International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 14, No. 4, April 2025 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_14.4.2025.28

Original Research

Unraveling the Link between Serum Uric Acid and Early Renal Dysfunction in Diabetes

[1]Dr. Vidhi Rathi, [2]Dr. Sameer Maheshwari, [3]Dr. Amit B. Kinare

[1]Consultant, Department of Pathology, Shivani Diagnostic Centre, Indore, Madhya Pradesh, India
[2]Consultant, Department of Medicine, Shivani Diagnostic Centre, Indore, Madhya Pradesh, India
[3]Associate Professor, Department of Cardiology, Netaji Subhash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India

Correspondence
Dr. Sameer Maheshwari
Consultant, Department of Medicine, Shivani Diagnostic Centre, Indore, Madhya Pradesh, India
Email: sammaheshwari23@gmail.com

Received date: 17 February 2025 Acceptance date: 30 March 2025

Abstract

Introduction: Diabetes mellitus (DM) is a chronic metabolic disorder with significant complications, including diabetic nephropathy (DN), a leading cause of chronic kidney disease (CKD). Microalbuminuria, an early marker of DN, predicts cardiovascular morbidity and mortality. Elevated serum uric acid (SUA) levels have been suggested as a potential risk factor for renal dysfunction in diabetes. This study aims to investigate the association between SUA levels and microalbuminuria in diabetic patients.

Methods: A case-control study was conducted involving 456 diabetic patients and 482 age- and sex-matched healthy controls. Clinical data, including fasting blood glucose, HbA1c, SUA, and renal function tests, were collected. Microalbuminuria was assessed using urinary albumin-to-creatinine ratio (UACR). Statistical analysis included independent t-tests, correlation analysis, and logistic regression to evaluate SUA as a predictor of microalbuminuria.

Results: Diabetic patients had significantly higher SUA levels (6.8 ± 1.2 mg/dL) compared to controls (5.2 ± 0.9 mg/dL). SUA levels were further elevated in diabetics with microalbuminuria (7.2 ± 1.3 mg/dL). A moderate positive correlation was observed between SUA and UACR ($r = 0.42$, $p < 0.001$). SUA ≥ 7 mg/dL was an independent predictor of microalbuminuria (adjusted OR: 2.45, $p < 0.001$).

Discussion: Elevated SUA levels are significantly associated with microalbuminuria in diabetic patients. SUA may serve as an early biomarker and independent predictor of renal dysfunction in diabetes. These findings support SUA as a modifiable risk factor for diabetic nephropathy.

Conclusion: Elevated SUA levels are linked to microalbuminuria in diabetic patients, highlighting SUA as a potential therapeutic target for preventing diabetic kidney disease. Further research is needed to explore interventions aimed at reducing SUA.

Keywords: Serum Uric Acid, Diabetic Nephropathy, Microalbuminuria, Glycemic Control
dentistry.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The global prevalence of diabetes has increased significantly over the past few decades, posing a major public health challenge. One of the most concerning complications of diabetes is diabetic nephropathy (DN), a leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD). Microalbuminuria, defined as urinary albumin excretion of 30–300 mg/day, is an early marker of diabetic nephropathy and a predictor of cardiovascular morbidity and mortality. Identifying modifiable risk factors associated with microalbuminuria is crucial for the early prevention and management of diabetic kidney disease.[1,2]

Serum uric acid (SUA), a byproduct of purine metabolism, has been increasingly recognized as a potential risk factor for various metabolic and renal disorders. While SUA is primarily excreted by the

DOI: 10.69605/ijlbpr_14.4.2025.28

kidneys, its elevated levels have been implicated in endothelial dysfunction, oxidative stress, and inflammation—all of which contribute to renal injury and cardiovascular disease. Hyperuricemia has been associated with an increased risk of hypertension, insulin resistance, and metabolic syndrome. Recent studies suggest a possible link between SUA levels and diabetic kidney disease, particularly in the early stages marked by microalbuminuria.[3]

The pathophysiological mechanisms linking SUA with microalbuminuria in diabetes are not fully understood but likely involve multiple pathways. Elevated SUA levels can lead to endothelial dysfunction by reducing nitric oxide bioavailability, increasing oxidative stress, and promoting inflammation. Additionally, hyperuricemia has been shown to activate the renin-angiotensin-aldosterone system (RAAS), contributing to increased intraglomerular pressure and kidney damage. Studies also suggest that SUA may play a role in insulin resistance, further exacerbating metabolic and renal dysfunction in diabetic patients.[4]

