Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 69 Issue 06 | 2026
DOI: 10.5281/zenodo.20792416

EFFICACY OF COMBINATION OF METFORMIN AND INSULIN VERSUS INSULIN ALONE IN PREGNANT WOMEN WITH GESTATIONAL DIABETES MELLITUS

Dr. ASRA KHALID CH*
Postgraduate Resident (Main Author), Capital Development Authority Hospital CDA, Islamabad.
*Corresponding Author Email: Asrakhalidch@Gmail.Com

Dr. SHEEBA NOREEN
Gynaecologist, (Training Supervisor), Capital Development Authority Hospital CDA, Islamabad.
Email: Dr.Sheebanoreen@Gmail.Com

Dr. HADIA AZIZ
Associate Professor, Capital Development Authority Hospital CDA, Islamabad.
Email: Drhadia88@Gmail.Com

SANI ZAHRA
Postgraduate Resident, Capital Development Authority Hospital CDA, Islamabad.
Email: Sz.Zahra1414@Gmail.Com

Dr. NOREEN FATIMA
Postgraduate Resident, Capital Development Authority Hospital CDA, Islamabad.
Email: Noreenfatima1993@Gmail.Com

Dr. HUSNA AMJAD ABBASI
Postgraduate Resident, Capital Development Authority Hospital CDA, Islamabad.
Email: Husnaamjad5@Gmail.Com

Abstract

Background: Gestational diabetes mellitus (GDM) is a common pregnancy complication associated with adverse maternal and fetal outcomes. Insulin is the standard treatment; however, metformin is increasingly used due to oral route and improved compliance. **Objective:** To compare the efficacy of metformin plus insulin with insulin alone in achieving glycemic control among pregnant women with GDM. **Methods:** This randomized controlled trial was conducted at Capital Development Authority Hospital, Islamabad. A total of 62 pregnant women with GDM not controlled with diet were randomly allocated into two groups (n = 31 each). Group A received insulin alone, while Group B received metformin in addition to insulin. Glycemic control was assessed using fasting blood glucose (<95 mg/dl) and 2-hour postprandial glucose (<120 mg/dl). Data were analyzed using SPSS. **Results:** Baseline characteristics were comparable between groups. A significantly higher proportion of patients achieved glycemic control in the metformin plus insulin group compared to the insulin-alone group (83.9% vs 41.9%, $p = 0.001$). The combination group had lower follow-up fasting glucose (90.32 ± 3.93 vs 94.63 ± 4.18 mg/dl, $p < 0.001$), lower postprandial glucose (113.94 ± 4.34 vs 119.71 ± 7.16 mg/dl, $p < 0.001$), and shorter time to control (7.16 ± 2.27 vs 25.55 ± 10.59 days, $p < 0.001$). **Conclusion:** Metformin combined with insulin is more effective than insulin alone in achieving glycemic control in GDM and reduces the time required to achieve target glucose levels.

Keywords: Gestational Diabetes Mellitus, Glycemic Control, Insulin Therapy, Metformin, Pregnancy.

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 69 Issue 06 | 2026
DOI: 10.5281/zenodo.20792416

INTRODUCTION

Gestational diabetes mellitus (GDM) is a manifestation of carbohydrate intolerance characterized by hyperglycemia of variable severity that usually develops or first becomes apparent during pregnancy (1). GDM is one of the most common metabolic disorders in pregnancy and is associated with a significant maternal and fetal morbidity (2). On a worldwide basis, however, approximately 7% of all pregnancies are complicated by GDM, resulting in more than 2 million cases annually (3). However, the reported prevalence ranges from 1% to 28%, depending on the population sample of the studied demographic cohort and the diagnostic criteria used (4). Suboptimal glycemic control in GDM is a risk factor in a wide range of adverse maternal and neonatal sequelae, including pre-eclampsia, macrosomia, birth trauma, neonatal hypoglycemia, and increased rates of caesarean delivery (5). In addition, people diagnosed with GDM are at greatly increased risk for the development of impaired glucose tolerance and type 2 diabetes mellitus in the following years (6).

