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Assessing the efficacy and safety of combined glimepiride and metformin therapy in type 2 diabetes mellitus management

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Abstract

Background: The fixed drug combination (FDC) of glimepiride and metformin effectively controls blood glucose and improves glycated hemoglobin (HbA1c). This study aimed to evaluate the effectiveness and safety of the FDC of glimepiride and metformin in managing type-2 diabetes mellitus (T2DM).

Materials and Methods: This retrospective, non-comparative, multi-center cross-sectional study was conducted at tertiary care centers in Nepal. Adult patients (aged 18 years or older) with T2DM were included. Primary outcomes included changes in HbA1c, fasting plasma glucose (FPG), and postprandial glucose (PPG) levels.

Results: A total of 287 patients were included in the study, with a mean age of 55.6 years and a predominance of females (62.41%). The average body mass index was 27.49 kg/m^2 and the median duration of T2DM was 4 years. Common risk factors included obesity (53.31%), smoking (45.30%), and a sedentary lifestyle (36.59%). The most prevalent treatment regimen was the combination of glimepiride 1 mg and metformin 1000 mg sustained release (54.77%). Post-glimepiride and metformin 1000 mg sustained release, the mean changes in HbA1c, FPG, and PPG were significant, with reductions of 2.45%, 64.53 mg/dL, and 102.64 mg/dL, respectively ($P<0.001$, each). Overall, physicians evaluated the efficacy and tolerability as good to excellent responses in a higher proportion of patients (94.9% and 96.2%, respectively).

Conclusion: The combination of glimepiride and metformin 1000 mg sustained release effectively improves glycemic control in patients with T2DM while demonstrating a favorable safety profile

Keywords: Fasting plasma glucose; Glycated hemoglobin; Glycemic control; Obesity

1. Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder that is rapidly emerging as a global health challenge, affecting millions of individuals worldwide [1]. According to estimates from the International Diabetes Federation (IDF), the prevalence of diabetes was 9.6% in 2021 and is projected to rise to 10.4% by 2030 [2]. Uncontrolled diabetes is associated with various long-term complications, such as cardiovascular disease, retinopathy, neuropathy, and

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nephropathy, which can significantly reduce the quality of life and lead to premature mortality. Therefore, it is crucial to effectively manage diabetes to prevent these complications and enhance overall health outcomes [3].

Effective management of diabetes mellitus necessitates a comprehensive approach encompassing lifestyle modifications, pharmacotherapy, and sometimes insulin therapy to attain and sustain glycemic control and mitigate associated complications [4]. Meanwhile sulfonylureas work by stimulating insulin release from pancreatic beta cells, helping to lower blood glucose levels in patients with T2DM [5, 6]. This approach is crucial for attaining effective control of blood glucose levels and preventing the chronic complications associated with diabetes [7].

Metformin, a commonly used antidiabetic, improves insulin action and binding with minimal liver impact and a short half-life. It lowers blood glucose by reducing liver glucose production and intestinal absorption [8, 9]. Glimepiride, a third-generation sulfonylurea used to manage T2DM, leads to increased insulin release and improved glucose uptake. Unlike other sulfonylureas, glimepiride has a prolonged action of up to 24 h with better CV safety profile [10, 11].

Monotherapy of a glucose-lowering agent shows an increasing failure of blood glucose control over time, eventually requiring a number of antidiabetic medications in combination or insulin [12]. To delay complications and progression in T2DM, achieving optimal glycemic control is crucial. When metformin alone is insufficient, sulfonylureas and insulin are frequently used, particularly in Asian countries [13].

The recent post-trial monitoring study found that early intensive glycemic control with sulfonylurea, insulin, or metformin led to long-term reductions in the risk of death, myocardial infarction, and microvascular disease, with benefits lasting up to 24 years. Achieving near normoglycemia early in diabetes management appears crucial for minimizing lifelong diabetes-related complication [14].

Clinical studies, including those from the United Kingdom Prospective Diabetes Study (UKPDS), have demonstrated that this combination therapy is generally more effective than using either drug alone [15, 16].

Despite their widespread use, there remains a need for ongoing evaluation of these medications' efficacy and safety profiles in diverse patient populations. The FDC of glimepiride and metformin is frequently utilized to harness the complementary mechanisms of action of these drugs, yet their combined effects on long-term glycemic control and safety have not been comprehensively evaluated in T2DM patients in Nepal. This study aimed to evaluate the effectiveness and safety of combining metformin and glimepiride for managing T2DM.

