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ORIGINAL ARTICLE

Hyperuricemia in diabetic kidney disease patients presenting to a tertiary care hospital of Khyber Pakhtunkhwa: a cross sectional Study

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ABSTRACT

Background: Hyperuricemia is commonly observed in patients with diabetic kidney disease (DKD) and is believed to contribute to worsening renal outcomes. Limited local data exist to highlight the burden of hyperuricemia in these patients in Pakistan. We want to determine the prevalence of hyperuricemia in patients with DKD presenting to a tertiary care hospital in Khyber Pakhtunkhwa.

Methods: This Descriptive cross-sectional study was conducted at the Nephrology unit of Lady Reading Hospital, Peshawar, from May to October 2024. A total of 237 patients having T2DM and chronic kidney disease were enrolled using non-probability consecutive sampling. DKD was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 and/or albuminuria >30 mg/g for more than 3 months. Hyperuricemia was characterized by serum uric acid concentrations above 7.0 mg/dL in males and 6.0 mg/dL in females. The data were analyzed using SPSS version 24, with a p-value of ≤ 0.05 considered statistically significant.

Results: Of the 237 participants, 127 (53.6%) were males and 110 (46.4%) females, with a mean age of 51 ± 9.02 years. Hyperuricemia was observed in 131 patients (55.3%). The condition was more prevalent in females than in males ($p < 0.05$). A significant association was noted between hyperuricemia and the duration of diabetic kidney disease.

Conclusion: Hyperuricemia is highly prevalent among diabetic kidney disease patients, affecting over half of the studied population. These findings underscore the need for routine screening and early intervention to potentially slow disease progression and reduce related complications.

Keywords: Chronic Kidney Disease, Diabetes Mellitus, Diabetic Kidney Disease, Hyperuricemia, Uric Acid

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Introduction

Diabetic kidney disease (DKD), a major microvascular complication of diabetes, is a leading cause of end-stage renal disease (ESRD). It is defined by a sustained eGFR <60 mL/min/1.73 m² and/or albuminuria >30 mg/g for over three months in patients with long-term diabetes, after excluding other CKD causes (1, 2). DKD usually appears after 10 years of diabetes (or ≥5 years in type 1), but may be present at diagnosis in type 2. As diabetes becomes more prevalent, DKD adds to healthcare burden and is linked to high morbidity and mortality (3). It affects 30–40%

of diabetics, significantly increasing their cardiovascular risk (4, 5). Contributing factors include hyperglycemia-induced oxidative stress, inflammation, and profibrotic pathways that damage glomeruli and tubulointerstitial tissue (6).

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Hyperuricemia, defined as serum uric acid >7 mg/dL in men and >6 mg/dL in women (7), is increasingly recognized in DKD for its role in worsening renal outcomes. It results from excessive production or reduced excretion, especially with impaired renal function (8). It can be both a cause and consequence of renal failure, influenced by genetics, diet, and ethnicity (9). Genetic variations in urate transporters may explain higher hyperuricemia rates in Asian populations (10, 11). In DKD, it may worsen kidney injury via oxidative stress, inflammation, endothelial dysfunction, RAAS activation, and reactive oxygen species (12). This perpetuates a cycle of renal damage and uric acid buildup.

Studying hyperuricemia in DKD offers insights into patients' metabolic profiles and highlights the need for early intervention. Regular uric acid monitoring may help identify those at greater risk of rapid progression. Its association with cardiovascular complications further underscores its clinical importance (13, 14).

This study explores hyperuricemia prevalence in DKD patients at a tertiary care center in Khyber Pakhtunkhwa, aiming to understand its impact on disease progression and guide better treatment strategies. Managing hyperuricemia with diet and medications may slow progression to ESRD and reduce healthcare burden.

Methods

This study was conducted at the Nephrology Unit of MTI, Lady Reading Hospital, Peshawar, from May to October 2024. The Institutional Ethical and Review Board (Approval No. 251/LRH/MTI) granted ethical approval. A non-probability consecutive sampling technique was employed.

Assuminga 19% prevalence of hyperuricemia in DKD patients, a sample size of 237 was calculated using the WHO calculator with a 95% confidence level and 5% margin of error (15). Adult patients with CKD secondary to type 2 diabetes attending the Nephrology OPD were consecutively enrolled until the target was met. Patients with type 1 diabetes, known hyperuricemia conditions (e.g., gout, malignancies, psoriasis, hemolytic disorders), and those taking medications known to raise serum uric acid levels were excluded. All participants provided written informed permission after being explained the study's purpose and potential benefits.

