The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 3, 2025

# EFFECTS OF DAPA/ EMPA ON SERUM URIC ACID LEVELS IN HOSPITALIZED TYPE 2 DIABETES MELLITUS PATIENTS

**Dr Elleyyeen Avais[*1], Dr Ghulam Hussain Ibrahim[2], Dr Fawad Ahmed[3], Dr Rida Al Sunnah[4], Dr Muhammad Faizan[5], Dr Muhammad Waqas Ahmed Qureshi[6]**

[*1,4,5,6]*Registrar Medicine PEMH Rawalpindi*
[2,3]*Classified Medical Specialist CMH Abbottabad*

[*1]elleyyeen@gmail.com,[2]drhussainibrahim@gmail.com

**DOI:** https://doi.org/10.5281/zenodo.17455228

**Keywords**
*Blood Glucose, Sodium-Glucose Transporter 2 Inhibitors, Type 2 Diabetes Mellitus, Uric Acid*

**Article History**
*Received: 11 Jan 2025*
*Accepted: 21 Feb 2025*
*Published: 23 March 2025*


**Corresponding Author: ***
**Dr Elleyyeen Avais**

**Abstract**

***Background:*** *Metabolic disorders like hyperuricemia have been long associated with Diabetes mellitus and are found to be associated with DM in very complex manners.*

***Objectives:*** *To observe whether Sodium-Glucose Transporter 2 Inhibitors decrease serum uric acid levels in patients with type 2 diabetes mellitus*

***Methods:*** *This prospective observational study was conducted at the Medicine Department of Pak Emirates Military Hospital, Rawalpindi. The patients were divided into two Groups: one Group received a Sodium-Glucose Transporter 2 Inhibitor (Group S), and the other Group continued their routine oral anti-hyperglycaemic treatment (Group D). Group S received empagliflozin 10-25 mg daily, whereas Group D received metformin and glimepiride alone or in combination to maintain a fasting blood sugar <110 mg/dl. The primary parameter observed at the end of four weeks post-medication was the difference in uric levels between Groups.*

***Results:*** *Mean age of patients was 47.77±4.67 years in Group S versus 47.43±4.64 years in Group D (p=0.016). Levels of serum uric acid in Group S were 7.81±0.72 mg/dl before and 6.46±0.57 mg/dl at the end of the study (p=0.001). In Group D, levels of serum uric acid were 8.10±0.75 mg/dl before and 8.05±0.68 mg/dl at the end of the study (p=0.167). The difference was statistically higher in Group S when compared to Group D, in which no statistically significant difference was observed.*

***Conclusion:*** *Sodium-Glucose Transporter 2 Inhibitors significantly decrease serum uric levels while also modestly decreasing body weight and body mass index.*

## INTRODUCTION

Diabetes mellitus is one of the major diseases with a high prevalence worldwide. According to estimates furnished by International Diabetes Federation (IDF), the prevalence of diabetes worldwide was 10.5% in 2021 (536.6 million) and is projected to rise to 12.2% by 2045 (783.2 million).[1] This makes diabetes among the top ten prevalent diseases in the world.[2] The enormity of this disease causes significant morbidity and mortality in affected patients as well as cripple hospital resources worldwide[3]. It becomes imperative to prevent diabetes by early detection, screening, and

treatment of risk factors and managing complications in those affected by the disease.

Hyperuricemia is caused by a defective process of purine metabolism, resulting in high serum uric acid levels in the blood.[4] In various studies, hyperuricemia has been associated to co-exist with patients of diabetes mellitus.[5] It has also been implicated as a risk factor for diabetes mellitus in patients with poor glycaemic control and impaired glucose tolerance. This strong association then becomes a matter of considerable importance since studies show that increased waist circumference, dyslipidaemia, insulin resistance and hypertension are all factor predisposing to increase uric acid levels in patients with diabetes mellitus.[6] This points toward the management of uric acid and its levels must be controlled in patients presenting with the complaint with co-existing diabetes mellitus since it leads to cardiovascular and renal complications as the disease progresses, and if levels remain uncontrolled.[7]

SGLT-2 (sodium glucose co-transporter 2) inhibitors have been gaining importance as excellent treatment option for diabetic patients due to their superior cardiovascular and renal profile, excellent glycaemic control, and their role in reducing serum uric acid levels and preventing gout episodes as well.[8,9] This makes SGLT-2 inhibitors as a very feasible treatment option in type-II diabetic patients with increased uric acid levels. The aim of this study is to observe whether SGLT-2 inhibitors decrease serum uric acid levels in patients with type II diabetes mellitus effectively while maintaining a good glycaemic control when compared to other anti-diabetic drug classes.

## PATIENTS AND METHODS

This prospective-observational study was carried out at the Department of Medicine, Pak Emirates Military Hospital, Rawalpindi, from July 2024 to December 2024 after approval from the ethical review board vide letter no. A/28/ERC/541/23. Patients were included in the study (minimum sample size 196) using the WHO calculator, keeping the confidence interval at 95%, margin of error at 7% with the incidence of hyperuricemia in patients with type II diabetes mellitus at 53.5%.[10]

All patients with type II diabetes mellitus with a body mass index (BMI) < 28 kg/m$^2$, serum uric acid levels of more than 7 mg/dl in males and 6 mg/dl in females were included. Moreover, patients with controlled diabetes (HbA1c <7%) while on anti-diabetic drugs other than SGLT-2 inhibitors, and patients with controlled hypertension (BP < 140/90 mm Hg) were also included. Patients on anti-gout medication, those on medications affecting uric acid levels (aspirin, niacin, pyrazinamide, immunosuppressants, etc.), and those with major respiratory, cardiovascular, and renal diseases were excluded.

The study included patients as per the inclusion and exclusion criteria furnished. The patients were divided into two Groups with one Group receiving SGLT-II inhibitor (Group S) (n=105) and one Group on their routine oral anti-hyperglycaemic drugs (Group D) (n=105). The method of sampling was non-probability consecutive sampling by computer generated random list. Before the commencement of the treatment regimen, laboratory investigation like serum uric acid levels, blood sugar fasting and HbA1c levels were taken after 12 hours fasting period and documented. The same was done after completion of study at 4 weeks. Group S received empagliflozin 10-25 mg daily, whereas Group D received metformin and glimepiride alone or in combination to maintain a fasting blood sugar <110 mg/dl. The fasting blood sugar of all patients was checked at a weekly interval after an 8-hour fast with a sample taken in the morning. Patients were advised to refrain from taking sugar, beverages and diets affecting glycaemic index for the duration of the study. Patient, doctor, and staff were blinded to the study protocol throughout the duration of the study. Primary endpoint at the end of four weeks post-medication was the difference in uric levels between both Groups, whereas changes in weight and BMI were secondary endpoints.

Demographic data was statistically described in terms of mean and SD, frequencies, and percentages as appropriate. An independent sample Student's t-test was used to compare statistically significant changes for primary and secondary endpoints. A p-value of <0.05 was considered statistically significant. All statistical calculations were performed using Statistical Package for the Social Sciences 26.0.

## RESULTS

A total of 210 patients were included in the study as per the inclusion criteria furnished earlier. Mean age of patients was 47.77±4.67 years in Group S versus 47.43±4.64 years in Group D (p=0.016). Mean weight

of patients was 81.75±4.78 kg in Group S versus 81.92±4.64 kg in Group D (p=0.272). Mean duration of diabetes mellitus varied between

8.08±0.67 years in Group S versus 8.01±0.70 in Group D (p=0.109). When comparing mean uric acid levels before the start of the study, the mean value was 7.81±0.72 mg/dl in Group S compared to 8.10±0.75 in Group D (p=0.06). The value of HbA1c (glycosylated haemoglobin) was 5.650.48% in Group S versus 5.710.45% in Group D (Table 1)
.

*Table 1: Demographic and Baseline Parameters between the Groups*

| **Variable** | **Group S** (n=105) | **Group D** (n=105) | **p-value** |
|---|---|---|---|
| **Age** (Years) | 47.77±4.67 | 47.43±4.64 | 0.016 |
| **Body Weight** (Kg) | 81.75±4.78 | 81.92±4.64 | 0.272 |
| **Duration Of Diabetes** (Years) | 8.08±0.67 | 8.01±0.70 | 0.109 |
| **BMI** ($Kg/m^2$) | 25.38±1.31 | 25.04±1.48 | 0.001 |
| **Blood Pressure** (mmHg) | 83.20±4.03 | 82.99±3.97 | 0.06 |
| **Fasting Blood Sugar** (mg/dL) | 96.60±3.03 | 96.34±3.16 | 0.09 |
| **Mean HbA1c** (%) | 5.64±0.48 | 5.71±0.45 | 0.004 |
| **Serum Uric Acid Levels** (mg/dL) | 7.81±0.72 | 8.10±0.75 | 0.006 |

*BMI: Body Mass Index; HbA1C: Glycosylated haemoglobin*

When observing the primary endpoint, levels of serum uric acid in Group S were 7.81±0.72 mg/dl before and 6.46±0.57 mg/dl at the end of study (p=0.001). In Group D, levels of serum uric acid were 8.10±0.75 mg/dl at the start and 8.05±0.68 mg/dl at the end of study (p=0.167). The difference was statistically higher in Group S when compared to Group D, in which no statistically significant difference was observed, as shown in Table 2.
Secondary endpoints between both Groups showed that mean body weight was significantly reduced from 81.75±4.78 kg to 76.55±8.61 kg in Group S (p<0.001), whereas the change in weight was not statistically significant (p=0.633) in Group D, as body weight did not show a reduction (81.92±4.64 kg before and 82.14±4.71 kg) at the end of study. BMI showed a change, as in Group S, the BMI reduced from 25.381.31% to 23.231.24% showing a statistically significant decrease (p=0.001). However, in Group D, the change was not significant. Details are shown in Table 2.

*Table 2: Comparison Of Primary and Secondary Parameters Between the Groups*

| Variable | **Group S** (n=105) | | | **Group D** (n=105) | | |
|---|---|---|---|---|---|---|
| | **Before Therapy** | **After Therapy** | **p-value** | **Before Therapy** | **After Therapy** | **p-value** |
| Serum Uric Acid Levels **(mg/dL)** | 7.81±0.72 | 6.46±0.57 | **0.001** | 8.10±0.75 | 8.05±0.68 | **0.167** |
| Body Weight **(Kg)** | 81.75±4.78 | 76.55±8.61 | **0.001** | 81.92±4.64 | 82.14±4.71 | **0.663** |
| BMI **(Kg/m$^2$)** | 25.38±1.31 | 23.23±1.24 | **0.001** | 25.04±1.48 | 25.08±1.41 | **0.762** |

*BMI: Body mass index*

## DISCUSSSION

The study was carried out at a centre of excellence to observe the outcome in hyperuricemic diabetic patients and to see whether SGLT-2 inhibitors tend to have a statistically significant effect in decreasing serum uric acid levels while adequately controlling blood sugar levels in these patients. This study was one of the very few studies done in this demographic area, as well as at the national level.[11] The mechanism by which SGLT-2 inhibitors decrease blood sugar levels is the inhibition of sodium glucose co-transporter 2, which prevents reabsorption of glucose from the proximal convoluted tubules.[12] With the added benefit of decreasing serum uric acid levels as observed in this study, as well as some work done at the regional level, it is a very promising regimen for patients with diabetes. The statistically significant level of fall in uric acid levels is in line with international studies, and the proposed mechanism of the SGLT-2 class of drugs is hypothesised to be their action on the GLUT-9 transporter in the renal collecting tubules, exchanging extracellular glucose and enhancing urate secretion.[13] Based on these findings, these drugs have provided good results in decreasing uric acid levels, and studies have also shown a decrease in the number of gout flares in susceptible individuals.[14]

A meta-analysis also showed a decrease in serum uric acid levels with the use of SGLT-2 inhibitors, and some drugs had a dose-dependent effect.[15] Similarly, in this study, serum uric acid was significantly reduced after use of an SGLT-2 inhibitor. The excellent renal and cardiovascular profile of these drugs has also been stated in various studies.[8,16] Not only do they decrease uric acid levels and prevent metabolic syndrome in susceptible diabetes mellitus patients, but they are also shown to have a good effect in lowering serum glucose levels and modestly affect weight loss in these patients as well.[17] The effect of lipid dysfunction and increased uric acid levels in diabetics is also shown to increase insulin resistance and increase beta-cell dysfunction in the islet of Langerhans.[18] Another systematic review and meta-analysis found the SGLT-2 inhibitors beneficial in reducing hyperuricemia in patients suffering from type 2 diabetes, although a few of the drugs were found to be better than the others.[19,20] In present research, empagliflozin significantly reduced the serum uric acid levels and BMI in diabetic population. A retrospective study showed improvement in gout, serum uric acid levels and heart functions with the use of SGLT-2 inhibitors.[21] The findings of this research are in coherence with their findings with respect to uric acid level reduction.

The limitations of this study are those of a single centre, a small sample size and short duration. A multi-centre study with a prolonged duration at a large scale will better understand the effect of SGLT-2 inhibitors on metabolic and renal parameters in type 2 Diabetes Mellitus.

## CONCLUSION

SLGT-2 inhibitors significantly decrease serum uric levels while also modestly decreasing body weight and BMI. This highlights their role in managing and addressing the metabolic derangements in diabetic patients.

**ETHICAL APPROVAL:** The Study was conducted after approval from the ethical review board vide letter reference no. A/28/ERC/541/23
**CONFLICT OF INTEREST:** None
**FUNDING SOURCE:** None

## AUTHOR CONTRIBUTION

**EA, GH, MI:** Substantial contributions to study design, conceptualisation, data analysis, critical review and gave final approval of the version to be published
**FA, RS, MA:** Contributed towards study design, data collection, critical review and gave final approval of the version to be published

## REFERENCES

Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas. Diabetes research and clinical practice. 2019;157:107843. doi: 10.1016/j.diabres.2019.107843.

Smokovski I. Burden of Diabetes Prevalence. Managing Diabetes in Low Income Countries: Providing Sustainable Diabetes Care with Limited Resources. Cham: Springer; 2021:1-12. doi:10.1007/978-3-030-51469-3_1

Gomes MB, Rathmann W, Charbonnel B, Khunti K, Kosiborod M, Nicolucci A, et al. Treatment of type 2 diabetes mellitus worldwide: baseline patient characteristics in the global DISCOVER study. Diabetes Res Clin Pract. 2019;151:20-32. doi: 10.1016/j.diabres.2019.03.024.

James A, Ke H, Yao T, Wang Y. The role of probiotics in purine metabolism, hyperuricemia and gout: mechanisms and interventions. Food Rev Int. 2021:1-17. doi:10.1080/87559129.2021.1904412.

Arersa KK, Wondimnew T, Welde M, Husen TM. Prevalence and Determinants of Hyperuricemia in Type 2 Diabetes Mellitus Patients Attending Jimma Medical Center, Southwestern Ethiopia, 2019. Diabetes Metab Syndr Obes. 2020;13:2059-67. doi: 10.2147/DMSO.S252825.

Yanai H, Adachi H, Hakoshima M, Katsuyama H. Molecular biological and clinical understanding of the pathophysiology and treatments of hyperuricemia and its association with metabolic syndrome, cardiovascular diseases and chronic kidney disease. nt J Mol Sci. 2021;22(17):9221. doi: 10.3390/ijms22179221.

Gong M, Wen S, Nguyen T, Wang C, Jin J, Zhou L. Converging relationships of obesity and hyperuricemia with special reference to metabolic disorders and plausible therapeutic implications. Diabetes Metab Syndr Obes. 2020;13:943-62. doi: 10.2147/DMSO.S232377.

Cowie MR, Fisher M. SGLT2 inhibitors: mechanisms of cardiovascular benefit beyond glycaemic control. Nat Rev Cardiol. 2020;17(12):761-72. doi: 10.1038/s41569-020-0406-8.

Copur S, Demiray A, Kanbay M. Uric acid in metabolic syndrome: Does uric acid have a definitive role? Eur J Intern Med. 2022;103:4-12. doi: 10.1016/j.ejim.2022.04.022.

Alqahtani SAM, Awan ZA, Alasmary MY, Al Amoudi SM. Association between serum uric acid with diabetes and other biochemical markers. J Family Med Prim Care. 2022;11(4):1401-9. doi: 10.4103/jfmpc.jfmpc_1833_21.

Hussain M, Elahi A, Hussain A, Iqbal J, Akhtar L, Majid A. Sodium-Glucose Cotransporter-2 (SGLT-2) Attenuates Serum Uric Acid (SUA) Level in Patients with Type 2 Diabetes. J Diabetes Res. 2021;2021:9973862. doi: 10.1155/2021/9973862.

Nelinson DS, Sosa JM, Chilton RJ. SGLT2 inhibitors: a narrative review of efficacy and safety. J Osteopath Med. 2021 Feb 1;121(2):229-39. doi: 10.1515/jom-2020-0153.

Novikov A, Fu Y, Huang W, Freeman B, Patel R, van Ginkel C, et al. SGLT2 inhibition and renal urate excretion: role of luminal glucose,

GLUT9, and URAT1. Am J Physiol Renal Physiol. 2019;316(1):F173-F185. doi: 10.1152/ajprenal.00462.2018.

Bailey CJ. Uric acid and the cardio-renal effects of SGLT2 inhibitors. Diabetes Obes Metab. 2019 Jun;21(6):1291-98. doi: 10.1111/dom.13670.

Zhao Y, Xu L, Tian D, Xia P, Zheng H, Wang L, et al. Effects of sodium-glucose co-transporter 2 (SGLT2) inhibitors on serum uric acid level: A meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2018;20(2):458-62. doi: 10.1111/dom.13101.

McGuire DK, Shih WJ, Cosentino F, Charbonnel B, Cherney DZ, Dagogo-Jack S, et al. Association of SGLT2 Inhibitors With Cardiovascular and Kidney Outcomes in Patients With Type 2 Diabetes: A Meta-analysis. JAMA Cardiol. 2021;6(2):148-58. doi: 10.1001/jamacardio.2020.4511.

Herat LY, Matthews J, Azzam O, Schlaich MP, Matthews VB. Targeting Features of the Metabolic Syndrome Through Sympatholytic Effects of SGLT2 Inhibition. Curr Hypertens Rep. 2022;24(3):67-74. doi: 10.1007/s11906-022-01170-z.

Yaribeygi H, Sathyapalan T, Maleki M, Jamialahmadi T, Sahebkar A. Molecular mechanisms by which SGLT2 inhibitors can induce insulin sensitivity in diabetic milieu: A mechanistic review. Life Sci. 2020;240:117090. doi: 10.1016/j.lfs.2019.117090.

Xin Y, Guo Y, Li Y, Ma Y, Li L, Jiang H. Effects of sodium glucose cotransporter-2 inhibitors on serum uric acid in type 2 diabetes mellitus: A systematic review with an indirect comparison meta-analysis. Saudi J Biol Sci. 2019;26(2):421-26. doi: 10.1016/j.sjbs.2018.11.013.

Hu X, Yang Y, Hu X, Jia X, Liu H, Wei M, et al. Effects of sodium-glucose cotransporter 2 inhibitors on serum uric acid in patients with type 2 diabetes mellitus: A systematic review and network meta-analysis. Diabetes Obes Metab. 2022;24(2):228-38. doi: 10.1111/dom.14570.

Akbar U, Khan S, Dani SS, Umer AM, Shafique N, Muhibullah F, et al. The Role of SGLT2 Inhibitors in Managing Hyperuricemia, Gout, And Cardiovascular Outcomes in Patients with Diabetes and Heart Failure. JACC. 2025;85(Suppl 12):1660. doi:10.1016/S07351097(25)02144-8