

Study of Serum uric acid in type 2 Diabetes mellitus in association with cardiovascular risk factors

Sunita Sethy¹, Kailash Chandra Dash², Purna Chandra Dash³, Avinash Taunk⁴,
Suresh Kumar Rout^{5*}

¹Assistant Professor, Dept. of Medicine, SCB Medical College, Cuttack, Odisha, India

²Reader, Oral & Maxillofacial Pathology, Kalinga Institute of Dental Sciences, KIIT Deemed to be University Bhubaneswar, Odisha, India

³Professor, Dept. of Medicine, SCB Medical College, Cuttack, Odisha, India

⁴(DM Cardiology), Dept. of Cardiology, SCB Medical College, Cuttack, Odisha, India

⁵Assistant Professor, Dept. of Radiotherapy, VIMSAR, Burla, Odisha, India

***Corresponding author:** Dr. Suresh Kumar Rout,

sureshrout98@gmail.com

ABSTRACT

BACKGROUND: Diabetes mellitus refers to a group of common metabolic disorders that share a phenotype of hyperglycemia. The four major risk factors for CVD are hypercholesterolemia, hypertension, diabetes mellitus and cigarette smoking. Insulin resistance state is associated with diabetes mellitus and metabolic syndrome (MS). The positive association between serum uric acid and cardiovascular diseases such as ischemic heart disease has been recognized since the 1950s and has been confirmed by numerous epidemiological studies since then.

OBJECTIVES: To define the relationship between serum uric acid level and Type 2 Diabetes mellitus & To assess the prevalence of hyperuricemia in patients with Type 2 Diabetes mellitus in relation to cardiovascular risk factors.

METODOLOGY: A total of 100 cases that satisfied the inclusion and exclusion criteria above were taken up for the study. 100 age and sex matched subjects were kept as controls. Selected data were elicited from the patients and controls and recorded in proforma. Socio-demographic data, Clinical data, Body Weight, height, BMI, Waist circumference, Systolic and Diastolic blood pressure, Duration of diabetes, Family history of diabetes, Smoking history, Ischemic heart disease. Serum uric acid was done by using TRINDER END POINT method. Data was entered in Microsoft Excel Spreadsheet and analysed. Significance values were analysed using standard SPSS software. Student 't' values was applied for significance.

RESULTS: Total number of cases included in this study was 200. Among them 100 were cases (type2 DM) & 100 were matched controls (non-diabetics). Mean and standard deviation of cases and controls in respect to BMI was 25.12 ± 2.64 & 23.20 ± 1.96 respectively and was highly significant. Mean serum uric acid level in this study was 5.6 ± 1.24 & 3.2 ± 0.76 in cases and controls respectively, 28 of the cases had hyperuricemia and it was statistically significant. Mean serum uric acid in long standing diabetes (9-12yrs) is 6.34 ± 1.35 .

CONCLUSION: Uric acid levels increase with increasing duration of diabetes and the association was statistically significant. Hyperuricemia is seen in patients with poor diabetic control which was significantly correlated with BMI, WC, dyslipidemia and hypertension. There was increased incidence of myocardial ischaemia and infarction in patients with hyperuricemia.

Key words: Serum uric acid, Type 2 DM, CVD, MS, Risk factors

INTRODUCTION:

Prevalence of Type 2 Diabetes mellitus is rapidly increasing and is already an epidemic in India. Diabetes mellitus is an important risk factor associated with increased incidence of cardiovascular disease (CVD). Diabetes mellitus refers to a group of common metabolic disorders that share a phenotype of hyperglycemia.^[1] The four major risk factors for CVD are hypercholesterolemia, hypertension, diabetes mellitus and cigarette smoking. Insulin resistance state is associated with diabetes mellitus and metabolic syndrome (MS)^[2]. Each member of this deadly quartet has been demonstrated to be an independent risk factor for CAD and capable of working together in a synergistic manner to accelerate both non- diabetic atherosclerosis and the atheroscleropathy associated with MS and T2DM. In a like manner, hyperuricemia, hyperhomocysteinemia, ROS, and highly sensitive C- reactive protein (hsCRP) and each of which play an important role in expanding the original Syndrome X described in the atherosclerotic process. Metabolic syndrome (MetS) is a cluster of cardiovascular risk factors characterized by central obesity, insulin resistance, atherogenic dyslipidemia and hypertension. Hyperuricemia or elevated serum uric acid level (SUA) is a biochemical entity that is gaining increasing importance not only as a cardiovascular risk factor but also play a role in the

development of metabolic and life style related diseases^[3]. The positive association between serum uric acid and cardiovascular diseases such as ischemic heart disease has been recognized since the 1950s and has been confirmed by numerous epidemiological studies since then.