Consequently, achieving optimal glycemic control at all points in the pregnancy is still of paramount importance in the therapeutic management of GDM to avoid both immediate and long-term complications. Historically, insulin administration has been considered to be the reference pharmacologic intervention for women with GDM who cannot attain adequate glycemic control with diet and lifestyle modification alone (7). While insulin therapy efficaciously reduces circulating glucose concentrations, it requires frequent injections, strict monitoring, as well as increased risk of maternal hypoglycemia and maternal excessive weight gain (8). These constraints have led to a growing interest in alternative or adjunctive pharmacotherapeutic choices (8).

Oral antidiabetic drugs have become attractive alternatives because they are easy to use, cost-effective, and have better patient compliance. Among these, metformin has received considerable attention due to its favorable pharmacological characteristics and known safety profile in pregnancy (9). Metformin (a biguanide antidiabetic) improves glycemic regulation by a range of mechanisms: inhibition of hepatic gluconeogenesis, increased peripheral insulin sensitivity, increased glucose uptake in skeletal muscle and hepatic cells, reduction of circulating free fatty acids by antilipolytic effects and enhancement of glucose utilization by the intestines (10). Compared with insulin, metformin is associated with a lower incidence of hypoglycemia, reduced maternal weight gain, and improved patient adherence due to its oral formulation (11).

Historical clinical investigations involving metformin in GDM have yielded mixed results: some studies have shown glycemic control equivalent to insulin, while others have shown better results when metformin is used in combination with insulin (12). A study reported a treatment success rate of 82.3% in a group of women receiving a combination of metformin and insulin therapy, compared with 44.1% in a group receiving only insulin therapy, suggesting a possible synergistic effect (13). Notwithstanding, an expanding body of international data supporting metformin in GDM treatment, data specific to South Asian populations on the efficacy of combination therapy with insulin are limited. Within

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 69 Issue 06 | 2026
DOI: 10.5281/zenodo.20792416

the confines of Pakistan, the prevalence of GDM and its associated maternal and perinatal complications remains at a significant level of magnitude, and thus highlights the need for effective, cost-efficient, and patient-oriented therapeutic regimes. Accordingly, this investigation was undertaken to evaluate the efficacy of metformin and insulin concomitant therapy and insulin monotherapy to achieve glycemic control in pregnant women diagnosed with GDM. By assessing clinically relevant glycemic endpoints and potential effect modifiers such as maternal age, body mass index, gestational age, and a history of GDM, this study aimed to generate region-specific evidence to inform clinical decision-making. The resultant data may elucidate the effect of adjunctive metformin therapy on glycemic control whilst simultaneously reducing the therapeutic burden in resource-constrained healthcare environments.

METHODOLOGY

This randomized controlled trial was conducted in the department of Obstetrics and Gynecology at the Capital Development Authority Hospital in Islamabad. The study involved a period of three months after approval of the research protocol by the institutional ethical review board (Approval No. IRB-127 dated: 09-12-2025). A total of 62 pregnant women with a diagnosis of gestational diabetes mellitus were included. The required sample size was calculated based on an expected efficacy rate of 44.1% for insulin monotherapy and 82.3% for combined metformin-insulin therapy, with a confidence level of 95%, statistical power of 90%, and the World Health Organization's online calculator.

Accordingly, 31 subjects were assigned to each of the two intervention arms. Participants were recruited using consecutive non-probability sampling from patients attending the outpatient and emergency departments of the hospital. Inclusion criteria included pregnant women who were diagnosed with gestational diabetes mellitus that was not well controlled by alteration of diet, gestational age 28-34 weeks, body mass index between 25 and 35 kg/m2, and singleton pregnancy. Eligibility was further narrowed to women aged from 20 to 45 years.

Exclusion criteria were previous diagnosed pre-existing diabetes mellitus (type 1 or type 2) before pregnancy, known hypersensitivity or adverse reaction to metformin, or short maternal stature and a gross degree of pelvic contraction that may require elective caesarean section. FBS ≥92 mg/dl and 2h ≥153 mg/dl were considered as gestational diabetes mellitus.

