RESEARCH PAPER

Evaluation of Fractional Uric Acid Excretion in Type 2 Diabetes patients treated with SGLT2 Inhibitors

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ABSTRACT

Introduction: An increased serum uric acid (UA) level, usually greater than 357 mmol/L in women and 416 mmol/L in males, is known as hyperuricemia. Hyperuricemia is linked to an increased risk of hypertension, cardiovascular events, and the onset and advancement of chronic kidney disease (CKD). A new class of antidiabetic drugs called sodium-glucose cotransporter-2 (SGLT-2) inhibitors lowers plasma glucose levels by boosting urine glucose excretion and decreasing renal reabsorption. However, little is known about sodium-glucose cotransporter 2 (SGLT2) inhibitors and the fractional excretion of uric acid.

Materials and Methods: The study included patients aged 18–65 years with type 2 diabetes who were eligible for SGLT2 inhibitor therapy which was conducted in the Department of Biochemistry JNMC.28 patients attending KLEs Endocrine OPD were enrolled in this study. Serum uric acid, serum creatinine, Urine uric acid, and Urine creatinine levels were estimated and FEUA was calculated using the formula.

Results: Blood uric acid levels ranged from 1.01 to 7.88 mg/dL at baseline, with a mean of 5.05 ± 1.65 mg/dL. Serum creatinine levels ranged from 0.58 to 3.42 mg/dL, with an average of 1.25 ± 0.61 mg/dL. Urine uric acid levels ranged from 21.73 to 141.32 mg/dL, with a mean of 74.4 ± 35.6 mg/dL. Urinary creatinine levels ranged from 68.44 to 243.44 mg/dL, with an average of 148.43 ± 55.69 mg/dL. The ratio of renal excretion of uric acid ranged from 2.56% to 41.23%, with an average of 14.52 ± 10.72%. Conclusion: The study showed that SGLT2 inhibitor medication significantly lowers serum uric acid levels while increasing fractional excretion of uric acid in patients with type 2 diabetes. These results suggest that, regardless of variations in serum creatinine or glomerular filtration rate, SGLT2 inhibitors have strong uricosuric effects by increasing renal uric acid clearance.

Keywords: Fractional uric acid excretion, SGLT2inhibitors, Diabetes, Renal damage

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INTRODUCTION

An increased serum uric acid (UA) level, usually greater than 357 mmol/L in women and 416 mmol/L in males, is known as hyperuricemia [1]. Obesity, the metabolic syndrome, and high sugar and purine intake are significant risk factors for hyperuricemia. Once known as the "rich man's disease" (because only the wealthy could afford a diet of red meat, wild game, shellfish, and organ meats), gout is a classic disorder of excess nutrients, especially an excess of glucose and purines [2,3,4].

Urate crystals are deposited in the kidneys (nephrolithiasis) and joints (gout) as a result of either excessive UA production or poor excretion [5,6]. Hyperuricemia is linked to an increased risk of hypertension, cardiovascular events, and the onset and advancement of chronic kidney disease (CKD) [7]. According to reports, coupled asymptomatic hyperuricemia affects 60% of CKD patients [8].

In order to manage asymptomatic hyperuricemia, non-pharmacologic therapies that concentrate on dietary and lifestyle changes are essential [9, 10]. Xanthine oxidase inhibitors continue to be the first-line pharmacological treatment for symptomatic cases [11]. However, dosage issues, side effects, and patient nonadherence frequently limit the efficacy of existing urate-lowering treatments [12]. This emphasizes the necessity of looking for safer and more successful alternative medicines. A new class of antidiabetic drugs called sodium-glucose cotransporter-2 (SGLT-2) inhibitors lowers plasma glucose levels by boosting urine glucose excretion and decreasing renal reabsorption [13]. It is still uncertain how precisely SGLT2 inhibitors encourage the excretion of uric acid. Nevertheless, no studies using medications that decrease uric acid have produced encouraging outcomes. However, little is known about sodium-glucose cotransporter 2 (SGLT2) inhibitors and the fractional excretion of uric acid, which have been linked to kidney-protective effects in part because they lower plasma uric acid. In order to determine the impact of SGLT2 inhibitors on serum uric acid and fractional excretion of uric acid in patients with Type 2 Diabetes Mellitus, the current study was conducted.

