International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 11, November 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.11.2024.110

ORIGINAL RESEARCH

A comparative study to assess the relationship between serum uric acid and blood glucose levels in type2 diabetes patient and healthy individual in tertiary care centre

[1]Dr. Kuldeep Johar, [2]Dr. Vishal Yadav, [3]Dr. R.K. Jha, [4]Dr. Ankita Santosh Vishwakarma

[1]PG Student, [2]Professor, [3]Professor & HOD, Department of General Medicine, Sri Aurobindo Medical College & Postgraduate Institute, Indore, M.P., India
[4]Medical Officer, Mukhymantri Sanjeevni Clinic Bada Bangarda, Indore, M.P., India

Corresponding Author
Dr. Kuldeep Johar
PG Student, Department of General Medicine, Sri Aurobindo Medical College & Postgraduate Institute, Indore, M.P., India

Received Date: 15 September, 2024 Accepted Date: 17 October, 2024

ABSTRACT

Background: Serum uric acid (SUA), a by product of purine metabolism, has been variably associated with type 2 diabetes mellitus (T2DM), with studies suggesting positive, negative, or no correlation. Given the mixed findings, this study explores the correlation between SUA and glycemic parameters among individuals with T2DM and healthy controls. **Method:** An analytical cross-sectional study was conducted at Sri Aurobindo Institute of Medical Sciences, Indore, India, over 18 months (September 2022–February 2024). The study included 250 participants: 125 with T2DM and 125 healthy controls. Fasting blood glucose (FBG), postprandial blood glucose (PPBG), HbA1c, and SUA levels were measured. Data were analyzed using descriptive statistics, t-tests, chi-square tests, and Spearman's correlation, with a p-value <0.05 considered statistically significant. **Results:** Diabetics exhibited significantly higher FBG, PPBG, HbA1c, and SUA levels compared to healthy controls. SUA levels were positively correlated with FBG ($\rho = 0.320$, $p < 0.001$) and PPBG ($\rho = 0.328$, $p < 0.001$) across the total population, although significance diminished after adjusting for age, BMI, hypertension, and lifestyle factors in regression analysis. **Conclusion:** Modified SUA levels did not show a significant independent correlation with diabetes mellitus. After accounting for metabolic, lifestyle, and clinical factors, SUA levels remained largely unaffected by glycemic parameters, suggesting that SUA may not independently predict diabetes risk. Future research should control for additional covariates to clarify SUA's role in T2DM.

Keywords: Serum Uric Acid, Type 2 Diabetes Mellitus, Glycemic Parameters, Fasting Blood Glucose, Postprandial Blood Glucose, HbA1c

INTRODUCTION

Uric acid is the ultimate degradation product of purine nucleotide metabolism. It is a weak diprotic acid functioning as a pro-oxidant.[1,2] he action is contingent upon the surrounding environment, including the onset of disease, location, and the oxidative conditions within tissues.[3, 4]The prevalence of hyperuricemia is elevated in both developed and developing nations, [5]and elevated uric acid levels may exert a toxic effect, promoting the precipitation of uric acid crystals in joints and tissues, resulting in complications such as gout, nephrolithiasis, and chronic nephropathy.[4]

A positive correlation between elevated Serum Uric Acid (SUA) and diabetes has been documented, while others have reported no correlation [9,10]or an inverse relationship.[11-13]SUA exhibits a positive correlation with serum glucose levels in healthy individuals.[14]

Nonetheless, this correlation is not uniform between healthy and diabetic individuals.[10, 15] SUA is regarded as a significant and independent risk factor for diabetes; however, a study has indicated a low serum level of uric acid in a hyperglycaemic state.[12] Most individuals undergo a period of impaired glucose tolerance prior to the onset of diabetes, and

DOI: 10.69605/ijlbpr_13.11.2024.110

during this interval, the correlation between elevated levels of SUA and the risk of developing type II Diabetes Mellitus remains ambiguous. [10, 15]

The objective of this study was to evaluate any alterations in SUA levels. Therefore, a study is required to ascertain the significance of serum uric acid in diabetes mellitus by assessing the correlation between glycaemic parameters and serum uric acid levels across varying glucose tolerance statuses. The correlation between elevated SUA levels and the risk of type II Diabetes mellitus (DM) remains ambiguous. [10, 15]

The objective of this study was to evaluate any alterations in SUA levels. Therefore, a study is required to ascertain The importance of serum uric acid in diabetes mellitus by assessing the correlation between glycaemic parameters and serum uric acid levels across various glucose tolerance statuses.

