### Research Article

# Correlation of Serum Uric Acid Levels and Type-2 Diabetes Mellitus in A Tertiary Care Hospital

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#### **ABSTRACT:**

**Background:** Type 2 diabetes mellitus (T2DM) is associated with insulin resistance, metabolic syndrome, and oxidative stress. Serum uric acid (SUA) levels have been linked to T2DM, but the relationship remains unclear. This study was aimed to assess the association between SUA levels and duration of diabetes, glycemic control (HbA1c), and markers of metabolic syndrome in patients with T2DM.

Materials & Methods: This hospital-based cross-sectional observational study included patients with T2DM aged ≥18 years, attending the OPD of General Medicine department. Patients with renal disorders, uricosuric drugs, renal calculi, chemotherapy, or unwilling participants were excluded.

**Results:** Mean age was  $51.69\pm15.104$  years, with 55.6% females. Mean duration of diabetes was  $11.55\pm6.47$  years in patients with normal SUA levels and  $10.70\pm7.09$  years in those with increased SUA levels. Significantly higher proportions of cases with raised SUA levels had HbA1c >8.5% (66.2% vs. 49.3%), whereas normal SUA levels had HbA1c <7.5% (31.3% vs. 11.7%). The association between SUA and HbA1c was statistically significant.

**Conclusion:** This study suggests a positive correlation between serum uric acid levels and poor glycemic control in patients with type 2 diabetes mellitus.

**KEYWORDS:** Serum Uric Acid; Type 2 Diabetes Mellitus; Glycemic Control; Metabolic Syndrome; Insulin Resistance.

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#### **INTRODUCTION:**

Chronic hyperglycemia as a result of diabetes leads to various metabolic aberrations, causing damage to various organ systems, leading to microvascular as well as macrovascular complications. Diabetes is associated with certain risk factors such as advancing age, physical inactivity, unhealthy diet, obesity, family history etc. The key risk factors associated with diabetes are insulin resistance and metabolic syndrome. The insulin resistance could be attributed to production of reactive oxygen species (ROS) as a result

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of oxidative stress, which is postulated to be a major link for beta cell dysfunction, as well as impaired glucose tolerance in type 2 diabetes mellitus (T2DM).

[3,4] Apart from this, free radicals are formed and as a preventive measure, the generation of antioxidants in the body is increased. [5]

Uric acid, the end product of purine metabolism is one of the most abundant antioxidant in the plasma. <sup>[6]</sup> Uric acid can act as an antioxidant as well as strong reducing agent and has free radical scavenging property. <sup>[7]</sup> Hyperuricemia may be due to overproduction of urate, the soluble form of uric acid or

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its decreased elimination, or both. Raised serum uric acid levels and deposition of urate is seen in certain conditions such as gout, acute and chronic nephropathy, urolithiasis etc. [8] There is also an increasing evidence suggesting possible link between hyperuricemia and various disorders including diabetes, obesity, hypertension, dyslipidemia, insulin resistance, inflammation, cardiovascular diseases and peripheral vascular diseases. [9-16]

Though a causal relationship between hyperuricemia and diabetes is not established, three mechanisms have been postulated suggesting the positive association between diabetes and raised uric acid concentration. First, metabolic syndrome associated with diabetes induces high oxidative stress, and raised serum uric acid levels further worsens this condition. Second, uric acid act as stimulator for proliferation of vascular smooth muscles, leading to endothelial dysfunction. Third, increased renal glomerular pressure in cases with hyperuricemia affect the sodium reabsorption in kidneys. Further, literature suggest that fructose increases the production of uric acid, promoting insulin resistance and T2DM rapidly. [18]

A positive link between diabetes and uric acid levels have been reported by few of the previous studies conducted in Western countries. Measurements of serum uric acid levels may be of help in patients with diabetes mellitus if it is shown to be correlated with worsening of diabetes mellitus (DM). The present study was therefore conducted at a tertiary care centre to study the association of serum uric acid levels with duration of DM and Diabetes control (HbA1c) as well as to correlate serum uric acid level with markers of metabolic syndrome in diabetic patient.