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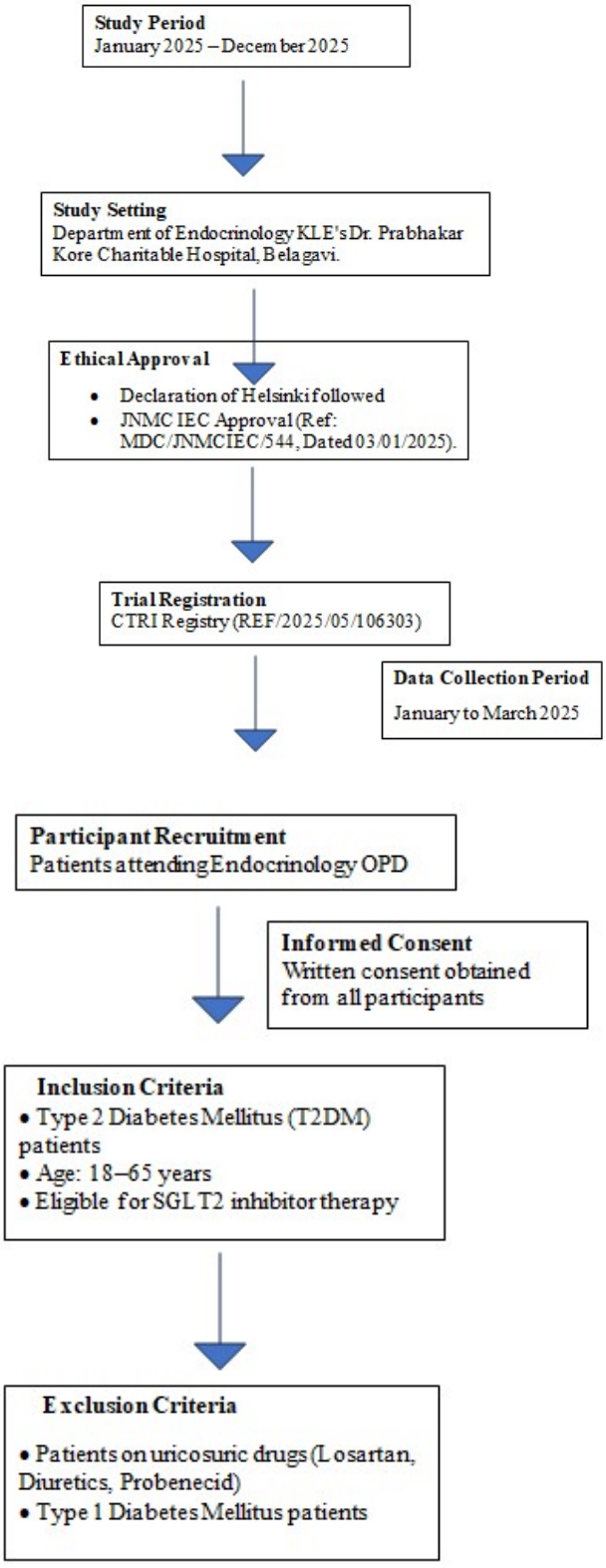
MATERIALS AND METHODS



The sample size was calculated using the formula for comparing paired means:

$$n = \frac{(Z\alpha + Z_{1-\beta})^2 \, (SD_1^2 + SD_2^2)}{(\overline{x_1} - \overline{x_2})^2}$$

$Z_{\frac{\alpha}{z}}$ = 1.96 (95% confidence Interval)

$Z_{1-\beta}$ = 0.84 (80% power of the test)

A sample size of 28 individuals was determined using the above statistical formula to identify clinically significant variations in the primary outcomes based on preliminary data.

