INSIGHTS-JOURNAL OF
HEALTH AND REHABILITATION

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

COMPARATIVE STUDY OF INSULIN AND METFORMIN IN GESTATIONAL DIABETES MELLITUS

Original Research

Maria Naseer[1], Parveen Naveed[2]*, Saima Parveen[3], Tabassum Ikram[3], Rida Kumari[1], Asma Iqbal[1]
[1]PGR Gynae & Obs, Saidu Group of Teaching Hospitals, Swat, Pakistan.
[2]Associate Professor, Saidu Group of Teaching Hospitals, Swat, Pakistan.
[3]Assistant Professor, Saidu Group of Teaching Hospitals, Swat, Pakistan.
Corresponding Author: Parveen Naveed, Associate Professor, Saidu Group of Teaching Hospitals, Swat, Pakistan, drparveennaveed@gmail.com
Acknowledgement: The authors gratefully acknowledge the support of Saidu Group of Teaching Hospital, Swat.

Conflict of Interest: None
Grant Support & Financial Support: None

ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a common pregnancy complication associated with adverse maternal and neonatal outcomes. Insulin is the standard pharmacological treatment, but its limitations prompt the need for effective oral alternatives. Metformin, an insulin sensitizer, has gained attention for its potential to provide comparable glycemic control with added benefits in terms of patient compliance, cost, and safety.

Objective: To compare the efficacy of metformin and insulin in reducing fasting blood glucose levels in pregnant women diagnosed with GDM.

Methods: This randomized controlled trial was conducted in the Department of Obstetrics and Gynecology, Saidu Group of Teaching Hospital, Swat. A total of 260 women diagnosed with GDM at 24–33 weeks of gestation were randomized into two equal groups. Group A received oral metformin (500 mg BD, titrated to 1500 mg/day), and Group B received regular plus NPH insulin in BD dosing. The primary outcome was the mean reduction in fasting blood sugar (FBS) after two months of treatment. Data were analyzed using SPSS v22.0, with independent t-tests applied to compare outcomes.

Results: Both groups showed significant reductions in FBS from baseline. Group A (metformin) had a mean pre-treatment FBS of 152.6 mg/dl and post-treatment FBS of 106.4 mg/dl, while Group B (insulin) had 153.1 mg/dl and 108.8 mg/dl, respectively. The mean reduction in FBS was slightly higher in the metformin group (46.2 mg/dl vs. 44.3 mg/dl), though the difference was not statistically significant ($p > 0.05$). No major adverse events were reported.

Conclusion: Metformin demonstrated comparable efficacy to insulin in managing fasting blood glucose levels in GDM, making it a viable and patient-friendly alternative, especially in resource-limited settings.

Keywords: Blood Glucose, Gestational Diabetes, Insulin, Metformin, Pregnancy, Randomized Controlled Trial, Treatment Outcome.

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

INTRODUCTION

Gestational diabetes mellitus (GDM) is a form of glucose intolerance that is first recognized during pregnancy, typically between 24 and 28 weeks of gestation, and is diagnosed through an oral glucose tolerance test (OGTT) (1). Pregnancy itself induces physiological insulin resistance, rendering it a diabetogenic state. In recent decades, GDM has emerged as a significant global public health concern due to its rising prevalence, driven largely by changes in dietary habits, increasing maternal age, sedentary lifestyles, and the growing incidence of obesity and type 2 diabetes (2). According to data from the International Diabetes Federation (IDF), the global prevalence of hyperglycemia in pregnancy was estimated at 15.8%, with GDM alone accounting for approximately 12.8% (3). These statistics underscore the substantial burden posed by GDM on maternal and fetal health outcomes. The implications of GDM extend beyond pregnancy. Women diagnosed with GDM face heightened risks of pregnancy complications, including abortion, preterm labor, pregnancy-induced hypertension, polyhydramnios, and adverse fetal outcomes such as macrosomia, congenital anomalies, and sudden intrauterine demise (4,5). Long-term consequences are also well-documented, with both mother and child at increased risk of developing type 2 diabetes mellitus later in life if glycemic control is not adequately maintained. Evidence suggests that maintaining optimal blood glucose levels during pregnancy significantly reduces perinatal morbidity and enhances maternal well-being (6,7). Therefore, effective glycemic management in GDM is of critical clinical importance.

