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Original article

Efficacy and Safety of Metformin, Injectable Insulin, and Sulfonylureas in Type 2 Diabetes Management: A Comparative Evaluation in Libyan Patients

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Abstract
Type 2 Diabetes Mellitus (T2DM) is a major health burden in Libya, where metformin, sulfonylureas, and insulin remain the main therapeutic options. This study evaluated the efficacy and safety of these agents, alone and in combination, with emphasis on glycemic control and organ function. A cross-sectional analysis was conducted at the Diabetes and Endocrinology Hospital in Tripoli between September 2025 and January 2026, enrolling 81 patients aged 30–75 years with confirmed T2DM. Participants were assigned to five therapeutic groups, and fasting blood glucose, HbA1c, renal indices, and hepatic enzymes were measured. Combination therapy, particularly insulin plus metformin, achieved superior glycemic control with lower HbA1c compared to sulfonylurea monotherapy. Renal impairment was most evident in the sulfonylurea plus metformin group, while hepatic enzyme elevations were more pronounced with sulfonylurea alone. In contrast, insulin plus metformin demonstrated more favorable hepatic outcomes. These findings highlight the advantages of combination therapy but emphasize the need for individualized treatment and careful monitoring of renal and hepatic function in resource-limited settings.
Keywords: Type 2 Diabetes Mellitus, Metformin, Insulin, Sulfonylureas, Glycemic Control, Renal Function, Hepatic Function, Combination Therapy, HbA1c, Libya.

Introduction

Type 2 Diabetes Mellitus (T2DM) represents a significant and escalating global health challenge, with an estimated prevalence of 537 million people in 2021, a figure projected to rise to 700 million by 2045 (1). The disease is pathologically characterized by a progressive loss of β-cell insulin secretion, often superimposed on a background of underlying insulin resistance (2). The prevalence of insulin resistance and its strong association with key biochemical markers—such as lipids and glycated hemoglobin (HbA1c)—are critical factors in disease progression, a relationship underscored by regional studies conducted in Tarhuna City (3). The chronic nature of T2DM necessitates effective and safe therapeutic strategies to mitigate its multifaceted complications, requiring a comprehensive approach that extends beyond glycemic control alone.

Despite the continuous evolution of pharmacological options, metformin, sulfonylureas, and insulin remain cornerstone therapies in the management of T2DM. Metformin is universally recommended as the first-line pharmacotherapy owing to its robust glucose-lowering efficacy, favorable cardiovascular safety profile, minimal risk of hypoglycemia, and potential for modest weight loss (4). Its primary mechanism of action involves the reduction of hepatic glucose production and the enhancement of peripheral glucose uptake and utilization. However, its clinical utility can be constrained by gastrointestinal side effects and, in rare cases, the risk of lactic acidosis, particularly in patients with significant renal impairment (5).

When metformin monotherapy proves insufficient to achieve glycemic targets, sulfonylureas (SUs) and insulin become crucial for treatment intensification. As insulin secretagogues, SUs effectively lower HbA1c levels by stimulating endogenous insulin release from pancreatic β-cells. Although cost-effective and potent, their mechanism is intrinsically linked to a notable risk of hypoglycemia and weight gain (4). Furthermore, concerns have been raised regarding their long-term durability and cardiovascular safety in comparison to newer agents (6,7). Concurrently, the management of dyslipidemia is a key component of comprehensive T2DM care, with studies confirming the integral role of statin therapy in controlling lipid profiles within this patient population (8).

Injectable insulin remains the most potent glucose-lowering therapy available, indispensable for patients with severe hyperglycemia or marked β-cell dysfunction. By supplementing or replacing deficient endogenous insulin, it effectively normalizes glycemia across the full spectrum of T2DM progression. Nevertheless, its application is associated with considerable challenges, including a heightened risk of hypoglycemia, the potential for substantial weight gain, and the practical burdens of daily injections and intensive self-monitoring (2). The clinical decision to initiate and titrate insulin must therefore carefully balance these risks against the imperative of achieving stringent glycemic targets to prevent microvascular complications (9,10). The primary objectives of this study was to evaluate and compare the effectiveness and safety of different glucose-lowering therapies—metformin, insulin, and sulfonylureas—by assessing their

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impact on glycemic control (fasting blood glucose and HbA1c), renal and hepatic function parameters, and treatment-related adverse effects, with HbA1c serving as the primary clinical outcome measure.