A thorough medical history and physical examination was performed to take the baseline values (before starting SGLT2 inhibitors). According to the treating Endocrinologist clinical assessment, patients were started on SGLT2 inhibitor therapy (Dapagliflozin 10 mg) along with their current antidiabetic drugs. Patients returned for a follow-up assessment following three months of SGLT2 inhibitor medication.

Spot urine samples (10 mL) were collected in sterile containers, and fasting blood samples (3 mL) were obtained by venipuncture in plain or gel vacutainer tubes at baseline and three-month follow-up visits.

Serum was extracted from blood samples by centrifuging them for ten minutes at 3000 rpm. Enzymatic techniques were used to measure serum uric acid (mg/dl), serum creatinine (mg/dl), urine uric acid (mg/dl), and urine creatinine (mg/dl) on a fully automated analyser (Roche/Hitachi Cobas c 311, Cobas 501/502). Quality control procedures were followed according to manufacturer guidelines.

FEUA was calculated using the formula:

FEUA (%) = (Urine uric acid × Serum creatinine) / (Urine creatinine × Serum uric acid) × 100

Statistical Analysis

SPSS software (version 23.0) was used to analyse the data. The mean ± standard deviation (SD) was used to express continuous variables. The Kolmogorov-Smirnov test was used to determine whether the distribution was normal. Biochemical parameters were compared between baseline and the three-month follow-up using paired t-tests. The association between urine uric acid and FEUA was evaluated using Pearson correlation analysis. Statistical significance was defined as a two-tailed p-value of less than 0.05.

RESULTS

The pre-intervention demographic and biochemical characteristics of the 28 participants are shown in Table 1. There were 14 male and 14 female patients in the sample population, indicating an equal distribution of genders. The average age of the participants, which ranged from 28 to 74 years, was 48.86 ± 12.5 years, as evident that most of them were middle-aged and typically had type 2 diabetes. Blood uric acid levels ranged from 1.01 to 7.88 mg/dL at baseline, with a mean of 5.05 ± 1.65 mg/dL. Serum creatinine levels ranged from 0.58 to 3.42 mg/dL, with an average of 1.25 ± 0.61 mg/dL. Urine uric acid levels ranged from 21.73 to 141.32 mg/dL, with a mean of 74.4 ± 35.6 mg/dL. Urinary creatinine levels ranged from 68.44 to 243.44 mg/dL, with an average of 148.43 ± 55.69 mg/dL. The ratio of renal excretion of uric acid ranged from 2.56% to 41.23%, with an average of 14.52 ± 10.72%. %. This indicates diversity in uric acid excretion across participants at the start of the trial.

Table 1: Baseline patient characteristics (n = 28)

Variable	Min.	Max.	Mean	SD
Gender	Female (14) / Male (14)			
Age (years)	28	74	48.86	12.5
Serum uric acid (mg/dl)	1.01	7.88	5.05	1.65
Serum creatinine (mg/dl)	0.58	3.42	1.25	0.61
Urine uric acid (mg/dl)	21.73	141.32	74.4	35.6
Urine creatinine (mg/dl)	68.44	243.44	148.43	55.69
Fraction excretion	2.56	41.23	14.52	10.72

Biochemical indicators at baseline and following three months of SGLT2 inhibitor treatment are compared in Table 2. After three months, the average blood uric acid level dropped significantly from 5.05 ± 1.65 mg/dL to 2.99 ± 1.68 mg/dL (p = 0.001). Though not considerably (p = 0.395), serum creatinine levels dropped from 1.25 ± 0.61 mg/dL to 1.19 ± 0.58 mg/dL. After three months, urinary uric acid levels dropped from 74.4 ± 35.6 mg/dL at baseline to 52.48 ± 35.97 mg/dL (p = 0.005). The urine creatinine level also decreased, with a significant impact (p = 0.001), from 148.43 ± 55.69 mg/dL to 79.63 ± 36.24 mg/dL.