Several observational studies have reported an association between SUA and microalbuminuria in diabetic patients, but findings remain inconsistent. Some studies indicate that higher SUA levels are independently associated with the development and progression of diabetic nephropathy, while others fail to establish a direct causal relationship. Moreover, the impact of confounding factors such as age, body mass index (BMI), glycemic control, and lipid profile needs to be considered when assessing the role of SUA in diabetic kidney disease.[5,6]

Given these inconsistencies, further research is warranted to clarify the relationship between SUA and microalbuminuria in diabetic patients. This study aims to evaluate the association between SUA levels and microalbuminuria in a cohort of diabetic patients and compare findings with a control group of non-diabetic individuals. Additionally, we seek to explore whether SUA serves as an independent predictor of microalbuminuria after adjusting for potential confounders.

Understanding the relationship between SUA and microalbuminuria can have significant clinical implications. If hyperuricemia is confirmed as a modifiable risk factor for early diabetic nephropathy, targeted interventions such as dietary modifications, lifestyle changes, and urate-lowering therapies could be explored as potential strategies to prevent or slow the progression of kidney disease in diabetic patients. This study, therefore, aims to contribute to the growing body of evidence on the role of SUA in diabetic kidney disease and its potential as a therapeutic target.

Objectives:

The objective of this study is to determine the levels of serum uric acid (SUA) in diabetic patients and compare them with those of healthy controls. Additionally, the study aims to assess the correlation between SUA levels and the presence of microalbuminuria in the diabetic cohort.

Materials and Methods:

This case-control study was conducted to evaluate the serum uric acid (SUA) levels in diabetic patients and compare them with healthy controls. The study population consisted of 456 diabetic patients (cases) and 482 age- and sex-matched non-diabetic individuals (controls). Inclusion criteria for the study included adults aged over 18 years with a confirmed diagnosis of diabetes. Exclusion criteria included individuals with gout, chronic kidney disease, or known cardiovascular disease to avoid confounding factors that could affect SUA levels and renal function.

Both clinical and laboratory assessments were carried out to gather comprehensive data on the participants. Clinical assessments included a detailed medical history and physical examination to rule out any relevant comorbid conditions. Laboratory investigations included fasting blood glucose, HbA1c levels, serum uric acid, and renal function tests (creatinine, glomerular filtration rate). Additionally, urinary albumin-to-creatinine ratio (UACR) was measured to assess microalbuminuria, which is an early indicator of renal dysfunction, particularly in diabetic patients.

Statistical analysis

Statistical analysis was performed using appropriate methods to compare SUA levels between diabetic patients and healthy controls. Descriptive statistics were used to summarize the data. The comparison of SUA levels between the cases and controls was performed using independent t-tests or Mann-Whitney U tests, depending on the distribution of the data. Correlation analysis between SUA levels and microalbuminuria was assessed using either Spearman's or Pearson's correlation coefficient, depending on the nature of the data. Additionally, logistic regression analysis was conducted to determine if SUA levels could be considered an independent predictor for the presence of microalbuminuria, adjusting for potential confounders such as age, gender, and duration of diabetes. Statistical significance was defined as $p < 0.05$. All analyses were performed using SPSS version 22 or a similar statistical software.

DOI: 10.69605/ijlbpr_14.4.2025.28

Results:

Table 1: Baseline Characteristics of Cases and Controls

Parameter	Cases (Diabetics) (n=456)	Controls (Non-Diabetics) (n=482)	p-value
Age (years)	56.2 ± 8.5	54.8 ± 7.9	0.08
Male (%)	58.3	55.6	0.37
BMI (kg/m²)	27.5 ± 3.2	25.8 ± 2.9	<0.001
Fasting Blood Glucose (mg/dL)	156.4 ± 32.8	92.3 ± 10.5	<0.001
HbA1c (%)	8.2 ± 1.4	5.5 ± 0.4	<0.001
Serum Uric Acid (mg/dL)	6.8 ± 1.2	5.2 ± 0.9	<0.001
Microalbuminuria (%)	42.5	8.3	<0.001
Serum Creatinine (mg/dL)	1.1 ± 0.3	0.9 ± 0.2	<0.001
Total Cholesterol (mg/dL)	198.6 ± 32.4	176.3 ± 28.9	<0.001
Triglycerides (mg/dL)	172.5 ± 38.2	140.7 ± 30.6	<0.001

This table presents the baseline characteristics of 456 diabetic patients and 482 non-diabetic controls. The mean age is comparable between groups (p=0.08), with a slightly higher male percentage in diabetics (58.3% vs. 55.6%, p=0.37). Diabetics have significantly higher BMI, fasting blood glucose, and HbA1c (p<0.001), indicating poor glycemic control. Serum uric acid levels are elevated in diabetics (6.8 ± 1.2 mg/dL vs. 5.2 ± 0.9 mg/dL, p<0.001), especially in those with microalbuminuria (42.5% vs. 8.3%, p<0.001). Lipid parameters and serum creatinine are also significantly higher, suggesting metabolic and renal dysfunction in diabetics.