Materials and Methods

Study Design and Population

This cross-sectional analytical study was conducted at the Diabetes and Endocrinology Hospital in Tripoli, Libya, from September 2025 to January 2026. A total of 81 adult patients (aged 30–75 years) with a confirmed diagnosis of type 2 diabetes mellitus who had been on their current therapy for at least six months were enrolled. All included patients had type 2 diabetes, and their treatment regimens were selected and monitored with caution.

Classification of Treatment Groups

Participants were classified into five therapeutic groups:

1. Metformin
2. Insulin
3. Sulfonylurea
4. Insulin + Metformin
5. Sulfonylurea + Metformin

Data Collection and Laboratory Markers

After an overnight fast of 8–12 hours, venous blood samples were collected to measure fasting blood glucose (FBG), glycated hemoglobin (HbA1c), serum creatinine, estimated glomerular filtration rate (eGFR), and liver enzymes (AST and ALT) using standardized automated analyzers.

Statistical Analysis

Data were analyzed using SPSS version 27. One-way ANOVA was applied to compare biochemical markers across the five groups, while Chi-square tests were used to assess associations between therapy type and categorical variables. Statistical significance was set at $p < 0.05$.

Results

The study assessed the effects of different glucose-lowering therapies on glycemic control, renal function, and liver function in patients with type 2 diabetes mellitus. Data analysis revealed variations across treatment groups, including both monotherapies (metformin, insulin, sulfonylureas) and combination therapies (insulin + metformin, sulfonylurea + metformin). The detailed findings are presented in the following tables and figures.

The study cohort consisted of 81 patients, with a predominance of females (61.7%) compared to males (38.3%).

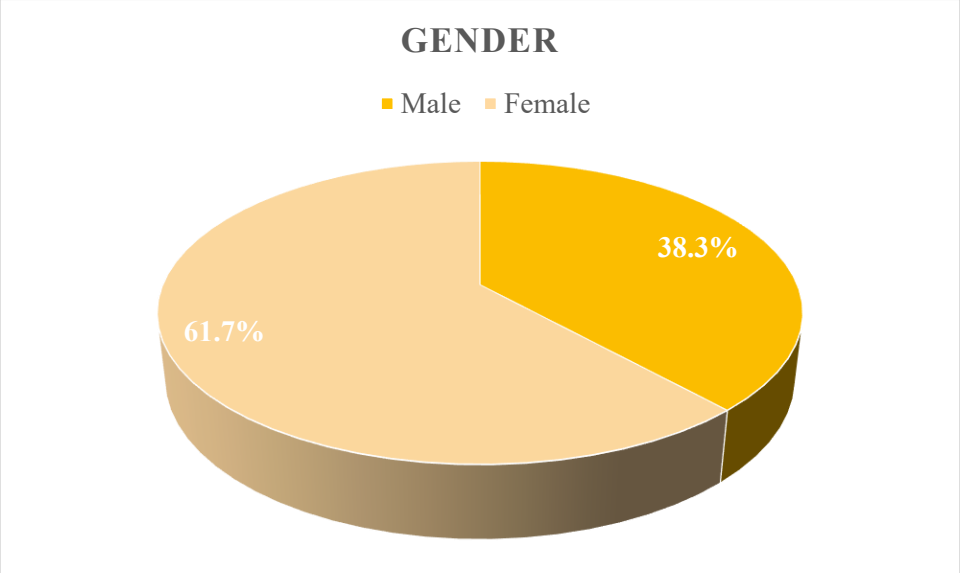

Figure1. Gender Distribution of the Study Population

The figure illustrates the percentage distribution of gender among the study population (N=81). Females constituted the majority, representing 61.7% of the cohort, while males accounted for 38.3%. This predominance of females in type 2 diabetes mellitus within the studied community. Gender distribution is an important baseline characteristic.

