

Group 2 (Only CVA): 50 patients having stroke (CVA) without diabetes mellitus (DM)

Group 3 (Only DM): 50 patients having diabetes mellitus (DM) without stroke (CVA)

Age distribution

In our study mean age of total patients are 64.60 ± 7.41 years, among them group 1 (CVA+DM) is 64.68 ± 8.02 years, group 2 (Only CVA) is 66.28 ± 6.62 years and group 3 (Only DM) is 62.84 ± 7.25 years (**Figure 1 and Table 1**).

Sex distribution

There are 91 (61%) male patients and 59 (39%) female patients included in our study. Among them in group 1 (CVA + DM), 29 (58%) patients are male and 21 (42%) patients are female, in group 2 (Only CVA), 32 (64%) are male and 18 (36%) are female and in group 3 (Only DM) 30 (60%) are male and 20 (40%) are female. So stroke is more common in men (**Figure 2, Figure 3 and Table 2**).

Two main parameters were taken namely uric acid and lipid profile in this study which is quantitative data. To know whether the data is normally distributed or not the Test of Normality (Kolmogorov –Smirnov test) is done (**Table 3**).

This values are normally distributed as because the Test of Normality (Kolmogorov – Smirnov test) shows significance level 0.200 which is greater than 0.05.

As this was a normally distributed quantitative data so that parametric test was done. We had to compare mean uric acid between Group 1 & Group 2 and between Group 1 & Group 3. So unpaired t-test was done.

This is a cross sectional observational study including a total of 150 patients out of which 50 patients have CVA+ DM, 50 patients have Only CVA and 50 patients have Only DM. This study is done to

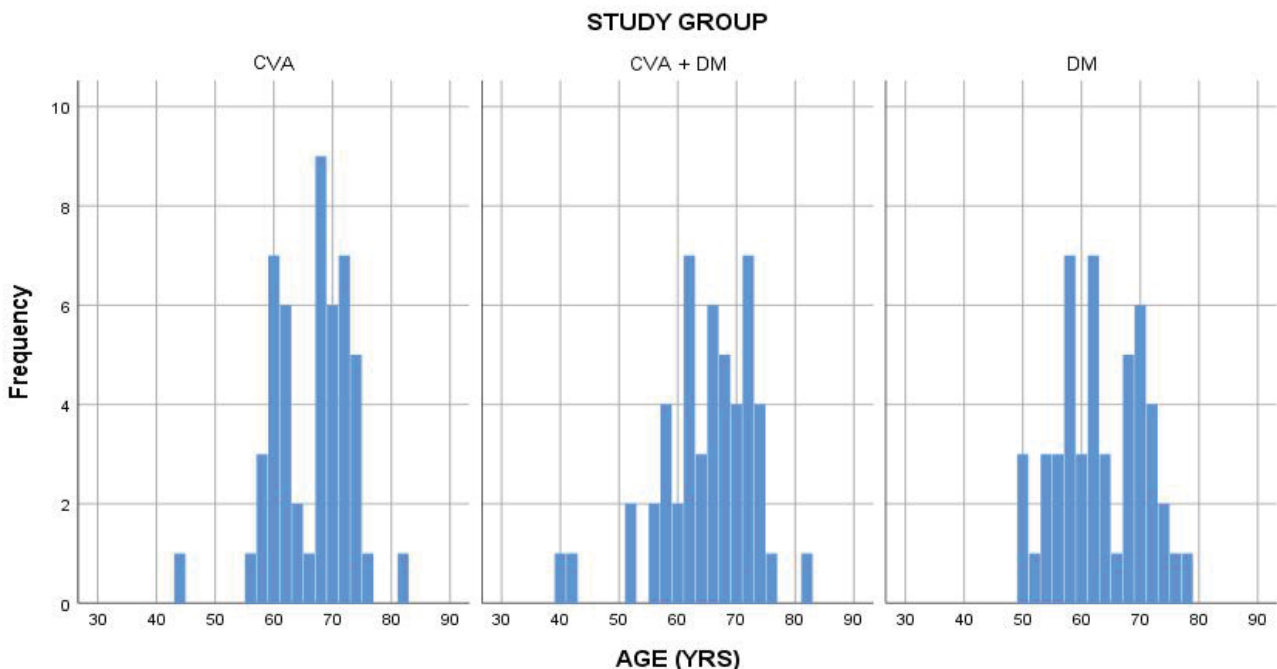


Figure 1 Histogram showing distribution of age among study groups.

Table 1 Mean age of study population.