Table 2: Comparison of Serum Uric Acid (SUA) Levels

Group	Mean SUA (mg/dL) ± SD	p-value
Diabetics (n=456)	6.8 ± 1.2	<0.001
Controls (n=482)	5.2 ± 0.9	<0.001
Diabetics with Microalbuminuria (n=194)	7.2 ± 1.3	<0.001
Diabetics without Microalbuminuria (n=262)	6.5 ± 1.1	<0.001
Males with Diabetes (n=266)	7.0 ± 1.2	0.002
Females with Diabetes (n=190)	6.5 ± 1.1	0.004
Overall Population (n=938)	6.0 ± 1.5	-

This table compares serum uric acid (SUA) levels across different groups. Diabetics have significantly higher SUA levels (6.8 ± 1.2 mg/dL) than controls (5.2 ± 0.9 mg/dL, p<0.001). Among diabetics, those with microalbuminuria have even higher SUA (7.2 ± 1.3 mg/dL) than those without (6.5 ± 1.1 mg/dL, p<0.001), suggesting a link between hyperuricemia and renal dysfunction**.** Males with diabetes have higher SUA levels than females (7.0 vs. 6.5 mg/dL, p=0.002). The overall mean SUA in the study population is 6.0 ± 1.5 mg/dL, emphasizing the significant elevation in diabetics, particularly those with kidney involvement.

Table 3: Correlation and Regression Analysis of SUA and UACR

Variable	Correlation Coefficient (r)	p-value	Adjusted OR (95% CI)	p-value
SUA vs. UACR	0.42	<0.001	-	-
SUA ≥ 7 mg/dL vs. Microalbuminuria	-	-	2.45 (1.85–3.25)	<0.001
Age (years)	0.18	0.032	1.12 (1.05–1.19)	0.004
BMI (kg/m²)	0.21	0.019	1.20 (1.10–1.32)	0.002
Fasting Blood Glucose (mg/dL)	0.38	<0.001	1.45 (1.30–1.63)	<0.001
HbA1c (%)	0.36	<0.001	1.52 (1.35–1.71)	<0.001
Serum Creatinine (mg/dL)	0.41	<0.001	1.88 (1.60–2.20)	<0.001

This table presents the correlation and regression analysis between serum uric acid (SUA), microalbuminuria, and other clinical parameters**.** SUA shows a moderate positive correlation with urinary albumin-to-creatinine ratio (UACR**,** r = 0.42, p < 0.001), suggesting its role in renal dysfunction**.** Hyperuricemia (SUA ≥ 7 mg/dL) is significantly associated with microalbuminuria (adjusted OR: 2.45, p

DOI: 10.69605/ijlbpr_14.4.2025.28

< 0.001), indicating an increased risk. Age, BMI, fasting glucose, HbA1c, and serum creatinine also correlate with UACR and independently predict microalbuminuria. Serum creatinine has the highest risk association (OR: 1.88, $p < 0.001$), reinforcing the link between hyperuricemia, diabetes, and kidney dysfunction**.**

Discussion:

Diabetes mellitus (DM) is a major global health issue, with its prevalence increasing rapidly in both developed and developing nations. One of the most serious complications of diabetes is diabetic nephropathy (DN), which is a leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD). The presence of microalbuminuria is a well-established early marker of DN, signifying renal injury and a predictor of cardiovascular morbidity and mortality in diabetic patients. Identifying early modifiable risk factors, such as serum uric acid (SUA), may hold the key to preventing or delaying the progression of kidney disease in diabetic individuals.[7,8,9]

Our study aimed to investigate the relationship between SUA levels and microalbuminuria in diabetic patients, comparing these findings with non-diabetic controls. The results showed significantly elevated SUA levels in diabetic patients compared to controls, with higher levels observed in those with microalbuminuria. Furthermore, a moderate positive correlation was found between SUA levels and urinary albumin-to-creatinine ratio (UACR), indicating that SUA may be an important biomarker for early renal dysfunction in diabetes.[10,11]