Diabetes was identified through patient history, medical documentation, and standard diagnostic thresholds (FBS ≥126 mg/dL, RBS ≥200 mg/dL, or HbA1c ≥6.5%). Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m², calculated using the MDRD formula.

Each participant provided a 5 mL venous blood sample. Hyperuricemia was characterized by serum uric acid levels exceeding 7.0 mg/dL in males and 6.0 mg/dL in females.

Demographic and clinical data such as age, gender, height, weight, body mass index (BMI), residential location (urban or rural),

duration of diabetes and CKD, hypertension status, and serum uric acid level were recorded using a structured data collection form. The inclusion and exclusion criteria were strictly followed to minimize selection bias.

Data analysis was conducted using SPSS version 24. Quantitative variables, including age, height, BMI, and duration of illness, were summarized as mean ± standard deviation. Categorical variables such as gender, hypertension, and hyperuricemia were reported as frequencies and percentages. The data were stratified by age and gender. The chi-square test was employed to compare categorical variables, with a p-value ≤0.05 considered statistically significant. Findings were illustrated through tables and graphical representations.

Results

A total of 237 patients with diabetic kidney disease were enrolled in the study. Among them, 127 (53.7%) were male and 110 (46.4%) were female. The overall mean age of participants was 51 ± 9.02 years. Gender-wise, the mean age was 52.86 ± 8.72 years for females and 49.96 ± 9.12 years for males. An independent t-test revealed a statistically significant difference in age between male and female participants (t = 2.05, p = 0.042).

Table 1. Age Distribution of Participants (n = 237)

Age Group (Years)	Frequency	Percentage (%)
31–40	37	15.6
41–50	65	27.4
51–60	71	30.0
>60	64	27.0
Total	**237**	**100.0**

The average body mass index (BMI) was 27.57 ± 2.57 kg/m², placing the majority of patients in the overweight category. The mean duration of diabetic kidney disease (DKD) was 4.57 ± 3.18 years. The cohort's mean serum uric acid level was 7.23 ± 2.26 mg/dL

Hyperuricemia was observed in 131 patients (55.3%). Gender-wise analysis showed that 59 males and 72 females had hyperuricemia, while 68 males and 38 females had normal uric acid levels (Table 2). The frequency of hyperuricemia was notably higher among female patients, which may reflect gender-specific thresholds and physiological differences.

Table 2. Gender-wise Frequency of Hyperuricemia

Gender	Hyperuricemia	Normal Uric Acid	Total
Male	59	68	127
Female	72	38	110
Total	**131**	**106**	**237**

Age-wise distribution of hyperuricemia is detailed in Table 3. The highest frequency was noted in the 51–60 years age group, followed by those aged 61 and above. A trend of increasing hyperuricemia prevalence with age was observed.

Table 3. Age-wise Distribution of Hyperuricemia

Age Group (Years)	Hyperuricemia (↑Uric Acid)*	Normal Uric Acid	Total
31–40	25	14	39
41–50	28	34	62
51–60	31	39	70
>60	47	19	66
Total	**131**	**106**	**237**

Figure 1 illustrates the relationship between the duration of diabetic kidney disease and the presence of hyperuricemia. Patients with longer disease duration were more likely to exhibit elevated serum uric acid levels, suggesting a potential progressive link between DKD severity and metabolic derangements.

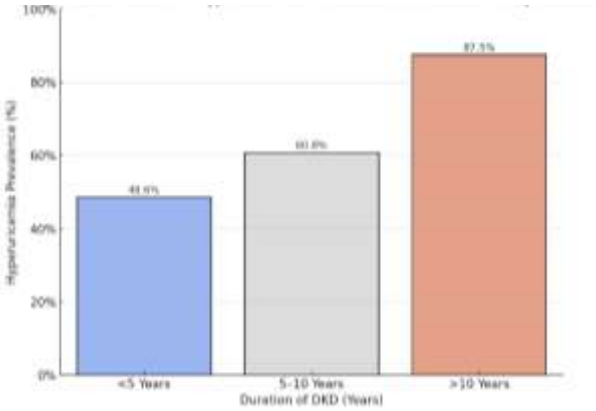

Figure 1. Correlation of Hyperuricemia with Duration of Diabetic Kidney Disease

Table 4. Summary of Clinical and Biochemical Characteristics

Variable	Mean ± SD
Age (years)	51.00 ± 9.02
BMI (kg/m²)	27.57 ± 2.57
Duration of DKD (years)	4.57 ± 3.18
Serum Uric Acid (mg/dL)	7.23 ± 2.26

These findings highlight the need for regular monitoring of serum uric acid levels in patients with DKD as part of a comprehensive management strategy to mitigate renal and cardiovascular complications.

