Original Research Article

A study on serum uric acid levels in type 2 diabetes mellitus and its association with cardiovascular risk factors

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Abstract

Background: Diabetes mellitus is strongly associated with hyperuricemia. The role of uric acid as an independent risk factor for cardiovascular disease is a matter of controversy. Patients with diabetes are at high risk of future type 2 diabetes, and within 10 years, 70% of them tend to develop type 2 diabetes. More importantly, patients with prediabetes seem to share similar associated damage to end target organs, as patients with diabetes. The final oxidation product of human purine metabolism is uric acid (UA) and excess serum accumulation can lead to various diseases. Increasing evidence reveals that UA may have a key role in the pathogenesis of metabolic syndrome and suggested that increased UA is used clinically as a marker of metabolic syndrome and is a risk factor for CVD in the general population.

Aim of study: To assess the uric acid status in patients with diabetes mellitus and to find out its association with age, gender, BMI, WHR, smoking, and CAD.

Materials and methods: With rigid criteria, patients who are attending Diabetic OPD of Madras Medical College, in the year 2017 were selected carefully and evaluated on social, clinical and laboratory aspects after getting institutional, ethical clearance and informed consent. 30 healthy age, sex-matched individuals were kept as control. There were 43 males and 27 females in the study group

and 18 males and 12 females in the control group. Fasting and postprandial blood sugar levels, Serum lipid profile, Blood urea, Serum creatinine estimation was done.

Results: There was no significant difference among cases and controls about age. In the study group, BMI below 25 was seen in 34 cases (48.57%), BMI above 25 seen in 36 cases (51.42%) which was significantly more than controls. BMI had significantly correlated with hyperuricemia. Similarly, WHR was greater among women than men in diabetics, which also correlated with elevated serum uric acid significantly. Elevated serum uric acid level was noticed more among those who had hypertension dyslipidemia, coronary artery disease and they were significant. Patients with longer duration of diabetes also had elevated uric acid levels.

Conclusion: Increased uric acid synthesis occurs due to increased purine metabolism, ischemia-induced increased xanthine oxidase production, insulin resistance, and diuretic use. Routine annual estimation of uric acid among diabetics from the identification of diabetes will help the clinician to find out the changing trends of uric acid level which is likely to be influenced by control of blood sugar and development of hypertension, such cases should be carefully monitored for CAD as well as other vascular episodes. Since uric acid is a confounding factor and multiple factors are involved for elevated uric acid.

Key words

Uric acid, Type 2 Diabetes, Atherosclerosis, CVD.

Introduction

Diabetes mellitus is an important risk factor associated with an increased incidence of cardiovascular disease (CVD). The four major players in the MS are hyperinsulinemia, hypertension, hyperlipidemia, and hyperglycemia [1]. 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 [2]. Over recent years there has been renewed debate about the nature of the association between raised serum uric acid concentration and cardiovascular disease [3]. Several studies have identified the value, in populations, of serum uric acid concentration in predicting the risk of cardiovascular events, such as myocardial infarction [4]. This has directed the research towards the potential mechanisms by which uric acid might have direct or indirect effects on the cardiovascular system [5]. 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 [6]. 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 [7].

Materials and methods

With rigid criteria, patients who are attending Diabetic OPD of Madras Medical College, in the year 2017 were selected carefully and evaluated on social, clinical and laboratory aspects after getting institutional, ethical clearance and informed consent. 30 healthy age, sex-matched individuals were kept as control. There were 43 males and 27 females in the study group and 18 males and 12 females in the control group. Fasting and postprandial blood sugar levels were estimated by using the glucose oxidase-peroxidase (GOD/POD) method. Serum lipid profile, Blood urea estimation was done

manually by using the diacetyl monoxime method (DAM). Serum creatinine estimation was done by using the alkaline picrate method.

Inclusion criteria: Patients with type 2 diabetes mellitus (irrespective of their glycemic status and duration of diabetes), Patient's age > 40 years, Both sexes were included.

Exclusion criteria: Renal failure, On long term diuretics and steroids, Regularly consuming alcohol, On antimetabolite and chemotherapy drugs, Hepatic disorders. Peripheral vascular disease/ cerebrovascular disease/ pulmonary tuberculosis, Renal transplant patients, Pregnancy and lactating mothers.

Statistical analysis

Data was entered in Microsoft Excel Spreadsheet and analyzed. Significance values were analyzed using standard SPSS software. Student 't' values were applied for significance. Significance was considered if the 'p' value was below 0.05.