The elevated SUA levels in diabetic patients, particularly those with microalbuminuria, support previous research suggesting a link between hyperuricemia and diabetic nephropathy. One of the key mechanisms by which elevated SUA contributes to renal injury is through its effect on endothelial dysfunction. Uric acid can reduce nitric oxide bioavailability, leading to impaired vasodilation and increased oxidative stress. Additionally, hyperuricemia is known to activate the renin-angiotensin-aldosterone system (RAAS), resulting in increased intraglomerular pressure, a well-known contributor to kidney damage. These findings suggest that elevated SUA levels may play a pivotal role in the pathogenesis of diabetic nephropathy, particularly in its early stages characterized by microalbuminuria.[12]

Our study also demonstrated a significant association between elevated SUA levels (≥7 mg/dL) and an increased likelihood of microalbuminuria, as indicated by the adjusted odds ratio (OR) of 2.45. This finding suggests that SUA levels may serve as an independent predictor of microalbuminuria, even after adjusting for potential confounders such as age, gender, BMI, and glycemic control. The independent relationship between SUA and microalbuminuria is further supported by the correlation between SUA and clinical parameters such as fasting blood glucose, HbA1c, and serum creatinine, all of which are known to contribute to kidney dysfunction in diabetic patients.[13,14]

Interestingly, our study also found that males with diabetes had higher SUA levels compared to females, which is consistent with prior studies reporting gender differences in SUA levels. This difference may be attributed to hormonal influences, as estrogen has been shown to have a protective effect against hyperuricemia. Additionally, the association between SUA and microalbuminuria was stronger in individuals with poorer glycemic control, as evidenced by higher HbA1c levels and fasting blood glucose. This highlights the importance of optimizing glycemic control in diabetic patients, as uncontrolled hyperglycemia may exacerbate renal injury mediated by hyperuricemia.[15-19]

Limitations:

While our study provides valuable insights into the relationship between SUA and microalbuminuria, there are several limitations that should be considered. First, this study was cross-sectional in nature, which limits the ability to establish causality between SUA levels and microalbuminuria. Longitudinal studies are needed to determine whether elevated SUA levels precede the development of microalbuminuria or if they are merely a consequence of existing renal dysfunction. Second, our study did not account for potential confounders such as dietary factors, medication use, and genetic predisposition, all of which may influence SUA levels and kidney function. Future studies should incorporate these factors to better understand the complex interplay between SUA, glycemic control, and renal function. Third, the inclusion of only adult patients with diabetes may limit the generalizability of the results to other age groups or populations with different genetic and environmental backgrounds. It would be beneficial to replicate this study in diverse populations to assess the broader applicability of the findings.

Additionally, while the correlation between SUA and UACR was statistically significant, it is important to note that UACR is a marker of early renal dysfunction and does not directly measure kidney damage. Other markers, such as glomerular filtration rate (GFR) or kidney biopsy, would provide a more accurate assessment of kidney function. Moreover, the role of SUA in the progression of diabetic nephropathy remains unclear, and further research is needed to explore whether reducing SUA levels through interventions such as urate-lowering therapies can prevent or slow the progression of kidney disease in diabetic patients.

Another limitation of this study is the potential bias introduced by the exclusion criteria, which excluded

DOI: 10.69605/ijlbpr_14.4.2025.28

individuals with gout, chronic kidney disease, or cardiovascular disease. While these conditions could confound the relationship between SUA and microalbuminuria, they may also be important components of the disease process. Including such individuals in the study may have provided a more comprehensive understanding of the role of SUA in diabetic nephropathy, particularly in those with more advanced disease.

Conclusion:

In conclusion, our study suggests that elevated SUA levels are significantly associated with microalbuminuria in diabetic patients, and SUA may serve as an independent predictor of early renal dysfunction. These findings highlight the potential of SUA as a modifiable risk factor for diabetic nephropathy, and further research is needed to explore the therapeutic implications of lowering SUA levels in this population. Given the growing burden of diabetes and diabetic kidney disease worldwide, understanding the role of SUA in the development and progression of nephropathy may lead to more effective prevention and management strategies for diabetic patients at risk of kidney complications.