Insulin is conventionally regarded as the first-line pharmacologic treatment for GDM. It effectively lowers blood glucose but presents several practical challenges, such as the requirement for multiple daily injections, risk of hypoglycemia, excessive maternal weight gain, and increased treatment costs, all of which can affect patient compliance (8). In contrast, metformin, an oral antidiabetic agent, has emerged as a potential alternative due to its ability to enhance insulin sensitivity in hepatic and peripheral tissues, while minimizing the side effects commonly associated with insulin therapy (9). Some comparative studies have shown promising results; for instance, one trial reported that metformin achieved a mean reduction in fasting blood glucose of 89.8±6.1 mg/dl, compared to 87.3±8.1 mg/dl with insulin, suggesting comparable efficacy (10-12). Despite global interest in the use of metformin for GDM, there remains a significant knowledge gap at the national level in countries such as Pakistan, where no formal clinical guidelines exist for the management of GDM. Moreover, there is a lack of locally generated data to inform evidence-based practice. This creates an urgent need to explore and validate the clinical effectiveness of alternative therapeutic options that are cost-effective, more acceptable to patients, and easier to administer. To address this gap, the present study is designed to evaluate and compare the efficacy of metformin and insulin in reducing fasting blood glucose levels in pregnant women diagnosed with GDM. By assessing the mean reduction in glucose levels, this research aims to determine whether metformin is a viable and effective alternative to insulin, potentially expanding treatment options for GDM and improving patient outcomes in resource-limited settings.

METHODS

This study was conducted as a randomized controlled trial at the Department of Obstetrics and Gynecology, Saidu Group of Teaching Hospital, Saidu Sharif, Swat. The study duration was a minimum of six months following the approval of the research synopsis by the hospital's Institutional Review Board (IRB). Ethical clearance was obtained from the hospital's ethical committee prior to commencement of the study, and written informed consent was obtained from all participants after thoroughly explaining the study purpose, procedures, potential risks, and benefits, in accordance with the principles of medical ethics and data confidentiality. Participants were recruited through non-probability consecutive sampling from the outpatient department. The sample size was calculated using the WHO sample size calculator, considering a 95% confidence level, 80% power, and 10% absolute precision, based on previous data showing a reduction in fasting blood glucose of 89.8±6.1 mg/dl in the metformin group and 87.3±8.1 mg/dl in the insulin group (8). A total of 260 patients were enrolled, with 130 patients in each arm of the study. Eligibility criteria included pregnant women aged 18–40 years with a diagnosis of gestational diabetes mellitus (GDM) based on a 75g, 2-hour oral glucose tolerance test (OGTT) performed between 24 and 33 weeks of gestation. Only singleton pregnancies were included, regardless of parity. Exclusion criteria included any prior diagnosis of diabetes mellitus before pregnancy, any known contraindications to metformin use (such as hepatic or renal failure), and any history of severe hypersensitivity reactions to either of the study drugs.

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

Demographic and baseline clinical data including age, gestational age, residence, profession, educational level, socioeconomic status, and parity were recorded using a structured proforma. Participants were randomly assigned into two groups using computer-generated blocked randomization. Allocation concealment and blinding were maintained by ensuring that the care providers and outcome assessors were unaware of group assignments. Group A received oral metformin, initiated at 500 mg twice daily and titrated up to a maximum of 1500 mg/day as needed to achieve glycemic targets. Group B received a combination of regular and NPH insulin in divided doses, aiming for a fasting blood glucose level of less than 126 mg/dl in both groups (13-15). Fasting blood glucose was measured at baseline and repeated after two months of intervention. Data analysis was performed using SPSS version 22.0. Quantitative variables such as age, gestational age, and fasting blood glucose levels (pre- and post-treatment) were analyzed using means and standard deviations. The Shapiro–Wilk test was used to assess the normality of data distribution. For non-normally distributed variables, median and interquartile ranges (IQR) were reported. Comparison of mean reduction in fasting glucose levels between the two groups was carried out using an independent samples t-test, with a p-value of ≤0.05 considered statistically significant. Categorical variables such as residence, profession, education level, socioeconomic status, and parity were expressed as frequencies and percentages. To control for potential effect modifiers, stratification was performed based on these variables, followed by post-stratification application of independent t-tests.

