

# Relationship Between Diabetes and Hyperuricemia in Zakho City – Kurdistan Region of Iraq: A Retrospective Cross-Sectional Study

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## Abstract

**Objective:** This retrospective cross-sectional study aimed to explore the prevalence of hyperuricemia among patients with type 2 diabetes mellitus and identify associated factors.

**Methods:** A total of 228 adult patients diagnosed with type 2 diabetes mellitus were included in this study. Data including demographic characteristics, clinical parameters, and serum uric acid levels were collected from medical records. Patients were categorized into two groups based on uric acid levels: hyperuricemia ( $\geq 7$  mg/dL for males,  $\geq 6$  mg/dL for females) and non-hyperuricemic. Descriptive statistics and unpaired t-tests were utilized for analysis.

**Results:** A total of 228 patient were included (60.53% of them were female), according to standard guidelines hyperuricemia was defined as ( $\geq 7$  mg/dl for male and  $\leq 6$  mg/dl for female) among them, 39.47% exhibited hyperuricemia. Mean uric acid level was  $5.84 \pm 2.03$ . Significant associations were observed between uric acid levels and age ( $P = 0.0003$ ), marital status ( $P = 0.0358$ ), duration of diabetes ( $P = 0.0013$ ), and HbA1c levels ( $P < 0.0001$ ). However, other factors such as gender, smoking status, family history of diabetes, body mass index, and waist circumference did not show significant associations with uric acid levels.

**Conclusion:** This study highlights a notable prevalence of hyperuricemia among patients with type 2 diabetes mellitus. Factors such as older age, longer duration of diabetes, and poorer glycemic control were associated with higher uric acid levels. These findings underscore the importance of monitoring and managing uric acid levels in diabetic patients to mitigate potential metabolic complications. Further prospective studies are warranted to elucidate the underlying mechanisms and clinical implications of this relationship.

**Keywords:** Diabetes mellites, hyperuricemia, uric acid level, Zakho, Iraq

## Introduction

Type 2 diabetes mellitus (T2DM) is a chronic condition characterized by hyperglycemia resulting from insulin resistance and impaired insulin secretion.<sup>1</sup> Sustained hyperglycemia can lead to both microvascular complications affecting the eyes, nerves and kidneys, as well as macrovascular complications including cardiovascular disease.<sup>2</sup> Therefore, optimizing glycemic control is a key goal in T2DM management.

Worldwide there has been a notable global rise in the prevalence of hyperuricemia. Numerous studies have been conducted to evaluate the association of high serum uric acid levels in different groups to various chronic diseases.<sup>3-8</sup> During the past few decades, the Middle Eastern countries, including Kurdistan region of Iraq, has witnessed a significant economic and environmental advancements.<sup>9</sup> The traditional way of life, marked by its distinctive features, dietary practices, and physical activity routines, has shifted towards a more modernized western lifestyle.<sup>10,11</sup>

Emerging evidence suggests that elevated serum uric acid levels may be linked to poorer glycemic control in T2DM patients.<sup>12,13</sup> Uric acid is the final product of purine metabolism, and hyperuricemia has been associated with obesity, hypertension, dyslipidemia and insulin resistance.<sup>14</sup> Several studies have found positive correlations between serum uric acid levels and hemoglobin A1c (HbA1c), a marker of glycemic control, in T2DM patients.<sup>15,16</sup> A 2020 meta-analysis of 18 studies found a significant positive association between uric acid levels and HbA1c.<sup>17</sup> Furthermore, baseline uric acid was identified as an independent predictor of future glycemic control in a 5-year prospective study of patients with new-onset

T2DM.<sup>18</sup> The mechanisms by which uric acid may impact glucose metabolism are not fully elucidated. Proposed pathways include uric acid-induced inflammation, oxidative stress, and vascular dysfunction.<sup>19</sup>

Limited research has been conducted to investigate the relationship between diabetes and hyperuricemia among general population in Kurdistan Region, Iraq. In this study we aimed to explore the percentage of hyperuricemia and correlation of hyperuricemia to glycemic control indexed by HbA1c in our patients.

## Material and Methods

### Study Design and Data Collection

This was a retrospective cross-sectional study conducted in Zakho city, Kurdistan Region, Iraq. The records of all patients who visited the Zakho Diabetes Center at Zakho General Hospital from January 1, 2022, to May 1, 2023, were examined. A total of 228 patients were included, all of whom were 18 years of age and older and had been diagnosed with type 2 diabetes mellitus.