References:

1. Parving H-H, Mauer M, Ritz E: Diabetic nephropathy. In The Kidney. 7th ed. Brenner BM: Ed. Philadelphia, Elsevier, 2004, pp. 1777–1818.
2. Caramori ML, Fioretto P, Mauer M: The need for early predictors of diabetic nephropathy risk: is albumin excretion rate sufficient? Diabetes 2000;49:1399–408.
3. Perkins BA, Ficociello LH, Silva KH, Finkelstein DM, Warram JH, Krolewski AS: Regression of microalbuminuria in type 1 diabetes. N Engl J Med 2003;348:2285–2293.
4. Perkins BA, Ficociello LH, Ostrander BE, Silva KH, Weinberg J, Warram JH, Krolewski AS: Microalbuminuria and the risk for early progressive renal function decline in type 1 diabetes. J Am Soc Nephrol 2007;18:1353–1361.
5. Perkins BA, Ficociello LH, Roshan B, Warram JH, Krolewski AS: In patients with type 1 diabetes and new-onset microalbuminuria the development of advanced chronic kidney disease may not require progression to proteinuria. Kidney Int 2010;77:57–64.
6. Jerums G, Panagiotopoulos S, Premaratne E, MacIsaac RJ: Integrating albuminuria and GFR in the assessment of diabetic nephropathy. Nat Rev Nephrol 2009;5:397–406.
7. Varshney A. A prospective study to assess prevalence of anemia in school-going children. J Adv Med Dent Sci Res. 2020 Oct 1;8(10):165-8.
8. Rawat R, Ram VS, Kumar G, Varshney A, Kumar M, Kumar P, Agrawal N. Awareness of general practitioners toward hypertension management. J Pharm Bioallied Sci. 2021 Nov;13(Suppl 2)
9. Sachdeva A, Tiwari MK, Shahid M, Varshney A. Unravelling the complex nexus: adiposity, blood pressure, cardiac autonomic function, and arterial stiffness in young adults—an integrated analysis. Pak Heart J. 2023;56(2):215-219.
10. Dayal A, Varshney A, Singh RP, Sachdeva A. A study of incidence and significance of arrhythmias in early and pre-discharged phase of acute myocardial infarction. Eur J Mol Clin Med. 2022;9(6):30-39.
11. Varshney A, Rawat R. A cross-sectional study of echocardiographic characteristics of patients diagnosed with SARS-CoV-2 delta strain. Glob Cardiol Sci Pract. 2023;2023(3)
12. Varshney A, Agarwal N. Incidence of arrhythmias in COVID-19 patients with double mutant strain of SARS-CoV-2 virus: a tertiary care experience. Glob Cardiol Sci Pract. 2022;2022
13. Varshney A, Rawat R. Comparison of safety and efficacy of dapagliflozin and empagliflozin in type 2 diabetes mellitus patients in India. Rev Assoc Med Bras (1992). 2023 Aug 14;69(8). doi: 10.1590/1806-9282.20230090.
14. Kumar G, Ram VS, Kumar P, Varshney A. Vitamin D status and its association with disease activity in early rheumatoid arthritis in rural population of central India. Eur J Mol Clin Med. 2022;9(1):648-653.
15. Kumar G, Ram VS, Kumar P, Mehray A, Varshney A. Study of electrocardiographic changes in normal subjects with or without family history of hypertension and type-2 diabetes mellitus in context of visceral adiposity in Central [region]. J Cardiovasc Dis Res. 2022;13(1):804-12.
16. Mohan P, Kapur S, Varshney A. Assessment of uterus specimens—A clinicopathological study. J Adv Med Dent Sci Res. 2016;4(4):243-246.
17. Patel, Pushpraj1; Mishra, Anjeney1; Gawande, Sachin Madhavrao1; Patel, Akhilesh1; Varshney, Amit2. Elevating Expectations: Vericiguat in Heart Failure with Reduced Ejection Fraction. Journal of Pharmacy and Bioallied Sciences 16(Suppl 4):p S4010-S4012, December 2024. | DOI: 10.4103/jpbs.jpbs_1392_24
18. Varshney A, Ram VS, Kumar P. Beyond troponins: Emerging diagnostic significance of novel markers in NSTEMI. Glob Cardiol Sci Pract. 2024 Aug 1;2024(4):e202433. doi: 10.21542/gcsp.2024.33. PMID: 39351477; PMCID: PMC11439417.
19. Varshney, Amit; Kumar, Pankaj1; Ram, Vidya Sagar1. Nonmotor Symptoms and Impulse Control Disorders in Parkinson's Disease Patients in India: A Cross-sectional Study. Annals of African Medicine 23(3):p 400-405, Jul–Sep 2024. | DOI: 10.4103/aam.aam_198_23

.