Study Group	Number (N)	Mean Age (Years)	Standard Deviation (SD)
CVA + DM	50	64.68	8.022
Only CVA	50	66.28	6.624
Only DM	50	62.84	7.249
Total	150	64.60	7.407

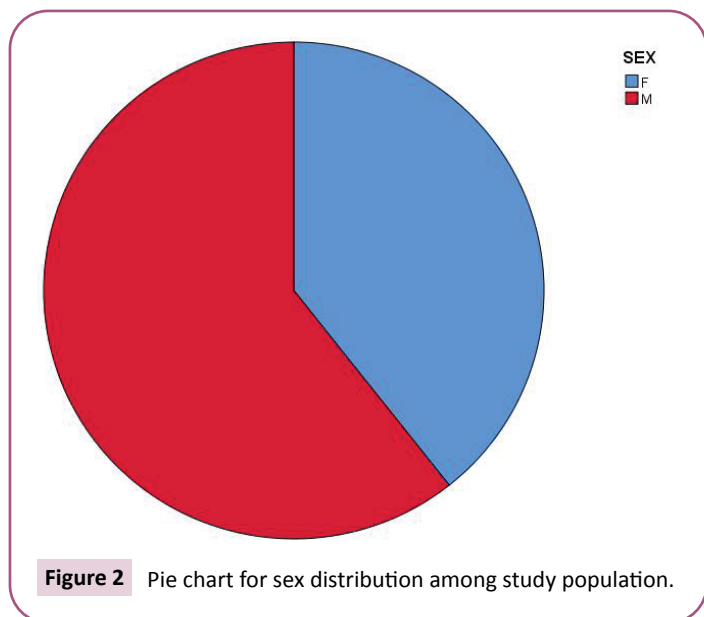


Figure 2 Pie chart for sex distribution among study population.

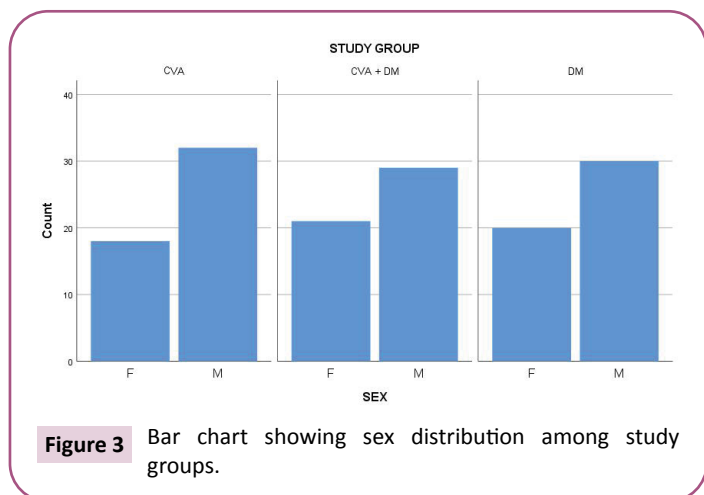


Figure 3 Bar chart showing sex distribution among study groups.

find out whether there is any association of serum concentration of Uric acid and Lipid profile in Stroke patients with Diabetes mellitus [9,10].

The study is done among the patients admitted in Neurology/ Medicine Indoor or attended OPD of Burdwan Medical College & Hospital. The patients are taken according to the inclusion and exclusion criteria [11]. Uric acid and Lipid profile levels were estimated by standard method and Statistical analysis was done by using SPSS.

It is found that, mean uric acid level in patients of CVA+DM group is 8.172 ± 1.366 mg/dl, in Only CVA group is 6.235 ± 1.247 mg/dl and in Only DM group is 5.911 ± 1.528 mg/dl. The differences of mean uric acid level in between CVA+DM group and Only CVA group; & CVA+DM group and Only DM group are statistically significant (p value<0.05).

In this study, mean Cholesterol level among patients having CVA with DM is 220.640 ± 34.254 mg/dl, in patients having Only CVA is 216.440 ± 35.635 mg/dl and in patients having Only DM is 184.780 ± 22.489 mg/dl. The mean difference of Cholesterol level

between CVA+DM group and Only CVA group is statistically not significant (p value >0.05) but between CVA+DM group and Only DM group is statistically significant (p value <0.05).

In our study we found mean Triglyceride level among patients having CVA with DM is 302.500 ± 49.513 mg/dl, patients having Only CVA is 158.240 ± 26.496 mg/dl and in patients with Only DM is 233 ± 47.596 mg/dl and the mean difference of TG level among the three groups (CVA+DM, Only CVA, Only DM) are statistically significant (p value <0.05).

In this study, mean HDL cholesterol level in CVA+ DM group is 24.960 ± 4.548 mg/dl, in Only CVA group is 38.480 ± 4.769 mg/dl and in Only DM group is 30.480 ± 5.953 mg/dl and mean difference of HDL -C level among the three groups (CVA+DM, Only CVA, Only DM) are statistically significant (p value <0.05).

