e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(9); 1661-1665

Original Research Article

Evaluating Hyperuricemia as a Risk Factor for Early Diabetic Kidney Disease Using Regression Analysis

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Received: 14-07-2025 / Revised: 13-08-2025 / Accepted: 14-09-2025
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Conflict of interest: Nil

Abstract:

Background: Diabetic Kidney Disease (DKD) is a major microvascular complication of T2DM mellitus and remains a leading cause of chronic kidney disease worldwide. Hyperuricemia has recently gained attention as a potential modifiable risk factor contributing to the onset and progression of DKD. Understanding this correlation may aid in identifying high-risk patients at an earlier stage.

Aim: To evaluate hyperuricemia as an independent risk factor for early DKD using regression analysis.

Methods: At Rama Medical College-Hospital & Research Center in Kanpur, Uttar Pradesh, a six-month observational cross-sectional study was carried out. One hundred T2DM patients in all were enrolled. Information was gathered on clinical history, demographics, and laboratory tests such as urine albumin-creatinine ratio, eGFR, serum uric acid, and serum creatinine. Uric acid levels were used to stratify the patients into groups. SPSS version 23.0 was used for the statistical analysis, which applied multiple regression models, correlation, t-tests, and chi-square.

Results: Hyperuricemia was present in 36% of participants. Patients with hyperuricemia had significantly higher serum creatinine (1.18 ± 0.24 mg/dL vs. 0.92 ± 0.18 mg/dL), lower eGFR (72.5 ± 12.3 vs. 88.6 ± 14.7 mL/min/1.73m²), and higher urine albumin-creatinine ratio (41.7 ± 15.2 vs. 26.3 ± 12.8 mg/g) compared to those with normal uric acid levels ($p < 0.05$ for all). After controlling for age, sex, HbA1c, BMI, and length of diabetes, multiple regression analysis verified hyperuricemia as an independent predictor of decreased eGFR ($\beta = –0.42$, $p < 0.001$).

Conclusion: In patients with T2DM, hyperuricemia was independently and strongly associated with early diabetic kidney damage. It might be a helpful indicator for determining who is more likely to have renal impairment.

Recommendations: Routine monitoring of serum uric acid in diabetic patients should be encouraged, and strategies targeting uric acid reduction may be considered as part of preventive measures to delay DKD progression. Large-scale prospective research is necessary to confirm these results.

Keywords: Hyperuricemia, DKD, T2DM Mellitus, eGFR, Regression Analysis.

Introduction

DKD, which affects a large percentage of individuals with T2DM, is one of the most dangerous microvascular consequences of the condition. It increases cardiovascular morbidity and mortality and causes end-stage renal disease (ESRD). DKD is still a major cause of chronic kidney disease (CKD) worldwide, placing a significant strain on healthcare systems despite advancements in blood pressure and glucose control [1,2].

Hyperuricemia, defined as elevated serum uric acid (SUA) levels, has emerged in recent years as a potential modifiable risk factor in the pathogenesis and progression of DKD. Observational and cross-sectional studies have reported that higher SUA correlates with worse renal function, increased albuminuria, and greater risk of DKD, even after adjustment for traditional risk factors such as hypertension, duration of diabetes, (BMI), and glycemic control [3–5]. For instance, a large Chinese cross-sectional study involving over 3000

type 2 diabetic patients found that hyperuricemia was independently correlated with DKD, with higher prevalence of DKD among hyperuricemic individuals versus those with normal uric acid levels (68.3% vs. 41.5%) [3]. Similarly, another Chinese investigation stratifying patients by KDIGO risk categories showed that higher SUA values corresponded to higher risk of DKD progression [6].

Mechanistic evidence supports these epidemiologic correlations. Elevated uric acid is thought to contribute to renal injury through multiple pathways including endothelial dysfunction, oxidative stress, activation of inflammatory processes (e.g. IL-1, IL-6, TNF-α), and up-regulation of the renin-angiotensin system. Uric acid can impair nitric oxide bioavailability, promote vascular smooth muscle proliferation, and induce tubulointerstitial fibrosis and mesangial expansion [7,8]. A study of T2DM patients found correlations between high SUA and markers of tubular damage and renal inflammation (urinary KIM-1, IL-1, IL-6, TNF-α) [7]. Moreover, a Mendelian randomization study published in 2024 has suggested a causal link between genetically predicted increases in SUA and the risk of diabetic nephropathy, although not for other microvascular complications such as retinopathy or neuropathy [9].

Despite growing evidence, several questions remain unresolved. It is unclear what threshold of SUA constitutes risk in different populations, whether hyperuricemia is an early marker or driver of DKD, and how much its independent effect persists after adjusting for confounders like duration of diabetes or baseline kidney function. In settings such as India, data are relatively sparse but crucial given high diabetes prevalence and sociocultural determinants of diet, obesity, and healthcare access.

