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COMPARATIVE STUDY OF GLYCAEMIC CONTROL AND RENAL FUNCTION AMONG PATIENTS RECEIVING METFORMIN WITH SGLT2 INHIBITORS VERSUS METFORMIN WITH DPP-4 INHIBITORS

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ABSTRACT

Background: Type 2 diabetes mellitus requires sustained glycaemic management and monitoring of renal complications. Metformin is frequently combined with sodium-glucose cotransporter-2 (SGLT2) inhibitors or dipeptidyl peptidase-4 (DPP-4) inhibitors, making comparative assessment clinically important. **Aim:** To compare glycaemic control, renal function, and adverse events among patients receiving metformin with SGLT2 inhibitors versus metformin with DPP-4 inhibitors.

Materials and Methods: This hospital-based prospective observational comparative study included 112 patients with type 2 diabetes mellitus at a tertiary care hospital. Group A comprised 56 patients receiving metformin with SGLT2 inhibitors, while Group B comprised 56 patients receiving metformin with DPP-4 inhibitors. Demographic characteristics, fasting and postprandial plasma glucose, HbA1c, serum creatinine, estimated glomerular filtration rate (eGFR), urinary albumin-to-creatinine ratio (UACR), biochemical parameters, and adverse events were assessed. Data were analysed using IBM SPSS Statistics version 28.0, with $p<0.05$ considered statistically significant.

Results: Mean HbA1c was significantly lower in Group A than Group B (7.03 ± 0.73% versus 7.75 ± 0.81%; $p<0.001$). Fasting plasma glucose (139.28 ± 21.89 versus 157.65 ± 24.00 mg/dL; $p<0.001$) and postprandial plasma glucose (201.60 ± 33.06 versus 222.35 ± 30.96 mg/dL; $p=0.001$) were also significantly lower. HbA1c below 7.00% was achieved by 50.00% versus 17.86% of patients ($p<0.001$). Mean eGFR was higher (84.58 ± 13.94 versus 74.87 ± 12.45 mL/min/1.73 m²; $p<0.001$), whereas median UACR was lower (18.90 versus 40.54 mg/g; $p<0.001$) in Group A. Genital infections were more frequent in Group A (14.29% versus 1.79%; $p=0.032$).

Conclusion: Metformin with SGLT2 inhibitors was associated with more favourable glycaemic and renal parameters than metformin with DPP-4 inhibitors. However, genital infections were more frequent, emphasizing the importance of individualized treatment selection and safety monitoring.

Keywords: Type 2 diabetes mellitus; Metformin; SGLT2 inhibitors; DPP-4 inhibitors; Renal function.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a major and expanding public health challenge associated with persistent hyperglycaemia, metabolic dysfunction, and progressive damage to multiple organ systems. Its increasing prevalence places considerable pressure on patients, healthcare professionals, and tertiary care services, particularly where cardiovascular and renal complications coexist. Although the condition is primarily characterized by impaired insulin secretion and insulin resistance, its clinical consequences extend far beyond abnormal blood glucose concentrations. Effective management