Treatment effectiveness was defined as satisfactory glycemic control, operationalized as fasting blood glucose <95mg/dl and 2-hour postprandial blood glucose <120mg/dl at follow-up. Following confirmation of eligibility and achievement of written informed consent, participants were randomly allocated within 2 groups (treatment groups) using block randomization. Group A (Insulin Group) was given human insulin in divided doses, with a starting total daily dose of 0.8 units/kg. Two-thirds of this dose were administered in the morning before breakfast, and the remaining one third in the evening before dinner.

ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 69 Issue 06 | 2026
DOI: 10.5281/zenodo.20792416

Insulin doses were then further adjusted as per glycemic monitoring to get sugars under control. Group B (Metformin + Insulin Group) started oral metformin 500mg once a day with food and laboratory monitored dose increment with 500mg per week as required, with maximum 2500 mg per day. In addition to metformin, insulin doses were titrated based on serial glucose monitoring to achieve target glycemic levels.

Ethical approval was obtained from the ethics committee of the hospital before the study began. Eligible patients were recruited from the outpatient and emergency departments. After explaining the aims and possible benefits of the study, written informed consent was obtained by all participants. Baseline demographic and clinical data were recorded on a structured proforma. All participants were subjected to laboratory investigations such as fasting and random blood glucose determinations and oral glucose tolerance test conducted within the pathology department of the hospital to ascertain the diagnosis of GDM. Patients were followed in antenatal clinics every two weeks up to 36 weeks of gestation, and then on a weekly basis until delivery.

Furthermore, fasting and 2-hour blood glucose levels were monitored on each visit to assess glycemic control and effectiveness of treatment. Data were entered and analyzed using version 26 of Statistical Package for Social Sciences (SPSS). Continuous variables were summarized as means and SD, categorical variables as frequencies and percentages.

The primary outcome, i.e. treatment effectiveness, was compared between the two groups by means of the Chi square test. Stratification was conducted to examine for possible effect modifiers, such as maternal age, gestational age at birth, BMI and previous history of gestational diabetes. Regression analyses were performed and a p-value < 0.05 was considered statistically significant.

RESULTS

A total of 62 pregnant women with gestational diabetes mellitus were included in the study and equally allocated into two treatment groups: insulin alone ($n = 31$) and metformin plus insulin ($n = 31$). The majority of participants were multigravida (88.7%), while 11.3% were primigravida. A previous history of gestational diabetes mellitus was present in 27.4% of participants (Table 1).

The descriptive statistics was also performed (Table 2). Normality testing using the Shapiro–Wilk test showed that all continuous variables were normally distributed ($p > 0.05$).

Table 1: Distribution of Participants According to Baseline Characteristics (N = 62)

Variable	Frequency (n)	Percentage (%)
Treatment Group		
Insulin alone	31	50.0
Metformin + insulin	31	50.0

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 69 Issue 06 | 2026
DOI: 10.5281/zenodo.20792416

Parity		
Multigravida	55	88.7
Primigravida	7	11.3
Previous History of GDM		
No	45	72.6
Yes	17	27.4

Table 2: Descriptive Statistics of Continuous Variables

Variable	Mean ± SD
Maternal age (years)	31.76 ± 4.83
Gestational age (weeks)	30.63 ± 1.49
Height (cm)	159.47 ± 4.97
Weight (kg)	74.83 ± 6.98
BMI (kg/m²)	29.43 ± 2.50

The independent-samples t-test showed that the two treatment groups were comparable at baseline, with no statistically significant differences (all $p > 0.05$). However, significant differences were observed in follow-up outcomes (Table 3).

Compared with the insulin-alone group, the metformin-plus-insulin group had lower mean follow-up FBS, lower mean follow-up PPBS, and a markedly shorter mean time to achieve glycemic control (Table 4).