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Table 1. Baseline Characteristics of the Study Population

Clinical Parameter	N	Minimum	Maximum	Mean ± SD
Age (years)	81	34.0	74.0	55.9 ± 9.2
Weight (kg)	81	55.0	140.0	79.8 ± 15.9
BMI (kg/m²)	79	21.7	66.6	31.7 ± 9.3
Diabetes Duration (years)	81	1.0	37.0	10.1 ± 7.4
Fasting Blood Glucose (mg/dL)	81	99.0	377.0	183.8 ± 74.9
HbA1c (%)	81	5.7	11.8	8.0 ± 1.4
Creatinine (mg/dL)	81	0.6	1.9	0.86 ± 0.29
GFR (ml/min)	81	40.2	277.5	103.5 ± 40.3
AST (U/L)	81	6.5	43.0	19.5 ± 9.0
ALT (U/L)	81	5.0	64.6	19.8 ± 12.3

The study cohort consisted of 81 patients with type 2 diabetes mellitus, with a mean age of 55.9 years and a mean BMI of 31.7 kg/m², indicating an overweight to obese population. The average duration of diabetes was approximately 10 years, reflecting a chronically affected group. Biochemical parameters revealed a mean fasting blood glucose of 183.8 mg/dL and HbA1c of 8.0%, consistent with suboptimal glycemic control. Renal function markers showed a mean creatinine of 0.86 mg/dL and GFR of 103.5 ml/min, suggesting preserved renal function in most patients, though with wide variability. Liver enzymes (AST and ALT) were within the upper normal range, with mean values of 19.5 U/L and 19.8 U/L, respectively, indicating no overt hepatic dysfunction at baseline.

Table 2. Comparative Effects of Glucose-Lowering Therapies on Glycemic Control

Therapy	N	Mean FBG (mg/dL) ± SD	Mean HbA1c (%) ± SD
Sulfonylurea	4	115.5 ± 5.2	9.85 ± 0.17*
Insulin	29	189.9 ± 71.6	8.31 ± 1.53
Metformin	18	191.8 ± 95.9	8.00 ± 1.58
Insulin + Metformin	16	172.8 ± 53.2	7.66 ± 0.76*
Sulfonylurea + Metformin	14	193.1 ± 79.7	7.47 ± 1.01*
Total	81	183.8 ± 74.9	8.05 ± 1.38

**p=0.017 for HbA1c (ANOVA). Significant differences were observed between sulfonylurea vs. combined therapies. No significant differences in FBG (p=0.374).*

Table 3. Comparative Effects of Glucose-Lowering Therapies on Renal Function

Therapy	N	Mean Creatinine (mg/dL) ± SD	Mean GFR (ml/min) ± SD
Sulfonylurea	4	0.75 ± 0.06	126.2 ± 20.1
Insulin	29	0.84 ± 0.33	109.8 ± 30.8
Metformin	18	0.82 ± 0.22	123.6 ± 62.6*
Insulin + Metformin	16	0.78 ± 0.16	87.0 ± 14.1*
Sulfonylurea + Metformin	14	1.10 ± 0.35*	76.7 ± 24.0*

**p=0.016 for creatinine, *p=0.003 for GFR (ANOVA). Sulfonylurea+Metformin is associated with higher creatinine and lower GFR compared to Metformin.*

Table 4. Comparative Effects of Glucose-Lowering Therapies on Liver Function

Therapy	N	Mean AST (U/L) ± SD	Mean ALT (U/L) ± SD
Sulfonylurea	4	28.0 ± 17.3*	37.0 ± 31.9*
Insulin	29	17.5 ± 6.5	19.2 ± 11.0
Metformin	18	19.2 ± 8.2	21.2 ± 8.6
Insulin + Metformin	16	16.9 ± 8.1	12.3 ± 7.2*
Sulfonylurea + Metformin	14	24.6 ± 10.2	23.1 ± 10.1

**p=0.024 for AST, *p=0.003 for ALT (ANOVA). Sulfonylurea associated with higher liver enzymes compared to insulin and combined therapies.*

The comparative analysis of glucose-lowering therapies revealed distinct differences in glycemic control and biochemical parameters among patients with type 2 diabetes mellitus.

Although fasting blood glucose (FBG) did not differ significantly across treatment groups (p=0.374), HbA1c levels demonstrated statistically significant variation (p=0.017). Patients treated with sulfonylurea monotherapy exhibited the highest HbA1c values (9.85 ± 0.17%), whereas combined regimens (Insulin + Metformin and Sulfonylurea + Metformin) were associated with lower HbA1c levels (7.47–7.66%). These

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findings underscore the superior efficacy of combination therapy in achieving long-term glycemic control compared to sulfonylurea alone.

Creatinine levels varied significantly among groups (p=0.016), with sulfonylurea + metformin therapy showing elevated values (1.10 ± 0.35 mg/dL). Similarly, glomerular filtration rate (GFR) differed significantly (p=0.003), with sulfonylurea + metformin associated with reduced renal clearance (76.7 ± 24.0 ml/min) compared to metformin monotherapy (123.6 ± 62.6 ml/min). These results suggest a potential adverse impact of sulfonylurea-containing regimens on renal function, warranting careful monitoring in clinical practice.

Significant differences were also observed in hepatic enzymes. AST levels were higher in the sulfonylurea group (28.0 ± 17.3 U/L, p=0.024), while ALT was markedly elevated in sulfonylurea monotherapy (37.0 ± 31.9 U/L, p=0.003) compared to insulin + metformin (12.3 ± 7.2 U/L). These findings indicate that sulfonylurea therapy may be associated with hepatic stress, whereas combined regimens appear to exert a hepatoprotective effect.

Table 5. Association Between Glucose-Lowering Therapies and Glycemic Control Improvement

Therapy	No (n, %)	Yes (n, %)	Partial (n, %)	Total (n, %)
Sulfonylurea	2 (50.0)	2 (50.0)	0 (0.0)	4 (100.0)
Insulin	0 (0.0)	21 (72.4)	8 (27.6)	29 (100.0)
Metformin	2 (11.1)	6 (33.3)	10 (55.6)	18 (100.0)
Insulin + Metformin	0 (0.0)	14 (87.5)	2 (12.5)	16 (100.0)
Sulfonylurea + Metformin	0 (0.0)	10 (71.4)	4 (28.6)	14 (100.0)
Total	4 (4.9)	53 (65.4)	24 (29.6)	81 (100.0)

Pearson Chi-Square = 32.113, df = 8, p < 0.001. Significant association observed between therapy type and glycemic control improvement.

Table 6. Association Between Glucose-Lowering Therapies and Side Effects

Therapy	No (n, %)	Yes (n, %)	Total (n, %)
Sulfonylurea	0 (0.0)	4 (100.0)	4 (100.0)
Insulin	17 (58.6)	12 (41.4)	29 (100.0)
Metformin	10 (55.6)	8 (44.4)	18 (100.0)
Insulin + Metformin	8 (50.0)	8 (50.0)	16 (100.0)
Sulfonylurea + Metformin	4 (28.6)	10 (71.4)	14 (100.0)
Total	39 (48.1)	42 (51.9)	81 (100.0)

Pearson Chi-Square = 7.555, df = 4, p = 0.109. No statistically significant association between therapy type and side effects.