therefore requires sustained glycaemic control, reduction of modifiable cardiovascular risks, and early recognition of kidney impairment. Contemporary estimates of the global diabetes burden emphasize the importance of accessible and effective long-term treatment strategies.[1] The relationship between glycaemic control and diabetic complications is complex and influenced by disease duration, age, body composition, blood pressure, and associated metabolic abnormalities. Persistent hyperglycaemia contributes to endothelial dysfunction, oxidative stress, inflammation, and microvascular injury, thereby increasing the likelihood of diabetic kidney disease and other complications. Glycated haemoglobin (HbA1c) provides an estimate of longer-term glycaemic exposure, whereas fasting and postprandial plasma glucose reflect different aspects of daily glucose regulation. Current approaches to T2DM management emphasize individualizing treatment according to glycaemic targets, weight, hypoglycaemia risk, comorbid conditions, patient preferences, and the broader benefits of the available medications.[2] Metformin remains a widely used foundation of pharmacological treatment because it reduces hepatic glucose production, improves insulin sensitivity, and has a well-established clinical profile. However, progressive deterioration in pancreatic beta-cell function and ongoing insulin resistance may prevent adequate glycaemic control with metformin alone. Additional glucose-lowering agents are frequently prescribed to achieve individualized targets while limiting treatment-related complications. The selection of second-line therapy has consequently become an important clinical decision rather than a choice based exclusively on glucose concentrations. Particular consideration is required when patients have obesity, hypertension, cardiovascular disease, albuminuria, or declining kidney function, because these characteristics can influence both medication suitability and long-term treatment priorities.[3] Dipeptidyl peptidase-4 (DPP-4) inhibitors represent one class commonly combined with metformin in routine practice. These agents inhibit degradation of endogenous incretin hormones, thereby enhancing glucose-dependent insulin secretion and suppressing inappropriate glucagon release. Their generally weight-neutral profile, oral administration, and relatively low intrinsic risk of hypoglycaemia make them convenient options for selected patients. Nevertheless, the magnitude and durability of glucose lowering may vary with baseline glycaemic status and disease progression. Comparative evaluation of metformin-based regimens is therefore clinically relevant, particularly when differences in individual characteristics or coexisting renal disease may influence the choice of additional medication.[4] Sodium-glucose cotransporter-2 (SGLT2) inhibitors provide an alternative mechanism by reducing glucose reabsorption in the proximal renal tubules and promoting urinary glucose excretion. Their action is largely independent of pancreatic insulin secretion, distinguishing them from incretin-based therapy. Beyond glucose reduction, SGLT2 inhibition can influence body weight, blood pressure, intraglomerular haemodynamics, and renal sodium handling. These effects have increased interest in their use among individuals with diabetes who are at risk of kidney disease. Nevertheless, treatment requires attention to volume depletion, genital infections, kidney function, and other clinical factors that may affect safety and suitability.[5] The kidney is central to both the complications and pharmacological management of T2DM. Chronic hyperglycaemia and associated hypertension can promote glomerular injury, albumin leakage, and progressive loss of filtration capacity. In this setting, clinical assessment should extend beyond serum creatinine alone. Estimated glomerular filtration rate (eGFR) reflects filtration function, while the urinary albumin-to-creatinine ratio (UACR) provides complementary information about kidney injury. These measurements are particularly useful when evaluating treatment groups with potentially different renal and cardiovascular risk profiles. Their interpretation also requires consideration of baseline kidney status, concurrent medications, and the possibility that observational differences may not represent treatment effects.[6]

MATERIALS AND METHODS

The present study was designed as a hospital-based, prospective observational comparative study to evaluate and compare glycaemic control and renal function among patients with type 2 diabetes mellitus (T2DM) receiving metformin in combination with sodium-glucose cotransporter-2 (SGLT2) inhibitors or dipeptidyl peptidase-4 (DPP-4) inhibitors. The study aimed to assess differences in glycaemic parameters, renal function indicators, metabolic profiles, and associated clinical characteristics between the two treatment groups. The study was conducted at a tertiary care hospital in the Departments of General Medicine. Patients attending the diabetic clinic, general medicine outpatient department, and associated follow-up services were screened for eligibility. Clinical examinations, laboratory investigations, and relevant treatment details were recorded using a structured data collection proforma. A total of 112 patients diagnosed with type 2 diabetes mellitus were included using a consecutive sampling technique. Eligible patients were categorized into two groups according to their prescribed antidiabetic combination therapy. Group A comprised 56 patients receiving metformin with SGLT2 inhibitors, whereas Group B comprised 56 patients receiving metformin with DPP-4 inhibitors.

Inclusion Criteria

Patients aged 18 years and above with an established diagnosis of type 2 diabetes mellitus were eligible for

inclusion. Patients receiving either metformin with an SGLT2 inhibitor or metformin with a DPP-4 inhibitor for at least three months, with stable treatment regimens, were considered. Participants were required to have available glycaemic and renal function investigations and to provide written informed consent.

Exclusion Criteria

Patients with type 1 diabetes mellitus, gestational diabetes, acute kidney injury, advanced chronic kidney disease requiring dialysis, or an estimated glomerular filtration rate below 30 mL/min/1.73 m² were excluded. Patients with severe hepatic dysfunction, active malignancy, acute systemic infections, pregnancy, or lactation were excluded. Individuals receiving systemic corticosteroids or additional glucose-lowering medications likely to influence the comparison were also excluded.

Methodology

Detailed demographic and clinical information was collected, including age, sex, body mass index (BMI), duration of diabetes, family history, smoking status, alcohol consumption, and associated comorbidities. History of hypertension, dyslipidaemia, cardiovascular disease, and chronic kidney disease was documented. Anthropometric measurements included height, weight, and BMI. Systolic and diastolic blood pressure were recorded using standardized procedures. Current antidiabetic medications, drug dosages, treatment adherence, and concomitant medications, particularly antihypertensive and renoprotective agents, were documented.

Assessment of Glycaemic Control

Glycaemic control was assessed using fasting plasma glucose (FPG), two-hour postprandial plasma glucose (PPPG), and glycated haemoglobin (HbA1c). Fasting blood samples were collected following an overnight fast of 8–12 hours. Plasma glucose concentrations were measured using standardized enzymatic methods, while HbA1c was estimated using a standardized laboratory method. HbA1c below 7.00% was considered a conventional indicator of satisfactory glycaemic control, while recognizing individualized treatment targets. The mean values of glycaemic parameters and the proportions achieving glycaemic targets were compared between both groups.

Assessment of Renal Function

Renal function was evaluated using serum creatinine, blood urea, estimated glomerular filtration rate (eGFR), and urinary albumin-to-creatinine ratio (UACR). Serum creatinine was measured using a standardized laboratory assay, and eGFR was calculated using the 2021 CKD-EPI creatinine equation. Urinary albumin excretion was assessed using spot urine samples. An eGFR below 60 mL/min/1.73 m² was categorized as reduced renal function, while UACR ≥30 mg/g indicated increased urinary albumin excretion. These parameters were compared to assess differences in renal profiles between treatment groups.

Additional Biochemical and Safety Parameters

Additional biochemical investigations included serum sodium, potassium, total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol. Clinical records were reviewed for documented hypoglycaemic episodes, urinary tract infections, genital infections, dehydration, and other treatment-related adverse events. These parameters were evaluated to provide a broader assessment of the metabolic and clinical profiles associated with both treatment combinations.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 28.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution. Categorical variables were presented as frequencies and percentages. The independent samples Student's t-test or Mann–Whitney U test was applied for intergroup comparisons of continuous variables. The Chi-square test or Fisher's exact test was used for categorical variables. Pearson's or Spearman's correlation analysis was performed to assess relationships between glycaemic and renal parameters. Multivariable linear regression was used, where appropriate, to adjust for potential confounding factors. A p-value less than 0.05 was considered statistically significant.

RESULTS

Table 1. Comparison of Baseline Demographic and Clinical Characteristics Between the Two Study Groups (N=112)

Table 1 presents the baseline demographic and clinical characteristics of the 112 patients included in the study. The mean age was 55.30 ± 8.69 years in Group A and 55.91 ± 9.37 years in Group B, with no statistically significant difference (p=0.723). Male patients constituted 46.43% and 57.14% of the respective groups (p=0.257). The mean BMI was 26.96 ± 3.32 kg/m² in Group A and 26.57 ± 3.20 kg/m² in Group B (p=0.532), while the mean duration of diabetes was 9.36 ± 3.48 and 8.46 ± 3.68 years, respectively (p=0.190). Hypertension was observed in 46.43% and 48.21% of patients, whereas dyslipidaemia was present in 51.79% and 35.71%, respectively. Cardiovascular disease was recorded in 7.14% of Group A and 17.86% of Group B patients, while ACE inhibitor/ARB therapy was documented in 48.21% and 39.29%, respectively. None of the baseline demographic or clinical characteristics showed a statistically significant intergroup difference (p>0.05).

Table 2. Comparison of Glycaemic Control Parameters Between the Two Study Groups (N=112)

Table 2 demonstrates significant differences in glycaemic control parameters between the two treatment groups. The mean fasting plasma glucose

was significantly lower in Group A (139.28 ± 21.89 mg/dL) compared with Group B (157.65 ± 24.00 mg/dL), with p<0.001. Similarly, mean postprandial plasma glucose was 201.60 ± 33.06 mg/dL in Group A and 222.35 ± 30.96 mg/dL in Group B (p=0.001). The mean HbA1c was significantly lower among patients receiving metformin with SGLT2 inhibitors (7.03 ± 0.73%) than among those receiving metformin with DPP-4 inhibitors (7.75 ± 0.81%; p<0.001). Satisfactory glycaemic control, defined as HbA1c below 7.00%, was observed in 50.00% of Group A patients compared with 17.86% of Group B patients (p<0.001). Conversely, HbA1c ≥8.00% was recorded in 8.93% and 37.50% of patients, respectively (p<0.001).

Table 3. Comparison of Renal Function Parameters Between the Two Study Groups (N=112)

Table 3 compares renal function parameters between patients receiving metformin with SGLT2 inhibitors and those receiving metformin with DPP-4 inhibitors. The mean serum creatinine was significantly lower in Group A (0.93 ± 0.18 mg/dL) compared with Group B (1.06 ± 0.19 mg/dL; p<0.001), while mean blood urea levels were 25.72 ± 7.83 and 28.94 ± 7.14 mg/dL, respectively (p=0.025). The mean estimated glomerular filtration rate was significantly higher in Group A (84.58 ± 13.94 mL/min/1.73 m²) than in Group B (74.87 ± 12.45 mL/min/1.73 m²; p<0.001). The median urinary albumin-to-creatinine ratio was 18.90 mg/g (IQR: 11.39–31.05) in Group A compared with 40.54 mg/g (IQR: 23.56–72.61) in Group B (p<0.001). Reduced eGFR below 60 mL/min/1.73 m² was observed in 1.79% and 16.07% of patients, respectively (p=0.016). Furthermore, increased urinary albumin excretion (UACR ≥30 mg/g) was present in 26.79% of Group A and 66.07% of Group B patients (p<0.001).

Table 4. Comparison of Lipid Profile and Serum Electrolyte Parameters Between the Two Study Groups (N=112)

Table 4 presents the comparison of lipid profile and serum electrolyte parameters between the two groups. Mean total cholesterol levels were 180.51 ± 28.32 mg/dL in Group A and 182.79 ± 28.71 mg/dL in Group B, without a statistically significant difference (p=0.673). The mean triglyceride concentration was comparatively higher in Group A (162.65 ± 37.04 mg/dL) than in Group B (152.01 ± 32.26 mg/dL), although the difference was not statistically significant (p=0.108). Mean LDL cholesterol was 105.95 ± 28.87 mg/dL and 110.05 ± 30.27 mg/dL, respectively (p=0.465), whereas HDL cholesterol levels were 42.03 ± 7.66 mg/dL and 42.54 ± 7.50 mg/dL (p=0.723). Serum sodium concentrations were nearly identical in both groups, measuring 138.25 ± 2.45 and 138.21 ± 2.10 mEq/L, respectively (p=0.925). Similarly, serum potassium levels were 4.26 ± 0.30 mEq/L in Group A and 4.35 ± 0.33 mEq/L in Group B (p=0.118).

Table 5. Comparison of Documented Adverse Events Between the Two Study Groups (N=112)

Table 5 illustrates the distribution of documented adverse events among patients receiving the two antidiabetic combination therapies. Hypoglycaemic episodes were observed in 3.57% of Group A patients compared with 8.93% of Group B patients, although the difference was statistically insignificant (p=0.438). Urinary tract infections were documented in 10.71% and 7.14% of patients, respectively (p=0.742). However, genital infections were significantly more frequent in Group A (14.29%) than in Group B (1.79%), with a statistically significant difference (p=0.032). Dehydration episodes were recorded in 7.14% of Group A and 3.57% of Group B patients (p=0.679). At least one recorded adverse event was observed in 30.36% of patients receiving metformin with SGLT2 inhibitors compared with 17.86% receiving metformin with DPP-4 inhibitors (p=0.122).

Table 6. Multivariable Regression Analysis of the Association Between Treatment Group and Glycaemic and Renal Parameters (N=112)

Table 6 presents the multivariable regression analysis evaluating the association between treatment group and glycaemic and renal function parameters after adjustment for potential confounding factors. Patients receiving metformin with SGLT2 inhibitors demonstrated an adjusted mean HbA1c that was 0.81 percentage points lower than that of patients receiving metformin with DPP-4 inhibitors (adjusted difference: −0.81; 95% CI: −1.11 to −0.51; p<0.001). Similarly, Group A was associated with a significantly higher adjusted eGFR, with a mean difference of +10.44 mL/min/1.73 m² (95% CI: +5.71 to +15.18; p<0.001). The adjusted geometric mean ratio for UACR was 0.42 (95% CI: 0.32–0.54; p<0.001), indicating that the adjusted geometric mean UACR in Group A was approximately 58.00% lower than in Group B.

Table 1: Comparison of Baseline Demographic and Clinical Characteristics Between the Two Study Groups (N=112)

Parameters	Group A (n=56)	Group B (n=56)	p-value
Age (years), mean ± SD	55.30 ± 8.69	55.91 ± 9.37	0.723
Male	26 (46.43%)	32 (57.14%)	0.257
BMI (kg/m²), mean ± SD	26.96 ± 3.32	26.57 ± 3.20	0.532
Duration of diabetes (years)	9.36 ± 3.48	8.46 ± 3.68	0.190
Systolic BP (mmHg)	132.62 ± 13.17	135.29 ± 12.37	0.271
Diastolic BP (mmHg)	81.08 ± 7.81	82.27 ± 6.34	0.377
Hypertension	26 (46.43%)	27 (48.21%)	0.850
Dyslipidaemia	29 (51.79%)	20 (35.71%)	0.086
Cardiovascular disease	4 (7.14%)	10 (17.86%)	0.151
ACE inhibitor/ARB therapy	27 (48.21%)	22 (39.29%)	0.341

Table 2: Comparison of Glycaemic Control Parameters Between the Two Study Groups (N=112)

Glycaemic parameters	Group A (n=56)	Group B (n=56)	p-value
Fasting plasma glucose (mg/dL)	139.28 ± 21.89	157.65 ± 24.00	<0.001
Postprandial plasma glucose (mg/dL)	201.60 ± 33.06	222.35 ± 30.96	0.001
HbA1c (%)	7.03 ± 0.73	7.75 ± 0.81	<0.001
HbA1c <7.00%	28 (50.00%)	10 (17.86%)	<0.001
HbA1c ≥8.00%	5 (8.93%)	21 (37.50%)	<0.001

Table 3: Comparison of Renal Function Parameters Between the Two Study Groups (N=112)

Renal parameters	Group A (n=56)	Group B (n=56)	p-value
Serum creatinine (mg/dL)	0.93 ± 0.18	1.06 ± 0.19	<0.001
Blood urea (mg/dL)	25.72 ± 7.83	28.94 ± 7.14	0.025
eGFR (mL/min/1.73 m²)	84.58 ± 13.94	74.87 ± 12.45	<0.001
UACR (mg/g), median (IQR)	18.90 (11.39–31.05)	40.54 (23.56–72.61)	<0.001
eGFR <60 mL/min/1.73 m²	1 (1.79%)	9 (16.07%)	0.016
UACR ≥30 mg/g	15 (26.79%)	37 (66.07%)	<0.001

Table 4: Comparison of Lipid Profile and Serum Electrolyte Parameters Between the Two Study Groups (N=112)

Biochemical parameters	Group A (n=56)	Group B (n=56)	p-value
Total cholesterol (mg/dL)	180.51 ± 28.32	182.79 ± 28.71	0.673
Triglycerides (mg/dL)	162.65 ± 37.04	152.01 ± 32.26	0.108
LDL cholesterol (mg/dL)	105.95 ± 28.87	110.05 ± 30.27	0.465
HDL cholesterol (mg/dL)	42.03 ± 7.66	42.54 ± 7.50	0.723
Serum sodium (mEq/L)	138.25 ± 2.45	138.21 ± 2.10	0.925
Serum potassium (mEq/L)	4.26 ± 0.30	4.35 ± 0.33	0.118

Table 5: Comparison of Documented Adverse Events Between the Two Study Groups (N=112)

Adverse events	Group A (n=56)	Group B (n=56)	p-value
Hypoglycaemic episodes	2 (3.57%)	5 (8.93%)	0.438
Urinary tract infections	6 (10.71%)	4 (7.14%)	0.742
Genital infections	8 (14.29%)	1 (1.79%)	0.032
Dehydration episodes	4 (7.14%)	2 (3.57%)	0.679
Any recorded adverse event	17 (30.36%)	10 (17.86%)	0.122

Table 6: Multivariable Regression Analysis of the Association Between Treatment Group and Glycaemic and Renal Parameters (N=112)

Outcome variable	Adjusted effect (Group A versus Group B)	95% confidence interval	p-value
HbA1c (%)	−0.81	−1.11 to −0.51	<0.001
eGFR (mL/min/1.73 m²)	+10.44	+5.71 to +15.18	<0.001
UACR (ratio of geometric means)	0.42	0.32 to 0.54	<0.001

DISCUSSION

The present study included 112 patients with type 2 diabetes mellitus, equally distributed between metformin with SGLT2 inhibitors (Group A) and metformin with DPP-4 inhibitors (Group B). The mean age was 55.30 ± 8.69 years in Group A and 55.91 ± 9.37 years in Group B (p=0.723), while the mean BMI was 26.96 ± 3.32 and 26.57 ± 3.20 kg/m², respectively (p=0.532). The mean duration of diabetes was 9.36 ± 3.48 years in Group A and 8.46 ± 3.68 years in Group B (p=0.190). These findings indicated broadly comparable baseline demographic characteristics. Scott et al. (2018), in the CompoSIT-R randomized clinical trial involving 613 treated patients, reported a higher mean age of 67.10 years, mean BMI of 31.60 kg/m², and mean diabetes duration of 10.60 years. Their study also demonstrated a greater reduction in HbA1c with sitagliptin (−0.51%) than dapagliflozin (−0.36%; p=0.006), contrasting with the more favourable glycaemic findings in the SGLT2 inhibitor group of the present study. These differences emphasize the potential influence of patient characteristics, renal function, and treatment selection on glycaemic outcomes.[7] The present study demonstrated significantly more favourable glycaemic parameters among patients receiving metformin with SGLT2 inhibitors compared with those receiving metformin with DPP-4 inhibitors. Mean fasting plasma glucose was 139.28 ± 21.89 mg/dL in Group A compared with 157.65 ± 24.00 mg/dL in Group B (p<0.001), while mean postprandial plasma glucose was 201.60 ± 33.06 and 222.35 ± 30.96 mg/dL, respectively (p=0.001). The mean HbA1c was also significantly lower in Group A (7.03 ± 0.73%) than in Group B (7.75 ± 0.81%; p<0.001). Comparable findings were reported by Lavalle-González et al. (2013), who conducted a randomized trial involving 1,284 patients receiving background metformin therapy. At 52 weeks, the reductions in HbA1c were 0.73%, 0.88%, and 0.73% with canagliflozin 100 mg, canagliflozin 300 mg, and sitagliptin 100 mg, respectively. Canagliflozin 300 mg demonstrated significantly greater HbA1c reduction than sitagliptin, with a between-group difference of −0.15 percentage points (95% CI: −0.27 to −0.03). Thus, both studies support favourable glycaemic outcomes with certain SGLT2 inhibitor regimens, although the

present study compared observed values rather than treatment-induced changes.[8] Regarding glycaemic target achievement, the present study observed that 28 patients (50.00%) receiving metformin with SGLT2 inhibitors achieved HbA1c below 7.00%, compared with 10 patients (17.86%) receiving metformin with DPP-4 inhibitors (p<0.001). Conversely, HbA1c ≥8.00% was documented in only 8.93% of Group A patients compared with 37.50% of Group B patients (p<0.001). These findings are broadly consistent with those reported by Häring et al. (2014), who evaluated empagliflozin added to metformin in 637 patients. After 24 weeks, the adjusted mean HbA1c reductions were 0.70% and 0.77% with empagliflozin 10 mg and 25 mg, respectively, compared with 0.13% with placebo (p<0.001). Approximately 38.00–39.00% of patients receiving empagliflozin achieved HbA1c below 7.00%, compared with 13.00% receiving placebo. The higher proportion achieving glycaemic targets in Group A of the present study is consistent with the effectiveness of SGLT2 inhibitor-based therapy in supporting glucose control, although differences in study design and comparator treatment limit direct equivalence.[9] The present study demonstrated significant differences in renal function parameters between the two treatment groups. Mean serum creatinine was lower in Group A (0.93 ± 0.18 mg/dL) compared with Group B (1.06 ± 0.19 mg/dL; p<0.001), while mean eGFR was significantly higher in Group A (84.58 ± 13.94 mL/min/1.73 m²) than in Group B (74.87 ± 12.45 mL/min/1.73 m²; p<0.001). Similar evidence supporting favourable renal outcomes with SGLT2 inhibitors was reported by Melzer Cohen et al. (2023) in a real-world propensity score-matched cohort involving 19,648 patients. The incidence of the composite kidney-specific outcome was 6.90 events per 1,000 patient-years with SGLT2 inhibitors compared with 9.50 events per 1,000 patient-years with DPP-4 inhibitors. SGLT2 inhibitor treatment was associated with a significantly lower risk of kidney-specific outcomes (HR: 0.72; 95% CI: 0.61–0.86; p<0.001) and a slower annual decline in eGFR, with an adjusted between-group difference of 0.49 mL/min/1.73 m² per year. These results support the potential renal advantages associated with SGLT2 inhibitors, although the cross-sectional renal differences in the present study cannot establish slower kidney-function decline.[10] The present study further identified significantly lower urinary albumin excretion among patients receiving metformin with SGLT2 inhibitors. The median UACR was 18.90 mg/g (IQR: 11.39–31.05) in Group A compared with 40.54 mg/g (IQR: 23.56–72.61) in Group B (p<0.001). Furthermore, increased urinary albumin excretion (UACR ≥30 mg/g) was observed in 26.79% and 66.07% of patients, respectively (p<0.001). These findings may be compared with those of Pollock et al. (2019), who conducted the DELIGHT randomized clinical trial among patients with type 2 diabetes and chronic kidney disease. At 24 weeks, dapagliflozin alone produced a 21.00% greater reduction in UACR than placebo (95% CI: −34.10% to −5.20%; p=0.011), whereas dapagliflozin combined with saxagliptin produced a 38.00% greater reduction (95% CI: −48.20% to −25.80%; p<0.001). Although this trial involved patients with more advanced renal impairment and different treatment combinations, its findings demonstrate the albuminuria-lowering potential of dapagliflozin and provide relevant evidence for interpreting the lower UACR observed in Group A.[11] The present study also demonstrated a significantly lower prevalence of reduced renal function among patients receiving metformin with SGLT2 inhibitors. An eGFR below 60 mL/min/1.73 m² was observed in only 1 patient (1.79%) in Group A compared with 9 patients (16.07%) in Group B (p=0.016). Mean blood urea levels were also significantly lower in Group A (25.72 ± 7.83 mg/dL) than in Group B (28.94 ± 7.14 mg/dL; p=0.025). These observations can be compared with Au et al. (2022), who conducted a population-based cohort study involving 6,333 SGLT2 inhibitor users and 25,332 DPP-4 inhibitor users, with a median follow-up of 3.80 years. Their analysis demonstrated that SGLT2 inhibitor use was associated with a significantly lower risk of end-stage renal disease (HR: 0.51; 95% CI: 0.42–0.62; p<0.001) and acute renal failure (HR: 0.59; 95% CI: 0.48–0.73; p<0.001). The authors also reported a slower decline in eGFR among SGLT2 inhibitor users, although findings regarding albuminuria were inconsistent across analyses. These findings support an association between SGLT2 inhibitor therapy and more favourable renal outcomes, but do not establish that the differences in the present study resulted from treatment.[12] The present study revealed no statistically significant differences in lipid profile and serum electrolyte parameters between the two treatment groups. Mean total cholesterol was 180.51 ± 28.32 mg/dL in Group A compared with 182.79 ± 28.71 mg/dL in Group B (p=0.673), while LDL cholesterol levels were 105.95 ± 28.87 and 110.05 ± 30.27 mg/dL, respectively (p=0.465). Mean HDL cholesterol was 42.03 ± 7.66 mg/dL in Group A and 42.54 ± 7.50 mg/dL in Group B (p=0.723). Serum sodium and potassium concentrations also showed no significant intergroup differences (p=0.925 and p=0.118, respectively). Schernthaner et al. (2013), in a randomized trial involving 755 patients receiving background metformin and sulfonylurea, reported that canagliflozin 300 mg produced a 7.60% increase in HDL cholesterol compared with 0.60% with sitagliptin 100 mg at 52 weeks. LDL cholesterol increased by 11.70% with canagliflozin and 5.20% with sitagliptin, while triglyceride changes were modest in both groups. Unlike the present study, which showed no significant differences in absolute lipid values, their findings demonstrated differences in lipid changes over time. The variation may reflect differences in concomitant therapy, baseline metabolic characteristics, and duration of treatment assessment.[13] The assessment of adverse events in the present study demonstrated significant variation

in the occurrence of genital infections between the two groups. Genital infections were documented in 8 patients (14.29%) receiving metformin with SGLT2 inhibitors compared with 1 patient (1.79%) receiving metformin with DPP-4 inhibitors (p=0.032). Urinary tract infections were observed in 10.71% and 7.14% of patients, respectively (p=0.742), while hypoglycaemic episodes occurred in 3.57% and 8.93% (p=0.438). Overall adverse events were recorded in 30.36% of Group A patients compared with 17.86% of Group B patients, without a statistically significant difference (p=0.122). Comparable findings were reported by Lega et al. (2019), who conducted a population-based study involving 21,444 new SGLT2 inhibitor users and 22,463 new DPP-4 inhibitor users. Their study demonstrated a significantly increased risk of genital mycotic infections among SGLT2 inhibitor users (adjusted HR: 2.47; 95% CI: 2.08–2.92; p<0.001), whereas the adjusted hazard ratio for urinary tract infections was 0.89 (95% CI: 0.78–1.00; p=0.05). These results are consistent with the higher frequency of genital infections observed in Group A and highlight the importance of monitoring genitourinary adverse events during SGLT2 inhibitor therapy.[14] The multivariable regression analysis in the present study demonstrated statistically significant associations between treatment category and glycaemic and renal function parameters after adjustment for potential confounding factors. Patients receiving metformin with SGLT2 inhibitors had an adjusted mean HbA1c that was 0.81 percentage points lower (95% CI: −1.11 to −0.51; p<0.001) and an adjusted mean eGFR that was 10.44 mL/min/1.73 m² higher (95% CI: 5.71–15.18; p<0.001) than those receiving metformin with DPP-4 inhibitors. The adjusted geometric mean ratio for UACR was 0.42 (95% CI: 0.32–0.54; p<0.001), indicating approximately 58.00% lower adjusted geometric mean urinary albumin excretion in Group A. These findings may be considered alongside those of Perkovic et al. (2019), who conducted the CREDENCE randomized clinical trial involving 4,401 patients with type 2 diabetes and albuminuric chronic kidney disease. During a median follow-up of 2.62 years, the primary composite renal and cardiovascular outcome occurred at rates of 43.20 and 61.20 events per 1,000 patient-years in the canagliflozin and placebo groups, respectively, representing a 30.00% relative risk reduction (HR: 0.70; 95% CI: 0.59–0.82; p=0.00001). Although the trial provided stronger evidence of renal protection with canagliflozin, its population and comparator differed substantially from those of the present study.[15]

CONCLUSION

The present study demonstrated that patients receiving metformin with SGLT2 inhibitors had significantly better glycaemic control and more favourable renal function parameters compared with those receiving metformin with DPP-4 inhibitors. Lower HbA1c, fasting and postprandial glucose levels, reduced urinary albumin excretion, and higher eGFR were observed in the SGLT2 inhibitor group. However, genital infections were significantly more frequent among patients receiving SGLT2 inhibitors, while other adverse events showed no significant differences. These findings suggest that metformin with SGLT2 inhibitors may be a favourable therapeutic option for selected patients with type 2 diabetes mellitus, although larger prospective studies are required to establish long-term comparative benefits and safety.

