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A study of serum uric acid in type 2 diabetes mellitus and it's association with cardiovascular risk

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Abstract
Aim: To evaluate serum uric acid in type2 diabetes mellitus and it's association with cardiovascular risk.
Material and Methods: The present descriptive analytical study was done at Narayana Medical College, Nellore for one year among 100 cases of type 2 diabetes mellitus patients. Based on the criteria, patients were selected, and proforma containing history, clinical examination and investigation was prepared. Hyperuricemia has been arbitrarily defined as >7.0 mg/dL in men and >6. mg/dL in women. Data was collected and subjected to statistical analysis using SPSS software version 24.
Results: Out of 100 subjects, 48% were males and 52% were females. Hyperuricemia was reported among 14% of the subjects. Mean FBS was significantly higher in hyperuricemic subjects (184.83) as compared to subjects with normal uric acid (142.57). Mean uric acid increase with increase in duration of diabetes. Mean uric acid level was 6.91 and 5.02 mg/dl among subjects with and without hypertension respectively. When mean uric acid was acid was compared according to presence and absence of hypertension, significant difference was found. No difference was found among subjects with ischemic and infarction w.r.t. uric acid level.
Conclusion: Diabetic patients with raised serum uric acid levels should be carefully monitored for CAD as well as other vascular episodes.

Keywords: diabetes, uric acid, cardiovascular

Introduction
Diabetes Mellitus is a chronic disease linked to cardiovascular and renal problems, as well as a variety of microangiopathies, including metabolic syndrome. According to the International Federation of Diabetes, over 415 million adults worldwide suffer with diabetes, with estimates that this figure will rise to around 642 million by 2040 [1].
Uric acid (UA) is a final enzymatic product of purine metabolism in humans [2] and it is regulated by the xanthine-oxidoreductase enzyme, which converts hypoxanthine to xanthine and xanthine to uric acid.[3] An elevated concentration of UA is associated with a variety of cardiovascular conditions [4] The balance between the intake endogenous synthesis, excretion ratio and metabolism of purines determines the concentrations of Serum Uric Acid (SUA). Recent research has found that serum uric acid levels in people with prediabetes and early type 2 diabetes are greater than in healthy people [5]. Hyperuricemia has now been included to the list of metabolic disorders linked to metabolic syndrome's insulin resistance or hyperinsulinemia [6, 7].
Hyperglycemia and lipid metabolism disorder is also linked to a greater risk for vascular problems, kidney disease, nerve and retinal damage resulting in challenges in managing the disease adequately, especially in the presence of immune suppression, and predisposes individual to premature mortality. Moreover, this has cost and social implications for patients, their families, communities and the healthcare system. Currently, HUA in T2DM patients has been less well investigated in developing countries. Until now, the pathogenic role of UA in the development of the MetS is not complete, therefore, the aim of the study was to assess the serum uric acid in type2 diabetes mellitus and it's association with cardiovascular risk.

Material and Methods
Study Setting
This study was done at Narayana Medical College, Nellore

Study Design
Descriptive analytical study

Study Duration
One year

Study Subjects
Study was conducted on 100 cases of type 2 diabetes mellitus patients.

Inclusion Criteria
1. Patients with type 2 diabetes mellitus (irrespective of glycemic status and duration of diabetes).
2. Patient age more than 40years.
3. Both sex were included

Exclusion Criteria
1. Patients with
2. Renal failure
3. On long term diuretics and steroids
4. Regularly consuming alcohol
5. On antimetabolite and chemotherapy drugs
6. Hepatic disorder
7. Renal transplant patients
8. Pregnancy and lactating mothers

Data Collection
Based on the criteria, patients were selected, and proforma containing history, clinical examination and investigation was prepared.
Ethics committee approval was obtained before the start of the study by the Institutional Ethics Committee.