MATERIAL AND METHODS

Study Design: This study is an analytical cross-sectional study designed to investigate the relationship between serum uric acid and blood glucose levels in individuals with type 2 diabetes mellitus (T2DM) and healthy controls. Data collection was conducted at the Department of General Medicine, Sri Aurobindo Institute of Medical Sciences, from September 2022 to February 2024.

Study Setting: The study was conducted at Sri Aurobindo Institute of Medical Sciences (SAIMS) in Indore, India. Patients diagnosed with T2DM and healthy individuals presenting to the Department of Medicine and Endocrinology outpatient department (OPD) and wards were recruited.

Study Population

The study population consisted of two groups:

- Group 1 (Diabetic Group): Patients aged 18 years and above with confirmed T2DM, diagnosed according to standard clinical criteria, and presenting with biochemical reports.
- Group 2 (Control Group): Healthy, non-diabetic individuals aged 18 years and above, attending the OPD for routine check-ups.

Inclusion Criteria

- Individuals aged above 18 years.
- Group 1: Patients with confirmed T2DM attending the OPD or admitted to the hospital.
- Group 2: Healthy, non-diabetic individuals.

Exclusion Criteria

- Patients under the age of 18.
- Patients with type 1 diabetes mellitus.
- Patients on steroid therapy.
- Patients with acute infectious diseases.
- Non-consenting individuals.

Sample Size

A total sample size of 250 participants (125 per group) was calculated based on the prevalence of diabetes in India (8.9%) and an absolute error of 5%, with a 95% confidence interval.

Data Collection Tools and Procedures

A structured proforma was used to collect baseline demographic and clinical information for each participant. Informed written consent was obtained from all participants. Data were collected through a combination of patient history, clinical examination, and laboratory investigations, which were directly recorded onto the proforma.

Investigations

The following laboratory investigations were conducted for each participant:

- Fasting Blood Sugar (FBS)
- Postprandial Blood Sugar (PPBS)
- Glycated Hemoglobin (HbA1c)
- Serum Uric Acid (S. Uric Acid)
- Complete Blood Count (CBC)
- Erythrocyte Sedimentation Rate (ESR)

Procedure

1. Recruitment: Eligible patients diagnosed with T2DM and healthy controls visiting SAIMS OPD or wards were recruited after informed consent.
2. Data Collection: Personal and family history were collected through interviews. Laboratory values, including blood glucose levels and serum uric acid levels, were recorded from biochemical reports.
3. Diagnosis Confirmation: Blood glucose levels, HbA1c, and serum uric acid levels were tested to confirm the diagnosis of diabetes in patients and assess uric acid levels in both groups.

Statistical Analysis

Data were entered into Microsoft Excel 2010 and analyzed with appropriate statistical software. Descriptive statistics (mean, standard deviation) were calculated for continuous variables, while frequencies and percentages were calculated for categorical variables. A chi-square test or Fisher's exact test was used for categorical data comparison, while the Independent t-test or Mann-Whitney U test was employed for continuous variables. A p-value <0.05 was considered statistically significant.

DOI: 10.69605/ijlbpr_13.11.2024.110

RESULTS

Table 1: Baseline Characteristics of Study Participants (n=250)

Variables	Total Study Participants (n=250)	Diabetic Cases (n=125)	Non-Diabetic Controls (n=125)	p-value
Age (years)	52.0 (41.2-62.0)	57.0 (47.0-64.0)	44.0 (35.7-54.2)	<0.001
BMI (kg/m²)	24.2 (21.5-26.7)	24.7 (22.1-27.2)	23.9 (21.3-25.9)	0.005
SBP (mm of Hg)	124.0 (120.0-140.0)	130.0 (120.0-140.0)	121.0 (110.0-140.0)	0.016
DBP (mm of Hg)	80.0 (70.0-90.0)	80.0 (80.0-90.0)	80.0 (70.0-90.0)	0.019
FBG (mg/dl)	119.0 (95.0-151.7)	146.0 (122.7-180.0)	88.0 (84.0-94.0)	<0.001
PPBG (mg/dl)	181.0 (132.0-246.5)	235.5 (192.0-278.5)	116.0 (108.0-132.0)	<0.001
HbA1c (%)	6.1 (5.4-7.1)	6.9 (6.2-7.9)	5.2 (5.1-5.4)	<0.001
sUA (mg/dl)	5.6 (4.9-6.3)	5.8 (5.3-6.5)	5.2 (4.4-5.8)	<0.001

Abbreviations: BMI - Body Mass Index; SBP - Systolic Blood Pressure; DBP - Diastolic Blood Pressure; FBG - Fasting Blood Glucose; PPBG - Post-prandial Blood Glucose; HbA1c - Glycated Hemoglobin; sUA - Serum Uric Acid.