2. Material and methods

2.1. Study design

This was a retrospective, non-comparative, non-randomized, multi-centric real-world cross-sectional study conducted at tertiary care centers across Nepal. It involved the analysis of medical records of adult diabetic patients (>18 years) who had received treatment with glimepiride and metformin combination. The study was conducted in accordance with ethical guidelines and principles. The research was approved by the independent institutional review board and ethics committee.

2.2. Inclusion and exclusion criteria

Adult patients (aged 18 years or older) with T2DM were eligible for the study. Patients having incomplete data files or with any condition that, according to the discretion of the investigator, indicated that the patient was not suitable for inclusion in the study were excluded from this study.

2.3. Data collection

Demographic and baseline characteristics, including age, sex, body mass index (BMI), blood pressure, duration of T2DM, and risk factors, were retrieved from patient's medical records available at hospital/clinics and entered into case report forms.

2.4. Outcomes

Primary outcomes included changes in glycated hemoglobin (HbA1c), fasting plasma glucose (FPG), and postprandial glucose (PPG) levels using standard lab techniques. Secondary outcomes encompassed the frequency of hypoglycemic events in the last three months, any adverse events and physician assessments of treatment efficacy and safety.

2.5. Statistical analysis

Data were analyzed using a statistical package for the social sciences (SPSS) version 23.0. Descriptive analysis was used to present the study outcomes. Categorical variables were described as numbers and percentages. Continuous variables were summarized using means and standard deviations or medians and ranges, as appropriate. Pre- and post-treatment observations for HbA1c, FPG, and PPG were compared using paired t-test. A P-value of less than 0.05 was considered statistically significant

3. Results

A total of 287 patients were included in this study. Table 1 represents the demographic characteristics of the patients. The mean (SD) age of the 287 patients was 55.6 (11.73) years. Majority of the patients were female (62.41%). The mean (SD) body mass index (BMI) was 27.49 (8.98) kg/m^2. The mean systolic blood pressure (SBP) was 132.96 mmHg, whereas the mean diastolic blood pressure (DBP) was 83.49 mmHg. The median duration of T2DM among the patients was 4 years, ranging from 0.08 to 22.08 years. The most common risk factors among the patients included obesity (53.31%), followed by smoking (45.30%), sedentary lifestyle (36.59%) (Figure 1). Approximately 56% of the patients had a family history of diabetes. Additionally, the majority of patients had dyslipidemia (44.95%), followed by hypertension (37.28%).

Table 1 Demographic characteristics

Parameters	**Number of patients (N=287)***
Age (years), mean (SD), [n=283]	55.56 (11.73)
Sex [n=282]	
Male	106 (37.59)
Female	176 (62.41)
BMI (kg/m^2), mean (SD), [n=143]	27.49 (8.98)
Blood pressure, mean (SD), [n=279]	
SBP	132.96 (14.02)
DBP	83.49 (8.39)
Duration of T2DM (years), median (range)	4.0 (0.08-22.08)
Family history of diabetes	160 (55.75)
Family history of obesity	49 (17.07)
Diabetes complications	
Neuropathy	63 (21.95)
CAD	55 (19.16)
Nephropathy	29 (10.10)
Erectile dysfunction	29 (10.10)
Retinopathy	21 (7.32)
TIA	18 (6.27)
PAD	12 (4.18)
Foot ulcer	7 (2.44)
Any other**	5 (1.74)
Other comorbidities	
Dyslipidemia	129 (44.95)

Hypertension	107 (37.28)
NAFLD	51 (17.77)
Heart failure	20 (6.97)
Arthritis	16 (5.57)
Hyperuricemia	14 (4.88)
Sleep apnea	9 (3.14)
Hyperthyroidism	5 (1.74)
Urinary incontinence	2 (0.70)
Any other#	9 (3.14)

Data presented as n (%), unless otherwise specified. N=287*, unless otherwise specified. **Any other diabetic complication: No, n=3; Yes, n=1; COPD, n=1 #Any other comorbidities: No, n=3; COPD, n=1; hypothyroidism, n=2; RA, n=2; RA/hypothyroidism, n=1. BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; NAFLD, non-alcoholic fatty liver disease; PAD, peripheral artery disease; RA, rheumatoid arthritis; SD, standard deviation; T2DM, type 2 diabetes mellitus; TIA, transient ischemia attack