Table 3: Comparison of Baseline Characteristics Between Treatment Groups

Variable	Insulin	Metformin + Insulin	p-value
Age (years)	30.71 ± 4.64	32.81 ± 4.86	0.088
Gestational age (weeks)	30.78 ± 1.54	30.47 ± 1.44	0.408
BMI (kg/m²)	29.41 ± 2.77	29.45 ± 2.25	0.956
Baseline FBS	135.17 ± 5.58	132.49 ± 5.77	0.067
Baseline PPBS	164.29 ± 10.28	164.66 ± 10.75	0.893

Table 4: Comparison of Follow-Up Outcomes Between Groups

Variable	Insulin alone	Metformin + insulin	p-value
Follow-up FBS (mg/dL)	94.63 ± 4.18	90.32 ± 3.93	<0.001
Follow-up 2-hour PPBS (mg/dL)	119.71 ± 7.16	113.94 ± 4.34	<0.001
Days to achieve glycemic control	25.55 ± 10.59	7.16 ± 2.27	<0.001

A significantly higher proportion of participants in the metformin plus insulin group achieved good glycemic control compared to the insulin-only group. Among patients receiving insulin alone, only 13 out of 31 (41.9%) achieved good glycemic control, whereas 26 out of 31 (83.9%) patients in the metformin plus insulin group achieved target glycemic levels. (Figure 1).

Table 5: Comparison of Treatment Effectiveness Between Groups

Treatment Group	Effective n (%)	Not Effective n (%)	p-value
Insulin alone	13 (41.9%)	18 (58.1%)	
Metformin + insulin	26 (83.9%)	5 (16.1%)	0.001

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 69 Issue 06 | 2026
DOI: 10.5281/zenodo.20792416

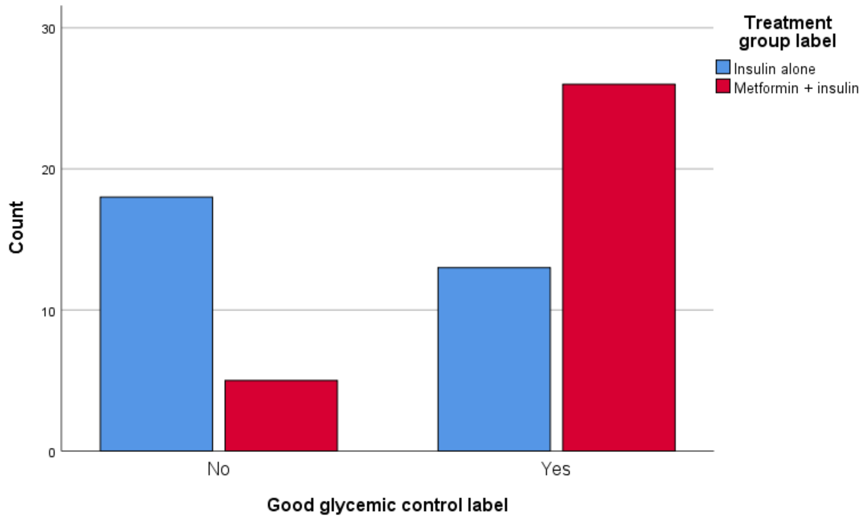
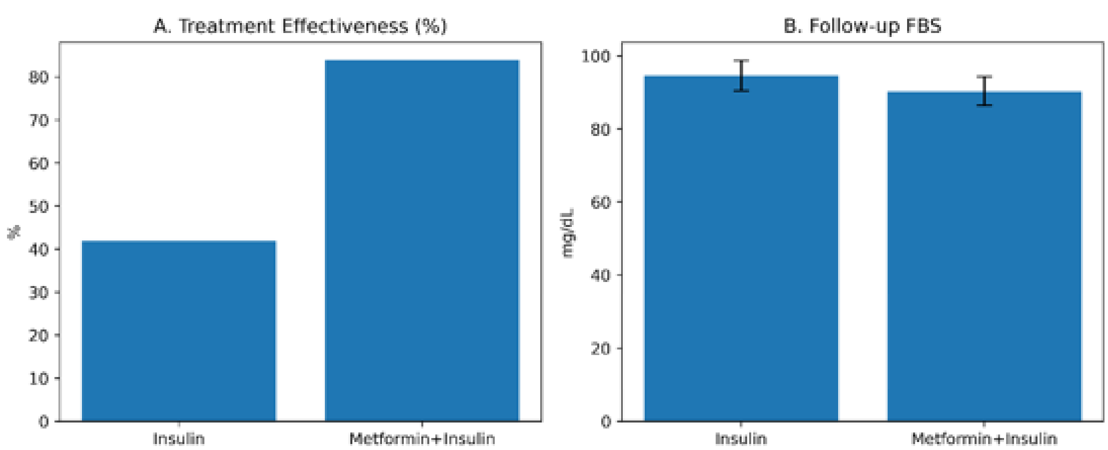


Figure 1: Proportion of participants achieving glycemic control in each treatment group

No statistically significant differences were observed between treatment groups across stratified variables including age, gestational age, BMI, parity, and previous history of GDM ($p > 0.05$), confirming homogeneity of groups. Multivariable logistic regression analysis demonstrated that none of the covariates were independently associated with treatment effectiveness ($p > 0.05$) (Table 6).