Table 2: Socio-Demographic and Clinical Characteristics Among Study Participants (n=250)

Variables	Total Study Participants (n=250)	Diabetic Cases (n=125)	Non-Diabetic Controls (n=125)	p-value
Sex				
Male	138 (55.2%)	78	60	**0.881**
Female	112 (44.8%)	47	65	
Diet				
Vegetarian	21 (8.4%)	11	10	0.820
Mixed	229 (91.6%)	114	115	
Smoking				
Non-smokers	210 (84.0%)	112	98	0.150
Smokers	40 (16.0%)	23	17	
Alcohol				
Non-alcoholic	214 (85.6%)	121	93	0.592
Alcoholic	36 (14.4%)	22	14	
Hypertension				
Yes	110 (44.0%)	73	37	0.065
No	140 (56.0%)	52	88	
Uric Acid Category				
Low	17 (6.8%)	10	7	0.038
Normal	204 (81.6%)	113	91	
High	29 (11.6%)	20	9	

Table 3: Correlation of Serum Uric Acid Levels with Glycemic Parameters

Dependent Variable (Serum Uric Acid)	FBG (mg/dl)	PPBG (mg/dl)	HbA1C (%)	Duration of Diabetes (years)
	ρ	p-value	ρ	p-value
Total Study Population (n=250)	0.320	<0.001	0.328	<0.001
Non-Diabetic Controls (n=125)	0.277	0.008	0.180	0.090
Diabetic Cases (n=125)	0.220	0.003	0.255	0.001

Notes: ρ - Correlation coefficient; p-value obtained from Spearman's correlation analysis.

Table 4: Multiple Linear Regression Analysis to Evaluate Association of sUA and Diabetes

Variables	Unadjusted B	Unadjusted p-value	Adjusted B	Adjusted p-value
FBG	0.009	<0.001	0.005	0.259
PPBG	0.005	<0.001	0.002	0.260
HbA1c	0.229	<0.001	-0.031	0.759
Study Group	0.347	<0.001	0.033	0.712

Notes: p-values from simple linear regression analysis; p-values from multiple linear regression analysis after adjusting for age, sex, diet, BMI, hypertension, alcohol, and smoking.

DOI: 10.69605/ijlbpr_13.11.2024.110

DISCUSSION

This study aimed to compare serum uric acid levels among diabetic patients, and non-diabetic control. We also examined its correlation with glycaemic parameters such as FBG, PPBG, and HbA1c levels. The demographic and clinical parameters, including age, BMI, SBP, and DBP, exhibited significant differences among the three groups. Unadjusted serum uric acid levels were significantly elevated in the diabetic group relative to the pre-diabetic and non-diabetic groups. We noted a progressive trend, with uric acid levels being highest in diabetics, followed by pre-diabetics, and lowest in non-diabetic participants. Serum uric acid exhibited a weak positive correlation with all glycaemic parameters (FBG, PPBG, and HBA1c), with the exception of the pre-diabetic group. Serum uric acid levels rose markedly with the prolonged duration of diabetes in the diabetic cohort. Nonetheless, after controlling for potential confounders (age, sex, diet, BMI, hypertension, alcohol consumption, and smoking), we observed no significant correlation between serum uric acid and the study group. Furthermore, serum uric acid levels exhibited no significant variation with an increase in any glycaemic parameters. The systolic blood pressure (SBP) and diastolic blood pressure (DBP) of the participants exhibited significant differences across the three groups. Unmodified serum uric acid concentrations were also markedly elevated in the diabetic group in comparison to the pre-diabetic and non-diabetic groups. The levels of uric acid exhibited a progressive trend, being highest in diabetics, followed by pre-diabetics, and lowest in non-diabetic participants. Serum uric acid exhibited a positive but weak correlation with all glycaemic parameters (FBG, PPBG, and HBA1c), with the exception of the pre-diabetic group. Serum uric acid levels rose significantly with the prolonged duration of diabetes in the diabetic cohort. Nonetheless, after controlling for potential confounders (age, sex, diet, BMI, hypertension, alcohol consumption, and smoking), we identified no significant correlation between serum uric acid and the study group. Furthermore, serum uric acid levels exhibited no significant variation with an increase in any glycaemic parameters.