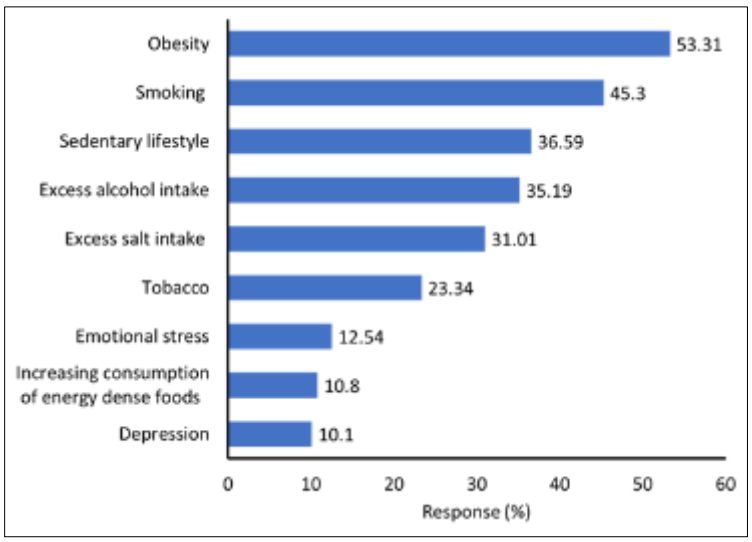

Figure 1 Risk factors

Among the 287 patients who used anti-diabetic drugs before initiation, the most common medications were metformin 1000 mg (20.56%), followed by glimepiride 1 mg + metformin 500 mg SR (19.16%), and glimepiride 1 mg + metformin 1000 mg SR (12.89%).

Table 2 represents the treatment and related observations. The most common regimen among patients was the combination of glimepiride 1 mg and metformin 1000 sustained release (SR) (54.77%), while 40.25% received it at a dose of 2 mg. The median duration of the treatment with this combination was 1.42 years. Majority of the patients adhered to a twice-daily medication regimen (69.10%). The most frequently used oral hypoglycemic agents (OHA) or concomitant medications were rosuvastatin (11.85%), followed by telmisartan (11.50%), and linagliptin and voglibose (each 6.27%). Other notable medications included aspirin (6.62%), empagliflozin and sitagliptin (each 5.57%), and amlodipine (4.88%). The primary reasons for initiating glimepiride and metformin 1000 mg SR were to improve HbA1c levels (76.31%), to control FPG (70.03%), and manage PPG (60.98%).

Table 2 Treatment and related observations

Parameters	Number of patients (N=287) *
Glimepiride Dose +Metformin 1000mg SR,	[n=241]
0.5 mg	10 (4.15)
1 mg	132 (54.77)
2 mg	97 (40.25)
3 mg	2 (0.83)
Duration (Year), median (IQR)	1.42 (0.5-3.17)
Frequency, [n=301]	
OD	93 (30.90)
BD	208 (69.10)
Reason for start Glimepiride and Metformin 1000 mg SR	
To improve HbA1c	219 (76.31)
To control FPG	201 (70.03)
To control PPG	175 (60.98)
Glycemic and Weight control	119 (41.46)
Due to Adverse Events	6 (2.09)

Data presented as n (%), unless otherwise specified.; N=287*, unless otherwise specified.; BD, twice a day; FPG, fasting plasma glucose; HbA1c, glycated haemoglobin; IQR, inter quartile range; OD, once a day; OHA, oral hypoglycemic agent; PPG, post prandial glucose; SR, sustained release.

Among the 287 patients, various concomitant medications were used, with antihypertensive (26.13%) and statin (21.95%) being the most frequently prescribed [Supplementary table 1].

The mean changes in HbA1c, FPG, and PPG before and after treatment with glimepiride and metformin 1000 mg SR were 2.45% (1.62-3.72, P<0.001), 64.53 mg/dL (57.75-71.31, P<0.001), and 102.64 mg/dL (95.84-109.43, P<0.001), respectively [Table 3].

