

Original Research

A study of plasma uric acid levels in patients with diabetes mellitus in comparison with normal subjects

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Abstract

Introduction: Serum uric acid has been shown to be associated with an increased risk of hypertension, cardiovascular disease, and chronic renal disease in previous epidemiological studies. However, the association between serum uric acid levels and diabetes mellitus is not clear. This study is aimed to define the relationship between serum uric acid and glucose levels in patients with diabetes mellitus.

Methods: It is a duration based case and control prospective observational study including 50 patients of type 2 diabetes mellitus and 50 controls. A detailed history, clinical examination and relevant investigations including serum uric acid and fasting blood glucose were done. Categorical variables were tabulated in frequency with percentage distribution and continuous variables were summarized in mean±SD. Two independent means were compared using the student t-test. The critical levels of significance of the results were considered at 0.05 levels i.e. $P < 0.05$ for statistical significance.

Results: The present study showed that there is a mild decrease in serum uric acid levels in patients with Type 2 diabetes mellitus and as the duration of diabetes increases there was decrease in serum uric acid levels. The patients with type 2 diabetes mellitus having poor glycemic control had less levels of serum uric acid.

Conclusion: Serum uric acid levels were mildly decreased in patients with Type 2 DM. It was more decreased in patients with Type 2 DM of longer duration and having poor glycemic control. The degree of reduction was directly proportional to the duration of Type 2 DM.

Keywords: Diabetes mellitus, hypouricemia, hyperglycemia, hyperuricemia, , uric acid

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Introduction

High serum uric acid levels have been shown to be associated with an increased risk of hypertension¹⁻³, cardiovascular disease^{2,4}, and chronic kidney disease⁵ in epidemiological studies. Hyperuricemia is a risk factor for peripheral arterial disease⁶, insulin resistance, and a component of the metabolic syndrome⁷. The association between serum uric acid (SUA) levels and diabetes mellitus (DM) is not clear. Some studies reported positive association⁸⁻¹³, whereas other studies reported no association¹⁴ or negative relationship¹⁵⁻¹⁶. However, most of the previous studies were conducted in the co-morbid population group^{8, 17}. Few studies have evaluated the SUA levels and its relationship with blood glucose concentrations in apparently healthy controls and such data is very limited from central region of India. This study aims to assess the relationship between SUA and fasting blood glucose levels in non-diabetic

healthy and diabetic individuals.

Material and Methods

This case and control observational study was conducted at the outpatient and inpatient units in department of general medicine, Netaji Subhash Chandra Bose Medical College Jabalpur, Madhya Pradesh, India. Duration period of the study was from 15th January 2019 to 31st August 2020. It was pre-approved by the Institutional Ethics Committee (IEC) for the final permission. After obtaining the permission of IEC the study was conducted. Fifty patients with type 2 diabetes mellitus (newly detected or already on treatment) and 50 normal subjects were included in the study. Considering the best availability of the patients by reviewing the previous records of this health facility, to achieve the maximum sample size we have randomly screened all patients and selected those who were already on treatment or

freshly detected diabetes mellitus. Patients with kidney disease, hepatic disorder, cardiovascular disease, myelo and lympho-proliferative disorder, psoriasis and alcoholics were excluded from the study. Pregnant and lactating females, individuals with a history of anti-hyperuricemic medications were also excluded from the study. Informed and written consent was obtained from each individual and the participation in the project was on voluntary basis. A detailed history and clinical examination was done. Venous blood samples were taken in the morning with the subjects fasting for 12 hours. The samples were then put into an ice-cooled box and transported to the lab at the department of Biochemistry. After centrifugation of blood samples at 3000 rpm for 15 min, the serum was isolated and stored at -20°C . The serum glucose concentration was measured within 3 h after of blood collection by glucose oxidase method. Serum uric acid (SUA) was measured by the uricase method. Routine blood investigations were also done. Diabetes was defined according to WHO criteria as a fasting blood plasma glucose ≥ 126 mg/dL, non-fasting plasma glucose ≥ 200 mg/dL¹⁸, or by clinical records of previously diagnosed patients. Hyperuricemia was defined if SUA concentration was > 7.5 mg/dL in males and > 7.0 mg/dL in females¹⁹ and hypouricemia was defined if SUA concentration was < 3.5 mg/dL in males and < 3.0 mg/dL in females²⁰.

