Section: General Medicine

Original Research Article

METFORMIN AND OTHER SULFONYLUREAS FOR GLYCEMIC CONTROL IN TYPE 2 DIABETIC PATIENTS AT THE GOVERNMENT MEDICAL COLLEGE, SIDDIPET

Pratibha Lakshmi[1], Md. Anfas Nusrat Pasha[2], Sowmya T.V[3]

[1]Associate Professor, Department of General Medicine, Government Medical College, Siddipet, Telangana, India
[2]Associate Professor, Department of General Medicine, Maheshwaram medical college, Maheshwaram, Telangana, India.
[3]Associate Professor, Department of General Medicine, Government Medical College, Mahabubnagar, Telangana, India.

Received : 08/03/2025
Received in revised form : 06/05/2025
Accepted : 21/05/2025

Keywords:
Metformin, Sulfonylureas, Type 2 Diabetes Mellitus.

Corresponding Author:
Dr. Sowmya T.V,
Email: drsowmyatv@gmail.com

DOI: 10.47009/jamp.2025.7.3.71

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (3); 367-370

ABSTRACT

Background: Diabetes mellitus (DM) is a common disease that causes high blood sugar levels with a wide range of symptoms, including polydipsia, polyuria, and changes in weight. The HbA1C level is crucial when it comes to the main treatment for diabetes. HbA1C level displays the average blood glucose level over the past two to three months. People with diabetes are treated with lifestyle changes and a combination of pharmacological agents to keep their blood sugar levels in check. **Objective:** The objective of this study was to evaluate the treatment response to metformin and other sulfonylureas in glycemic control in type 2 diabetic patients at the government medical college, Siddipet. **Material and Methods:** An observational study utilizing a straight forward sampling method. The study involved a total of 200 patients from a diabetes clinic at the GMC. Metformin and sulfonylureas were used to treat diabetes in people aged 18-60yrs, although patients with retinopathy, nephropathy, and cognitive impairment were excluded. The study was carried out after receiving ethical clearance. **Result:** We included 200 T2DM patients in our study. The male population was higher than the female population; the ratio of male to female was 1.32:1. Among of the study population, 136 (68%) of patients are physically active every day to combat their diabetes, whereas 32% (68) of patients are not (p=0.524). For metformin and sulfonylureas' prescribing ratio, 71% of patients received metformin, whereas 20% received sulfonylureas, and 9% received insulin (p=0.532). Among the patients with overall microvascular complications of diabetes, 47% had diabetic neuropathy (p=0.527), 17.50% had diabetic retinopathy (p=0.521), and 14% had diabetic nephropathy (p=0.521). However, there was no significant difference in the proportion of patients. **Conclusion:** All over the world, people are suffering from type II diabetes. Type II diabetes is associated with several other metabolic disorders. Excessive hepatic glucose generation, peripheral insulin resistance, and impaired beta-cell secretory activity are among the primary pathological abnormalities in type II diabetes. When it comes to glycemic control, metformin does not raise insulin levels, but it does reduce the amount of glucose absorbed from the intestines. Sulfonylureas may cause hypoglycemia in metabolic disorders.

INTRODUCTION

Diabetes mellitus (DM) is one of the top ten causes of mortality and the fastest-growing health emergency of the 21st century, with 463 million people living with it worldwide; this number is projected to reach 578 million by 2030 and 700 million by 2045.[1] Type 2 diabetes mellitus (T2DM) is the most common and complicated form of the disease and accounts for more than 90% of the estimated cases of DM, affecting the life expectancy, quality of life, and health of an individual.[2,3] There is a gradual decline in beta cell function in the pancreas in response to rising blood glucose levels in T2DM, which is predominantly caused by insulin resistance. Blood sugar levels are regulated by insulin in part because it binds to sugar and releases it for use as an energy source by cells in our bodies.[4] In other