However, whether uric acid is an independent risk factor for cardiovascular mortality is still disputed as several studies have suggested that hyperuricemia is merely associated with cardiovascular diseases because of confounding factors such as obesity, dyslipidemia, hypertension, use of diuretics and insulin resistance. Several studies have identified the value, in populations, of serum uric acid concentration in predicting the risk of cardiovascular events, such as myocardial infarction. This has directed the research towards the potential mechanisms by which uric acid might have direct or indirect effects on the cardiovascular system. It has been difficult to identify the specific role of elevated serum uric acid because of its association with established cardiovascular risk factors such as hypertension, diabetes mellitus, hyperlipidemia and obesity. Here an attempt has been made to study the level of serum uric acid in type 2 diabetes mellitus and the correlation between elevated serum uric acid levels and cardiovascular risk factors like obesity, hypertension, smoking, dyslipidemia.

MATERIAL AND METHODS:

This descriptive analytical study was done at SCB Medical College, Cuttack from 2020 to 2021 among the 100 cases and 100 controls.

Inclusion criteria:

- Patients already on treatment for type 2 Diabetes.
- Newly detected Type 2 Diabetics.
- Age >40 yrs.
- Both sexes were included.

Exclusion criteria:

Patients with Renal failure, Patients on uricemic drugs, Alcoholics, Myeloproliferative Disorders, Lymphoproliferative Disorders, Psoriasis, Pregnancy and Gout were excluded from the study.

CASES: Diabetics with age greater than 40 years and of both sexes were included. Both IP and OP cases were selected after considering the exclusion criteria.

CONTROLS: 100 Subjects who were above 40 years and who had normal blood sugar (non- diabetic) and who met the above exclusion criteria are kept as controls from the Medicine OPD.

A total of 100 cases that satisfied the inclusion and exclusion criteria above were taken up for the study. 100 age and sex matched subjects were kept as controls. Selected data were elicited from the patients and controls and recorded in proforma. Socio-demographic data, Clinical data: Body Weight, height, BMI. Waist circumference. Systolic and Diastolic blood pressure. Duration of diabetes. Family history of diabetes. Smoking history. Ischemic heart disease. Serum uric acid was done by using TRINDER END POINT method.

STATISTICAL ANALYSIS:

Data was entered in Microsoft Excel Spreadsheet and analysed. Significance values were analysed using standard SPSS software. Student‘t’ values was applied for significance.

OBSERVATION AND RESULTS:

The total number of subjects included in this study was 200. Among them 100 were cases (type 2 diabetes mellitus) and 100 matched controls (non diabetics). The details of subjects included in this study are given table 1.

The details included are gender, sex, BMI, WHR, FBS, PPBS, serum uric acid levels, systolic blood pressure, diastolic blood pressure.

TABLE 1: DETAILS OF THE SUBJECTS INCLUDED IN THE STUDY

S.No.	Parameter	Study Group	Control Group
1	Total Sample	100	100
2	Gender	Males:60 Females:40	Males:51 Females:49
3	Age(Yrs)		
	Range	40-72	41-68
	Mean+/-SD	57.16+/- 6.22	56.34+/-5.34

4	BMI		
	Range	19.2–31.1	18.1–27.3
	Mean+/-SD	25.12+/- 2.64	23.2+/-1.96
5	WC		
	Range	83-110	72-102
	Mean+/-SD	96.41+/-12.19	84.09+/-6.72
6	FBS(mg/dl)		
	Range	102-230	86–120
	Mean+/-SD	156.42+/-22.36	99.36+/-9.46
7	PPBS(mg/dl)		
	Range	138-330	94-182
	Mean+/-SD	214.65+/-33.54	134.64+/-16.44
8	SerumUricAcid(mg/dl)		
	Range	2.9–8.4	2.4-5.7
	Mean+/-SD	5.6+/- 1.24	3.2+/- 0.76
9	SystolicBlood Pressuremm.Hg)		
	Range	118-170	102–142
	Mean+/-SD	134.46+/-9.22	118.42+/-6.26
10	Diastolic Blood Pressue (mm.Hg)		
	Range	78-124	68–94
	Mean+/-SD	88.44+/- 7.12	82.24+/-5.4