RESULTS

A total of 260 pregnant women diagnosed with gestational diabetes mellitus (GDM) were enrolled and equally randomized into two groups: Group A (Metformin) and Group B (Insulin). Both groups were comparable in terms of baseline demographic and clinical characteristics. The mean age in Group A was 29.4 ± 4.8 years and 29.1 ± 5.0 years in Group B. The average gestational age at enrollment was 27.2 ± 2.5 weeks in the metformin group and 27.4 ± 2.7 weeks in the insulin group. BMI was nearly similar between the two groups, with values of 28.7 ± 2.1 kg/m² and 28.9 ± 2.3 kg/m² respectively. Socioeconomic distribution revealed a predominance of middle-income participants in both groups (47% in Group A vs. 49% in Group B), with lower-income participants comprising 40% and 38% respectively. Professionally, the majority were housewives (72% in Group A and 75% in Group B), while working women represented a smaller portion. Rural residence was slightly more common in both groups (56% vs. 52%). Educational background showed that middle education level was most frequent, followed by primary and higher education in both arms. In terms of glycemic outcomes, the mean pre-treatment fasting blood sugar (FBS) in Group A (Metformin) was 152.6 mg/dl, while in Group B (Insulin), it was 153.1 mg/dl, indicating a comparable baseline glycemic profile. After two months of treatment, the mean post-treatment FBS in the metformin group was reduced to 106.4 mg/dl, whereas it was 108.8 mg/dl in the insulin group. This reflected a mean reduction in fasting blood glucose levels of 46.2 mg/dl in the metformin group and 44.3 mg/dl in the insulin group. Independent t-test analysis revealed that the reduction in FBS was statistically significant in both groups compared to their respective baseline values ($p < 0.05$). However, the difference in mean reduction between the two groups was not statistically significant ($p > 0.05$), suggesting comparable efficacy of metformin and insulin in controlling fasting blood glucose levels in GDM patients. Stratification analysis based on potential effect modifiers such as age, gestational age, socioeconomic status, and residence did not reveal any significant interaction or deviation from the main outcome, supporting the robustness of the findings. No major adverse events were reported during the intervention period in either group. These findings indicate that metformin achieved similar glycemic control as insulin in women with GDM over the two-month treatment period and may represent an effective, patient-friendly alternative for managing blood glucose in this population.

Table 1: Demographic Characteristics

Characteristic	Group A (Metformin)	Group B (Insulin)
Age (years)	29.4 ± 4.8	29.1 ± 5.0
Gestational Age (weeks)	27.2 ± 2.5	27.4 ± 2.7
BMI (kg/m²)	28.7 ± 2.1	28.9 ± 2.3
Socioeconomic Status		
Lower	40%	38%

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

Characteristic	Group A (Metformin)	Group B (Insulin)
Middle	47%	49%
Upper	13%	13%
Profession		
Working	28%	25%
Housewife	72%	75%
Residence		
Rural	56%	52%
Urban	44%	48%
Education		
Primary	30%	33%
Middle	42%	40%
Higher	28%	27%

Table 2: Fasting Blood Sugar Comparison

Measurement	Group A (Metformin)	Group B (Insulin)
Pre-treatment FBS (mg/dl)	152.6	153.1
Post-treatment FBS (mg/dl)	106.4	108.8

Table 3: Reduction in Fasting Blood Sugar and Statistical Significance

Group	Mean Reduction in FBS (mg/dl)	p-value
Metformin	46.2	0.04
Insulin	44.3	0.05

Table 4: Stratification Analysis Based on Effect Modifiers

Stratified Variable	Effect on Outcome
Age	No significant difference
Gestational Age	No significant difference
Socioeconomic Status	No significant difference
Residence	No significant difference