Table 3 Pre-post-treatment observations

Parameters	Before Glimepiride and metformin 1000 mg SR	After Glimepiride and metformin 1000 mg SR	Mean change (95% CI)	P-value
HbA1c (%), [n=198]	11.09 (23.93)	8.63 (15.18)	2.45 (1.62, 3.72)	P<0.001
FPG (mg/dL), [n=207]	179.31 (50.40)	114.78 (18.55)	64.53 (57.75, 71.31)	P<0.001
PPG (mg/dL), [n=198]	273.52 (64.20)	170.88 (36.19)	102.64 (95.84, 109.43)	P<0.001

CI, confidence interval; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; PPG, post prandial glucose; SR, sustained release

The majority of patients (83.09%) did not experience hypoglycemic events in the last three months, while 15.07% experienced hypoglycemia. Additionally, 1.74% of patients reported other adverse events, including issues like frequent urination, gastric problems, and general wellness. The overall global assessment for efficacy and tolerability was good to excellent scale for a majority of the patients (91.60% and 93.91%, respectively) [Table 4].

Table 4 Outcomes

Parameters	Number of patients
Hypoglycemic event in the last 3 months, [n=272]	
Yes	41 (15.07)

No	226 (83.09)
Any other adverse events	5 (1.74)
Frequency of urination	1
Gastric	3
Generalized wellness	1
Physician global evaluation of efficacy, [n=238]	
Excellent	29 (12.18)
Very good	99 (41.60)
Good	90 (37.82)
Average	19 (7.98)
Fair	1 (0.42)
Physician global evaluation of safety, [n=230]	
Excellent	34 (14.78)
Very good	72 (31.30)
Good	110 (47.83)
Average	13 (5.65)
Fair	1 (0.43)

Data presented as n (%).; N=287*, unless otherwise specified.

4. Discussion

In 2020, the prevalence of T2DM in Nepal was 8.5% (95% CI 6.9–10.4%), slightly higher than the 8.4% (95% CI 6.2-10.5%) reported in 2014 [17, 18]. The management of T2DM remains a critical global health issue, necessitating effective and safe therapeutic strategies to control blood glucose levels and mitigate associated complications. Combination therapies involving oral anti-diabetic medications have led to better glycemic control and improved clinical outcomes, reducing health complications associated with diabetes. This study evaluated the efficacy and safety of the combination of glimepiride and metformin in patients with T2DM.

In the previous study, the median age of patients was 55 years, with 29.4% aged over 60, with a higher proportion of males (60.1%). In the present study, the average age was comparable to the previous study, however, the majority of female patients compared to male patients [19]. Similarly, this study identified a sedentary lifestyle, smoking, emotional stress, obesity, and family history as the most common risk factors.

Overweight and obesity are important risk factors for DM. The previous nationwide study from Nepal showed that participants who were overweight and obese had about two times higher odds of having T2DM than those with a normal BMI [20]. Moreover, overweight and obesity have been increasing in Nepal, particularly among women [21]. A study by Hills et al. estimated the prevalence of overweight in Nepal at 16.7%, with a higher rate among women (19.6%) than men (13.6%). Obesity is strongly associated with an increased risk of early-onset T2DM and cardiovascular disease [22]. Moreover, the study by Sinha et al., from India identified a sedentary lifestyle, smoking, emotional stress, obesity, and family history as the most common risk factors [23]. These results align with findings from Agrawal et al. and Keller et al., which also highlighted alcohol consumption, sedentary lifestyle, smoking, overnutrition, and physical inactivity as strong risk factors for T2DM [24, 25]. A recent cross-sectional study found that smoking, obesity, and a family history of diabetes were significantly linked to the prevalence of the disease [26]. Similarly, the present study identified obesity (53.31%), smoking (45.30%), and a sedentary lifestyle (36.59%) as prominent comorbid conditions, with 56% of patients having a family history of diabetes, underscoring its critical role as a predictor for T2DM. The current study indicates that obesity, smoking, and a sedentary lifestyle are key risk factors for T2DM, highlighting the considerable influence of a family history of diabetes in predicting the disease.

Unnikrishnan et al. study found that 667 patients (46.6%) were treated with a combination of glimepiride 2 mg and metformin in dosages of 500, 850, or 1000 mg [27]. In a study by Prasanna KM et al., the most commonly used regimens were glimepiride 2 mg and metformin 500 mg (32.3%), and glimepiride 1 mg and metformin 500 mg (27.9%) (19). Moreover, in a study by Kim HS, et al., the average daily doses were 2.5 mg of glimepiride and 627 mg of metformin for the glimepiride and metformin FDC group [28]. In contrast, in the present study, 54.77% of patients were prescribed glimepiride at a dose of 1 mg, while 40.25% received it at a dose of 2 mg.