#### **MATERIALS & METHODS:**

The present study was conducted as a hospital based cross sectional observational study on patients with DM attending the OPD of Medicine and Endocrinology department, People's College of Medical Sciences and Research Centre & associated People's Hospital Bhopal, during the study period of 18 months i.e. from 01 November 2022 to 30 April 2024. The present study included patients with T2DM aged 18 years or older who provided informed consent. Excluded were patients with renal disorders, those taking uricosuric drugs, or with a history of renal calculi, chemotherapy, or unwilling participants, as well as individuals under 18. Written consent was obtained from all the study participants in consent form, after explaining them nature and purpose of study with the help of participant's information sheet.

The patients were ensured that confidentiality will be maintained and option to withdraw from the study was always kept open.

After obtaining ethical clearance from Institute's ethical committee, all the patients with T2DM satisfying the inclusion and exclusion criteria were enrolled. Detailed history regarding sociodemographic variables such as age, gender, etc. was obtained and entered in prescribed questionnaire. All the patients were then subjected to detailed clinical history, which included data regarding mode of presentation, duration of symptoms, duration of diabetes etc. History regarding diabetic medications, insulin, comorbid conditions along with past medical and surgical history if any was obtained and entered in the questionnaire. All the patients were then subjected to general physical and systemic examination. Their height and weight were obtained and BMI was calculated. Apart from this, waist hip ratio and blood pressure were obtained for all the cases.

All the patients were then subjected to blood investigations, for which 2 ml venous blood was collected in EDTA tubes and plain tube under all aseptic precautions. The blood obtained was subjected to analysis of serum uric acid level and HbA1c. The presence of serum uric acid level above 7 mg/dl and 6 mg/dl was considered hyperuricemia for males and females respectively.

Data was collected and analysis was done using IBM SPSS software version 20. Categorical variables were expressed as frequency and proportion whereas continuous data was expressed as mean and standard deviation. Association of uric acid levels with duration of diabetes, HbA1c levels and components of metabolic syndrome was done using Chi square test (for categorical variables) or independent t test or ANOVA (for continuous variables). Correlation of uric acid levels with various diabetic parameters was done using Pearson Correlation Coefficient and was interpreted as *p*-value of less than 0.05 was considered statistically significant.

#### **RESULTS:**

In present study, mean age of patients with T2DM was 51.69±15.104 years and majority i.e. 27.8% cases belonged to 51 to 60 and more than 60 years of age. Only 11.1% cases belonged to 31 to 40 years whereas 12.5% cases belonged to less than 30 years of age (Table 1). In present study, more than half of the cases with T2DM were females (55.6%), whereas only 44.4% of the cases were males (Table 2). As observed from Table 3, mean duration of diabetes in patients with normal uric acid levels was 11.55±6.47 years

Table 1: Distribution of cases according to age.

Age (years)	Frequency (n=144)	Percentage	
=30	18	12.5	
31-40	16	11.1	
41-50	30	20.8	
51-60	40	27.8	
>60	40	27.8	
Mean±SD	5	51.69 ±15.104	

Table 2: Distribution of cases according to gender.

Gender	Frequency (n=144)	Percentage
Male	64	44.4
Female	80	55.6

whereas in cases with increased uric acid levels was  $10.70\pm7.09$  years. Majority of cases had duration of diabetes in the range of 6 to 15 years irrespective of serum uric acid levels (p>0.05). Mean body mass index in patients with normal uric acid levels was  $25.055\pm3.46$  whereas in cases with increased uric acid levels was  $24.46\pm3.29$  kg/m2. Majority of cases with normal as well as increased serum uric acid levels were obese (49.3% and 42.9%) and the observed association of uric acid with BMI was statistically insignificant (p>0.05) (Table 4).

Mean WHR in patients with normal uric acid levels was  $0.88\pm0.13$  whereas in cases with increased uric acid levels was  $0.86\pm0.12$ . Majority of cases with normal as well as increased serum uric acid levels had high WHR (64.2% and 55.8%) and we found no significant association of uric acid with waist hip ratio (p>0.05) (Table 5).

In present study, significantly higher proportions of cases with raised serum uric acid levels had raised HBA1c above 8.5% (66.2% vs. 49.3%),

whereas significantly higher proportions of cases with normal uric acid levels had HbA1c values below 7.5% (31.3% vs. 11.7%). The observed association of serum uric acid levels with HbA1c was statistically significant (p<0.05) (Table 6).