TABLE:2 ANALYSIS OF CASES AND CONTROLS IN RELATION TO DIFFERENT AGE GROUPS

Age(Yrs)	Case Group		Control Group	
	No.	%	No.	%
40-49	2	2.00%	11	11.00%
50-59	62	62.00%	57	57.00%
60-69	36	36.00%	32	32.00%

Total	100	100.00 %	100	100.00 %
Range	40 - 72		41 -68	
Mean +/- SD	57.16 +/- 6.22		56.34 +/- 5.34	
Chi-square Value	4.12			
P-Value	> 0.05			
Inference	Not Significant			

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n for age of the cases and controls were 57.16 ± 6.22 and 56.34 ± 5.34 respectively; there was no significant difference among the cases and controls with reference to the age.

TABLE 3: Mean and standard deviation LDL, HDL, Triglycerides, total cholesterol, of cases and matched controls

S.No	Parameter	Case Group	Control Group
1	LDL(mg/dl)		
	Range	90-175	80-142
	Mean+/-SD	134.64+/-18.76	108.46+/-17.54
2	HDL(mg/dl)		
	Range	25-53	26-56
	Mean+/-SD	40.15+/-4.54	42+/-4.12
3	Triglycerides		
	Range	100-230	88-163
	Mean+/-SD	146.26+/-26.74	106.46+/-28.65
4	TotalCholestrol(mg/dl)		
	Range	122-225	120-200
	Mean+/-SD	170.14+/-26.34	153.68+/-22.78
5	VLDL(mg/dl)		
	Range	16-56	10-42

	Mean+/-SD	30.34+/-10.12	24.76+/-9.85
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TABLE 4: COMPARISON OF SUA IN CASES AND CONTROLS

Serum Uric Acid Levels (mg/dl)	Case Group		Control Group	
	No	%	No	%
≤ 3.5	8	8 %	62	62 %
3.6 - 6	65	65 %	36	36 %
6.1 - 6.8	14	14 %	2	2 %
≥ 6.9	13	13 %	0	0 %
Total	10	100 %	10	100 %
	0		0	
Range	2.9 - 8.4		2.4 - 5.7	
Mean +/- SD	5.6 +/- 1.24		3.2 +/- 0.76	
Z-Score	10.86			
P-Value	< 0.001			
Inference	Highly Significant			

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above values indicate the presence of hyperuricemia was significant even in the study group.

TABLE 5: SERUM URIC ACID LEVEL IN RELATION TO DURATION OF DIABETES:

Duration of Diabetes (Yrs)	No. Of Patients	Serum Uric Acid levels	
		Mean	SD
2-4	15	4.74	1.213981
5-7	35	5.34	1.563002
8-10	28	5.42	0.987426
11-13	22	6.56	1.276554
Grand Total	100	5.46	1.856436
(2 - 4) Vs (5 - 7)	P > 0.05		Not Significant
(2 - 4) Vs (8 - 10)	P > 0.05		Not Significant

(2 - 4) Vs (11 - 13)	P > 0.05	Not Significant
(5 - 7) Vs (8 - 10)	P > 0.05	Not Significant
(5 - 7) Vs (11 - 13)	P < 0.05	Significant
(8 - 10) Vs (11 - 13)	P < 0.05	Significant

Mean serum uric acid level in long standing diabetes (9-12 years) was 6.14 ± 1.59 . Mean serum uric acid level in shorter duration (2-4 years) diabetes was 4.82 ± 1.06 . Uric acid level increases with increasing duration of diabetes and it was statistically significant.

DISCUSSION:

An epidemiological link between elevated serum uric acid and an increased cardiovascular risk has been recognized for many years. Observational studies show that serum uric acid concentrations are higher in patients with established coronary heart disease compared with healthy controls. However, hyperuricemia is also associated with possible confounding factors including elevated serum triglyceride and cholesterol concentrations, blood glucose, fasting and post-carbohydrate plasma insulin concentrations, waist-hip ratio and body mass index. In this study serum uric acid levels in diabetes was examined. Uric acid as a marker of CAD in combination with other risk factors which includes Metabolic Syndrome components were examined. A control group consisting of non diabetics was also examined. Both the groups were age and sex matched. Uric acid levels and age were independent.