Operational definitions
Diabetes Mellitus
FPG -126 mg/dl (7.0 mmol/l): Fasting is defined as no caloric intake for at least 8 h. OR
Symptoms of hyperglycaemia and casual plasma glucose -200 mg/dl (11.1mmol/l). Casual is defined as any time of day without regard to time since last meal. The classic symptoms of hyperglycaemia include polyuria, polydipsia, and unexplained weight loss. OR
2-h plasma glucose -200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.[8]

Hyperuricemia
Hyperuricemia has been arbitrarily defined as >7.0 mg/dL in men and >6. mg/dL in women.[9]

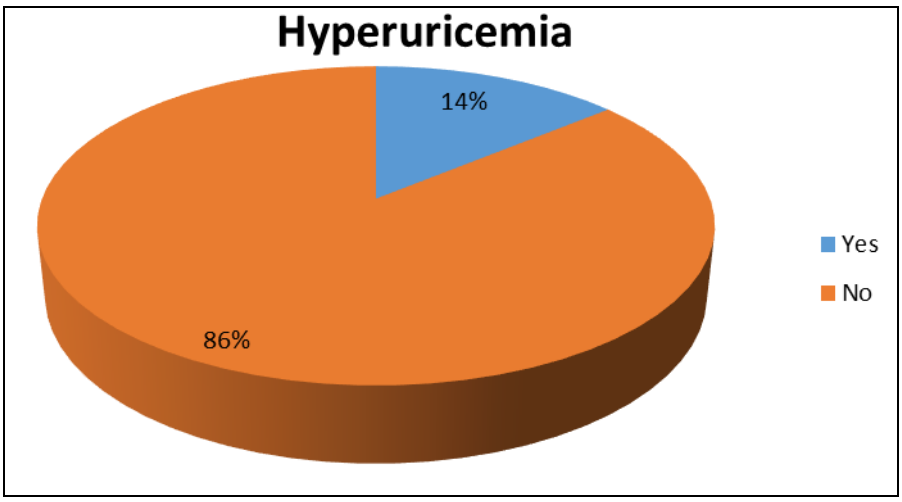
Statistical analysis
Data was collected and subjected to statistical analysis using SPSS software using SPSS software version 24. t test and anova test were used to identify significant difference. p vale<0.05 was considered as statistically significant.

Results
Table 1 show the basic profile among the study subjects. Out of 100 subjects, 48% were males and 52% were females. Mean age (in years), blood uric acid (mg/dl), FBS (mg/dl), BMI, WHR, CPKMB, Total Cholesterol, TGL and LDL among the study subjects was 55.16±7.35, 6.51±0.62, 157.04±26.15, 26.22±1.36, 0.21± 0.54, 65.38±12.86, 179.81±25.22, 143.84±13.64 and 47.21±7.24 respectively.

Table 1: Basic profile among the study subjects

Variables	Mean	SD
Age (in years)	55.16	7.35
Blood Uric acid (mg/dl)	6.51	0.62
FBS (mg/dl)	157.04	26.15
BMI	26.22	1.36
WHR	0.21	0.54
CPKMB	65.38	12.86
Total Cholesterol	179.81	25.22
TGL	143.84	13.64
LDL	47.21	7.24
Male, N (%)	48 (48%)	
Female, N (%)	52 (52%)	

Hyperuricemia was reported among 14% of the subjects (graph 1).



Graph 1: Uric acid among the study subjects

Mean FBS was significantly higher in hyperuricemic subjects (184.83) as compared to subjects with normal uric acid (142.57). Mean uric acid increase with increase in duration of diabetes. When uric acid was acid was compared according to FBS level and duration of diabetes, significant difference was found (table 2).

Table 2: Hyperuricemia based on FBS and duration of diabetes

Hyperuricemia	Mean FBS (mg/dl)	SD	t test	p value
Yes	184.83	19.21	5.91	0.012*
No	142.57	30.24		
Duration of Diabetes	Mean Uric acid (mg/dl)	SD	Anova test	p value
2-4 years	4.37	0.43	3.51	0.039*
5-8 years	5.71	0.72		
>8 years	6.96	0.69		

*: statistically significant

Mean uric acid level was 6.91 and 5.02 mg/dl among subjects with and without hypertension respectively. When mean uric acid was acid was compared according to presence and absence of hypertension, significant difference was found. Ischemia and infarction was reported in 19 and 6 subjects respectively. No difference was found among subjects with ischemic and infarction w.r.t. uric acid level (table 3).