### Inclusion and Exclusion Criteria

Inclusion criteria were type 2 Diabetes Mellites patient, age more than 18 years, having a glycated hemoglobin (HbA1c) level measured in the past 3 months and no changes to diabetic medications in the same periods. Exclusion criteria include: Type 1 Diabetes, pregnancy, active cancer treatment, glucocorticoid therapy, recent hospitalization and chronic kidney disease.

## Data Collection

Demographic and clinical data were collected through review of patient's medical record and included: age, sex, marital status, residence, smoking status, family history of Diabetes, body mass index, waist circumference, Diabetes duration and most recent HbA1c. Blood samples were collected by venipuncture after an 8 to 10 hour overnight fast. Serum uric acid levels were measured enzymatically with an audit diagnostic URCA Flex® reagent cartridge. HbA1c was measured using high-performance liquid chromatography HPLC-D-10 system (Bio-Rad Laboratories, Inc. USA).

## Study Tool

Patients were divided into 2 groups, group 1 those without hyperuricemia and group 2 those with hyperuricemia, hyperuricemia was defined as more than or equal to 7 mg/dL for male and more than or equal to 6 mg/dL for female.<sup>20</sup>

## Statistical Analysis

Descriptive statistics using (GraphPad Prism) was used to compare both groups (those with and those without hypouricemia) regarding sex, residence, family history, smoking status, duration of diabetes (newly diagnosed vs already diagnosed), body mass index, waist circumference and whether diabetes is controlled or not. A p-value of less than 0.05 was considered statistically significant.”

## Ethical Statement

The Ethics and Scientific Committee approved the final version of the survey at the University of Zakho, College of Medicine, Kurdistan Region of Iraq. Informed consent was obtained from all participants.

## Results

### Basic Demographic Characteristics

In this study, 228 patients were included, among them 138(60.53%) were female, participants age ranged from 27 to 76 years (the mean age:  $52.62 \pm 10.93$  years), 78 patients (34.21%) were active smoker, 159 patients (69.74%) were having positive family history for diabetes mellitus in their 1st degree relatives and 90 patients (39.47%) in our study sample were having hyperuricemia (Table 1).

## Factors Affecting Uric Acid Level

When we studied the factors affecting uric acid level using unpaired t-test method, we found that the factors that has a significant association with uric acid level were age, marital status, duration of diabetes and Hba1c% level p. value respectively were (0.0003, 0.0358, 0.0013, <0.0001). Other factors did not show significant association with uric acid level (Table 2).

## Discussion

Hyperuricemia, a condition characterized by high levels of uric acid in the blood, has been found to have a significant correlation with an elevated risk of developing Diabetes Mellitus, as evidenced by several studies.<sup>21-23</sup> One of

Table 1. Basic demographic characteristics of the study

Age (years)	Frequency (f) /Mean $\pm$ SD	Percentage
21–30	7	3.07
31–40	23	10.09
41–50	66	28.95
51–60	81	35.53
61–70	43	18.86
71–80	8	3.51
Mean $\pm$ SD	$52.62 \pm 10.93$	
Gender		
Male	90	39.47
Female	138	60.53
Smoker	78	34.21
Family history of diabetes	159	69.74
Age at diagnosis of DM (years)	$46.16 \pm 10.86$	
Duration of DM (years)	$6.45 \pm 6.53$	
BMI (kg/m <sup>2</sup> )	$29.45 \pm 6.06$	
HbA1c (%)	$9.03 \pm 2.24$	
Uric acid	$5.84 \pm 2.03$	39.47%
Waist circumference	$90.61 \pm 12.60$	

Table 2. Factors affecting uric acid level

Factors	Normal	Hyperuricemia	P value	CI 95%
Smoking	47/138 (34.06%)	31/90 (34.44%)	0.4933	–0.3078 to 0.6374
Residence (Inside city)	125/138 (90.58%)	83/90 (92.22%)	0.2345	–0.1765 to 0.7182
Marital status (Married)	136/138 (98.55%)	86/90 (95.56%)	0.0358	0.06077 to 1.759
Family history	97/138 (70.29%)	62/90 (68.89%)	0.2816	–0.2653 to 0.9079
Age (average $\pm$ Std)	$52.33 \pm 11.05$	$53.07 \pm 10.78$	0.0003	–15.14 to –4.473
Duration of diabetes	$5.34 \pm 6.12$	$8.17 \pm 6.80$	0.0013	–4.534 to –1.118
HbA1c% (average $\pm$ Std)	$8.31 \pm 1.74$	$10.15 \pm 2.47$	<0.0001	–2.495 to –1.358
BMI (average $\pm$ Std)	$29.59 \pm 5.95$	$29.25 \pm 6.25$	0.6872	–1.292 to 1.957
Waist circumference (average $\pm$ Std)	$90.1 \pm 12.82$	$91.39 \pm 12.28$	0.4519	–4.654 to 2.079