But after three months, uric acid excretion increased dramatically from 14.52 ± 10.72% at baseline to 36.24 ± 28.5% (p = 0.001). These results demonstrate that uric acid metabolism and urine excretion measurements were significantly impacted by SGLT2 inhibitor medication, whereas serum creatinine stayed rather constant over the course of the follow-up period.

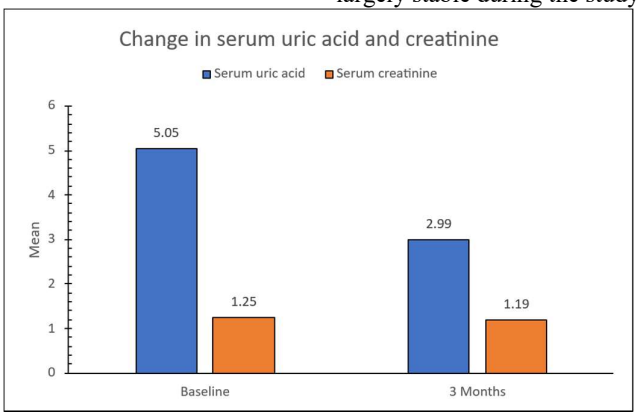
Table 2: Comparison of Parameters Prior to and Following Three Months of Administration with SGLT2 Inhibitors.

Variable	Time	Mean	SD	MD	t value	p value
Serum uric acid	Baseline	5.05	1.65	2.06	6.204	0.001*
	3 months	2.99	1.68			
Serum	Baseline	1.25	0.61	0.06	0.865	0.395

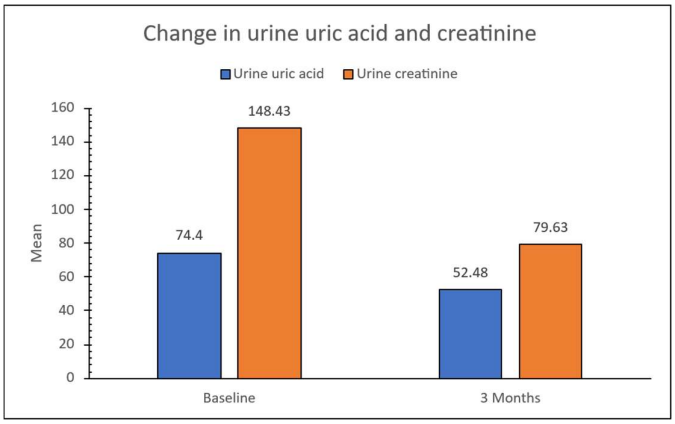
creatinine	3 months	1.19	0.58			
Urine uric acid	Baseline	74.4	35.6	21.92	3.057	0.005*
	3 months	52.48	35.97			
Urine creatinine	Baseline	148.43	55.69	68.8	8.285	0.001*
	3 months	79.63	36.24			
Fraction excretion	Baseline	14.52	10.72	-21.72	-4.613	0.001*
	3 months	36.24	28.5			

Table 2: Comparison of parameters before and 3 months after sodium-glucose cotransporter-2 inhibitor administration [*p-value is computed using paired t-test].

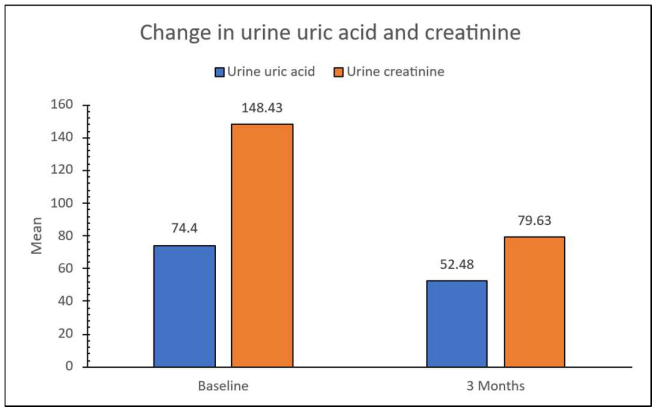
The variations in blood uric acid and creatinine levels before and after beginning SGLT2 inhibitor therapy are displayed in Graph 1. After three months, the mean blood uric acid level decreased significantly, from 5.05 mg/dL at the beginning to 2.99 mg/dL. On the other hand, blood creatinine levels only marginally dropped from 1.25 mg/dL to 1.19 mg/dL, suggesting that renal function was largely stable during the study period.



Graph 1: Changes in serum uric acid and serum creatinine levels from baseline to 3 months after initiation of SGLT2 inhibitor therapy.

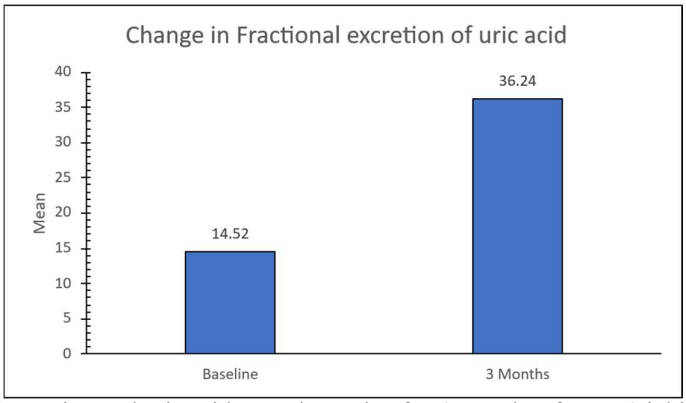


The variations in urine creatinine and uric acid levels during the course of the three-month treatment period are shown in Graph 2. After three months of treatment, the mean urine creatinine level dropped from 148.43 mg/dL to 79.63 mg/dL and the mean urinary uric acid level dropped from 74.4 mg/dL to 52.48 mg/dL. These findings show that urine biochemical markers significantly decreased over the course of the follow-up period.



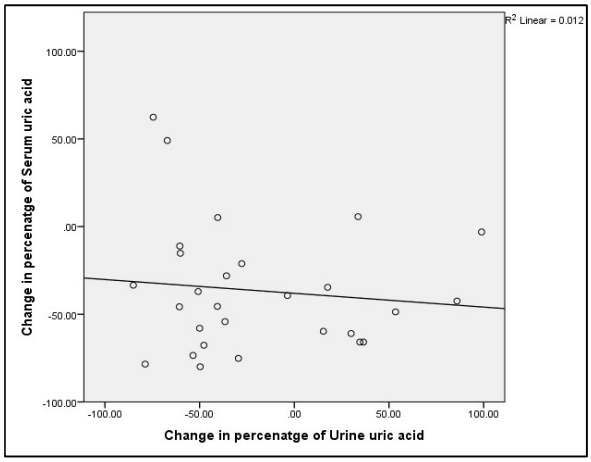
Graph 2: Change in urinary uric acid and urinary creatinine levels during the 3-month treatment period

The renal uric acid excretion ratio change after three months of SGLT2 inhibitor therapy is shown in Graph 3. Over the course of the study, the mean FEUA increased significantly from 14.52% at baseline to 36.24% following therapy, indicating a notable increase in uric acid excretion via the kidneys.



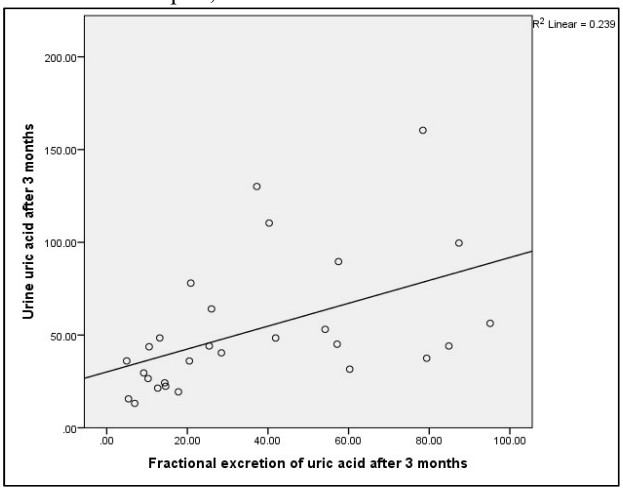
Graph 3: Change in renal uric acid excretion ratio after 3 months of SGLT2 inhibitor therapy