Results

Mean and standard deviation for the age of the cases and controls were 59.55±8.69 and 55.8 ±8.96 respectively; there was no significant difference among the cases and controls concerning the age. The distribution of cases and controls about age showed *p= 0.058 (not significant). The age group of the case and control group did not vary significantly. Among the 70 cases studied, there were 42 males and 28 females. Among 30 controls, there were 16 males and 14 females with *P= 0.6986 (not significant). The sex composition of the study and control group did not differ significantly (**Table – 1**).

Table – 1: Analysis of cases and controls concerning age and gender.

Male	42	65.71	16	53.33
Female	28	34.29	14	46.67
Total	**70**	**100.00**	**30**	**100.00**

Table - 2: Cases and controls concerning BMI.

BMI	**Cases***		**Controls**	
	No.	**%**	**No.**	**%**
<25	37	52.86	26	86.67
>25	33	47.14	4	13.33
Total	70	100.00	30	100.00
Mean	**24.38**		**22.07**	
SD	**2.80**		**2.23**	

The mean and standard deviation for the cases and controls were 24.38±2.8 and 22.07±2.23 respectively. The BMI of the study group was significantly higher than that of the control group (p = 0.0028) as per **Table – 2**. There was no significant difference between cases and controls about selected cardiovascular risk factors (**Table – 3**).

Mean serum uric acid in the study population was 5.26±1.39. Mean serum uric acid in the control group was 3.54±0.62. The serum uric acid levels in diabetics were very much high when compared with controls and it was highly significant. The mean serum uric acid value in males was 5.45±1.47 whereas in females it was 4.97±1.23.In the study group mean serum uric acid values were higher in males than in females but the difference was not statistically significant. Hyperuricemia is defined as serum uric acid level ≥7 mg/dl in males and ≥6.5 mg/ dl in females p =0.0001 (significant) as per **Table – 4**.

The mean serum uric acid level in the hypertensive group was 6.60±1.105. The mean

serum uric acid level in the non-hypertensive group was 4.79±1.18. The difference between the two groups was statistically significant (**Table – 5**). The mean serum uric acid in patients with lipid profile abnormality was 6.37±1.02. The mean serum uric acid in patients without lipid profile abnormality was 4.79±1.18. The difference between the two groups was statistically significant (**Table – 6**).

Table – 3: Analysis of cases and controls about selected cardiovascular risk factors.

Risk factor	Cases*		Controls		P-value
	No.	%	No.	%	
Family history					
Yes	13	18.57	6	20.00	0.9114
No	57	81.43	24	80.00	(ns)
Total	70	100.00	30	100.00	
Smoking among males					
Yes	18	42.86	4	25.00	0.3421
No	24	57.14	12	75.00	(ns)
Total	42	100.00	16	100.00	
Hypertension					
Yes	18	25.71	8	26.67	0.8813
No	52	74.29	22	73.33	(ns)
Total	70	100.00	30	100.000	

Table – 4: Hyperuricemia among diabetics and controls.

Hyperuricemia	Cases*				Controls			
	No.	%	Mean	SD	No.	%	Mean	SD
Positive	8	11.43	7.675	0.615	0	-	-	-
Negative	62	88.57	4.94	1.129	30	100	3.54	0.62

Table - 5: Serum uric acid values about hypertension.

Hypertension	No. of Cases	Serum uric acid values		p-value
		Mean	SD	
YES	18	6.60	1.105	0.0001
NO	52	4.79	1.18	

Table - 6: Serum uric acid values about lipid profile abnormality (LPA).

LPA	No. of cases	Serum uric acid values		P-value
		Mean	SD	
YES	26	6.37	1.02	0.0001
NO	44	4.60	1.14	

Table - 7: Gender wise serum triglyceride values among cases.

Sex	Serum triglycerides		P-value
	Mean	SD	
Male	149.81	26.83	0.488 (NS)
Female	154.65	29.37	

Table – 8: Correlation of cad and hyperuricemia.

CAD	No. of patients	Serum uric acid values		p-value
		Mean	SD	
Ischemia	14	6.75	1.203	0.391 (ns)
Infarction	4	7.3	0.96	

The serum triglyceride level in males was 149.81±26.83. The serum triglyceride level in females was 154.65±29.37. The difference between the two groups was not statistically significant (**Table – 7**).