Discussion

This study reveals that hyperuricemia is highly prevalent among patients with diabetic kidney disease (DKD), affecting 55.3% of the studied cohort. This finding has critical implications, especially within the context of a developing region such as Khyber Pakhtunkhwa, where metabolic disorders and their complications are often underdiagnosed and under-managed. The strong association observed between hyperuricemia and prolonged duration of DKD underscores the need to consider serum uric acid levels as both a diagnostic and prognostic biomarker in this population.

The overall prevalence reported in this study aligns with findings from other regional studies conducted in similar patient populations. A study from Pakistan by Gulzar et al. reported hyperuricemia in 52% of type 2 diabetic patients with nephropathy (16). Similarly, Mohsin et al. found elevated uric acid levels in 56.4% of pre-dialysis CKD patients, highlighting the overlap between hyperuricemia and progressive renal dysfunction (17). Our findings also reinforce the concept that hyperuricemia is not merely a bystander but potentially a key player in accelerating renal decline, as proposed by Johnson et al., who suggested uric acid may activate pro-inflammatory pathways, oxidative stress, and endothelial dysfunction, all of which can worsen renal outcomes (18).

One significant and novel observation in our study is the higher frequency of hyperuricemia in female patients (65.4%) compared to males (46.5%), despite males generally having a higher physiological threshold for uric acid. This gender difference may be partially attributed to hormonal and post-menopausal changes affecting urate metabolism, but also points toward the necessity for tailored screening thresholds and clinical awareness in female DKD patients. While many studies have observed higher baseline uric acid in males due to testosterone-mediated uricosuria, the reversal seen here might suggest gender-specific vulnerability in DKD populations that merits further research.[12]

The observed relationship between BMI and hyperuricemia is also noteworthy. The mean BMI in our cohort was 27.57 kg/m², indicating overweight status, which is consistent with the well-established association between obesity and hyperuricemia. Obesity contributes to insulin resistance; reduced renal urate excretion, and

increased urate production (9). Thus, lifestyle interventions targeting weight reduction may not only benefit glycemic control but also ameliorate hyperuricemia, potentially slowing DKD progression.

Importantly, our data support the hypothesis that serum uric acid levels increase with the duration of diabetic kidney disease (DKD), as patients with longer disease duration showed significantly higher uric acid concentrations suggesting a cumulative metabolic burden or progressive decline in urate excretion. This is consistent with international evidence linking longer-standing diabetes and renal dysfunction with increasing hyperuricemia (3). The role of hyperuricemia as both a marker and potential driver of disease progression raises important questions about the timing and indications for urate-lowering therapy.

While the causal relationship between hyperuricemia and DKD progression remains debated, emerging evidence from interventional studies provides cautious optimism. Kim et al. showed that urate-lowering therapies such as allopurinol and febuxostat may have renoprotective effects, though findings have been inconsistent and require larger randomized trials for confirmation (8). If validated, early identification and management of hyperuricemia could represent a low-cost adjunctive strategy to delay the need for renal replacement therapy in resource-limited settings.

This study's contribution is particularly significant due to the limited data on uric acid disturbances in Pakistani DKD populations. By offering localized evidence, this research adds to the body of knowledge required for crafting regional guidelines and screening protocols. The incorporation of routine uric acid testing in the management of DKD patients could aid in risk stratification and individualizing treatment plans, particularly in healthcare systems where access to advanced diagnostics or nephrology services may be constrained.

However, this study is not without limitations. The cross-sectional design precludes causality inference, and the convenience sampling method may introduce selection bias. Additionally, we did not assess the influence of dietary habits, socioeconomic status, or medication history (such as the use of urate-lowering agents), all of which could confound the association between DKD and hyperuricemia. Future longitudinal studies with broader sampling and controlled variables are needed to clarify causation and explore whether intervention on hyperuricemia translates into tangible clinical benefits in this demographic.