Prior research has yielded varied outcomes. Two meta-analyses indicate a positive correlation between sUA levels and the onset of T2DM. Both analyses, even after adjusting for metabolic and behavioural confounders, indicated that serum uric acid may be an independent risk factor for type 2 diabetes mellitus (T2DM).The correlation between sUA and T2DM diminished upon accounting for these covariates. An elevated level of uric acid correlates with heightened oxidative stress and inflammation. This may result in heightened insulin resistance, thereby exacerbating the risk of diabetes.[16,17] A study conducted in eastern Nepal indicated a notable and incremental rise in serum uric acid levels among non-diabetic, pre-diabetic, and diabetic individuals. Nevertheless, the study failed to account for the influence of important covariates such as BMI, age, SBP, and DBP in addition to the various glycaemic parameters.[18]

Conversely, certain studies have demonstrated an inverse relationship between serum uric acid and diabetes.[19-21] A substantial (n = 18,825) multi-ethnic study examined data from the third National Health and Nutrition Examination Survey (NHANES), revealing that elevated serum uric acid (sUA) levels were inversely correlated with diabetes mellitus, even after controlling for metabolic, behavioural, and clinical variables.[19]Nan et al. reported in their study that serum uric acid levels increased with rising fasting blood glucose (FBG) in non-diabetic and pre-diabetic groups, but decreased with elevated FBG levels within the diabetic range. The results were adjusted for covariates such as age, BMI, triglyceride levels, and history of cardiovascular diseases.[20] Haque et al. also documented a notable reduction in serum uric acid levels in pre-diabetic individuals.

and diabetic individuals compared to non-diabetics.[21]Impaired re-absorption of uric acid from the proximal tubule, attributed to elevated glucose concentration, has been proposed as a likely mechanism for reduced uric acid levels.[19-21] Alqahtani et al. reported significantly elevated serum uric acid levels in the pre-diabetic cohort. HbA1C levels were employed to categorise the study population in their research.[23] A prospective cohort study from the Osaka health survey indicated that elevated serum uric acid levels heightened the risk of hypertension but did not affect the risk of type 2 diabetes mellitus in Japanese men.[22] A comprehensive theory concerning the relationship between uric acid and diabetes risk has yet to be formulated. In the absence of coherent data, a simplistic cause-and-effect mechanism is inadequate to elucidate the trend in both directions. Diabetes mellitus and uric acid metabolism and transport are influenced by various factors, including lifestyle, diet, genetic composition, ethnicity, oxidative stress, inflammatory conditions, co-morbidities, and pharmacological agents, among others.[24-27] A comprehensive comprehension of the intricate interaction between these identified and unidentified factors, coupled with rigorous and suitable research methodologies for their assessment, may ultimately elucidate these inconsistent outcomes. Clinical and molecular studies are anticipated. The primary limitation of our study was the selection bias inherent in the hospital-based design. Consequently, these findings may not be relevant to the general population. It is advisable to conduct additional community-based prospective studies that include significant covariates.

CONCLUSION

The analysis showed that serum uric acid (sUA) levels did not exhibit a significant independent correlation

DOI: 10.69605/ijlbpr_13.11.2024.110

with pre-diabetes or diabetes mellitus. While sUA levels appeared higher in diabetic cases in unadjusted analyses, this association diminished after controlling for confounding factors such as age, sex, diet, BMI, hypertension, alcohol use, and smoking. Adjusted analyses revealed that sUA levels remained relatively stable despite increases in fasting blood glucose (FBG), postprandial blood glucose (PPBG), and HbA1c levels. These findings highlight the complexity of metabolic interactions influencing sUA levels, suggesting that future studies should carefully account for multiple covariates to clarify potential links between sUA and glycemic status.