REFERENCES

1. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109119. doi: 10.1016/j.diabres.2021.109119.
2. Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, et al. Management of hyperglycaemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 2022;65(12):1925-1966. doi: 10.1007/s00125-022-05787-2.
3. American Diabetes Association Professional Practice Committee. 9. Pharmacologic approaches to glycemic treatment: Standards of Care in Diabetes—2025. Diabetes Care. 2025;48(Suppl 1):S181-S206. doi: 10.2337/dc25-S009.
4. GRADE Study Research Group. Glycemia reduction in type 2 diabetes—glycemic outcomes. N Engl J Med. 2022;387(12):1063-1074. doi: 10.1056/NEJMoa2200433.
5. Heerspink HJL, Stefánsson BV, Correa-Rotter R, Chertow GM, Greene T, Hou FF, et al. Dapagliflozin in patients with chronic kidney disease. N Engl J Med. 2020;383(15):1436-1446. doi: 10.1056/NEJMoa2024816.
6. Herrington WG, Staplin N, Wanner C, Green JB, Hauske SJ, Emberson JR, et al. Empagliflozin in patients with chronic kidney disease. N Engl J Med. 2023;388(2):117-127. doi: 10.1056/NEJMoa2204233.
7. Scott R, Morgan J, Zimmer Z, Lam RLH, O'Neill EA, Kaufman KD, et al. A randomized clinical trial of the efficacy and safety of sitagliptin compared with dapagliflozin in patients with type 2 diabetes mellitus and mild renal insufficiency: the CompoSIT-R study. Diabetes Obes Metab. 2018;20(12):2876-2884. doi: 10.1111/dom.13473.
8. Lavalle-González FJ, Januszewicz A, Davidson J, Tong C, Qiu R, Canovatchel W, et al. Efficacy and safety of canagliflozin compared with placebo and sitagliptin in patients with type 2 diabetes on background metformin monotherapy: a randomised trial. Diabetologia. 2013;56(12):2582-2592. doi: 10.1007/s00125-013-3039-1.
9. Häring HU, Merker L, Seewaldt-Becker E, Weimer M, Meinicke T, Broedl UC, et al. Empagliflozin as add-on to metformin in patients with type 2 diabetes: a 24-week, randomized, double-blind, placebo-controlled trial. Diabetes Care. 2014;37(6):1650-1659. doi: 10.2337/dc13-2105.
10. Melzer Cohen C, Schechter M, Rozenberg A, Yanuv I, Sehtman-Shachar DR, Fishkin A, et al. Long-term, real-world kidney outcomes with SGLT2i versus DPP4i in type 2 diabetes without cardiovascular or kidney disease. Clin J Am Soc Nephrol. 2023;18(9):1153-1162. doi: 10.2215/CJN.0000000000000218.
11. Pollock C, Stefánsson B, Reyner D, Rossing P, Sjöström CD, Wheeler DC, et al. Albuminuria-lowering effect of dapagliflozin alone and in combination with saxagliptin and effect of dapagliflozin and saxagliptin on glycaemic control in patients with type 2 diabetes and chronic kidney disease

(DELIGHT): a randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol. 2019;7(6):429-441. doi: 10.1016/S2213-8587(19)30086-5.
12. Au PCM, Tan KCB, Cheung BMY, Wong ICK, Li HL, Cheung CL. Association between SGLT2 inhibitors vs DPP4 inhibitors and renal outcomes among patients with type 2 diabetes. J Clin Endocrinol Metab. 2022;107(7):e2962-e2970. doi: 10.1210/clinem/dgac164.
13. Schernthaner G, Gross JL, Rosenstock J, Guarisco M, Fu M, Yee J, et al. Canagliflozin compared with sitagliptin for patients with type 2 diabetes who do not have adequate glycemic control with metformin plus sulfonylurea: a 52-week randomized trial. Diabetes Care. 2013;36(9):2508-2515. doi: 10.2337/dc12-2491.
14. Lega IC, Bronskill SE, Campitelli MA, Guan J, Stall NM, Lam K, et al. Sodium glucose cotransporter 2 inhibitors and risk of genital mycotic and urinary tract infection: a population-based study of older women and men with diabetes. Diabetes Obes Metab. 2019;21(11):2394-2404. doi: 10.1111/dom.13820.
15. Perkovic V, Jardine MJ, Neal B, Bompoint S, Heerspink HJL, Charytan DM, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. N Engl J Med. 2019;380(24):2295-2306. doi: 10.1056/NEJMoa1811744.