Statistical analysis

Data was entered in a Microsoft Excel worksheet and all the categorical (qualitative) variables were coded numerically. Further data was transported in SPSS 20 for Windows for statistical analysis. Categorical variables were tabulated in frequency with percentage distribution and continuous variables were summarized in mean \pm SD. Chi-square analysis and/or Fisher's exact were applied to compare 2 x 2 contingency tables as appropriate. Two independent means were compared using the student t-test. The normality test was applied before using parametric tests. The critical levels of significance of the results

were considered at 0.05 levels i.e. $P < 0.05$ for statistical significance.

Results

The total number of subjects included in this study was 100. Among these 100 subjects, 50 were patients of type 2 DM, and 50 were controls. The age of the subjects with Type 2 DM ranged from 35 to 79 years. The age of the control ranged from 35 to 75. The mean and the standard deviation for age of patients with Type 2 DM, and controls were 52.8 ± 10.1 and 45.5 ± 10.3 respectively. There was no significant difference among the cases and the controls with reference to the age. The details of patients with $\text{FBS} > 180\text{mg/dl}$ and $\text{FBS} \leq 180\text{mg/dl}$ are given in the **Table-1**. The mean and standard deviation of serum uric acid level of patients with type 2 DM whose $\text{FBS} > 180\text{mg/dl}$ and $\text{FBS} \leq 180\text{mg/dl}$ was 2.61 ± 0.31 and 3.75 ± 0.93 respectively. The results were statistically significant. The details of fasting, postprandial blood sugar in control group are shown in the **Table-2**. The mean and standard deviation for FBS was 89.72 ± 14.20 similarly for PPBS was 122.86 ± 8.24 which implicates the glycemic status. Serum uric acid in diabetic population and control varied from 2.1 to 4.8 and 3.1 to 5.8mg/dl respectively. The mean and standard deviation of uric acid among diabetics was 2.96 ± 0.53 while in control it was 4.16 ± 0.91 respectively. The details are shown in the **Table-3**. The serum uric acid levels of diabetics was mildly decreased, compared with controls it was highly significant. Forty-one cases had hypouricemia in patients with Type 2 DM while 7 in controls. One control had hyperuricemia and none in patients with Type 2 DM. The results are shown in **Table-4**. This table clearly shows that the prevalence of hypouricemia is more in diabetic patients when compared to controls. Mean serum uric acid was less in patients with Type 2 DM of longer duration ($> 8\text{yrs}$), 2.64 ± 0.23 when compared to patients with Type 2 DM of shorter duration ($< 5\text{yrs}$). This is shown in the **Table-5**. Uric acid level decreases with increasing duration of Diabetes and it was statistically significant.

Table:1 Blood Sugar Distribution among Patients with Type 2 DM In Relation To Serum Uric Acid

Fasting Blood Sugar (FBS)	No. of case	Mean Serum Uric Acid Level	Standard Deviation
$\text{FBS} > 180\text{mg/dl}$	33	2.61	0.31
$\text{FBS} \leq 180\text{mg/dl}$	17	3.75	0.93

Table:2 Blood sugar distribution in control group

Blood Sugar	Mean	Standard Deviation
FBS*	89.72	14.20
PPBS†	122.86	8.24

* FBS- Fasting Blood Sugar ; † PPBS- Post Prandial Blood Sugar

Table:3 Serum uric acid levels in diabetics and controls

Serum Uric Acid (mg/dl)	Cases		Controls	
	Mean	Standard Deviation	Mean	Standard Deviation
	2.96	0.53	4.16	0.91

(p- value < 0.0001)

Table:4 Analysis of Hypouricemia and Hyperuricemia in Cases and Controls

Serum Uric Acid	Study Group			
	Diabetic		Control	
	Number	Percentage	Number	Percentage
Normal	09	18.00	42	84.00
Hypouricemia	41	82.00	07	14.00
Hyperuricemia	00	00.00	01	02.00

p < 0.0001

Table: 5 Serum Uric Acid Level In Relation to Duration of Diabetes

Duration of Diabetes	Number of Cases	Mean S.U.A*	S.D †
< 5 years	16	3.39	0.51
5-8 years	23	2.82	0.47
> 8 years	11	2.64	0.23