the potential rationales behind this relationship lies in the notable connection between hyperuricemia and insulin resistance, a key factor in the pathogenesis of Diabetes Mellitus.<sup>6</sup> Other explanation is the role that hyperuricemia may play in the acceleration of pancreatic beta cell death, which can further exacerbate the development of diabetes.<sup>24</sup> Approximately, 1 in 11 new cases of diabetes were statistically attributed to hyperuricemia.<sup>25</sup> Given the prevalence of hyperuricemia in the population, it becomes imperative to delve deeper into its mechanisms and how it impacts the pathophysiology of diabetes.<sup>26</sup> This study aims to investigate the prevalence of hyperuricemia and its correlation with glycemic control, indexed by HbA1c levels, among our patients. Understanding this relationship is crucial for improving patient management and developing preventive measures for associated health complications.

The prevalence of hyperuricemia in our study sample was 39.47% which was comparable to (Verah et al) a cross sectional study done in Uganda and they found that the prevalence of hyperuricemia in diabetic patients was 38.57%.<sup>27</sup> Our study investigates the link between glycosylated hemoglobin (HbA1c) levels and uric acid concentrations. Through careful analysis, we found a statistically significant association between high HbA1c levels and heightened serum uric acid levels, this positive correlation was also the case in Babakir et al and Bandaru et al.<sup>28,29</sup> This positive correlation may point to a potential interaction between glucose metabolism and uric acid regulation, providing insight into the intricate physiological processes underlying these biomarkers. Some researchers proposed that the possible mechanism linking hyperuricemia to poorly controlled blood sugar in people with diabetes may be related to the elevated blood sugar interfering with the reabsorption of uric acid in the kidneys, specifically in the proximal tubule portion of the nephron.<sup>30,31</sup>

Mean age in our study was  $46.16 \pm 10.86$  which was comparable to other studies,<sup>32,33</sup> and there was significant association between age and hyperuricemia ( $P = <0.001$ ) which was also the case in Singh, S.K., et al.<sup>32</sup> This association mainly is related to reduced glomerular function in elderly patients<sup>34</sup> and to that people with advanced age have markedly decreased hormones and enzymes that play role in decreasing uric acid.<sup>35</sup> Furthermore, aside from age, married patients exhibited a notably elevated uric acid level ( $P = 0.036$ ). This observation may be attributed to the higher average age of married patients compared to their single counterparts. Further investigations are needed to explore such a relationship.

Our data revealed positive correlation between the duration of type 2 diabetes and the level of uric acid. These findings were also evident in Niharika et al. and Kalyani et al.,<sup>36,37</sup>

while other study done by Stephen et al concluded that longer duration of diabetes being linked to a greater decline in uric acid concentration.<sup>38</sup> The decrease in the uric acid levels was attributed to possible changes in lifestyle or medication use subsequent to a diabetes diagnosis which may have role in altering uric acid production.

Smoking history, residence (whether inside or outside the city), family history of diabetes, and anthropometric measures like (body mass index and waist circumference) were not found to have significant association with hyperuricemia. This in contrast to other studies where these factors were found to have significant correlation with hyperuricemia.<sup>39-47</sup> This may not be easy to explain as it may be related to several intermingling factors including sample size, study design in addition to genetic variations between population.

This study has limitations. First, the study was performed retrospectively; hence, it may have some gaps when collecting and analyzing data. Second, since this study relied only upon a single center (University of Zakho - College of Medicine), generalization to other populations or settings may be limited. Third, the sample size for this study was small being 228 subjects which could reduce its analysis power statistically and ability to detect meaningful relationships. A larger prospective multicenter study is needed to investigate the relationships between uric acid levels and other factors is needed.

## Conclusion

Our study has given us useful insights into the prevalence and probable causative factors of hyperuricemia among type 2 diabetes mellitus patients.

Our analysis revealed significant association between hyperuricemia and some demographic and clinical variables such as; age, marital status, duration of diabetes and HbA1c levels. Therefore, these results indicate the necessity of taking them into consideration when dealing with patients diagnosed with type 2 diabetes mellitus.

Larger scale prospective studies across different populations are needed to confirm these results or build on them further. These studies will additionally enhance our understanding of the relationship between hyperuricemia and factors associated with diabetes, thereby offering improved strategies for preventing and managing diabetic complications.

## Conflict of Interest

The authors declare no conflict of interest. ■

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