Conclusion

This study underscores the importance of routine screening for hyperuricemia in patients with diabetic kidney disease (DKD), reinforcing its potential role in disease progression. The findings align with existing literature while contributing novel regional data, offering valuable insights that may support more personalized management strategies for DKD.

Recommendations:

Furthermore, the observed associations highlight the need for further research to elucidate the underlying mechanisms linking hyperuricemia and DKD. Such investigations could inform the development of future treatment guidelines tailored to high-risk populations in this region.

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References

1. Tuttle KR, Bakris GL, Bilous RW, Chiang JL, de Boer IH, Goldstein-Fuchs J, et al. Diabetic kidney disease: a report from an ADA consensus conference. *Am J Kidney Dis.* 2014;64(4):510–33.
2. American Diabetes Association. 10. Microvascular complications and foot care. *Diabetes Care.* 2023;46(Suppl 1):S135–51.
3. Alicic RZ, Rooney MT, Tuttle KR. Diabetic kidney disease: challenges, progress, and possibilities. *Clin J Am Soc Nephrol.* 2017;12(12):2032–45.
4. Duru OK, Middleton T, Tewari MK, Norris KC. The landscape of diabetic kidney disease in the United States. *Curr Diab Rep.* 2019;19(3):17.
5. Rossing P, Persson F, Frimodt-Møller M. Prognosis and treatment of diabetic nephropathy: recent advances and perspectives. *Nephrol Ther.* 2018;14(Suppl 1):S31–7.
6. Han Y, Ma W, He T, Song Z, Huang X, Gong S. Association of uric acid with diabetic kidney disease in patients with type 2 diabetes: a meta-analysis. *BMC Endocr Disord.* 2020;20(1):1.
7. Johnson RJ, Nakagawa T, Sanchez-Lozada LG, Shafiu M. Sugar, uric acid, and the etiology of diabetes and obesity. *Diabetes.* 2013;62(10):3307–15.
8. Kim IY, Kim JH, Kim MJ, Kwak H, Lee S, Lee Y, et al. Effect of uric acid lowering therapy on renal outcomes: a systematic review and meta-analysis. *Am J Nephrol.* 2020;51(5):372–87.
9. Liu P, Chen Y, Wang B, Zhang F. Dietary factors and the risk of hyperuricemia: meta-analysis and systematic review. *Nutr Rev.* 2018; 76(4):310–21.
10. Kodama S, Saito K, Yachi Y, Asumi M. Association between serum uric acid and development of type 2 diabetes. *Diabetes Care.* 2009; 32(9):1737–42.
11. Fox IH, Kelley WN. Studies on the mechanismof fructose-induced hyperuricemia in man. *Metabolism.* 1972; 21(8):713–21.
12. Kuwabara M, Borghi C, Cicero AFG, Jafar TH, Johnson RJ, Kang DH, et al. Elevated serum uric acid and cardiovascular disease: a narrative review. *Heart.* 2020;106(10):726–35.
13. Kanbay M, Jensen T, Solak Y, Le M. Uric acid in metabolic syndrome: from an innocent bystander to a central player. *Eur J Intern Med.* 2016; 29:3–8.
14. Kuwabara M. Hyperuricemia, cardiovascular disease, and hypertension. *Pulse (Basel).* 2016;3(3–4):242–52.
15. Shah N, Amanullah SJ, Marwat MA. Association of hyperuricemia with diabetic nephropathy in type 2 diabetes mellitus. *Khyber J Med Sci.* 2014; 7(2):267.
16. Gulzar A, Muhammad K, Muhammad A, Babar M, Imran DK, Muhammad T. Frequency of hyperuricemia in type-2 diabetes mellitus and its relation with diabetic nephropathy. *Pak Armed Forces Med J.* 2023; 73(1):199–203.
17. Qayyum M, Butt B, Khan G. Hyperuricemia in pre-dialysis chronic kidney disease patients: a single centre experience. *Pak Armed Forces Med J.* 2019; 69(1):66–70.
18. Johnson RJ, Bakris GL, Borghi C, Chonchol MB, Feldman D, Lanaspa MA, et al. Hyperuricemia, acute and chronic kidney disease, hypertension, and cardiovascular disease: report of a scientific workshop organized by the National Kidney Foundation. *Am J Kidney Dis.* 2018;71(6):851–65.

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All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed.