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Original Article

The Relationship between SGLT-2 Inhibitors and Weight Reduction among Type 2 Diabetic Patients: A Descriptive Cross-Sectional Study

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ABSTRACT

Background: Sodium-Glucose Cotransporter-2 (SGLT-2) inhibitors are modern antidiabetic agents that work by preventing the kidneys from reabsorbing glucose, reducing Blood Glucose (BG) levels, and causing glucose to leave the body through urine. **Objectives:** Assessing the effectiveness of SGLT-2 inhibitor drugs for weight reduction in persons with Type 2 Diabetes (T2D) and identifying which treatment agents are associated with the most significant weight loss among individuals adhering to a standard, unrestricted diet. **Materials and Methods:** A retrospective study analyzed 136 patients who were treated with an SGLT-2 inhibitor for 12 months at Dr. Soliman Fakeeh Hospital (DSFH) between August 2023 and October 2024. The population was divided into seven treatment groups. Three monotherapy groups (dapagliflozin 10 mg, empagliflozin 10mg, or empagliflozin 25 mg) and four combined therapy groups that received these drugs with metformin. A treatment response was defined as a body weight loss of at least 5%. We used linear regression to find out the relationship between SGLT-2 inhibitors and weight reduction. **Results:** 58.8% of patients maintained stable weight (±2 kg). 25.7% of patients achieved clinically meaningful weight loss (> 2 kg), 5.1% of patients achieved ≥ 5% weight loss (clinical responders). Significant inverse connection between age and weight change ($r = -0.21$, $p = 0.016$). No significant weight changes were found overall (mean: -0.54 ± 3.92 kg, $p = 0.110$). No significant gender variances in weight change were observed ($p = 0.646$). **Conclusion:** SGLT-2 inhibitors did not produce significant weight loss over 12 months when patients followed a regular diet without dietary restrictions.

Keywords: SGLT-2 inhibitors, Weight reduction, Dapagliflozin, Empagliflozin.

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INTRODUCTION

Management of BG in diabetic patients reduces the occurrence of diabetes-related complications (Zayed *et al.*, 2024). Obesity is a significant global health issue. It is a primary factor in the onset and advancement of T2D and its consequences (Amjad *et al.*, 2022). Moreover, the incidence of obesity has increased due to various variables, including genetic predisposition, environmental influences, and the aging process (Lu *et al.*, 2024). Many pharmacological agents are currently used to treat T2D (El-Zahabi *et al.*, 2022). SGLT-2 inhibitors are modern antihyperglycemics that enhance glycemic control independently of insulin production, with a low risk of hypoglycemia (Lu *et al.*, 2024). Dapagliflozin and empagliflozin are classified as SGLT-2 inhibitors (Lopaschuk and Vermu, 2020; McGuire *et al.*, 2021). They work by preventing renal glucose reabsorption and enhancing urine glucose excretion (Rivera *et al.*, 2023; Rosen *et al.*, 2024; Simental-Mendia *et al.*, 2021). They are also linked to caloric expenditure, leading to weight reduction and decreased blood pressure (Singh and Singh, 2020; Song *et al.*, 2024; Zayed *et al.*, 2025).

There is limited data on the use of SGLT-2 inhibitors in Saudi Arabia; this paper includes a case series of local patients utilizing SGLT-2 inhibitors. This study sought to assess the efficacy of

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SGLT-2 inhibitors in promoting weight loss among a group of Saudi patients with T2D.

The study addresses the relationship between the SGLT-2 inhibitors empagliflozin and dapagliflozin in their monotherapy or combined with metformin and weight reduction. The major questions answered by this study are: What is the effect of SGLT-2 inhibitors on body weight in T2D patients? This is the core question that groups empagliflozin and dapagliflozin are assessed for. Does the effect on weight differ between the SGLT-2 inhibitors empagliflozin and dapagliflozin? This question compares the two specific drugs to determine which one has a stronger or more consistent effect. How does the treatment regimen (monotherapy vs. combination therapy) influence weight reduction? Is the weight loss different when the drug is taken alone versus with metformin? Does patient age influence the magnitude of weight reduction achieved with SGLT-2 inhibitors? Is the effectiveness of the treatment regimen (monotherapy vs. combination) different across various age groups? Are there differences in weight reduction response to SGLT-2 inhibitors between males and females? Does gender interact with the type of SGLT-2 inhibitor? These are the key questions this study will address.