Therefore, the purpose of this study is to investigate the relationship between hyperuricemia and early DKD in a cohort of 100 T2DM patients at Rama Medical College-Hospital & Research Center, Kanpur, over a 6-month period. After adjusting for age, gender, duration of diabetes, glycemic control, and other factors, we use regression analysis to investigate whether hyperuricemia functions as an independent risk factor for early DKD.

Methodology

Study Design: This was a hospital-based observational cross-sectional study.

Study Setting: The study was conducted at Rama Medical College-Hospital & Research Center, Kanpur, Uttar Pradesh, a tertiary care teaching hospital providing both inpatient and outpatient services. The institution caters to a diverse population, ensuring adequate patient representation for the study.

Study Duration: The study was conducted over a six-month period, allowing sufficient time for patient recruitment, data collection, and statistical analysis.

Participants: The study comprised 100 individuals with T2DM. Participants were recruited consecutively from outpatient and inpatient departments after fulfilling eligibility criteria and providing informed consent.

Inclusion Criteria: Patients aged 30–70 years with a confirmed diagnosis of T2DM mellitus of at least one year duration were eligible for inclusion. Only patients who consented to participate and who underwent complete biochemical investigations including serum uric acid and renal function tests were included.

Exclusion Criteria: Individuals having a documented history of cardiovascular disease, hypertension, or chronic renal disease, gout, liver disorders, or those on uric acid–lowering drugs were excluded. Pregnant and lactating women were also excluded from the study to avoid confounding influences.

Bias: Throughout the study period, subjects were enrolled one after the other to reduce selection bias. The use of calibrated instruments and standardized laboratory methods helped to eliminate information bias. Confounding factors such as hypertension and pre-existing renal disease were controlled by applying strict exclusion criteria.

Data Collection: Data was collected using a predesigned proforma that included demographic details, clinical history, physical examination findings, and relevant biochemical investigations. Blood samples were collected under aseptic precautions to estimate fasting blood sugar, HbA1c, serum creatinine, eGFR, and serum uric acid levels.

Procedure: The goals of the study were explained to the eligible patients, and their agreement was acquired. Venous blood samples were taken for biochemical analysis following a thorough history and physical examination. The estimated glomerular filtration rate (eGFR), which is derived from serum creatinine levels, was used to evaluate renal function. To assess the connection between hyperuricemia and early DKD, patients were divided into groups according to their uric acid levels, and their renal parameters were examined.

Statistical Analysis: SPSS version 23.0 was used to enter all of the data for statistical analysis. Whereas categorical variables were displayed as frequencies and percentages, continuous variables were represented as mean ± standard deviation. For group comparisons, independent t-tests and chi-square tests were employed. To evaluate the independent relationship between hyperuricemia and early DKD,

correlation and multiple regression analyses were conducted. P-values less than 0.05 were regarded as statistically significant.

Results

The study included one hundred participants with T2DM mellitus. Participants ranged in age from 32 to 70 years old, with a mean age of 54.6 ± 9.2 years. There were 42 (42%) female patients and 58 (58%) male patients out of 100. The average number of years with diabetes was 7.8 ± 3.4.

Table 1: Baseline Demographic and Clinical Characteristics (n=100)

Variable	Mean ± SD / n (%)
Age (years)	54.6 ± 9.2
Male	58 (58%)
Female	42 (42%)
Duration of diabetes (years)	7.8 ± 3.4
BMI (kg/m²)	26.2 ± 3.8
HbA1c (%)	8.1 ± 1.3
Fasting blood sugar (mg/dL)	162.4 ± 39.6

Most participants were middle-aged males, overweight, and had poor glycemic control with elevated HbA1c.

Distribution of Hyperuricemia: Out of the 100 participants, 36 (36%) had hyperuricemia (defined as serum uric acid >7 mg/dL in males and >6 mg/dL in females).

Table 2: Distribution of Participants by Serum Uric Acid Levels

Group	Frequency (n)	Percentage (%)
Normal uric acid	64	64%
Hyperuricemia	36	36%
Total	**100**	**100%**

More than one-third of diabetic patients were found to have hyperuricemia, suggesting its common occurrence in this population.

Renal Function in Relation to Hyperuricemia: The mean eGFR among patients with hyperuricemia was 72.5 ± 12.3 mL/min/1.73m², compared to 88.6 ± 14.7 mL/min/1.73m² in those with normal uric acid levels. This difference was statistically significant ($p < 0.001$).