Discussion

This cross-sectional evaluation compared glycemic indices and selected renal and hepatic biomarkers across commonly used glucose-lowering regimens in adults with T2DM in Tripoli. The main findings were: (1) HbA1c, but not FBG, differed significantly across therapy groups; (2) combination therapy groups showed lower HbA1c than sulfonylurea monotherapy; (3) the sulfonylurea + metformin group demonstrated a less favorable renal profile (higher creatinine, lower eGFR); and (4) liver enzymes were highest in the sulfonylurea monotherapy group.

In the present cohort, mean HbA1c was significantly different among regimens (p=0.017), whereas mean FBG was not (p=0.374). This pattern is clinically plausible, as HbA1c reflects long-term glycemic exposure, making it a more robust marker for comparing sustained regimen effects in cross-sectional designs. Sulfonylurea monotherapy was associated with the highest mean HbA1c (9.85%), underscoring a subgroup with suboptimal glycemic control. Conversely, combination therapies achieved lower HbA1c levels. Interestingly, the sulfonylurea group exhibited the lowest mean fasting blood glucose despite having the highest HbA1c. This apparent discrepancy may be explained by the very small sample size (n=4) and the fact that HbA1c reflects long-term glycemic exposure, whereas FBG represents a single measurement. Such variability underscores the limited reliability of FBG as a sole marker of glycemic control, with the sulfonylurea + metformin group showing the lowest (7.47%). This supports the concept that treatment intensification improves glycemic control, aligning with real-world evidence where adding a second agent to metformin leads to meaningful HbA1c reductions (1). The efficacy of combining sulfonylureas with metformin, as seen in our cohort, is well-documented, with studies like Sahin (2) showing significant HbA1c reductions with such combinations.

However, our data showed a higher mean FBG in the insulin and metformin monotherapy groups. This observation likely reflects confounding by indication, a common issue in non-randomized studies. Patients prescribed insulin often have a longer duration of disease or more severe baseline hyperglycemia, necessitating a more potent therapy (3). Similarly, the systematic review confirms that while insulin achieves

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superior HbA1c reduction compared to sulfonylureas, its use is associated with higher risks of hypoglycemia and weight gain, justifying its reservation for later stages of disease (4).

It is important to clarify that patients with chronic kidney or liver disease unrelated to diabetes were excluded from the study. The included cases had no prior history of chronic kidney or liver disease, ensuring that the effects of glucose-lowering therapies on renal and hepatic function could be accurately assessed. Our study identified significant differences in renal markers (creatinine p=0.016; eGFR p=0.003), with the sulfonylurea + metformin group showing the least favorable profile. This finding should not be interpreted as direct drug-induced nephrotoxicity. Instead, it likely reflects prescribing patterns where certain drug classes are used cautiously in patients with declining renal function. For example, sulfonylurea and insulin clearance are both affected by renal function, which can heighten hypoglycemia risk and necessitate dose adjustments (5,6). Metformin, while having a demonstrated cardiorenal protective profile (7), is typically dose-adjusted or discontinued as renal function severely declines, a practice supported by studies showing its safety in mild-to-moderate CKD but risk of accumulation in acute renal failure (8). Liver enzymes also differed significantly, with sulfonylurea monotherapy showing the highest mean AST and ALT. This may reflect underlying metabolic heterogeneity, such as non-alcoholic fatty liver disease, rather than direct hepatotoxicity. Concerns regarding the cardiovascular safety of sulfonylureas have been raised in large cohort studies (9), which found a higher incidence of major cardiovascular events in patients initiated on sulfonylureas compared to metformin. While our study did not assess cardiovascular outcomes, the observed renal and hepatic biomarker differences contribute to the ongoing debate about the long-term safety profile of this drug class.