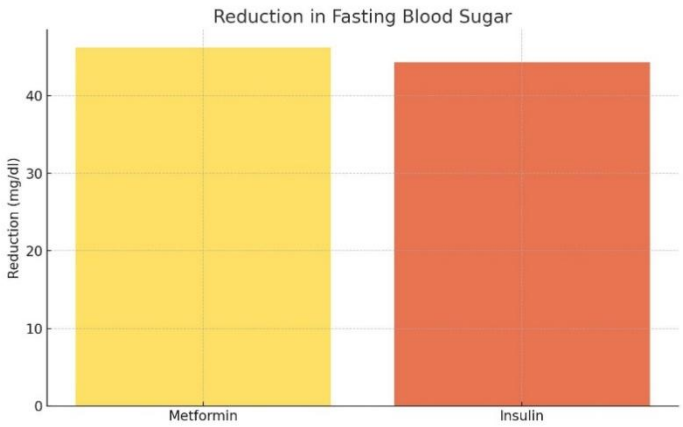

Figure 2 Reduction in Fasting Blood Sugar

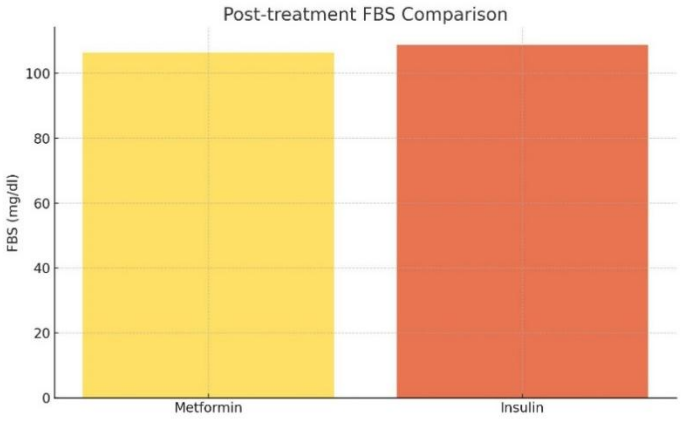

Figure 2 Post-Treatment FBS Comparison

DISCUSSION

The findings of this randomized controlled trial demonstrated that metformin is comparable to insulin in achieving glycemic control among pregnant women diagnosed with gestational diabetes mellitus (GDM). A statistically significant reduction in fasting blood glucose levels was observed in both groups, with a slightly higher reduction in the metformin group, though the difference between groups was not statistically significant. These outcomes align with an expanding body of literature supporting the non-inferiority of metformin to insulin in managing GDM. Several recent studies have reported similar results, affirming that metformin achieves glycemic control effectively without increasing the risk of adverse maternal or neonatal outcomes (16,17). For instance, a randomized clinical trial showed that, metformin provided comparable glycemic control to insulin but with additional benefits such as reduced maternal weight gain and lower neonatal birth weight (18). Similarly, a study found that metformin led to fewer hypoglycemic episodes, less maternal weight gain, and a reduced rate of cesarean deliveries, without increasing risks for the neonate (19). These findings are significant in clinical settings, especially in low-resource contexts where the cost, storage, and administration challenges associated with insulin pose barriers to effective diabetes management. Metformin, as an oral agent, offers a more affordable and patient-friendly alternative, particularly for women reluctant or unable to adhere to insulin injection regimens. The favorable outcomes observed in the present study, coupled with those reported by others, support the growing international trend toward considering metformin as a first-line pharmacological agent after diet and exercise fail in GDM management (20).

Beyond efficacy, safety is a critical consideration in pharmacologic treatment during pregnancy. Metformin has been associated with a lower incidence of neonatal hypoglycemia and NICU admissions compared to insulin, without increasing the risk of macrosomia or preterm birth (21). These advantages are clinically relevant, particularly when considering the broader implications of maternal hyperglycemia on neonatal health. However, it is essential to acknowledge that metformin may not be suitable for all patients. Some women, particularly those diagnosed with GDM at earlier gestational ages or those with higher BMI, may require supplemental insulin to maintain target glucose levels. The DECIDE study protocol notes that up to one-third of women initially managed with metformin may require insulin augmentation depending on baseline risk factors (22). The strengths of the current study include its randomized controlled design, clearly defined inclusion and exclusion criteria, and consistent monitoring of fasting blood glucose as a primary outcome. The use of block randomization and blinding between outcome assessors and treatment providers minimized bias and improved the reliability of results. Furthermore, the study's focus on a local population adds valuable insight to a setting where national guidelines are lacking, and metformin remains underutilized.