A multicenter study from Korea suggested that glimepiride and metformin FDC provide greater reductions in HbA1c compared to an increased dose of metformin alone (6.6% vs. 7.0%) and the adjusted mean difference between groups was 0.4% with statistical significance ($P < 0.001$) [28]. On parallel lines, the present study demonstrated that treatment with glimepiride and metformin 1000 mg SR resulted in mean changes of 2.45% in HbA1c (95% CI: 1.62% to 3.72%, $P < 0.001$). Similarly, another study also alluded that among overall patients, post-treatment of glimepiride and metformin FDC therapy significantly reduced the levels of HbA1c (8.3 vs. 7.0%; $P < 0.001$), as compared to pre-treatment levels [23]. In a study by Kim HS et al., HbA1c levels at baseline were comparable between the glimepiride and metformin FDC group (7.9%) and the metformin up-titration group (7.8%). By the end of the study period, HbA1c in the glimepiride and metformin FDC group decreased to 6.6%, while in the metformin UP group, it was 7.0%, with a significant adjusted mean difference of 0.4% ($P < 0.0001$) [28]. These findings suggest that the glimepiride and metformin 1000 mg SR combination significantly enhances glycemic control.

In a study by Sinha, et al., post-treatment with glimepiride and metformin FDC therapy significantly decreased FPG (173.0 mg/dL to 128.6 mg/dL, $P < 0.001$), and PPG (240.2 mg/dL to 166.7 mg/dL, $P < 0.001$) compared to pre-treatment levels [23]. Moreover, in a study by Kim HS et al., the glimepiride and metformin FDC group showed a mean reduction in fasting plasma glucose of -35.7 mg/dL, while the metformin up-titrated group had a reduction of -18.6 mg/dL, with a significant adjusted mean difference of -17.1 mg/dL ($P<0.0001$). The 2-h postprandial glucose levels decreased by 50.6 mg/dL in the glimepiride and metformin FDC group and 42.5 mg/dL in the metformin up-titrated group, with a non-significant adjusted mean difference of 8.1 mg/dL ($P=0.2681$) [28]. The results from the present study demonstrated that treatment with FDC of glimepiride and metformin 1000 SR resulted in mean changes of 64.53 mg/dL in FPG (95% CI: 57.75 to 71.31 mg/dL, $P< 0.001$), and 102.64 mg/dL in PPG (95% CI: 95.84 to 109.43 mg/dL, $P< 0.001$). The mean changes in FPG and PPG were higher than those reported in the existing literature. The present study suggests that treatment with glimepiride and metformin 1000 mg SR is highly effective in improving glycemic control.

A randomized placebo-controlled study found that adding glimepiride to metformin and insulin therapy in patients with T2DM for over 10 years effectively lowered HbA1c levels, with only minor hypoglycemic events [29]. Another study reported a total 100 hypoglycemic events among 41 patients using the glimepiride and metformin FDC, indicating a significantly higher incidence of hypoglycemia in this group. However, no severe hypoglycemic events were observed in either group [28]. Out of the 100 hypoglycemic events in the glimepiride and metformin FDC group, 58% of the individuals had blood glucose level above 70 mg/dL, and only 1.2% fell below 50 mg/dL. Although sulfonylureas were associated with a higher risk of hypoglycemia, glimepiride typically has a lower incidence of both mild and severe hypoglycemic events compared to traditional sulfonylureas [30, 31]. Whereas in present study the majority of patients (83.09%) did not experience hypoglycemic events in the last three months. The present study suggests that glimepiride and metformin 1000 mg SR have a favorable safety profile, with the majority of patients not experiencing hypoglycemic events over the last three months.

A previous multicenter study from India evaluated the combination of glimepiride and metformin among patients with T2DM (n = 1345). The result showed that the overall global assessment for efficacy and tolerability was rated as good to excellent by the majority of patients, with scores of 90.3% and 91.1%, respectively [23]. Likewise, in the present study, the overall global assessment for efficacy and tolerability was rated as good to excellent by the majority of HCPs (91.60% and 93.91%, respectively).