Table 6: Logistic Regression Analysis for Treatment Effectiveness

Variable	OR (Exp B)	p-value
Age	0.94	0.489
BMI	1.18	0.304
Gestational age	0.76	0.367
Previous GDM	0.87	0.885
Parity	0.79	0.506



Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 69 Issue 06 | 2026
DOI: 10.5281/zenodo.20792416

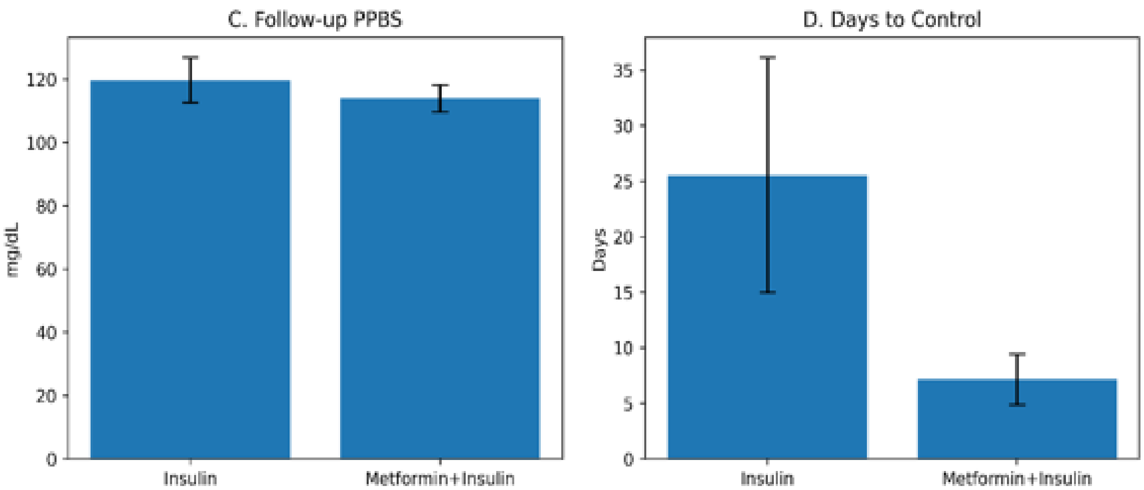


Figure 2 (A–D): Multi-panel representation of study outcomes. (A) Treatment effectiveness showing a higher proportion of patients achieving glycemic control in the metformin plus insulin group. (B) Comparison of follow-up fasting blood glucose levels with error bars (mean ± SD). (C) Comparison of follow-up postprandial glucose levels. (D) Comparison of time required to achieve glycemic control

The results of this study show that combination therapy (metformin and insulin) is much more effective than insulin alone in achieving glycemic control in pregnant women with GDM. The combination therapy not only led to better glycemic outcomes, but it also led to significantly reduced time to achieve glycemic control.

DISCUSSION

In this randomized controlled study involving 62 pregnant women with gestational diabetes mellitus (GDM), combination therapy with metformin and insulin demonstrated significantly superior glycemic outcomes compared with insulin alone. A substantially higher proportion of women in the metformin-plus-insulin group achieved good glycemic control (83.9% vs 41.9%). In addition, the combination group exhibited significantly lower follow-up FBS (90.32 ± 3.93 vs 94.63 ± 4.18 mg/dl) and 2-hour PPBS (113.94 ± 4.34 vs 119.71 ± 7.16 mg/dl). Notably, the time required to achieve glycemic control was markedly reduced in the combination group (7.16 ± 2.27 vs 25.55 ± 10.59 days), highlighting both efficacy and rapidity of response.