**Table 4**: Association between serum uric acid levels and BMI.

Body Mass Index	Uric Acid			
(kg/m2)	Normal(n=67)		Increase	ed(n=77)
	n	%	n	%
Underweight	1	1.5	2	2.6
Normal	14	20.9	23	29.9
Overweight	19	28.4	19	24.7
Obese	33	49.3	33	42.9
Mean±SD	25.055	±3.46	24.46 ±3	3.29
$X^2$	1.84			
<i>p</i> -value	0.61			

**Table 5**: Association between serum uric acid levels and Waist hip ratio.

	Uric Acid			
W-:-4 II: D -4:-	Normal(n=67)		Increas	sed(n=77)
Waist Hip Ratio	n	%	n	%
Normal	24	35.8	34	44.2
Increased	43	64.2	43	55.8
Mean±SD	$0.88 \pm 0.13$		$0.86 \pm 0.12$	
$X^2$	1.04			
<i>p</i> -value	0.31			

#### **DISCUSSION:**

This hospital based observational analytical, cross-sectional study examined the link between uric acid and diabetes in 144 patients with T2DM, who attended the OPD of Medicine and Endocrinology department of a tertiary care hospital at Bhopal, India. The average patient age in the early sixth decade, with a slight female majority. Although most had diabetes for over 6 years, there was no connection between uric acid levels and duration of diabetes. Similarly, weight (measured by BMI) and waist-hip ratio did not show a

**Table 3:** Association between serum uric acid levels and duration of diabetes.

	Uric Acid			
Duration Of Diabetes(years)	Normal(n=67) Increased (		i=77)	
	n	%	n	%
=5	14	20.9	20	26.0
6-10	19	28.4	21	27.3
11-15	20	29.9	21	27.3
>15	14	20.9	15	19.5
Mean±SD	11.55 ±6.47			10.70 ±7.09
$X^2$	0.53			
<i>p</i> -value	0.913			

Table 6: Association between serum uric acid levels and HbA1c levels.

		Uric A	Acid			
HbA1c -	Normal(n=67)		Normal(n=67)		Increase	ed(n=77)
	n	%	n	%		
<7.5	21	31.3	9	11.7		
7.5 - 8.5	13	19.4	17	22.1		
>8.5	33	49.3	51	66.2		
Mean±SD	$9.09 \pm 2.09$		10.08	±2.65		
$X^2$	8.54		_	_		
<i>p</i> -value	0.014					

significant link with uric acid levels. Blood pressure readings also seemed independent of uric acid. However, an interesting finding emerged when we observed blood sugar control. Hemoglobin A1c (HbA1c) is a measure of long-term blood sugar management. Here, the study identified a weak positive correlation. Patients with higher uric acid levels tended to have higher HbA1c, indicating poorer blood sugar control in diabetics. While the association was not very strong, it suggests a potential link between uric acid and how well diabetes is managed.

Average uric acid level found in this study was 7.13 mg/dL. Over half of the patients tested (53.5%) had elevated uric acid levels. The serum uric acid levels were significantly increased in cases  $(8.41 \pm 1.09)$  (p< 0.001) as compared to control group  $(4.34 \pm 0.66)$  in the study by Kaur J et al. [19] Similarly, Dhungana A et al investigated relationship between uric acid and blood sugar control in diabetes mellitus patients. They found 18.5% with hyperuricemia. They also found slightly higher uric acid in men than women. They found negative correlation between HbA1c, FBG, and PPBG in diabetes patients, suggesting potential inverse relationship. [20] Another alike study by Solanki HK et al found positive correlation between uric acid levels and diabetes duration with uric acid levels increased from 6.8 mg/dL to 7.7 mg/dL with longer diabetes duration  $(7-10 \text{ years})^{[21]}$ 

Kaire U et al reported average serum uric acid level of 5.10 mg/dL in T2DM patients. [22] Deb N et al found higher uric acid levels in diabetic patients vs. healthy controls and reported better blood sugar control associated with higher uric acid levels. [23] Modi AS et al detected lower serum uric acid levels in diabetic patients, but increased urinary uric acid excretion and positive correlation between blood sugar and urinary uric acid excretion was reported. [24] Deori R et al found high uric acid levels correlated with abnormal kidney function markers in diabetic and non-diabetic patients.

This suggests high uric acid as potential early indicator of kidney problems.  $^{[25]}$  In another study by Sidhu et al. (2017), diabetic patients had a uric acid level of 8 mg/dL, while healthy controls had a level of 3.7 mg/dL.