MATERIALS AND METHODS

The study is a retrospective analysis performed at DSFH, Jeddah, KSA, from August 2023 to October 2024. It was approved by the ethical committee of DSFH 526/IRB/2023. It analyzes data from 136 patients who received a minimum of 12 months of the following antidiabetic monotherapy: dapagliflozin 10 mg, once daily (Dapa 10), empagliflozin 10 mg, once daily (Empa 10), and empagliflozin 25 mg, once daily (Empa 10). Additionally, the following antidiabetic dual therapy: dapagliflozin 10mg + metformin 1000 mg, once daily (Dapamet 10), dapagliflozin 5 mg + metformin 1000 mg, once daily (Dapamet 5), empagliflozin 12.5 mg + metformin 1000 mg, once daily (Empamet 12.5), and empagliflozin 5 mg + metformin 1000 mg, once daily (Empamet 5). Statistical analysis was conducted using SPSS version 23.0 (IBM Corp., NY, USA) and DataStatePro. Online software (2024). Figure 1 shows the flow chart of the patients who were selected based on specific inclusion and exclusion criteria.

Inclusion criteria

The inclusion criteria were focused on the adult population ≥ 18 years old, who are suffering from T2D and use of dapagliflozin or empagliflozin as monotherapy or combined with metformin for longer than 12 months.

Exclusion criteria

Patients with gestational diabetes, T1DM who are taking insulin, or patients who are taking other antidiabetic medications, severe renal damage, or eGFR below the threshold for safe SGLT-2 inhibitor use, severe CV disease, Recurrent genital or urinary tract infections, conditions causing significant weight change independent of medication (e.g., untreated thyroid disorder, severe GIT diseases, active cancer). Pregnancy, lactation, or planned pregnancy. Use of medications that significantly impact

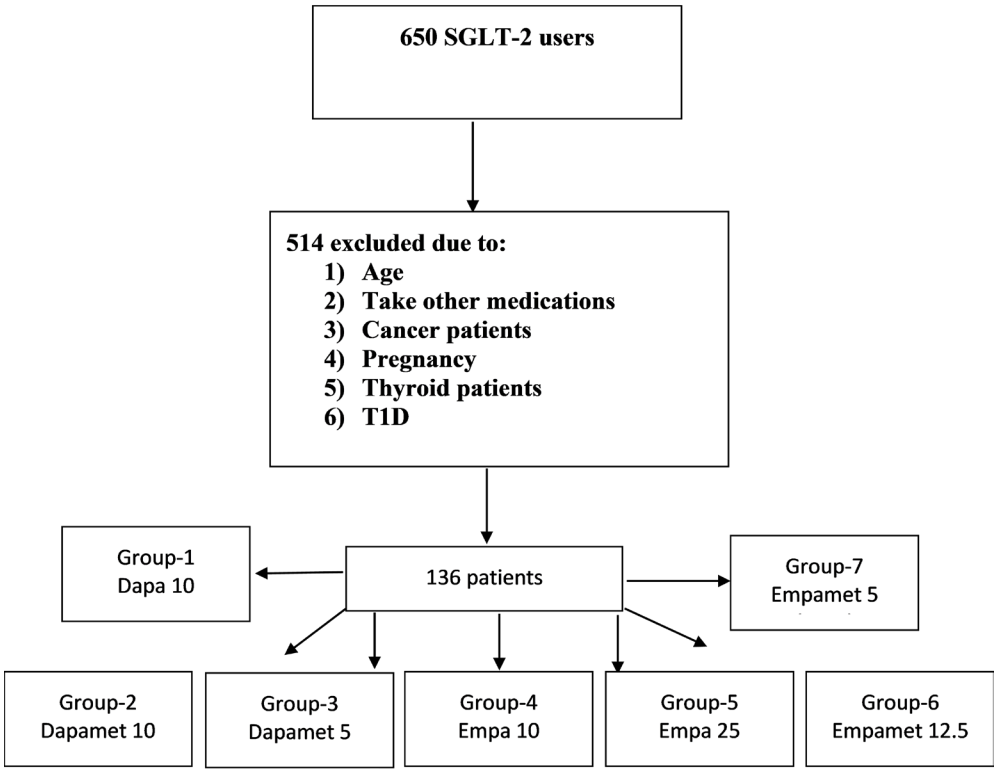

Figure 1: The flow chart shows the data from 136 patients who were treated with SGLT-2 inhibitors.

weight or appetite (e.g., chronic oral steroids, antipsychotics known for weight gain). Patients who are participating in a structured weight-loss program.