In this study, we found mean LDL cholesterol level among patients having CVA with DM is 135.140 ± 29.170 mg/dl, in patients with Only CVA is 146.300 ± 34.383 mg/dl and in patients with Only DM is 107.660 ± 19.818 mg/dl. The mean difference of LDL Cholesterol level between CVA+DM group and Only CVA group is statistically not significant (p value >0.05) but in between CVA+DM group and Only DM group is statistically significant (p<0.05).

In the present study, mean VLDL cholesterol level in CVA+ DM group is 60.180 ± 9.323 mg/dl, in Only CVA group is 31.660 ± 5.243 mg/dl and in Only DM group is 46.640 ± 9.503 mg/dl and mean difference of VLDL Cholesterol level among the three groups (CVA+DM, Only CVA, Only DM) are statistically significant (p value <0.05). In our present study we found that the mean HbA1C level in CVA +DM group is (9.12 ± 0.79) higher than the mean in Only DM group (7.95 ± 0.66) and the mean difference between these two groups are statistically significant (p value <0.05).

Discussion

In this study an effort was made to compare the level of the serum Uric acid & lipid profile among stroke patients having diabetes mellitus and stroke patients without having Diabetes mellitus and in patients having Only Diabetes mellitus [12]. Total 150 patients were taken (among them 50 patients of stroke (CVA) with diabetes mellitus (DM), 50 patients of stroke (CVA)

Table 2 Sex distribution among study group.

Study Group	Male	Female	Total
CVA + DM	29 (58%)	21 (42%)	50
Only CVA	32 (64%)	18 (36%)	50
Only DM	30 (60%)	20 (40%)	50
Total	91 (61%)	59 (39%)	150

Table 3 Kolmogorov-Smirnov test for checking normality.

Uric Acid (mg/dl)	Study Group	Kolmogorov-Smirnov			Shapiro-Wilk		
		Statistics	df	Sig.	Statistic	df	Sig.
	CVA	0.076	50	0.200*	0.984	50	0.709
	CVA + DM	0.080	50	0.200*	0.986	50	0.796
	DM	0.071	50	0.200*	0.969	50	0.221

without diabetes mellitus (DM) and 50 of diabetes mellitus (DM) without stroke).

Most of the patients of this study are above 50 years of age. Mean age of patients having stroke with Diabetes mellitus (CVA+DM) is 64.68 ± 8.022 years and of stroke patients (Only CVA) is 66.28 ± 6.624 years [13-15]. This is a well-known fact that incidence of stroke is more in older population. So this study is showing same type of finding.

The greater prevalence of stroke in men is well known, but recent issues emphasize the importance of stroke in women. Knowledge of sex differences might be of interest in improving preventive strategies and the in-hospital management of stroke patients. In our study, 21 patients were female out of 50 stroke patients (42%) in group 1 (CVA+DM) and 18 patients were female out of 50 patients (36%) in group 2 (Only CVA).

In this study, mean uric acid level in patients of CVA+DM group is 8.172 ± 1.366 mg/dl, in Only CVA group is 6.235 ± 1.247 mg/dl and in Only DM group is 5.911 ± 1.528 mg/dl. The differences of mean uric acid level in between CVA+DM group and Only CVA group; & CVA+DM group and Only DM group are statistically significant (p value < 0.05). This finding is similar with previous studies [16,17].

Hyperuricemia has previously been described as a strong predictor of well-defined cerebrovascular complications (stroke) in a Finnish cohort of patients with type 2 diabetes. Guan MP et al. also observed that the type 2 diabetic patients with stroke had significantly higher mean levels of serum uric acid than simple diabetic patients [18,19]. Hyperuricemia was associated with a significantly higher risk of both stroke incidence and mortality

[20]. Several patho-physiological mechanisms like endothelial dysfunction, oxidative metabolism, platelet adhesiveness and aggregation, related to hyperuricemia have been suggested.

Hyperuricemia is also found to be associated with elevated circulating levels of systemic inflammatory mediators such as monocytes chemo attractant protein-1, NF- κ B, interleukin-1 β , interleukin-6, and tumor necrosis factor- α , and vascular smooth muscle proliferation. Hypertension, one of the most common causes of stroke is closely related to hyperuricemia.

Conclusions

- Stroke is more common in older population with male predominance.
- The occurrence of stroke is quite high among female also.
- Hyperuricemia is a probable risk factor of stroke, in patients with Diabetes mellitus.
- Elevated total Cholesterol & LDL cholesterol levels are probable risk factors for developing stroke in patients with diabetes mellitus.
- Total cholesterol and LDL cholesterol levels are almost similarly elevated in diabetic stroke patients and non-diabetic stroke patients.
- High Triglyceride, high VLDL and reduced HDL Cholesterol are probable risk factors of stroke in patients with Diabetes mellitus.
- Chance of developing stroke is more in diabetic patients having greater HbA1C level.

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