REFERENCES

1. Remedios C, Shah M, Bhasker AG, Lakdawala M. Hyperuricemia: a reality in the Indian obese. Obes Surg. 2012 Jun;22 (6):945-8.
2. Choi HK, Mount DB, Reginato AM. Pathogenesis of gout. Ann Intern Med. 2005 Oct 4;143(7):499-516.
3. Hayden MR, Tyagi SC. Uric acid: A new look at an old risk marker for cardiovascular disease, metabolic syndrome, and type 2 diabetes mellitus: The urate redox shuttle. Nutr Metab (Lond). 2004 Oct 19;1(1):10.
4. Grassi D, Ferri L, Desideri G, Di Giosia P, Cheli P, Del Pinto R, et al. Chronic hyperuricemia, uric acid deposit and cardiovascular risk. Curr Pharm Des. 2013;19(13):2432-8.
5. Chen LY, Zhu WH, Chen ZW, Dai HL, Ren JJ, Chen JH, et al. Relationship between hyperuricemia and metabolic syndrome. J Zhejiang Univ Sci B. 2007 Aug;8(8):593-8.
6. Kodama S, Saito K, Yachi Y, Asumi M, Sugawara A, Totsuka K, et al. Association between serum uric acid and development of type 2 diabetes. Diabetes Care. 2009 Sep;32 (9):1737-42.
7. 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.
8. Kramer CK, von Muhlen 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.
9. Modi AS, Sahi N. Serum uric acid levels in type 2 diabetes mellitus. Indian J Basic Appl Med Res. 2018;7(3):459-63.
10. 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.
11. Rabari K, Samadhiya A, Saha S, Sharma A, Mirza AA, Naithani M. A study to assess serum uric acid level and its association with glycemic parameters in individuals with prediabetes and diabetes mellitus in a North Indian tertiary care hospital. Yuva J Med Sci. 2018;4 (2):12-8.
12. 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.
13. Bonakdaran S, Kharaqani B. Association of serum uric acid and metabolic syndrome in type 2 diabetes. Curr Diabetes Rev. 2014 Mar;10 (2):113-7.
14. Facchini F, Chen YD, Hollenbeck CB, Reaven GM. Relationship between resistance to insulin-mediated glucose uptake, urinary uric acid clearance, and plasma uric acid concentration. JAMA. 1991 Dec 4;266 (21):3008-11.
15. 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.
16. Kodama S, Saito K, Yachi Y, Asumi M, Sugawara A, Totsuka K, et al. Association between serum uric acid and development of type 2 diabetes. Diabetes care. 2009;32 (9):1737-42.
17. Jia Z, Zhang X, Kang S, Wu Y. Serum uric acid levels and incidence of impaired fasting glucose and type 2 diabetes mellitus: a meta-analysis of cohort studies. Diabetes Res Clin Pract. 2013;101 (1):88-96.
18. Khan SA, Mandal S. Significance of serum uric acid level in prediabetic and diabetic patients. Prog Med Sci. 2018;2(2):21-6.
19. Bandaru P, Shankar A. Association between Serum Uric Acid Levels and Diabetes Mellitus. Int J Endocrinol. 2011;2011:604715.
20. 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;76(1):68-74.
21. Haque T, Rahman S, Islam S, Molla NH, Ali N. Assessment of the relationship between serum uric acid and glucose levels in healthy, prediabetic and diabetic individuals. Diabetol Metab Syndr. 2019;11(1):49-56.
22. 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;19 (7):1209-15.
23. Alqahtani SA, Awan ZA, Alasmary MY,Al Amoudi SM. Association between serum uric acid with diabetes and other biochemical markers. J Family Med Prim Care. 2022;11 (4):1401-9.
24. Olokoba AB, Obateru OA, Olokoba LB. Type 2 diabetes mellitus: a review of current trends. Oman Med J. 2012; 27(4):269-73.
25. DeFronzo RA, Ferrannini E, Groop L, Henry RR, Herman WH, Holst JJ, et al. Type 2 diabetes mellitus. Nat Rev Dis Primers. 2015;1:15019.
26. Benn CL, Dua P, Gurrell R, Loudon P, Pike A, Storer RI, et al. Physiology of Hyperuricemia and Urate-Lowering Treatments. Front Med. 2018;5:160.
27. Joosten LAB, Crisan TO, Bjornstad P, Johnson RJ. Asymptomatic hyperuricaemia: a silent activator of the innate immune system. Nat Rev Rheumatol. 2020;16 (2):75-86.