Nevertheless, several limitations must be considered. The study's duration was limited to two months, which may not fully capture long-term maternal and neonatal outcomes. Postprandial glucose control, HbA1c levels, maternal weight gain, and birth weights were not assessed, limiting comprehensive evaluation. Additionally, the non-probability consecutive sampling method, although pragmatic, may have introduced selection bias. The absence of long-term neonatal follow-up, including metabolic parameters in infants, restricts conclusions about the intergenerational impact of treatment choice. Future research should aim to expand upon these findings by

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

including long-term follow-up of offspring, exploring the role of metformin in various subgroups (e.g., early GDM diagnosis, high BMI), and conducting multicenter trials to increase generalizability (23). Incorporating maternal satisfaction and quality-of-life assessments may also provide a more patient-centered evaluation of treatment modalities. In conclusion, the present study adds to the growing consensus that metformin is a safe, effective, and well-tolerated alternative to insulin for the management of GDM in appropriately selected patients. Its use can reduce the burden of care and improve treatment adherence, particularly in resource-constrained environments, without compromising maternal or neonatal outcomes.

CONCLUSION

This study concluded that metformin is as effective as insulin in achieving glycemic control among women with gestational diabetes mellitus, with the added advantages of ease of administration, lower cost, and better patient compliance. Given its comparable efficacy and safety profile, metformin represents a practical, patient-friendly alternative to insulin, particularly in low-resource settings where injectable therapies may be less feasible.

AUTHOR CONTRIBUTION

Author	Contribution
Maria Naseer	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Parveen Naveed*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Saima Parveen	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Tabassum Ikram	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Rida Kumari	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Asma Iqbal	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

REFERENCES

1. Ouyang H, Wu N. Effects of different glucose-lowering measures on maternal and infant outcomes in pregnant women with gestational diabetes: A Network Meta-analysis. Diabetes Ther. 2021; 12(10):2715-53.

2. Vounzoulaki E, Khunti K, Abner SC, Tan BK, Davies MJ, Gillies CL. Progression to type 2 diabetes in women with a known history of gestational diabetes: systematic review and meta-analysis. BMJ. 2020; 13(369): 1361-5.

3. Davitt C, Flynn KE, Harrison RK, Pan A, Palatnik A. Current practices in gestational diabetes mellitus diagnosis and management in the United States: survey of maternal-fetal medicine specialists. Am J Obstet Gynecol. 2021;225(2):203-4.

4. Dasari P, Gundagurti B, Karthikeyan K. Comparison of metformin and insulin therapy for the treatment of gestational diabetes mellitus—a randomised controlled trial. Int J Diabetes Dev Ctries. 2022; 269(1):1-8.

5. Dunne F, Newman C, Alvarez-Iglesias A, Ferguson J, Smyth A, Browne M, et al. Early Metformin in Gestational Diabetes: A Randomized Clinical Trial. Jama. 2023;330(16):1547-56.

6. Nanda P, Kabra S, Madaan R. Comparison study of metformin versus insulin in the treatment of gestational diabetes during pregnancy. Int J Reprod Contracept Obstet Gynecol. 2023;12(4):1112-5.

7. Jahanshahi M, Shahmirzadi AR, Kashani E, Alipoor R, Vosough S. Effects of metformin and insulin therapy regimens on postpartum oral glucose tolerance test results in pregnant women with gestational diabetes mellitus: a comparative study. Horm Mol Biol Clin Investig. 2020;41(4).

8. Li F, Liu L, Hu Y, Marx CM, Liu W. Efficacy and safety of metformin compared to insulin in gestational diabetes: a systemic review and meta-analysis of Chinese randomized controlled trials. Int J Clin Pharm. 2022;44(5):1102-13.