After three months of treatment, the scatter plot in Graph 4 illustrates the relationship between the percentage change in blood uric acid levels and the % change in urine uric acid levels. Only a minor portion of the variation was explained by the study's weak negative correlation (R2=0.012) between blood and urine uric acid levels. There appears to be no significant linear relationship between the two variables based on the dispersed distribution of data points.



Graph 4: Relationship between percentage difference in urine uric acid and percentage difference in serum uric acid levels after 3 months of therapy

Following three months of SGLT2 inhibitor therapy, Graph 5 shows the correlation between urine uric acid levels and the renal uric acid excretion ratio. Changes in FEUA explained around 23.9% of the variation in urine uric acid levels, according to the scatter plot, which revealed a moderately positive association (R^2=0.239). This result validates the conclusion that, after SGLT2 inhibitor medication, higher fractional excretion leads to improved urine elimination of uric acid.



Graph 5: Relationship between renal excretion of uric acid ratio and urine uric acid levels after 3 months of SGLT2 inhibitor therapy

DISCUSSION

According to this study, patients with diabetes experienced a rise in FEUA and a fall in serum UA levels following Dapagliflozin therapy as compared to pre-administration values. These findings are promising, and illustrate the clinical use fulness of SGLT2 inhibitor medication for renal protection, which may be helpful in treating T2DM patients to prevent the progression to ESRD.

The findings of this study are in accordance with other studies done by Zahao et al, which have showed that SGLT2 inhibitors lower serum uric acid levels in both diabetic and non-diabetic people. An elevated uric acid FE is the cause of this hypouricemic effect [14,15]. In 720 diabetic patients with glycosuria who participated in a community-based health care program, Andrade et al discovered a null prevalence of hyperuricemia and noticeably higher FEUA values [16].

A study done by Habeeb EA et al investigates how SGLT2i affects UA levels in a multicentre, real-world Saudi Arabian sample. This investigation, which was carried out across four significant medical facilities, showed that SGLT2i

Regardless of the use indication, treatment decreased UA levels.

UA-lowering results were constant across several subgroups, despite the fact that individuals with elevated baseline UA saw the most noticeable reductions [17].

Another important finding in this study was the absence of significant change in blood creatinine with SGLT2 inhibitor therapy (1.25 ± 0.61 vs 1.19 ± 0.58 mg/dL, p = 0.395). This is consistent with the excellent renal safety profile of SGLT2 inhibitors demonstrated in large clinical trials. Despite a little initial drop in eGFR, canagliflozin decreased the risk of renal disease progression by 34% in the CREDENCE study [18].

CONCLUSION

The study showed that SGLT2 inhibitor medication significantly lowers serum uric acid levels while increasing fractional excretion of uric acid in patients with type 2 diabetes. These results suggest that, regardless of variations in serum creatinine or glomerular filtration rate, SGLT2 inhibitors have strong uricosuric effects by increasing renal uric acid clearance.

LIMITATIONS OF THE STUDY

- Small sample size.
- No inter-group comparison

REFERENCES

1. Song P, Wang H, Xia W, Chang X, Wang M, An L. Prevalence and correlates of hyperuricemia in the middle-aged and older adults in China. Sci Rep. (2018) 8:4314. doi: 10.1038/s41598-018-22662-5
2. Schwartz SA. Disease of distinction. Explore (NY). 2006; 2:515–519.
3. Packer M. Role of deranged energy deprivation signaling in the pathogenesis of cardiac and renal disease in states of perceived nutrient over abundance. Circulation. 2020; 141:2095–2105.
4. Packer M. SGLT2 inhibitors: role in protective reprogramming of cardiac nutrient transport and metabolism. Nat Rev Cardiol. 2023; 20:443–462.