Table 3: Comparison of Renal Parameters in Patients with and without Hyperuricemia

Parameter	Normal Uric Acid (n=64)	Hyperuricemia (n=36)	p-value
Serum Creatinine (mg/dL)	0.92 ± 0.18	1.18 ± 0.24	<0.001*
eGFR (mL/min/1.73m²)	88.6 ± 14.7	72.5 ± 12.3	<0.001*
Urine Albumin-Creatinine Ratio (mg/g)	26.3 ± 12.8	41.7 ± 15.2	0.002*

*Statistically significant

Early diabetic kidney damage was indicated by considerably greater blood creatinine, poorer eGFR, and higher albuminuria in patients with hyperuricemia.

Regression Analysis: The independent relationship between hyperuricemia and renal impairment was assessed using multiple regression analysis, which was conducted after controlling for age, sex, BMI, length of diabetes, and HbA1c.

- Hyperuricemia was found to be a significant independent predictor of reduced eGFR ($\beta = -0.42$, $p < 0.001$).
- HbA1c and duration of diabetes also showed significant negative correlations with eGFR ($p < 0.05$).

Table 4: Multiple Regression Analysis for Predictors of Reduced eGFR

Variable	β Coefficient	p-value
Hyperuricemia	–0.42	<0.001*
Age	–0.15	0.07
Sex (Male)	–0.08	0.21
Duration of diabetes	–0.24	0.01*
HbA1c	–0.19	0.03*

*Statistically significant

Hyperuricemia showed the strongest independent correlation with reduced eGFR, even after adjusting for other confounding factors.

Summary of Findings

- 36% of diabetic patients had hyperuricemia.
- Patients with hyperuricemia had lower eGFR, higher serum creatinine, and greater albuminuria compared to those with normal uric acid levels.
- Regression analysis confirmed that hyperuricemia is an independent risk factor for early DKD.
- Compared to patients with normal uric acid levels, those with hyperuricemia had higher blood creatinine, decreased eGFR, and more albuminuria.
- Hyperuricemia is an independent risk factor for early diabetic kidney damage, according to regression analysis.

Discussion

The mean age of 100 T2DM patients in this cross-sectional study was 54.6 years, and men made up a slight majority (58%). A mean HbA1c above 8% indicated poor glycemic management and an average duration of diabetes of almost 8 years. 36% of subjects had hyperuricemia, which suggests that it is very common in diabetes people.

When compared to patients with normal uric acid levels, those with hyperuricemia showed noticeably worse renal metrics. They had higher urine albumin-creatinine ratios, decreased eGFR values, and raised serum creatinine levels—all indicators of early diabetic kidney impairment. Higher uric acid levels are strongly associated with early renal impairment in diabetes, as seen by the statistically significant difference between the two groups.

Moreover, multiple regression analysis showed that, even after controlling for confounding variables such age, sex, length of diabetes, BMI, and HbA1c, hyperuricemia was an independent predictor of decreased eGFR. While poor glycemic control and longer duration of diabetes also contributed significantly to declining renal function, hyperuricemia showed the strongest correlation.

These findings suggest that hyperuricemia is not just a coincidental metabolic abnormality but plays a potential role in the pathogenesis of DKD. Its high prevalence in diabetic patients and its independent correlation with renal dysfunction highlight the need for routine uric acid assessment in this group. Early detection and management of hyperuricemia could serve as an important preventive strategy in delaying the onset or progression of diabetic nephropathy, alongside conventional control of blood sugar levels.

Hyperuricemia is now recognized as a separate risk factor for the onset and advancement of DKD. Elevated uric acid was found to be a major predictor of the start and progression of DKD in a study of Chinese patients with T2DM, and logistic regression confirmed this relationship [10]. Similarly, another prospective cohort analysis demonstrated that hyperuricemia significantly contributed to a faster decline in (eGFR) and increased albuminuria in type 2 diabetic patients, even after adjusting for confounders [11].

Further support comes from cross-sectional data showing that hyperuricemia is independently correlated with the prevalence of microalbuminuria in T2DM, reinforcing its role in early renal impairment [12]. In addition, uric acid levels were found to predict the onset of early DKD, suggesting that hyperuricemia plays a role before significant renal dysfunction becomes apparent [13]. Beyond renal endpoints, evidence also indicates that hyperuricemia worsens both renal and cardiovascular outcomes in DKD patients, underscoring its dual impact on metabolic and vascular health [14]. Overall, the body of evidence after 2018 consistently supports hyperuricemia as a significant predictor of early DKD and its progression, making serum uric acid a valuable biomarker in regression-based risk assessment and a potential target for therapeutic intervention.

Conclusion

Hyperuricemia was found to be highly prevalent among diabetic patients and showed a significant independent correlation with early DKD. Patients with elevated uric acid levels had impaired renal function and greater albuminuria compared to those with normal levels. These findings suggest that routine monitoring and timely management of hyperuricemia, along with good glycemic control, may help in preventing or delaying the progression of diabetic nephropathy.

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