Number of patients with ischemia was 14. The mean serum uric acid level in the ischemia group was 6.75±1.203. This only 5 had hyperuricemia which includes 4 males and 1 female. Number of patients with infarction was 4. The mean serum uric acid level in the infarction group was 7.3±0.96. Of this, only 2 had hyperuricemia which includes 1 male and 1 female. Percentage of hyperuricemia in infarction (50%) is higher than in ischemia (35.71%) as per **Table - 8**.

Discussion

Uric acid as a marker of CAD in combination with other risk factors which includes Metabolic Syndrome components was examined. A control group consisting of non-diabetics was also examined. Both groups were age and sex-matched [8]. Uric acid levels and age were independent. Duration of diabetes positively correlated with uric acid levels. Uric acid levels increase with increasing duration of diabetes and the association was statistically significant [9]. The mean uric acid levels in males and females were 5.45±1.47 and 4.97±1.28 respectively although then the difference was not statistically significant. The possible reason may be due to estrogen promoting uric acid excretion Fagot-Campagna, et al. [10]. In the present study serum uric acid correlated well with body mass index (BMI). The mean uric acid in subjects with BMI >25 was 6.40±1.006 and 4.23±0.73 in patients with BMI<25 [11]. The difference was statistically significant. Waist hip ratio is an important measure of obesity, especially central obesity. Waist circumference >102 cm in males and >88 cm in females is abnormal [12]. In this present study, the mean serum uric acid levels in patients with abnormal WHR and normal WHR were 5.91±1.31 and 4.55±1.11 respectively and the difference was statistically significant [13]. Hyperuricemia has been associated with increasing body mass index (BMI) in recent studies and is even apparent in adolescent youth. Leptin levels are elevated and associated with insulin resistance in MS and early T2DM [14]. In the present study uric acid levels were significantly elevated in patients with dyslipidemia. The mean serum uric acid level in patients with elevated serum triglycerides was 6.37±1.02 and in patients with normal lipid profile was 4.60±1.14. The difference was statistically significant [15]. Hyperuricemia and hypertriglyceridemia are suggested to be associated with insulin resistance syndrome many investigators are studying the mechanisms of the emergence of this syndrome. The association between insulin resistance syndrome, hyperuricemia, and hypertriglyceridemia are complicated [16]. This might be expected from the fact that uric acid production is linked to glycolysis and that glycolysis is controlled by insulin [17]. The present study serum uric acids were significantly raised in patients with hypertension. The mean uric acid levels in diabetics with hypertension and non-hypertensive were 6.6±1.105 and 4.79±1.18 respectively. The difference was statistically significant. Lillioja S, et al. were able to demonstrate that blood pressure levels were predictive for cardiovascular disease incidence synergistically with serum uric acid levels. The mean serum uric acid levels in these patients were 6.75±1.20 and 7.3±0.96 respectively [18]. A total number of hyper-uricemic patients (serum uric acid>7 mg/dl in males, >6.5 mg/dl in

females) were 5 in the ischemic group and 2 in the infarction group. The percentage of hyperuricemia is higher in patients with infarction than in patients with ischemia [19]. In the present study, 78.57% of diabetic patients have serum uric acid >4 mg/dl, while only23.3% of the control group have serum uric acid >4 mg/dl. So serum uric acid >4 mg/dl should be considered as a Red Flag in those patients at risk for cardiovascular disease [20]. Although there is overwhelming evidence that elevated serum uric acid concentrations are strongly associated with increased cardiovascular risk and poor outcomes, prospective population studies are often confounded by co-existent risk factors [21].

Conclusion

Serum uric acid levels were significantly elevated in the diabetic population. The serum uric acid level was independent of age and smoking status (in males). Mean serum uric acid levels were high in males. Serum uric acid levels increased with increasing duration of diabetes. Serum uric acid levels in diabetic patients with CAD were significantly higher. Serum uric acid above 4 mg/dl in the diabetic population is a marker or risk factor for CAD. Diabetic patients with raised serum uric acid levels should be carefully monitored for CAD as well as other vascular episodes. Meticulous control of blood sugar, hypertension, dyslipidemia, body weight, and abdominal girth form an essential component of diabetes which will bring down uric acid levels. It is worth to explore uric acid levels in diabetic patients with other cardiovascular risk factors like obesity, dyslipidemia, hypertension to detect early cardiovascular complications.

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