* S.U.A - Serum Uric Acid ; † S.D – Standard Deviation

Discussion

The present study of serum uric acid levels in patients with Type 2 DM and in control group was carried out in the department of General Medicine. The patients were grouped into study group (patients with type 2 DM) and control group (normal patients). The purpose of the study was to study the relationship between serum uric acid levels in patients with type 2 DM in comparison with normal subjects. The main finding of our study was that the lowest plasma uric acid levels were found in diabetic patients. Plasma uric acid levels were clearly decreased, in diabetic patients and showed an inverse association with FBG concentration. This is in agreement with previous studies^{17, 21}, where a decreasing trend of SUA was observed with increasing blood glucose concentration. A negative association of plasma uric acid with overt diabetes was found earlier in several other studies^{15, 22}. Our results confirm this finding despite the methodological differences and the various diagnostic criteria for diabetes mellitus used in these studies. A plausible mechanism for the observed findings of the negative relationship between SUA and diabetes may be related to the inhibition of uric acid reabsorption in the proximal tubule of kidney by high glucose concentrations in diabetic individuals^{23, 24}. The low concentration of uric acid in serum might be the results of the uricosuric effect of glucose on uric acid, which may influence to increase the excretion and decrease reabsorption of uric acid from the kidney²⁵. Some studies have reported a positive association between SUA and diabetes^{8-10, 12}. Our study used the WHO criteria for diagnosis of diabetes mellitus and showed that plasma uric acid levels were clearly reduced in diabetic patients when compared with nondiabetic patients. In this study mean serum uric acid levels were less in patients with poorly controlled

diabetes when compare to patients with well controlled diabetes. The mean serum uric acid level was 2.61 ± 0.31 and 3.75 ± 0.93 in poorly controlled and well-controlled diabetic patients respectively. Derek G Cook et al²² showed that there was a positive relationship between serum glucose and serum uric acid concentrations, at higher levels of glucose serum uric acid levels decreased. He concluded that serum uric acid probably reflects the biochemical interaction between serum glucose and purine metabolism, with increased excretion of uric acid during hyperglycemia and glycosuria. Kodama S et al¹² in their study assessed systematical evaluation of association between serum uric acid level and subsequent development of Type 2 DM and concluded that serum uric acid level is positively associated with development of Type 2 DM regardless of various study characteristics and also concluded that further research should be attempted to determine whether it is effective to utilize serum uric acid level as a predictor of Type 2DM for its primary prevention. In our study patients with poor metabolic control and longer duration of diabetes were more susceptible to develop various complications including hypouricemia. Our study also shows that lower levels of serum uric acid was seen in patients with longer duration of diabetes when compared with shorter duration of diabetes, 2.64 ± 0.23 (>8yrs) vs 3.39 ± 0.51 (<5yrs). The difference was statistically significant. The possible reason may be due to increased excretion of uric acid over the years and modification of diet in renal disease. In this study 82% (N=41) patients of Type 2 DM had hypouricemia when compared to only 14% (N=7) in controls. The results were statistically significant. According to Derek G Cook et al,²² glomerular hyperfiltration, which accompanies diabetic nephropathy and,

functional abnormality of renal tubular urate handling lead to tubulointerstitial involvement, which contributes to hypouricemia in diabetic patients. There are some limitations in our study as cases were selected from a tertiary health care institute only; it does not represent the general population. Sample size was small due to ongoing Covid-19 and there were lot of cases with type 2 DM associated with systemic hypertension, which could not be taken in the present study due to exclusion criteria. The Uric acid level is subjected to vary based on other co morbidities.

Conclusion

Serum uric acid levels were mildly decreased in patients with Type 2 DM. It was more decreased in patients with Type 2 DM of longer duration and having poor glycemic control. The degree of reduction was directly proportional to the duration of Type 2 DM. These findings suggest that low serum uric acid level indicates impaired glucose metabolism and impaired control of blood sugar. Further studies are required to evaluate the reliability.

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References:

- Shankar A, Klein R, Klein BEK, Nieto FJ. The association between serum uric acid level and long-term incidence of hypertension: population based cohort study. *J Hum Hypertens.* 2006; 20:937-45.
- Klein R, Klein BE, Cornoni JC, Maready J, Cassel JC, Tyroler HA. Serum uric acid. Its relationship to coronary heart disease risk factors and cardiovascular disease, Evans County, Georgia. *Arch Intern Med.* 1973 Sep;132(3):401-10.
- Sundström J, Sullivan L, D'Agostino RB, Levy D, Kannel WB, Vasan RS. Relations of serum uric acid to longitudinal blood pressure tracking and hypertension incidence. *Hypertension.* 2005 Jan;45(1):28-33.
- Fang J, Alderman MH. Serum uric acid and cardiovascular mortality the NHANES I epidemiologic follow-up study, 1971-1992. National Health and Nutrition Examination Survey. *JAMA.* 2000 May 10; 283(18): 2404-10.
- Chonchol M, Shlipak MG, Katz R, Sarnak MJ, Newman AB, Siscovick DS, Kestenbaum B, Carney JK, Fried LF. Relationship of uric acid with progression of kidney disease. *Am J Kidney Dis.* 2007 Aug; 50(2): 239-47.
- Shankar A, Klein BE, Nieto FJ, Klein R. Association between serum uric acid level and peripheral arterial disease. *Atherosclerosis.* 2008 Feb; 196(2): 749-55.
- Yoo TW, Sung KC, Shin HS, Kim BJ, Kim BS, Kang JH, Lee MH, Park JR, Kim H, Rhee EJ, Lee WY, Kim SW, Ryu SH, Keum DG. Relationship between serum uric acid concentration and insulin resistance and metabolic syndrome. *Circ J.* 2005 Aug; 69(8): 928-33.
- Dehghan A, van Hoek M, Sijbrands EJ, Hofman A, Witteman JC. High serum uric acid as a novel risk factor for type 2 diabetes. *Diabetes Care.* 2008 Feb; 31(2): 361-2.
- Chien KL, Chen MF, Hsu HC, Chang WT, Su TC, Lee YT, Hu FB. Plasma uric acid and the risk of type 2 diabetes in a Chinese community. *Clin Chem.* 2008 Feb; 54(2): 310-6.
- Kramer CK, von Mühlen D, Jassal SK, Barrett-Connor E. Serum uric acid levels improve prediction of incident type 2 diabetes in individuals with impaired fasting glucose: the Rancho Bernardo Study. *Diabetes Care.* 2009 Jul; 32(7): 1272-3.
- Nakanishi N, Okamoto M, Yoshida H, Matsuo Y, Suzuki K, Tatara K. Serum uric acid and risk for development of hypertension and impaired fasting glucose or Type II diabetes in Japanese male office workers. *Eur J Epidemiol.* 2003; 18(6): 523-30.
- Kodama S, Saito K, Yachi Y, Asumi M, Sugawara A, Totsuka K, Saito A, Sone H. Association between serum uric acid and development of type 2 diabetes. *Diabetes Care.* 2009 Sep; 32(9): 1737-42.
- Modan M, Halkin H, Karasik A, Lusky A. Elevated serum uric acid—a facet of hyperinsulinaemia. *Diabetologia.* 1987 Sep; 30(9): 713-8.
- Taniguchi Y, Hayashi T, Tsumura K, Endo G, Fujii S, Okada K. Serum uric acid and the risk for hypertension and Type 2 diabetes in Japanese men: The Osaka Health Survey. *J Hypertens.* 2001 Jul; 19(7): 1209-15.
- Oda E, Kawai R, Sukumaran V, Watanabe K. Uric acid is positively associated with metabolic syndrome but negatively associated with diabetes in Japanese men. *Intern Med.* 2009; 48(20): 1785-91
- Nan H, Dong Y, Gao W, Tuomilehto J, Qiao Q. Diabetes associated with a low serum uric acid level in a general Chinese population. *Diabetes Res Clin Pract.* 2007 Apr; 76(1): 68-74.
- Bandaru P, Shankar A. Association between Serum Uric Acid Levels and Diabetes Mellitus. *Int J Endocrinol.* 2011;2011:604715.
- Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia. Geneva: World Health Organization; 2006.
- Emmerson BT. Identification of the causes of persistent hyperuricaemia. *Lancet.* 1991 Jun 15; 337(8755): 1461-3.
- Steele TH. Hypouricemia. *N Engl J Med.* 1979 Sep 6; 301(10): 549-50.
- Bonakdaran S, Kharraqani B. Association of serum uric acid and metabolic syndrome in type 2 diabetes. *Curr Diabetes Rev.* 2014 Mar; 10(2): 113-7.
- Cook DG, Shaper AG, Thelle DS, Whitehead TP. Serum uric acid, serum glucose and diabetes: relationships in a population study. *Postgrad Med J.* 1986 Nov; 62(733): 1001-6.
- Tuomilehto J, Zimmet P, Wolf E, Taylor R, Ram P, King H. Plasma uric acid level and its association with diabetes mellitus and some biologic parameters in a biracial population of Fiji. *Am J Epidemiol.* 1988 Feb; 127(2): 321-36.
- Herman JB, Medalie JH, Goldbourt U. Diabetes, prediabetes and uricaemia. *Diabetologia.* 1976 Mar; 12(1): 47-52.
- Pavani CH, Mohanty S, Dharwadkar AA. Hypouricemia in type 2 diabetes mellitus without nephropathy: a case control study. *Int J Clin Biochem Res.* 2018; 5:201-5.