5. Mandal AK, MountDB. Themolecular physiology of uric acid homeostasis. Annu Rev Physiol. (2015) 77:323–45. doi: 10.1146/annurev-physiol-021113 170343

6. Choi HK, Mount DB, Reginato AM. Pathogenesis of gout. Ann Intern Med. (2005) 143:499–516. doi: 10.7326/0003-4819-143-7-200510040-00009.

7. Sánchez-Briales P, Marques Vidas M, López-Sánchez P, López-Illázquez MV, Martín-Testillano L, Vedat-Ali A, Portolés J. The Uricosuric effect of SGLT2 inhibitors is maintained in the long term in patients with chronic kidney disease and type 2 diabetes mellitus. Journal of Clinical Medicine. 2024 Feb 27;13(5):1360.

8. Johnson RJ, Sanchez Lozada LG, Lanaspa MA, et al. Uric acid and chronic kidney disease: still more to do. Kidney Int Rep 2023; 8:229–39.

9. Dincer HE, Dincer AP, Levinson DJ. Asymptomatic hyperuricemia: to treat or not to treat. Cleve Clin J Med. (2002) 69:594–7. doi: 10.3949/ccjm.69.8.594.

10. Paul BJ, Anoopkumar K, Krishnan V. Asymptomatic hyperuricemia: is it time to intervene? Clin Rheumatol. (2017) 36:2637–44. doi: 10.1007/s10067-017-3825-0

11. Hainer BL, Matheson E, Wilkes RT. Diagnosis, treatment, and prevention of gout. Am Fam Physician. (2014) 90:831–6.

12. Sharma G, Dubey A, Nolkha N, Singh JA. Hyperuricemia, urate-lowering therapy, and kidney outcomes: a systematic review and meta-analysis. Ther Adv Musculoskelet Dis. (2021) 13:1759720X2110166. doi: 10.1177/1759720X211016619.

13. Zhang L, Zhang F, Bai Y, et al. Effects of sodium-glucose cotransporter- 2 (SGLT- 2) inhibitors on serum uric acid levels in patients with chronic kidney disease: a systematic review and network meta-analysis. BMJ Open Diab Res Care 2024;12:e003836. doi:10.1136/bmjdrc-2023-003836.

14. Suijk DL, van Baar MJ, van Bommel EJ, Iqbal Z, Krebber MM, Vallon V, Touw D, Hoorn EJ, Nieuwdorp M, Kramer MM, Joles JA. SGLT2 inhibition and uric acid excretion in patients with type 2 diabetes and normal kidney function. Clinical Journal of the American Society of Nephrology. 2022 May 1;17(5):663-71.

15. Chino, Y.; Samukawa, Y.; Sakai, S.; Nakai, Y.; Yamaguchi, J.; Nakanishi, T.; Tamai, I. SGLT2 inhibitor lowers serum uric acid through alteration of uric acid transport activity in renal tubule by increased glycosuria. Biopharm. Drug Dispos. 2014, 35, 391–404. [CrossRef] [PubMed]

16. Andrade JA, Kang HC, Greffin S et al: Serum uric acid and disorders of glucose metabolism: The role of glycosuria. Braz J Med Biol Res, 2014; 47: 917–23.

17. Habeeb EA, Ghaith AM, Alshehri AM, Aquil G, Afana AH, Alqarafi AH, Alahmed AA and Alkhezi OS (2025) Revealing the hidden impact of SGLT2 inhibitors on uric acid levels: a retrospective multicenter cohort study. Front. Endocrinol. 16:1667438. doi: 10.3389/fendo.2025.1667438.

18. Megumi Oshima, Meg J. Jardine, Rajiv Agarwal, George Bakris, Christopher P. Cannon, David M.et al.Insights from CREDENCE trial indicate an acute drop in estimated glomerular filtration rate during treatment with canagliflozin with implications for clinical practice,Kidney International,Volume 99, Issue 4,2021, 999-1009.