Our findings resonate with and extend previous research conducted in the Libyan context. The suboptimal glycemic control observed aligns with the findings of (10), who established a direct link between poor glycemic control and metabolic dysfunction in Tarhuna. Our work confirms this challenge persists across various therapeutic regimens. Furthermore, the importance of monitoring renal function in diabetic patients is profoundly illustrated by local research (11). Their study on patients undergoing hemodialysis, including those with diabetic kidney disease, highlights the severe end-stage consequences of poorly managed diabetes. Our findings of altered renal markers in certain treatment groups serve as an early-stage clinical corollary to the end-stage disease context described in (11), reinforcing the critical need for nephroprotective strategies in T2DM management in Libya. Finally, recognizing T2DM as a multifaceted metabolic disease is crucial. The work (12) on dyslipidemia in Tarhuna complements our study by underscoring the need to manage cardiovascular risk factors alongside glycemic control.

Strengths include the real-world therapy patterns and simultaneous assessment of glycemic, renal, and hepatic markers. Key limitations are the cross-sectional design (precluding causal inference), unequal group sizes (notably n=4 for sulfonylurea monotherapy), and potential confounding by indication.

Conclusion

In this study of adults with T2DM in Tripoli, combination therapies were associated with better long-term glycemic control compared to sulfonylurea monotherapy. Significant differences in renal and hepatic biomarkers were observed, with the sulfonylurea + metformin group exhibiting a less favorable renal profile, warranting careful patient selection and monitoring. These findings, contextualized by international evidence and local research (10–12), confirm the ongoing challenges in T2DM management in Libya. They reinforce the need for individualized therapy that considers glycemic efficacy alongside renal safety and broader metabolic health to mitigate the progression toward severe complications like end-stage kidney disease.

Conflict of interest. Nil

References

1. Zekarias A, Gebrie A, Tadesse Y. Patterns of treatment intensification in type 2 diabetes: Real-world evidence from resource-limited settings. Int J Diabetes Dev Ctries. 2019;39(4):678–85.
2. Sahin M. Comparative evaluation of gliclazide MR and glimepiride in combination with metformin in T2DM patients: A prospective study. Int J Diabetes Res. 2024;14(1):33–41.
3. Davies MJ, D'Alessio DA, Fradkin J, Kernan WN, Mathieu C, Mingrone G, et al. Management of Hyperglycemia in Type 2 Diabetes, 2018. Diabetes Care. 2018;41(12):2669–2701.
4. Vashisht R, Patel M, Shah K. Comparative safety and efficacy of insulin and sulfonylureas in type 2 diabetes: A systematic review. J Diabetes Res Clin Pract. 2023;205:110743.
5. Douros A, Dell'Aniello S, Yu OHY, Filion KB, Azoulay L, Suissa S. Sulfonylureas as second line drugs in type 2 diabetes and the risk of cardiovascular and hypoglycaemic events. BMJ. 2018;362:k2693.
6. Pina MI. Insulin metabolism and renal function: A physiological review. Nephrol Endocrinol Rev. 2020;12(3):201–15.
7. Petrie JR, Rossing P, Campbell IW. Metformin and cardiorenal outcomes: A review of clinical and observational evidence. Diabetes Vasc Dis Res. 2020;17(6):1–10.

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8. Shin ET. Descriptive analytical study on the use of metformin in diabetic patients with advanced chronic renal disease. J Nephrol Diabetes Res. 2025;18(2):112–20.
9. Roumie CL, Hung AM, Greevy RA, Grijalva CG, Liu X, Murff HJ, et al. Comparative effectiveness of sulfonylurea and metformin monotherapy on cardiovascular events in type 2 diabetes mellitus. Ann Intern Med. 2012;157(9):601–10.
10. Eshtiwey AA, Dakeal ME, Azgozi HA, Khalleefah AA, Abouzaid AA, Salem AO. Assessment of the Prevalence of Insulin Resistance in Tarhuna City. Afro-Asian J Sci Res. 2026;4(2):45–60.
11. Dakeal ME, Eshtiwe AA, Almakhrem AA. Analysis of Biochemical Profiles in Healthy Individuals, Chronic Kidney Disease, and Diabetic Kidney Disease Patients Undergoing Hemodialysis: A Cross-Sectional Study in Tarhuna, Libya. Journal of Libyan Academy Bani Walid. 2025 Dec 12:293-300.

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