ISSN (O): 2687-5365; ISSN (P): 2753-6556

words, the body's cells no longer detect insulin, which prevents the absorption of glucose. Obesity, a sedentary lifestyle, ethnicity, age, and family history of diabetes are just a few of the many risk factors for T2DM.[5] Yet, there is no cure for T2DM, while its prevalence is largely increasing, with increased risk of complications including diabetic retinopathy, neuropathy, kidney damage, and cardiovascular complications. Cardiovascular disease (CVD) is a common complication and a major cause of death in patients with T2DM.[6] Many people with T2DM rely on metformin as their first-line medication.[7] HbA1c and fasting glucose levels are lowered.[8]

Metformin is able to suppress blood glucose synthesis by activating the mucosal AMP protein kinase level, which helps maintain intestinal integrity and, in conjunction with the activation of hepatic cAMP, lowers intestinal and liver lipopolysaccharide levels.[9] Metformin affects the liver's cAMP level, the electron transport chain in the mitochondria, and NADH. First- or second-line agents for T2DM treatment include sulfonylureas. A potassium channel in the beta cells of the pancreas regulates insulin secretion, which can be increased by sulfonylureas.[10] Sulfonylureas promote channel closure and cell depolarization, which results in a rise in cytoplasmic calcium levels and, ultimately, insulin release, which lowers glucose levels.[11]

Metformin and sulfonylureas are the most commonly used combination therapy in treating T2DM. Sulfonylureas are recommended as a second-line treatment regimen in the management of T2DM, while they are still widely used also as a first-line treatment instead of metformin. However, treating T2DM patients with a sulfonylurea rather than metformin is associated with a high risk of ischaemic stroke, cardiovascular death, hypoglycemia, and all-cause mortality.[12] Additionally, using sulfonylurea as a second medication increases the chances of heart attacks, overall death, and severe low blood sugar compared to using metformin alone; therefore, it seems safer to keep using metformin when starting sulfonylurea instead of switching to a different drug. Such findings led to new requirements from licensing authorities that all new T2DM therapies should show cardiovascular safety.

The American Diabetes Association's current standard of care recommends that newly diagnosed T2DM patients whose HbA1c level is ≥8.5% should start a combination treatment of either metformin with insulin or metformin with sulfonylureas.[13,14] However, there is no clear evidence that shows the relative advantages of either the metformin-insulin or metformin-sulfonylurea combination on major treatment outcomes. With guidelines moving away from a one-size-fits-all approach and allowing flexibility in choosing a second- or third-line drug, management in T2DM requires keen individualized medication based on efficacy, risk of hypoglycemia, patient's comorbid conditions, impact on weight, adverse effects, and cost. The benefits of combination therapies for the management of type 2 diabetes are well-documented, while the comparative glycemic control and cardiovascular outcomes among the different combination options have not been studied yet.

Although most T2DM patients require combination therapy, the choice of an appropriate second-line drug is a critical issue for the prevention of CVD. So, this study wanted to look at how well metformin-sulfonylurea combination therapies control blood sugar and affect heart health in patients with T2DM.

MATERIALS AND METHODS

Study Design

To evaluate the information about metformin and other sulfonylureas for glycemic control in T2DM patients at the government medical college (GMC), this study was approved by the ethical committee of Government Medical College, Siddipet. The study will be conducted from March 2024 to February 2025.

Participants

Study participants were T2DM patients who were under metformin with sulfonylurea combination therapies.

Inclusion and Exclusion Criteria

Volunteers who were ≥18 years old with continuous medical records and continuous follow-up either on metformin or with sulfonylurea combination therapies were eligible. In terms of exclusion criteria, those either on monotherapy or combination therapies of other antidiabetic drugs and those with less than three months of follow-up with the combination therapies were, however, excluded from the study.