The study evaluates the weight-reduction effects of SGLT-2 inhibitors in patients following a regular, unrestricted diet to reflect real-world clinical conditions and to provide a realistic assessment of the drug's efficacy outside the structured lifestyle interventions. It also compares the findings with the established clinical trial data to reveal the distinct variations.

Baseline characteristics of the patients (N = 136)

We investigated 136 diabetic patients who visited the department of endocrinology at DSFH, Jeddah, Saudi Arabia, between August 2023 and October 2024. Among them, 74 (54%) were men and 62 (46%) were women. In this study, the patients were divided into seven treatment groups based on the antidiabetic medication. Group 1 includes 15 patients treated with Dapamet 10, group 2 includes 18 patients treated with Empa 10, group 3 includes 24 patients treated with Dapa 10, group 4 includes 6 patients treated with Emapamet 5, group 5 includes 57 patients treated with Empamet 12.5, group 6 includes 5 patients treated with Dapamet 5, and group 7 includes 11 patients treated with Empa 25. Table 1 summarizes the baseline characteristics of the patients, and Figure 2 shows the SGL-2 inhibitor distribution.

RESULTS

Weight change analysis

The mean and median weights for the baseline weight are extremely close to each other, which means that the baseline weight data are symmetrically distributed and not significantly skewed. The baseline weight range shows that there is a significant difference between the patients. The examination of weight changes shows that the whole group lost a very small amount of weight on average. The statistics indicate that most of the population sustained a consistent weight throughout the research duration. The high standard deviations show that the individual responses were very different from each other, with heterogeneous responses to SGLT-2 inhibitors.

The patients can be categorized based on weight change into five groups: The first group had a significant weight loss > 5 kg (13 patients), second group had a moderate loss 2-5 kg (23 patients), third group had a stable weight ±2 kg (79 patients), fourth group patients had a moderate weight gain 2-5 kg (18 patients), and fifth group had significant weight gain > 5 kg (3 patients). Figure 3 shows the weight categories, and Table 2 shows the weight change categories.

Subgroup analysis

Gender analysis

Statistical analysis indicated that gender did not influence weight change response to SGLT-2 inhibitors in this study, and there was no significant difference between genders. The mean weight change (Kg) for 74 males was -0.68 ± 3.95, and for 62 females was -0.37 ± 3.91. P-value was 0.6459, and T-value was -0.4604.

Age group analysis

Analysis of the age group in this experiment shows that the patients < 50 years (*n*=27) displayed slight weight gain (+0.84 kg), patients from 50-60 (*n*=35) showed (-0.3 Kg) weight loss, patients 60-70 (*n*=54) showed (-1.06 Kg) weight loss, older patients > 70 years (*n*=20) showed the greatest weight loss (-1.41 kg).

Correlation analysis

Age vs weight change

There is a statistically significant inverse relationship between age and weight change. Older patients tend to lose more weight on SGLT-2 inhibitors than younger patients. Pearson's r = -0.2056, indicating a weak negative correlation, and p-value = 0.0163, indicating a significant correlation.

Table 1: The baseline characteristics of the patients.

Variable	Total	p
Age	60.4 ± 10.6	0.341
Male	74 (54%)	0.841
Female	62 (46%)	0.621
Duration	11.6 ± 3.8	0.002*
Weight	82.52 ± 16.70	0.417
Height	1.62 ± 12.7	0.623
BMI	27.9 ± 5.24	0.721
SBP	135 ± 2.45	0.874
DBP	82 ± 4.56	0.421
HbA_{1c} (%)	7.9 ± 5.43	0.241
Fasting Plasma Glucose	154 ± 4.27	0.287
Total cholesterol (mg/dL)	148 ± 71.3	0.632
Triglycerides (mg/dL)	134 ± 42.7	0.451
HDL (mg/dL)	49.2 ± 21.3	0.254
LDL (mg/dL)	87.2 ± 25.3	0.351
eGFR (mL/min)	88.4 ±16.8	0.542
Cr (mg/dL)	0.84 ± 0.33	0.621
SGPT (ALT)	36 ± 12.5	0.412
A/C ratio (mg/dL)	14 ± 9.8	0.531

Values are displayed as mean ± SD or number (%), *p< 0.05.

Baseline weight vs weight change

The correlation study between them showed that weight does not predict weight change response to SGLT-2 inhibitors. Pearson's r = -0.0273, indicating no correlation, p-value = 0.7523, indicating no significant correlation between them.