Limitations

The study has several limitations that should be considered. The short duration of treatment and follow-up might not provide the long-term safety and efficacy of the interventions. Furthermore, the reliance on self-reported data for certain variables, such as adverse events, could introduce reporting biases.

5. Conclusion

The study demonstrates that the combination of glimepiride and metformin 1000 mg SR effectively reduces HbA1c, FPG, and PPG levels in patients with T2DM. The treatment shows a favorable safety profile, with the majority of patients

not experiencing any significant hypoglycemic events. Overall, glimepiride and metformin 1000 mg SR FDC is effective in improving glycemic control and is well-tolerated by patients, making them a viable option for managing T2DM.

Compliance with ethical standards

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Disclosure of conflict of interest

Aushili Mahule is an employee of USV Pvt Ltd. Mumbai. All other authors have nothing to declare.

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Statement of ethical approval

The research was approved by the independent institutional review board and ethics committee.

References

[1] Hossain MJ, Al-Mamun M, Islam MR. Diabetes mellitus, the fastest growing global public health concern: Early detection should be focused. Health Sci Rep. 2024;7(3):e2004.

[2] Magliano DJ, Boyko EJ; IDF Diabetes Atlas 10th edition scientific committee . IDF DIABETES ATLAS [Internet]. 10th edition. Brussels: International Diabetes Federation; 2021. Available from: https://www.ncbi.nlm.nih.gov/books/NBK581934/

[3] Bhattacharjee R, Rai M, Joshi P, Prasad A, Birla A. The Real DAPSI: A Real-World Retrospective Study on Assessing the Efficacy and Safety of a Fixed-Dose Combination of Dapagliflozin and Sitagliptin in the Indian Population. Cureus. 2023;15(10):e46767.

[4] Elkhalifa AME, Nazar M, Ali SI, et al. Novel Therapeutic Agents for Management of Diabetes Mellitus: A Hope for Drug Designing against Diabetes Mellitus. Life (Basel). 2024;14(1).

[5] LaSalle JR, Cross LB. Oral combination therapy with thiazolidinediones in type 2 diabetes. Am J Manag Care. 2006;12(14 Suppl):S369-81.

[6] Al-Saleh Y, Sabico S, Al-Furqani A, et al. Sulfonylureas in the Current Practice of Type 2 Diabetes Management: Are They All the Same? Consensus from the Gulf Cooperation Council (GCC) Countries Advisory Board on Sulfonylureas. Diabetes Ther. 2021;12(8):2115-32.

[7] Heo JH, Han KA, Hong JH, et al. Pioglitazone as Add-on Therapy in Patients with Type 2 Diabetes Mellitus Inadequately Controlled with Dapagliflozin and Metformin: Double-Blind, Randomized, Placebo-Controlled Trial. Diabetes Metab J. 2024;48(5):937-48.

[8] Vigneri R, Goldfine ID. Role of metformin in treatment of diabetes mellitus. Diabetes Care. 1987;10(1):118-22.

[9] Kirpichnikov D, McFarlane SI, Sowers JR. Metformin: an update. Ann Intern Med. 2002;137(1):25-33.

[10] Rosenstock J, Kahn SE, Johansen OE, et al. Effect of Linagliptin vs Glimepiride on Major Adverse Cardiovascular Outcomes in Patients With Type 2 Diabetes: The CAROLINA Randomized Clinical Trial. Jama. 2019;322(12):1155-66.

[11] Trerattanavong K, Tadi P. Glimepiride. StatPearls. Treasure Island (FL) with ineligible companies. Disclosure: Prasanna Tadi declares no relevant financial relationships with ineligible companies.: StatPearls Publishing Copyright © 2024, StatPearls Publishing LLC.; 2024.

[12] Turner RC, Cull CA, Frighi V, et al. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). UK Prospective Diabetes Study (UKPDS) Group. Jama. 1999;281(21):2005-12.

[13] Mohan V, Khunti K, Chan SP, et al. Management of Type 2 Diabetes in Developing Countries: Balancing Optimal Glycaemic Control and Outcomes with Affordability and Accessibility to Treatment. Diabetes Ther. 2020;11(1):15-35.