The internal validity of these findings is supported by the comparability of baseline characteristics between the two groups. There were no statistically significant differences in maternal age (30.71 ± 4.64 vs 32.81 ± 4.86 years), gestational age at enrollment (30.78 ± 1.54 vs 30.47 ± 1.44 weeks), BMI (29.41 ± 2.77 vs 29.45 ± 2.25 kg/m², $p = 0.956$), baseline FBS (135.17 ± 5.58 vs 132.49 ± 5.77 mg/dl, $p = 0.067$), and baseline PPBS (164.29 ± 10.28 vs 164.66 ± 10.75 mg/dl, $p = 0.893$). This homogeneity suggests that the

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 69 Issue 06 | 2026
DOI: 10.5281/zenodo.20792416

observed differences in outcomes are attributable to the intervention rather than confounding factors. The superiority shown of metformin based therapy in this study is consistent with the evidence from both regional and international research. In one trial performed in Pakistan, glycemic control was achieved (74.0%) with metformin compared with only 32.0% with insulin, an outcome very similar to our own (83.9% versus 41.9%) and confirming the improved efficacy of metformin-based regimens in similar populations (14). may offer potential benefits in South Asian populations, although further region-specific trials are needed.

Recent high quality evidence further supports the use of metformin to manage gestational diabetes mellitus (GDM) although findings differ by outcome measured (15). The EMERGE trial, for example, found that the primary composite endpoint of insulin initiation or fasting hyperglycemia occurred in 56.8 per cent of metformin group participants and 63.7 per cent of placebo group participants (risk ratio 0.89, p=0.13) and therefore suggested no statistically significant difference in the primary endpoint. Nevertheless, some maternal secondary outcomes were in favor of metformin such as earlier glycemic stabilization and improved patient-reported glycemic control (16). These results imply that if metformin is no superior to insulin overall in terms of composite endpoints, it still provides clinically meaningful benefits in maternal glycemic management.

Similarly, another multicenter study showed that 79% of women randomized to oral glucose lowering therapy were able to maintain glycemic control without the need for insulin, thus indicating the efficacy of oral agents in a significant proportion of patients randomized in this study. The trial, however, did not establish the non-inferiority for neonatal outcomes; large for gestational age infants occurred in 23.9 percent among the oral therapy group compared to 19.9 percent in the insulin group (17). These findings highlight the fact that whilst metformin based strategies are effective for glycemic control in mother, there is a need to further investigate their impact on neonatal outcomes.

A 2024 meta- analysis also supports the favorable maternal and neonatal profile of metformin. When compared with insulin, metformin was linked with lower risks of preeclampsia (RR 0.61), caesarean section (RR 0.91), macrosomia (RR 0.67), neonatal intensive care unit admission (RR 0.75), neonatal hypoglycemia (RR 0.55) and large for gestational age (RR 0.80) (18). These data provide the potential rationale that improving glycemic control with metformin will be associated with additional clinical benefits in the context of the heterogeneity which continues to exist across studies (19).

One of the most clinically important findings of our investigation is that glycemic control is achieved much quicker (7.16 vs. 25.55 days). This measure is frequently underreported in the literature but has important clinical implications as prolonged hyperglycemia during pregnancy has been associated with adverse fetal outcomes (20). Faster achievement of glycemic goals may therefore reduce cumulative fetal exposure to hyperglycemia and favor obstetric outcomes, a hypothesis worth confirming in larger studies. The benefits related to combination therapy are biologically plausible. Whereas metformin lowers the amount of glucose produced in the liver and improves insulin sensitivity in the peripheral

ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 69 Issue 06 | 2026
DOI: 10.5281/zenodo.20792416

tissues, insulin directly lowers the levels of glucose in the blood (21). This complementary mechanism perhaps is responsible for allowing for more effective glycemic regulation especially in insulin resistant states like GDM. Moreover, oral administration of metformin may have a beneficial effect on adherence of patients compared to injectable insulin, contributing further to better glycemic outcomes (11,22).