Medications analysis

Analysis of the antidiabetic medications implied that dapamet 10 showed the greatest weight loss (-2.3 kg). Combination therapies showed variable results. The high dose of empagliflozin 25 mg showed a slight weight gain. Most medications showed minimal weight change. Figure 4 illustrates the weight change by medication, and Table 3 shows the correlation analysis of medications.

Clinical outcomes

Clinically meaningful weight loss is expressed in percentage thresholds: Table 4 shows the threshold, number, percentage, and clinical significance.

Clinical responder analysis

Clinical responders are patients achieving ≥5% weight loss from baseline. In this experiment, 7 patients (5.1%) achieved ≥ 5% weight loss from baseline; however, 129 (94.9%) were non-responders. Clinical response distribution based on the weight loss showed that 80 patients (58.8%) were stable ± 2 kg, 35 patients (25.7%) had a weight loss ≥ 2 kg, and 21 patients (15.4%) had a weight gain.

DISCUSSION

This retrospective study of 136 patients on SGLT-2 inhibitors for 12 months with a regular diet revealed that there is no significant overall weight change (mean = -0.54 kg, p = 0.110). There was high heterogeneity in patient response (range = -0.20 kg to + 7 kg). Most patients maintained stable weight (58.8% within ± 2 kg). The patients showed a low clinical response rate (5.1% achieved ≥ 5% weight loss). The result was age-dependent as older patients lost more weight, p = 0.016. There was no gender difference in weight change outcomes. The reported studies (RCTs) of the SGLT-2 inhibitors reported mean weight loss of 2-3 Kg over 24-52 weeks, with a clinical response rate of ≥ 5% weight loss, ranging from 20-40%, and the weight loss is generally a result of glycosuria-induced caloric loss (200 to 300 kcal/day) (Tian *et al.*, 2022; Yang *et al.*, 2025). This study showed a lower mean weight change and response rate than reported RCTs. The RCTs have strict inclusion/exclusion criteria; however, this study follows a regular diet with no restrictions. The real-world population may be more heterogeneous, having variable baseline and glycemic control. Retrospective studies can't verify daily compliance, and real-world compliance is typically lower than in trials. The variable treatment duration may also affect the result. A notable discovery in the study is the inverse association between age and weight change (r = 0.21, p = 0.016), which can be elucidated by metabolic differences, eating patterns, comorbidities, and baseline glycemic control.

Table 2: Weight change categories.

Category	Number	Percentage
Significant Loss (> 5 kg)	13	9.6%
Moderate Loss (2-5 kg)	23	16.9%
Stable (±2 kg)	79	58.1%
Moderate Gain (2-5 kg)	18	13.2%
Significant Gain (> 5 kg)	3	2.2%

Table 3: The correlation analysis of medications.

Medication	Number	Mean weight change (kg)	Median (kg)	Mean % change
Dapamet 10	15	-2.38 ± 3.62	-1.00	2.77%
Emba 10	18	-1.19 ± 5.39	+0.35	1.74%
Dapa 10	24	-0.75 ± 4.64	0.00	1.04%
Embamet 5	6	-0.75 ± 2.40	-0.50	0.83%
Embamet 12.5	57	-0.01 ± 3.46	0.00	-0.14%
Dapamet 5	5	+0.26 ± 3.64	+1.00	-0.48%
Emba 25	11	+0.49 ± 2.36	0.00	-0.27%

Table 4: The threshold, number, percentage, and clinical significance.

Threshold	Number	Percentage	Clinical significance
≥10% loss	0.0%	0.0%	Very significant
≥5% loss	5.1%	5.1%	Clinically significant
≥3% loss	13.2%	13.2%	Modest benefit
<3% change	79.4%	79.4%	Minimal change
≥3% gain	7.4%	7.4%	Weight gain

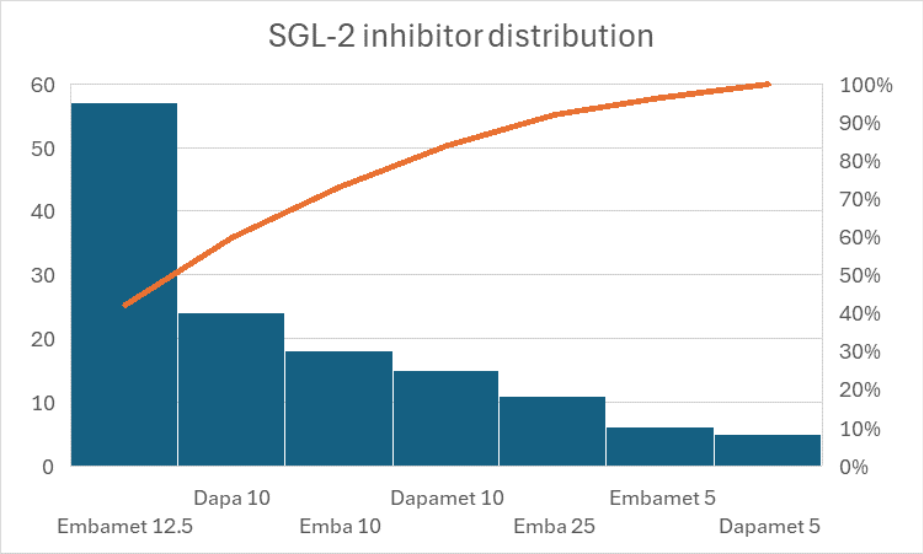

Figure 2: SGL-2 inhibitor distribution.

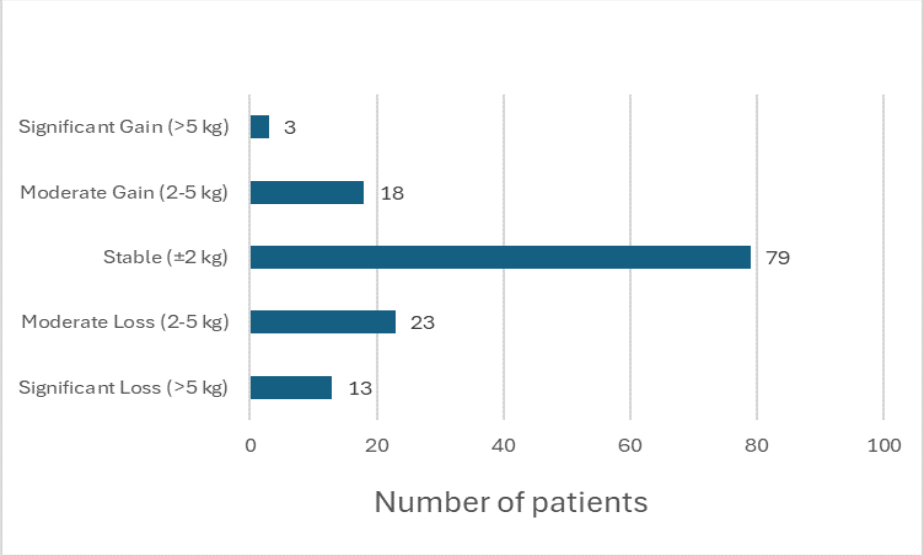

Figure 3: Weight change categories.

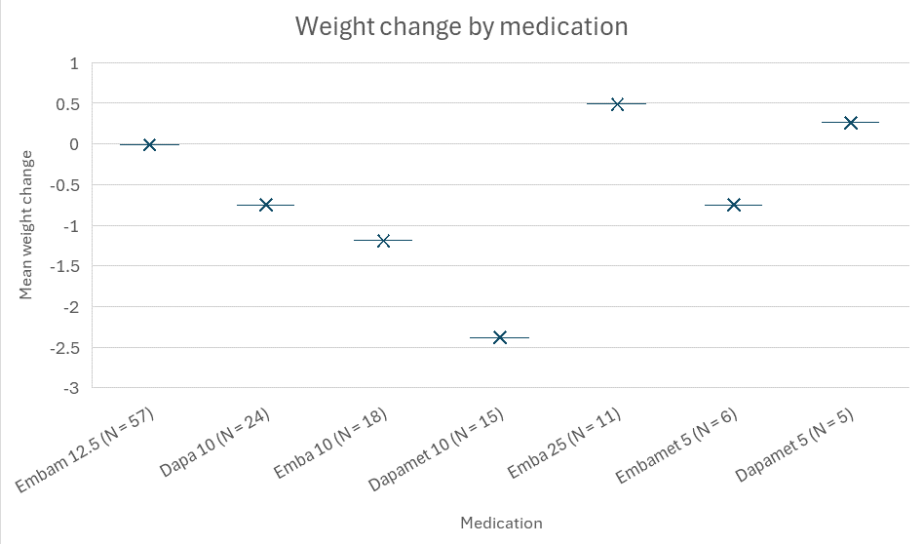

Figure 4: Weight changes due to medications.