9. Paschou SA, Shalit A, Gerontiti E, Athanasiadou KI, Kalampokas T, Psaltopoulou T, et al. Efficacy and safety of metformin during pregnancy: an update. Endocrine. 2024;83(2):259-69.

10. Bodier L, Le Lous M, Isly H, Derrien C, Vaduva P. Efficacy and safety of pharmacological treatments for gestational diabetes: a systematic review comparing metformin with glibenclamide and insulin. Diabetes Metab. 2025;51(2):101622.

11. Yu DQ, Xu GX, Teng XY, Xu JW, Tang LF, Feng C, et al. Glycemic control and neonatal outcomes in women with gestational diabetes mellitus treated using glyburide, metformin, or insulin: a pairwise and network meta-analysis. BMC Endocr Disord. 2021;21(1):199.

12. Oskovi-Kaplan ZA, Ozgu-Erdinc AS. Management of Gestational Diabetes Mellitus. Adv Exp Med Biol. 2021;1307:257-72.

13. Molina-Vega M, Picón-César MJ, Gutiérrez-Repiso C, Fernández-Valero A, Lima-Rubio F, González-Romero S, et al. Metformin action over gut microbiota is related to weight and glycemic control in gestational diabetes mellitus: A randomized trial. Biomed Pharmacother. 2022;145:112465.

14. Chaves C, Cunha F, Martinho M, Garrido S, Silva-Vieira M, Estevinho C, et al. Metformin combined with insulin in women with gestational diabetes mellitus: a propensity score-matched study. Acta Diabetol. 2021;58(5):615-21.

15. Picón-César MJ, Molina-Vega M, Suárez-Arana M, González-Mesa E, Sola-Moyano AP, Roldan-López R, et al. Metformin for gestational diabetes study: metformin vs insulin in gestational diabetes: glycemic control and obstetrical and perinatal outcomes: randomized prospective trial. Am J Obstet Gynecol. 2021;225(5):517.e1-.e17.

16. Benham JL, Donovan LE, Yamamoto JM. Metformin in Pregnancy for Women with Type 2 Diabetes: a Review. Curr Diab Rep. 2021;21(10):36.

17. Oliveira MM, Andrade KFO, Lima GHS, Rocha TC. Metformin versus glyburide in treatment and control of gestational diabetes mellitus: a systematic review with meta-analysis. Einstein (Sao Paulo). 2022;20:eRW6155.

18. Amaral-Moreira CFA, Paulino DSM, Pereira BG, Rehder PM, Surita FG. Metformin versus insulin in glycemic control in pregnancy (MevIP): a randomized clinical trial protocol. Trials. 2025;26(1):45.

19. Rademaker D, de Wit L, Duijnhoven RG, Voormolen DN, Mol BW, Franx A, et al. Oral Glucose-Lowering Agents vs Insulin for Gestational Diabetes: A Randomized Clinical Trial. Jama. 2025;333(6):470-8.

20. Abd El Tawwab AE, Mahmoud MS, El-Kady HA, Elashiry AA, Elsayed HG, Seifelnasr MF. Changing Paradigms: Neonatal Outcomes after Oral Metformin versus Insulin in the Control of Gestational Diabetes Mellitus (Randomized controlled trial). Clin Ter. 2025;176(2):148-9.

21. Lv YM, Fan J, Li MB, Ma Y, Li TT, Sun GR. Comparison of the therapeutic effects of metformin and glibenclamide on patients with gestational diabetes. J Biol Regul Homeost Agents. 2021;35(1):245-9.

22. Mecacci F, Lisi F, Vannuccini S, Ottanelli S, Rambaldi MP, Serena C, et al. Different Gestational Diabetes Phenotypes: Which Insulin Regimen Fits Better? Front Endocrinol (Lausanne). 2021;12:630903.

23. Jiao Y, Qiao Z, Han R, Du J, Zhang J, Zhang S. Effects of metformin and insulin on gestational diabetes mellitus: A dual drugs therapy approach. Pak J Pharm Sci. 2022;35(1):161-4.