Despite all these strengths, there are several limitations that should be recognized. Our study was done in one center with a small study size, which may limit the generalizability of the results. Additionally, neonatal effects and long term maternal and offspring effects were not assessed. Given ongoing concerns about the long-term metabolic effects of metformin exposure during pregnancy, additional studies are needed to begin to measure safety beyond the immediate perinatal phase.

CONCLUSION

Metformin plus insulin is more effective than insulin alone in achieving glycemic control in GDM, with faster stabilization and improved outcomes. This combination may be particularly valuable in resource-limited settings. Future multicenter studies should assess neonatal outcomes and long-term maternal effects.

Author Contributions

1st Author, Principal Author Concept, Drafting, Data Acquisition, Data analysis & Interpretation

2nd Author Final approval of the version to be published

3rd Author Concept & design, Critical review for important intellectual contents, Data analysis & Interpretation

4th Author Concept & design, Critical review for important intellectual contents

5th Author Data Curation & Data analysis & Interpretation

6th Author Critical Revision & final approval

References

1) Modzelewski R, Stefanowicz-Rutkowska MM, Matuszewski W, Bandurska-Stankiewicz EM. Gestational diabetes mellitus—recent literature review. Journal of clinical medicine. 2022 Sep 28; 11(19):5736. DOI: https://doi.org/10.3390/jcm11195736

2) Karkia R, Giacchino T, Shah S, Gough A, Ramadan G, Akolekar R. Gestational diabetes mellitus: association with maternal and neonatal complications. Medicina. 2023 Nov 29; 59(12):2096. DOI: https://doi.org/10.3390/medicina59122096

3) Guo L, Ma J, Tang J, Hu D, Zhang W, Zhao X. Comparative efficacy and safety of metformin, glyburide, and insulin in treating gestational diabetes mellitus: a meta-analysis. Journal of diabetes research. 2019; 2019(1):9804708. DOI: https://doi.org/10.1155/2019/9804708

4) Saeedi M, Cao Y, Fadl H, Gustafson H, Simmons D. Increasing prevalence of gestational diabetes mellitus when implementing the IADPSG criteria: A systematic review and meta-analysis. Diabetes Research and Clinical Practice. 2021 Feb 1; 172:108642. DOI: https://doi.org/10.1016/j.diabres.2020.108642

ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 69 Issue 06 | 2026
DOI: 10.5281/zenodo.20792416

5) Malaza N, Masete M, Adam S, Dias S, Nyawo T, Pheiffer C. A systematic review to compare adverse pregnancy outcomes in women with pregestational diabetes and gestational diabetes. International journal of environmental research and public health. 2022 Aug 31; 19(17):10846. DOI: https://doi.org/10.3390/ijerph191710846

6) Diaz-Santana MV, O'Brien KM, Park YM, Sandler DP, Weinberg CR. Persistence of risk for type 2 diabetes after gestational diabetes mellitus. Diabetes Care. 2022 Apr 1; 45(4):864-70. DOI: https://doi.org/10.2337/dc21-1430

7) Le DC, Vu TB, Tran TN, Nguyen TL, Nguyen TB, Nguyen DC, Hoang VT. The effectiveness of lifestyle changes in glycemic control among pregnant women with gestational diabetes mellitus. Medicina. 2023 Sep 1; 59(9):1587. DOI: https://doi.org/10.3390/medicina59091587

8) 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 & Metabolism. 2025 Mar 1; 51(2):101622. DOI: https://doi.org/10.1016/j.diabet.2025.101622

9) Judder MI, Islam M, Kaur H, Rahman R, Deka K, Kapil MJ, Pathak BJ, Sarma T, Islam MM. Therapeutic Trends in Diabetes Management: A Review on Oral Hypoglycemic Agents (OHAs) Utilization in Tertiary Care. Cardiovascular & Hematological Disorders-Drug Targets. 2025. DOI: https://doi.org/10.2174/011871529X414055250924050309

10) Szymczak-Pajor I, Wenclewska S, Śliwińska A. Metabolic action of metformin. Pharmaceuticals. 2022 Jun 30; 15(7):810. DOI: https://doi.org/10.3390/ph15070810