Monitoring uric acid levels could hold value, especially in diabetic patients with additional risk factors for hyperuricemia (obesity, high blood pressure, etc.). However, more research is required to establish clear guidelines for uric acid monitoring frequency and target levels in diabetic patients. In the present study, a significant correlation between elevated serum uric acid levels and poor glycemic control, as measured by HbA1c values was reported. Specifically 66.2% of patients with high uric acid levels had HbA1c >8.5%, compared to 49.3% with normal uric acid levels, indicating a 34.6% increased likelihood of poor glycemic control. Conversely, 31.3% of patients with normal uric acid levels achieved optimal glycemic control (HbA1c <7.5%), compared to 11.7% with elevated uric acid levels, suggesting a 166% increased likelihood of better glycemic control. Our study stands in concurrence with other studies. A comparable study by Sidhu et al found significantly higher serum uric acid levels in T2DM patients compared to controls (8.02 mg/dL vs 3.73 mg/dL) suggesting monitoring uric acid levels could indicate oxidative stress in T2DM. [26] Similarly, Ullah A et al linked poorly controlled blood sugar to high uric acid levels in diabetic patients, particularly adults and found a significant association between high blood sugar and uric acid levels. [8] Another study by Nan H et al found decreasing uric acid levels over time in participants who developed diabetes and higher baseline uric acid levels associated with increased diabetes risk in men. [10] Swarnalatha JC et al. (2019) identified independent association between uric acid levels and fasting blood sugar, blood pressure, BMI, and alcoholism status suggesting link between hyperuricemia and T2DM with hypertension. [8] Bhole V et al found high uric

acid levels to be an independent risk factor T2DM, even after accounting for other risk factors. [27] Another study Rao S et al found pre-diabetic patients had higher serum uric acid levels (4.88 mg/dL) compared to controls (3.84 mg/dL) and diabetic patients (3.78 mg/dL).[28] Fazlani KA et al linked higher uric acid levels in diabetic patients to unfavorable lipid profiles recommends monitoring uric acid and lipid profiles. [29] Shirsath A et al found approximately two-thirds of T2DM patients had elevated uric acid levels.[30] Panchani M et al found significant positive correlation between uric acid levels and HbA1c and fasting blood sugar in Monitoring uric acid levels could hold value, especially in diabetic patients with additional risk factors for hyperuricemia (obesity, high blood pressure, etc.). However, more research is required to establish clear guidelines for uric acid monitoring frequency and target levels in diabetic patients. In the present study, a significant correlation between elevated serum uric acid levels and poor glycemic control, as measured by HbA1c values was reported. Specifically 66.2% of patients with high uric acid levels had HbA1c >8.5%, compared to 49.3% with normal uric acid levels, indicating a 34.6% increased likelihood of poor glycemic control. Conversely, 31.3% of patients with normal uric acid levels achieved optimal glycemic control (HbA1c <7.5%), compared to 11.7% with elevated uric acid levels, suggesting a 166% increased likelihood of better glycemic control. Our study stands in concurrence with other studies. A comparable study by Sidhu et al found significantly higher serum uric acid levels in T2DM patients compared to controls (8.02 mg/dL vs 3.73 mg/dL) suggesting monitoring uric acid levels could indicate oxidative stress in T2DM. [26] Similarly, Ullah A et al linked poorly controlled blood sugar to high uric acid levels in diabetic patients, particularly adults and found a significant association between high blood sugar and uric acid levels. [8] Another study by Nan H et al found decreasing uric acid levels over time in participants who developed diabetes and higher baseline uric acid levels associated with increased diabetes risk in men. [10] Swarnalatha JC et al. (2019) identified independent association between uric acid levels and fasting blood sugar, blood pressure, BMI, and alcoholism status suggesting link between hyperuricemia and T2DM with hypertension. [8] Bhole V et al found high uric acid levels to be an independent risk factor T2DM, even after accounting for other risk factors. [27] Another study Rao S et al found pre-diabetic patients had higher serum uric acid levels (4.88 mg/dL) compared to controls (3.84 mg/dL) and diabetic patients (3.78 mg/dL). [28] Fazlani KA et al linked higher uric acid

levels in diabetic patients to unfavorable lipid profiles recommends monitoring uric acid and lipid profiles. Shirsath A et al found approximately two-thirds of T2DM patients had elevated uric acid levels. Panchani M et al found significant positive correlation between uric acid levels and HbA1c and fasting blood sugar in T2DM patients. [31] Farwa U et al found prediabetic patients had highest uric acid levels (6.07 mg/dL) compared to euglycemic and diabetic groups.