Older adults may have lower compensatory hyperphagia. They have age-related changes in appetite regulation and different hormonal responses to glycosuria. Older patients may have more stable dietary habits and be less likely to compensate for caloric loss. Greater disease burden in older patients affects their weight loss. Older patients may have higher BG and greater glycosuria, leading to greater weight loss.

Dapamet 10 showed the greatest mean weight loss (-2.38 kg). Embamet 12.5 showed minimal weight loss (-0.01 kg). There was no clear pattern favoring monotherapy or combination therapy due to variable results from the different formulations.

CLINICAL IMPLICATIONS

Patients should be counseled that significant weight loss is not guaranteed. The SGLT-2 inhibitors are mainly glucose-lowering agents, not weight loss agents. Average weight change in a real-world setting is minimal. Additionally, dietary intervention may be necessary for meaningful weight loss. The patient may unconditionally compensate for glycosuria-induced caloric loss. Structured nutrition programs should accompany SGLT-2 inhibitor therapy. Older patients may derive greater weight benefits. Individual response is highly variable. Patient-specific factors should be considered when setting weight-loss goals. Regular weight monitoring should be considered to identify responders and non-responders. Early identification of weight gain is important for intervention.

STRENGTHS AND LIMITATIONS

The key strengths of this study include real-world data reflecting actual clinical practice, patients eat a regular diet with no restriction, the sample size is adequate (N = 136), a comprehensive subgroup analysis was implemented to detect the various correlations, and the study is a 12-month follow-up.

The main limitations include that it is based on a retrospective observational model. Potential confounding variables may affect the result. Variable timing of weight measurement, small size of some groups, limited geographic area, and it may not be generalized to other populations.

FUTURE DIRECTIONS

Conduct prospective observational studies with comprehensive data collection, including measures of adherence, dietary intake, and physical activity. Conduct a long-term study for more than 12 months. Additionally, the study includes an assessment of changes in body composition (fat and muscle), hormonal and metabolic changes, appetite regulation, and energy expenditure. Compare with other SGLT-2 inhibitors to evaluate their effectiveness. Conduct randomized trials of SGLT-2 inhibitors with vs. without dietary counseling. Assessing optimal dietary intake to maximize weight loss and evaluation of compensatory eating behaviors.

CONCLUSION

This retrospective study was conducted to evaluate the association between SGLT-2 inhibitors and weight reduction in T2D patients. SGLT-2 inhibitors did not produce significant weight loss over 12 months when patients followed a regular diet without dietary restrictions. The majority of patients (58.8%) maintained steady weight, but only 25.7% experienced a little weight loss (exceeding 2 kg), and 5.1% achieved a clinically significant weight reduction (more than 5%). Age was the sole significant predictor of weight change, with older patients exhibiting greater weight reduction. Outcomes in the real world are different from those in clinical trials. This is probably because of differences in how patients are chosen, how they are counseled about their diets, and how their adherence is monitored. SGLT-2 inhibitors should not be prescribed primarily for weight loss without accompanying lifestyle modifications.

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ABBREVIATIONS

BG: Blood Glucose; **T2D:** Type 2 Diabetes; **SGLT-2:** Sodium–Glucose Cotransporter-2; **T1DM:** Type 1 Diabetes Mellitus; **DSFH:** Dr. Soliman Fakeeh Hospital; **IRB:** Institutional Review Board; **SPSS:** Statistical Package for the Social Sciences; **BMI:** Body Mass Index; **SBP:** Systolic Blood Pressure; **DBP:** Diastolic Blood Pressure; **HbA1c:** Glycated Hemoglobin; **HDL:** High-Density Lipoprotein; **LDL:** Low-Density Lipoprotein; **eGFR:** Estimated Glomerular Filtration Rate; **Cr:** Creatinine; **SGPT (ALT):** Serum Glutamic Pyruvic Transaminase (Alanine Aminotransferase); **A/C ratio:** Albumin-to-Creatinine Ratio; **CV:** Cardiovascular; **GIT:** Gastrointestinal Tract; **RCTs:** Randomized Controlled Trials.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

IRB STATEMENT

The study protocol was approved by the Institutional Review Board of Fakeeh College for Medical Sciences (FCMS), Jeddah, Saudi Arabia. IRB approval No. 526/IRB/2023.

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