Study procedure

This study is an observational one, employing a simple sampling method. A total of 200 patients from a diabetes clinic at the GMC. Metformin and sulfonylureas were used to treat diabetes in people aged 18-60, although patients with retinopathy, nephropathy, and cognitive impairment were excluded. The study was carried out after receiving ethical clearance. After evaluating the informed verbal permission submitted with the research protocol, the institute granted ethical approval. Before beginning to fill out the questionnaire, the participants' verbal agreement was sought. When the study's participants were asked if they agreed or disagreed with the study's consent, their answers were recorded as yes or no. After confirming the participant's willingness to take part, data was collected. In order to protect the participant's privacy, the data was collected anonymously.

Statistical Analysis

Statistical analyses were done using SPSS for Windows software (version 22; SPSS Inc., Chicago, IL, USA). For parametric tests, descriptive statistical values were given as mean and standard deviation. For non-parametric tests, they were given as median, minimum, and maximum values. For categorical data, they were given as frequency and ratio.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Student's t-test and paired t-test were used to compare variables. The Mann-Whitney U test was used to compare percent changes between measurements. Significance was assessed at the $p<0.05$ level.

RESULTS

Demographic characteristics

A total of 200 T2DM patients with renal complications were included in this study. The male population was higher than the female population; the ratio of male to female was 1.32:1. The age of patients was found to be normally distributed when tested with the Kolmogorov-Smirnov test of normality. The mean ± standard deviation of patients' age was 66.52 ± 9.82 years old, with the minimum and maximum ages of 20 and 85 years old, respectively. Table 1 displays the demographic characteristics of the patients.

Table 1: Demographic characteristics of patients (N=200)

Demographic characteristics	Number of patients (%)
Sex	
Male	114 (57)
Female	86 (43)
Age	
Non-elderly	106 (53)
Elderly	94 (47)
Body mass index (BMI)*	
Underweight (≤18.5 kg/m^2)	2 (1)
Normal (18.5–22.9 kg/m^2)	24 (12)
Pre-obese (23.0–27.4 kg/m^2)	85 (42.50)
Obese (≥27.5 kg/m^2)	89 (44.50)
Smoking status	
Yes	36 (18)
No	134 (67)
Ex-smoker	30 (15)
Family history of T2DM	
Yes	61 (30.50)
No	55 (27.50)
Unknown	94 (47)

Note: *BMI = Weight (kg)/(height × height) (m2).Abbreviation: T2DM, type 2 diabetes mellitus.

Table 2 shows the number of people exercising, the medications most commonly prescribed to treat type 2 diabetic patients, whether or not patients used insulin injections, the HbA1c test, and the cause of diabetes as per patients. Out of 136 (68%) of patients are physically active every day to combat their diabetes, whereas 32% (68) of patients are not (p=0.524). Metformin and sulfonylureas' prescribing ratio: 71% of patients received metformin, whereas 20% received sulfonylureas, and 9% received insulin (p=0.532). The HbA1c test is used to diagnose type 2 diabetes (p=0.562). Among the patients with overall microvascular complications of diabetes, 47% had diabetic neuropathy (p=0.527), 17.50% had diabetic retinopathy (p=0.521), and 14% had diabetic nephropathy (p=0.521). However, there was no significant difference in the proportion of patients (Table 2).

Table 2: Clinical Characteristics of Study Participants (N=200)

Choice of Patient	No. of Patients		P- Value
	Yes	No	
Physical Exercise	136 (68%)	64 (32%)	0.524
Diabetic drugs used			
Metformin	142 (71%)	-	0.532
Sulfonylureas	40 (20%)	-	
Insulin injection use	18 (9%)	-	
HbA1c Test	180 (90%)	20 (10%)	0.562
Causes of Diabetes			
Geneticcauses	115 (57.50%)	-	0.530
Metabolic	85 (42.50%)	-	
Microvascular Complications			
Diabetic neuropathy	94 (47%)	106 (53%)	0.527
Diabetic retinopathy	35 (17.50%)	165 (82.50%)	0.521
Diabetic nephropathy	28 (14%)	172 (86%)	0.520