Table 3: Association between serum uric acid levels and other CVD risk factors among diabetic subjects

Variables	N	Mean Uric acid (mg/dl)	SD	t test	p value
Hypertension					
Yes	24	6.91	0.71	11.17	<0.01
No	76	5.02	0.54		
CAD					
Ischemia	19	6.71	0.74	2.74	0.12
Infarction	6	7.03	0.59		

Discussion

Given the substantial link between uric acid levels in the blood and the development of coronary artery disease in people with type 2 diabetes, the current study was conducted to assess the serum uric acid in type2 diabetes mellitus and it's association with cardiovascular risk.

In our study, Hyperuricemia was reported among 14% of the subjects. Ischemia and infarction was reported in 19 and 6 subjects respectively. No difference was found among subjects with ischemic and infarction w.r.t. uric acid level. Mean uric acid level was 6.91 and 5.02 mg/dl among subjects with and without hypertension respectively. When mean uric acid was acid was compared according to presence and absence of hypertension, significant difference was found.

In a study by T. Murali Venkateswara Rao *et al* [10], hyperuricemia was much higher in diabetic population (11.43%) and none of the controls had hyperuricemia. Serum uric acids were significantly raised in patients with hypertension. In their review, Katsiki N *et al* [11] have concluded a strong association between the serum uric acid levels and diabetes and it' complications. Keenan T *et al* [12] have reported increased by Serum urate levels were not associated with T2DM, CHD, ischemic stroke, or HF. In contradiction to majority of the published studies on

the subject, this particular study has suggested, there is no causal role of uric acid and cardiovascular complications in diabetic population.

The difference was statistically significant. Studies by Li Q *et al* [13], Li LX *et al* [14] have demonstrated similar findings, but the study by Li LX *et al* [14] have also suggested, this association of hypertension and hyperuricemia may not translate into increased cardiovascular risk as proposed by many other studies.

Choi HK *et al* [15] have evaluated the correlation between gout and the future risk of type 2 diabetes among men with a high cardiovascular risk profile and confirmed that, among men with a high cardiovascular risk profile with gout, there is a higher risk of future risk of type 2 diabetes independent of other known risk factors. These study findings suggest a reverse causality and raises further questions on nature of the association of diabetes, serum uric acid and the diabetes related complications, especially coronary artery disease. Du L *et al* [16] confirmed the increased risk of diabetes related macro vascular complications, including CAD and cerebral infarction. From pooled estimates of 23 studies, the authors concluded that higher serum uric acid levels may contribute to cerebral infarction in patients with type 2 diabetes.

In our study; mean FBS was significantly higher in hyperuricemic subjects (184.83) as compared to subjects with normal uric acid (142.57). Mean uric acid increase with increase in duration of diabetes. When uric acid was acid was compared according to FBS level and duration of diabetes, significant difference was found. According to T. Murali Venkateswara Rao *et al* [10], the association between duration of diabetes and serum uric acid level was statistically significant. Studies by Gagliardi AC *et al* [17], Javorsky *et al* [18], Kramer CK [19] have reported similar association, along with strong influence of serum uric acid on future cardiovascular events.

In summary, although there is overwhelming evidence that elevated serum uric acid concentrations are strongly associated with increased cardiovascular risk and poor outcome, prospective population studies are often confounded by co-existent risk factors. In the present study serum uric acid positively correlated with duration of diabetes and cardiovascular risk factors like obesity (high BMI, abnormal waist hip ratio), hypertension, dyspidemia and the results were statistically significant.

Conclusion

In diabetics, serum uric acid levels were considerably higher. Those with dyslipidemia, high triglycerides, and hypertension had considerably higher serum uric acid levels. The amount of uric acid in the blood surge as the duration of diabetes increased.

Hence routine annual estimation of uric acid among diabetics from the identification of diabetes will help the clinician to find out the adequacy of

1. Control of glycemic status.
2. Control of dyslipidemia.
3. Development of hypertension.

Diabetic patients with raised serum uric acid levels should be carefully monitored for CAD as well as other vascular episodes.

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