However, in contrast to our study, Hague T et al reported higher serum uric acid levels in healthy individuals than pre-diabetics and diabetics and found negative association between uric acid and fasting blood glucose.[17] Dhungana A et al found negative correlation between uric acid and HbA1c, FBG, and PPBG in diabetes patients, suggesting potential inverse relationship. [20] Bandaru P et al (2011) found higher uric acid levels associated with lower diabetes risk, regardless of age, lifestyle, and health conditions. Highest uric acid group had nearly half the chance of diabetes. [33] Another study by Ganesh G et al found lower serum uric acid levels in diabetic patients vs. healthy controls, but difference was not statistically significant. No significant correlation between uric acid and blood glucose. [34]

Shabana S et al found hypertensive diabetics had lower serum uric acid levels than non-hypertensive diabetics and negative correlation between blood sugar and uric acid in diabetic patients.<sup>[35]</sup>

The possible reasons for Hyperuricemia worsening glycemic control could be either due to the oxidative stress or due to inflammation. High uric acid can act as a pro- oxidant, generating free radicals that damage pancreatic beta cells responsible for insulin production. This impaired insulin secretion can lead to hyperglycemia and contribute to poor glycemic control. Uric acid crystals can trigger inflammation in various tissues, including the adipose tissue and liver. <sup>[36]</sup> This chronic low-grade inflammation can impair insulin sensitivity in these tissues, further hindering blood sugar control.

Poorly controlled diabetes might also lead to hyperuricemia in the following manner. Firstly, poorly controlled diabetes with chronically elevated blood sugar levels can stimulate the production of uric acid through a process called purine nucleotide degradation. This increased production could overwhelm the body's uric acid excretion capacity, leading to hyperuricemia. Secondly, Diabetes can damage the kidneys over time, leading to decreased uric acid excretion. This impaired elimination, coupled with potentially increased production, could contribute to elevated uric acid

levels. Moreover, there are shared underlying metabolic pathways. Both hyperuricemia and hyperglycemia can be linked to insulin resistance, a condition where cells become less responsive to insulin's effects. This suggests potential shared metabolic pathways influencing both conditions. Increased dietary fructose intake has been linked to both hyperuricemia and insulin resistance. Fructose metabolism can generate precursors for uric acid production and impair insulin signaling, potentially contributing to the observed correlation. [9]

Other factors like genetic predisposition might influence both uric acid metabolism and insulin sensitivity, potentially creating a susceptibility to both hyperuricemia and poor glycemic control. Lifestyle factors like diet, physical activity, and body weight can influence both uric acid levels and diabetes management. These factors require further investigation to understand their potential role in the observed association.

The few limitations of the present study are that observed correlation does not clarify whether high uric acid levels contribute to poor glycemic control or vice versa. Patients with pre-existing risk factors for both hyperuricemia and hyperglycemia might have been recruited, leading to a spurious association. The study design does not account for potential confounding variables that could influence both uric acid and HbA1c. Factors like diet, physical activity, medications, and even socioeconomic status could play a role and need to be considered in future research designs that incorporate adjustments for these variables. Selection bias can occur if the study population avoids representing the broader diabetic population. Recruiting patients from a single tertiary care hospital might have enrolled individuals with more severe cases or those with specific characteristics that skew the results.

#### **CONCLUSION:**

To conclude, a significant association was found between raised serum uric acid levels and poor glycemic control (HbA1c >8.5%). Specifically, 66.2% of patients with hyperuricemia had HbA1c >8.5%, compared to 49.3% with normal uric acid levels. Conversely, 31.3% of patients with normal uric acid levels achieved optimal glycemic control (HbA1c <7.5%), compared to 11.7% with hyperuricemia. These findings suggest that serum uric acid levels may serve as a useful marker for identifying patients with type 2 diabetes mellitus at risk of poor glycemic control. Monitoring uric acid levels may aid in early detection and management of hyperglycemia,

potentially reducing the risk of microvascular and macrovascular complications associated with diabetes.

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#### **Conflicts of Interest**

There are no conflicts of interest.

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