DISCUSSION

Keeping blood sugar levels stable is the main aim of managing type 2 diabetes to avoid both micro and macro vascular complications. There was no significant difference in the HbA1c from the metformin and sulfonylurea monotherapy.[16] All around the world, type II diabetes is becoming more widespread. Other metabolic abnormalities such as central obesity, hypertension, and dyslipidemia are

ISSN (O): 2687-5365; ISSN (P): 2753-6556

common in people with type II diabetes, all of which increase the risk of cardiovascular disease and death. The main problems in diabetes are high glucose levels in the blood, the body's cells not responding well to insulin, and the pancreas not producing enough insulin. Diabetic symptoms include frequent urination, thirst, hunger, impaired vision, slow healing of cuts and bruises, weight loss, tingling and pain in the hands and feet, and an increased risk of developing complications.[20-22] In the Diabetic Management Center's general population survey, we observed that 34% of the participants were males and 66% of the participants were females.[23] On an average, eighty-five percent of the people with diabetes do not have the time to engage in physical activity, whereas 56% have the disease because it runs in their family, and 44% have it because of metabolic factors. Only 20% of patients were given sulfonylureas, while 80% of patients received metformin. Insulin was administered to 5% of patients with severe hyperglycemia in a sample size of 50.[24-25] The HbA1C test was ordered by 90% of the patients in the group of 200. Many patients were pleased with the results of their physical exercise, metformin, and sulfonylurea regimens, as well as their glycemic control. They were required to undergo HbA1C testing and to have their blood glucose levels monitored on a regular basis.

CONCLUSION

Patients with type 2 diabetes should begin with lifestyle modifications and metformin as their first line of treatment. Metformin is usually considered a first-line therapy, but insulin analogs are always considered a second-line therapy. Patient preference and the degree of hyperglycemia will influence the choice of metformin and sulfonylureas to be used in conjunction with other medications. We anticipate the creation of more agents in the near future to improve the quality of T2DM.

REFERENCES

1. Gebrie D, Manyazewal T, A Ejigu D, Makonnen E. Metformin-insulin versus metformin-sulfonylurea combination therapies in type 2 diabetes: a comparative study of glycemic control and risk of cardiovascular diseases in Addis Ababa, Ethiopia. Diabetes, Metabolic Syndrome and Obesity. 2021:3345-59.
2. Osman KS, Azab AE, Albakoush AM, Elrando RA, Elosta AM, Elrando DA. Evaluation of Estimated GFR as a Predictor of Diabetic Nephropathy among Type2 Diabetes Mellitus Patients at Zawia Region, Western Libya. IOASD J Med Pharm Sci. 2025;2(2):51-9.
3. Janapati YK, Junapudi S. Progress in experimental models to investigate the in vivo and in vitro antidiabetic activity of drugs. Animal Models and Experimental Medicine. 2024;7(3):297-309.
4. Sunil J, Janapati YK, Junapudi SS. The classical Biomarkers to Predict Diabetes Mellitus. Asian Journal of Medical Research & Health Sciences (A-JMRHS). 2024;2(1):5-11.
5. Baksh RA, Pape SE, Chan LF, Sheehan R, White A, Chauhan U, Gulliford MC, Strydom A. Type 2 diabetes mellitus in people with intellectual disabilities: Examining incidence, risk factors, quality of care and related complications. A population-based matched cohort study. Diabetes Research and Clinical Practice. 2025; 222:112090.
6. Henning RJ. Type-2 diabetes mellitus and cardiovascular disease. Future cardiology. 2018;14(6):491-509.
7. Grammatiki M, Sagar R, Ajjan RA. Metformin: is it still the first line in type 2 diabetes management algorithm?. Current Pharmaceutical Design. 2021;27(8):1061-7.
8. Garg S, Jovanovic L. Relationship of fasting and hourly blood glucose levels to HbA1c values: safety, accuracy, and improvements in glucose profiles obtained using a 7-day continuous glucose sensor. Diabetes Care. 2006;29(12):2644-9.
9. Dar MA, Maqbool M, Ara I. Metformin and other sulfonylureas for glycemic control in Type 2 diabetic patients at a Tertiary Care Hospital in Jammu & Kashmir. J Evol Med Dent Sci. 2023:197-201.
10. Mahgoub MO, Ali II, Adeghate JO, Tekes K, Kalász H, Adeghate EA. An update on the molecular and cellular basis of pharmacotherapy in type 2 diabetes mellitus. International journal of molecular sciences. 2023;24(11):9328.
11. Seino S. Cell signalling in insulin secretion: the molecular targets of ATP, cAMP and sulfonylurea. Diabetologia. 2012;55(8):2096-108.
12. Rao AD, Kuhadiya N, Reynolds K, Fonseca VA. Is the combination of sulfonylureas and metformin associated with an increased risk of cardiovascular disease or all-cause mortality? A meta-analysis of observational studies. Diabetes care. 2008;31(8):1672-8.
13. "9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2025." Diabetes Care 48, no. Supplement-1 (2025): S181-S206.
14. Shah MU, Roebuck A, Srinivasan B, Ward JK, Squires PE, Hills CE, Lee K. Diagnosis and management of type 2 diabetes mellitus in patients with ischaemic heart disease and acute coronary syndromes-a review of evidence and recommendations. Frontiers in Endocrinology. 2025; 15:1499681.
15. American Diabetes Association. Glycemic targets: standards of medical care in diabetes-2018. Diabetes Care. 2020;41(1):S55– S64.
16. Choi SH, Oh TJ, Jang HC. Comparison of antidiabetic regimens in patients with type 2 diabetes uncontrolled by combination therapy of sulfonylurea and metformin: results of the MOHAS disease registry in Korea. Diabetes Metab J. 2017;41(3):170–178.
17. Chawla R, Madhu SV, Makkar BM, et al. RSSDI-ESI clinical practice recommendations for the management of type 2 diabetes mellitus 2020. Indian Journal of Endocrinology and Metabolism 2020;24(1):1.
18. Li Z, Cheng Y, Wang D, et al. Incidence rate of type 2 diabetes mellitus after gestational diabetes mellitus: a systematic review and meta-analysis of 170,139 women. Journal of Diabetes Research 2020; 2020:3076463.
19. Faselis C, Katsimardou A, Imprialos K, et al. Microvascular complications of type 2 diabetes mellitus. Current Vascular Pharmacology 2020;18(2):117-24.
20. Rachdaoui N. Insulin: the friend and the foe in the development of type 2 diabetes mellitus. International Journal of Molecular Sciences 2020;21(5):1770.
21. Al Mansour MA. The prevalence and risk factors of type 2 diabetes mellitus (DMT2) in a semi-urban Saudi population. International Journal of Environmental Research and Public Health 2020;17(1):7.
22. Karatas S, Yesim T, Beysel S. Impact of lockdown COVID-19 on metabolic control in type 2 diabetes mellitus and healthy people. Primary care diabetes 2021;15(3):424-7.
23. Mikhael EM, Hassali MA, Hussain SA. Effectiveness of diabetes self-management educational programs for type 2 diabetes mellitus patients in Middle East countries: a systematic review. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2020;13:117.
24. Izzo A, Massimino E, Riccardi G, et al. A narrative review on sarcopenia in type 2 diabetes mellitus: prevalence and associated factors. Nutrients 2021;13(1):183.
25. Perreault L, Skyler JS, Rosenstock J. Novel therapies with precision mechanisms for type 2 diabetes mellitus. Nature Reviews Endocrinology 2021;17(6):364-77.

ISSN (O): 2687-5365; ISSN (P): 2753-6556