[14] Adler AI, Coleman RL, Leal J, et al. Post-trial monitoring of a randomised controlled trial of intensive glycaemic control in type 2 diabetes extended from 10 years to 24 years (UKPDS 91). Lancet. 2024;404(10448):145-155. doi: 10.1016/S0140-6736(24)00537-3. Epub 2024 May 18. PMID: 38772405

[15] Hermann LS, Scherstén B, Bitzén PO, et al. Therapeutic comparison of metformin and sulfonylurea, alone and in various combinations. A double-blind controlled study. Diabetes Care. 1994;17(10):1100-9.

[16] UKPDS 28: a randomized trial of efficacy of early addition of metformin in sulfonylurea-treated type 2 diabetes. U.K. Prospective Diabetes Study Group. Diabetes Care. 1998;21(1):87-92.

[17] Gyawali B, Sharma R, Neupane D, et al. Prevalence of type 2 diabetes in Nepal: a systematic review and meta-analysis from 2000 to 2014. Glob Health Action. 2015;8:29088.

[18] Shrestha DB, Budhathoki P, Sedhai YR, et al. Type 2 Diabetes Mellitus in Nepal from 2000 to 2020: A systematic review and meta-analysis. F1000Res. 2021;10:543.

[19] Prasanna Kumar KM, Seshadri K, Aravind SR, et al. Real-World Observational Study of Glimepiride and Metformin Fixed-Dose Combination Along With Insulin in the Management of Type 2 Diabetes Mellitus: Indian Experience. Cureus. 2021;13(1):e13020.

[20] Shrestha N, Karki K, Poudyal A, et al. Prevalence of diabetes mellitus and associated risk factors in Nepal: findings from a nationwide population-based survey. BMJ Open. 2022;12(2):e060750.

[21] Thapa SD, K.C sR, Gautam S, et al. Dyslipidemia in Type 2 Diabetes mellitus. Journal of Pathology of Nepal. 2017;7:1149.

[22] Hills AP, Arena R, Khunti K, et al. Epidemiology and determinants of type 2 diabetes in south Asia. Lancet Diabetes Endocrinol. 2018;6(12):966-78.

[23] Sinha B, Kant S, Bandyopadhyay S, et al. Clinical Utility of Glimepiride and Metformin Fixed-Dose Combination in Obese/Overweight Patients with Type 2 Diabetes Mellitus in Indian Settings. Chronicle of Diabetes Research and Practice. 2022;1(2):58-68.

[24] Agrawal P, Mercer A, Hassanali J, et al. Gender Differences in the Association Between Alcohol Use and Sedentary Behavior Among Adults. Am J Health Promot. 2018;32(7):1576-81.

[25] Keller S, Maddock JE, Hannöver W, et al. Multiple health risk behaviors in German first year university students. Prev Med. 2008;46(3):189-95.

[26] Asiimwe D, Mauti G, Ritah K. Prevalence and Risk Factors Associated with Type 2 Diabetes in Elderly Patients Aged 45-80 Years at Kanungu District. Journal of Diabetes Research. 2020;2020.

[27] Unnikrishnan Ag, Pandit K, George J, et al. Clinical Utilization Pattern of Multiple Strengths of Glimepiride and Metformin Fixed Dose Combinations in Indian Type 2 Diabetes Patients. J Assoc Physicians India. 2020;68(7):57-61.

[28] Kim HS, Kim DM, Cha BS, et al. Efficacy of glimepiride/metformin fixed-dose combination vs metformin uptitration in type 2 diabetic patients inadequately controlled on low-dose metformin monotherapy: A randomized, open label, parallel group, multicenter study in Korea. J Diabetes Investig. 2014;5(6):701-8.

[29] Nybäck-Nakell Å, Adamson U, Lins PE, et al. Adding glimepiride to insulin+metformin in type 2 diabetes of more than 10 years' duration--a randomised, double-blind, placebo-controlled, cross-over study. Diabetes Res Clin Pract. 2014;103(2):286-91.

[30] González-Ortiz M, Guerrero-Romero JF, Violante-Ortiz R, et al. Efficacy of glimepiride/metformin combination versus glibenclamide/metformin in patients with uncontrolled type 2 diabetes mellitus. J Diabetes Complications. 2009;23(6):376-9.

[31] Holstein A, Plaschke A, Egberts EH. Lower incidence of severe hypoglycaemia in patients with type 2 diabetes treated with glimepiride versus glibenclamide. Diabetes Metab Res Rev. 2001;17(6):467-73