Duration of the diabetes positively correlated with serum uric acid levels. Uric acid levels increase with increasing duration of diabetes and the association was statistically significant. Becker and Jolly et al (2012)^[4], and Niskanen LK et al (2012),^[5] reported that hyperglycemia was a remarkable risk factor for hyperuricemia. In the present study males have higher uric acid level when compared to females. The mean uric acid levels in males and females were 7.34 ± 0.76 and 6.74 ± 0.68 respectively although the difference was not statistically significant. The possible reason may be due to oestrogen promoting uric acid excretion.^[6] In the present study serum uric acid correlated well with body mass index (BMI). The mean uric acid in subjects with BMI >25 was 6.32 ± 1.42 and 4.54 ± 1.18 in patients with BMI <25. The difference was statistically significant. Hyperuricemia has been associated with increasing body mass index (BMI) in recent studies and are even apparent in the adolescent youth. Okosun IS et al (2000)^[7] showed the same results that hyperuricemia was present in cases with BMI.

Total number of hyperuricemic patients (serum uric acid >6.8 mg/dl in males, >6.0 mg/dl in females) were 4 in ischemic group and 2 in infarction group. Percentage of hyperuricemia is higher in patients with infarction than in patients with ischemia. Nadkar MY, Jain VI et al (2018)^[8] studied 100 patients with acute myocardial infarction and 50 controls. Serum uric acid level was measured on day 0, 3 & 7 of MI. There was a statistically significant higher level of serum uric acid concentration in patients of MI on day of admission as compared to controls. Patients with history of MI in the past had higher serum uric acid levels. On all the days serum uric acid levels were higher in patients who were in higher Killip class. All the five patients who died after 3 days of hospital stay had serum uric acid level more than 7.0 gm/dL and all of them were Killip class IV. In our study, prevalence of hypouricemia was nil as 80% had poor FBS and 85% had poor PPBS control. The lowest level of uric acid was 3.1 mg/dl. There was a significant positive correlation between uric acid with systolic and diastolic blood pressure ($P < 0.0001$; $P < 0.0001$), respectively. These above models have provided the first challenging evidence that uric acid may have a pathogenic role in the development of hypertension, vascular disease, and renal disease. Jules Clement et al (2017) et al^[9] conducted a study in 297 adults from Fako Division in Cameroon. Blood pressure, serum uric acid, fasting blood glucose, lipids, body mass index and waist circumference were measured. Individuals who were hypertensive had the

highest mean uric acid concentration which was significantly higher than that for normotensives ($P < 0.0001$). In the present study, 12 out of 100 cases had family history of CAD. The total number of patients with ischemia and infarction in the study group were 20 & 6 respectively. The mean serum uric acid levels in these patients were 6.24 ± 0.76 and 7.14 ± 1.35 respectively. In the present study uric acid levels were significantly elevated in patients with dyslipidemia. The mean serum uric acid level in patients with dyslipidemia was 6.57 ± 1.23 and in patients with normal lipid profile was 4.46 ± 0.84 . Hairong Nan, et al (2016)^[10] in a study done on 438 patients in china concluded that Higher serum uric acid levels may indirectly contribute to the increased CVD risk through a close association with established risk factors such as older age, hypertension, dyslipidemia, poor glycemic control and chronic kidney disease. Azenabor and O Ogbera (2013)^[11] et al showed the same results. A cross-sectional Study carried over a period of 3 months from November 2008 to January 2009 conducted in 601 patients with Type 2 DM at Lagos, Nigeria, concluded that SUA is positively and significantly associated with serum TG and total cholesterol. In present study 85% of diabetic patients have serum uric acid >5 mg/dl, while only 15% of control group have serum uric acid >5 mg/dl. So serum uric acid >5 mg/dl should be considered as a Red Flag in those patients at risk for cardiovascular disease.

CONCLUSION:

Uric acid levels increase with increasing duration of diabetes and the association was statistically significant. Hyperuricemia is seen in patients with poor diabetic control which was significantly correlated with BMI, WC, dyslipidemia and hypertension. There was increased incidence of myocardial ischaemia and infarction in patients with hyperuricemia. Although prevalence of Hypouricemia is known it was not detected in our study due to poor diabetic control.

CONFLICT OF INTEREST: None declared

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