11) Paschou SA, Shalit A, Gerontiti E, Athanasiadou KI, Kalampokas T, Psaltopoulou T, Lambrinoudaki I, Anastasiou E, Wolffenbuttel BH, Goulis DG. Efficacy and safety of metformin during pregnancy: an update. Endocrine. 2024 Feb; 83(2):259-69. DOI: https://doi.org/10.1007/s12020-023-03550-0

12) Boggess KA, Valint A, Refuerzo JS, Zork N, Battarbee AN, Eichelberger K, Ramos GA, Olson G, Durnwald C, Landon MB, Aagaard KM. Metformin plus insulin for preexisting diabetes or gestational diabetes in early pregnancy: the MOMPOD randomized clinical trial. Jama. 2023 Dec 12; 330(22):2182-90. DOI: https://doi.org/10.1001/jama.2023.22949

13) Picón-César MJ, Molina-Vega M, Suárez-Arana M, González-Mesa E, Sola-Moyano AP, Roldan-López R, Romero-Narbona F, Olveira G, Tinahones FJ, González-Romero S. Metformin for gestational diabetes study: metformin vs insulin in gestational diabetes: glycemic control and obstetrical and perinatal outcomes: randomized prospective trial. American journal of obstetrics and gynecology. 2021 Nov 1; 225(5):517-e1. DOI: https://doi.org/10.1016/j.ajog.2021.04.229

14) Javed N, Azra S, Ara Y, Masoom K. Metformin vs insulin in the management of gestational diabetes; a randomized controlled trial. Journal of the Society of Obstetricians and Gynaecologists of Pakistan. 2023 Apr 5; 13(1):5-8. Available at: https://www.jsogp.net/index.php/jsogp/article/view/592

15) He K, Guo Q, Ge J, Li J, Li C, Jing Z. The efficacy and safety of metformin alone or as an add-on therapy to insulin in pregnancy with GDM or T2DM: a systematic review and meta-analysis of 21 randomized controlled trials. Journal of Clinical Pharmacy and Therapeutics. 2022 Feb; 47(2):168-77. DOI: https://doi.org/10.1111/jcpt.13503

16) Dunne F, Newman C, Alvarez-Iglesias A, Ferguson J, Smyth A, Browne M, O'Shea P, Devane D, Gillespie P, Bogdanet D, Kgosidialwa O. Early metformin in gestational diabetes: a randomized clinical trial. Jama. 2023 Oct 24; 330(16):1547-56. DOI: 10.1001/jama.2023.19869

17) 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 Feb 11; 333(6):470-478. DOI: https://doi.org/10.1001/jama.2024.23410

ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 69 Issue 06 | 2026
DOI: 10.5281/zenodo.20792416

18) Wu R, Zhang Q, Li Z. A meta-analysis of metformin and insulin on maternal outcome and neonatal outcome in patients with gestational diabetes mellitus. The Journal of Maternal-Fetal & Neonatal Medicine. 2024 Jan 2; 37(1):2295809. DOI: 10.1080/14767058.2023.2295809

19) Berti GN, Garcia IG, Toledo JP, Tatemoto JR, Marino LW, Legori MD, Toledo SF. Metformin versus insulin in gestational diabetes mellitus: a systematic review. Revista Brasileira de Ginecologia e Obstetrícia. 2024; 46: e-rbgo89. DOI: 10.61622/rbgo/2024rbgo89

20) Venkatesh KK, Wu J, Trinh A, Cross S, Rice D, Powe CE, Brindle S, Andreatta S, Bartholomew A, MacPherson C, Costantine MM. Patient priorities, decisional comfort, and satisfaction with metformin versus insulin for the treatment of gestational diabetes mellitus. American journal of perinatology. 2024 May; 41(S 01):e3170-82. DOI: 10.1055/s-0043-1777334

21) Tarry-Adkins JL, Ozanne SE, Aiken CE. Impact of metformin treatment during pregnancy on maternal outcomes: a systematic review and meta-analysis. Sci Rep. 2021; 11: 9240. DOI: https://doi.org/10.1038/s41598-021-88650-5

22) Abbasi M, Heath B, McGinness L. Advances in metformin-delivery systems for diabetes and obesity management. Diabetes, Obesity and Metabolism. 2024 Sep; 26(9):3513-29. DOI: https://doi.org/10.1111/dom.15759