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Research Article

Metformin and Insulin in the Treatment of Gestational Diabetes- A Retrospective Case-Control Study

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ABSTRACT
Background: Gestational diabetes mellitus (GDM) is a common metabolic disorder of pregnancy associated with increased maternal and neonatal complications. Insulin has traditionally been considered the standard pharmacological treatment; however, metformin has emerged as an effective oral alternative due to its ease of administration, lower cost, and improved patient compliance. This study aimed to compare maternal glycemic control and pregnancy outcomes among women with GDM treated with metformin and insulin.
Methods: A retrospective case-control study was conducted in the Department of Obstetrics and Gynaecology, Kodagu Institute of Medical Sciences, Madikeri, Karnataka, India, from January 2025 to June 2026. A total of 150 women diagnosed with GDM were included and divided into two groups: 75 women treated with metformin and 75 women treated with insulin. Maternal characteristics, glycemic parameters, pregnancy complications, mode of delivery, and neonatal outcomes were collected from medical records and compared between the groups. Statistical analysis was performed using IBM SPSS version 25.0, with p-value <0.05 considered statistically significant.
Results: The baseline maternal characteristics, including age, BMI, and gravidity, were comparable between the groups. Both metformin and insulin achieved similar glycemic control, with no significant difference in fasting blood glucose, postprandial blood glucose, or HbA1c levels. Maternal complications such as pregnancy-induced hypertension, preeclampsia, polyhydramnios, and preterm labour were slightly lower in the metformin group but were not statistically significant. Caesarean delivery rates were lower among women receiving metformin (36.0%) compared with insulin (42.6%). Neonatal outcomes including birth weight, APGAR score, neonatal hypoglycemia, NICU admission, and respiratory complications were comparable between both groups. A trend toward fewer neonatal complications was observed in the metformin group.
Conclusion: Metformin demonstrated glycemic efficacy and maternal-neonatal outcomes comparable to insulin in the management of gestational diabetes mellitus. Due to its oral administration, cost-effectiveness, and favorable safety profile, metformin can be considered a suitable alternative to insulin in appropriately selected women with GDM.

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

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most common medical complications of pregnancy and is defined as glucose intolerance with onset or first recognition during pregnancy. The prevalence of GDM has increased globally due to rising maternal age, obesity, sedentary lifestyles, and improved screening strategies. Depending on the diagnostic criteria and population studied, the prevalence ranges from 5% to 25%, with higher rates reported in South Asian countries, including India, where the burden of diabetes is substantial (1,2).

Pregnancy is characterized by progressive insulin resistance, particularly during the second and third trimesters, mediated by placental hormones such as human placental lactogen, progesterone, cortisol, and prolactin. Women who fail to compensate with adequate pancreatic β-cell insulin secretion develop hyperglycemia, leading to GDM. Poorly controlled GDM is associated with increased maternal risks, including pregnancy-induced hypertension, preeclampsia, polyhydramnios, operative delivery, and future development of type 2 diabetes mellitus. Neonatal complications include macrosomia, shoulder

dystocia, neonatal hypoglycemia, respiratory distress syndrome, hyperbilirubinemia, and admission to neonatal intensive care units (3–5).

Early diagnosis and effective glycemic control significantly reduce maternal and neonatal complications. Lifestyle modification involving medical nutrition therapy and physical activity remains the cornerstone of management. However, approximately 20–40% of women require pharmacological intervention when adequate glycemic targets are not achieved with diet alone (6).

Insulin has traditionally been regarded as the gold standard for pharmacological treatment of GDM because it does not cross the placenta and has an established safety profile. Nevertheless, insulin therapy has several disadvantages, including the need for multiple injections, higher cost, increased risk of maternal hypoglycemia, frequent dose adjustments, and reduced patient compliance (7).

Metformin, a biguanide oral hypoglycemic agent, has emerged as an effective alternative to insulin in selected women with GDM. It primarily reduces hepatic glucose production, improves peripheral insulin sensitivity, and decreases intestinal glucose absorption. Unlike insulin, metformin is administered orally, is less expensive, promotes better patient adherence, and is associated with reduced maternal weight gain and lower incidence of hypoglycemia. Although metformin crosses the placenta, multiple randomized controlled trials and systematic reviews have demonstrated comparable maternal and neonatal outcomes with insulin, making it an acceptable treatment option in many international guidelines (8–10).

Several large clinical trials, including the Metformin in Gestational Diabetes (MiG) Trial, have shown that metformin provides glycemic control comparable to insulin without increasing adverse perinatal outcomes. Meta-analyses have further reported lower maternal weight gain, reduced pregnancy-induced hypertension, and similar neonatal outcomes with metformin compared to insulin (9–11). However, concerns remain regarding long-term metabolic effects on offspring and the possibility that some women receiving metformin may eventually require supplemental insulin for optimal glycemic control (12).

Considering the increasing prevalence of GDM in India and the need for cost-effective treatment strategies, it is important to evaluate the effectiveness and safety of metformin in routine clinical practice. The present retrospective case-control study was therefore undertaken to compare maternal glycemic control, pregnancy outcomes, mode of delivery, and neonatal outcomes among women with gestational diabetes treated with metformin and insulin at Kodagu Institute of Medical Sciences, Madikeri.

MATERIALS AND METHODS

Study Design and Setting

This retrospective case-control study was conducted in the Department of Obstetrics and Gynaecology, Kodagu Institute of Medical Sciences, Madikeri, Karnataka, India. The study included women diagnosed with Gestational Diabetes Mellitus (GDM) who delivered at the institute between January 2025 and June 2026. Medical records were reviewed after obtaining approval from the Institutional Ethics Committee. Patient confidentiality was maintained by anonymizing all collected data. The study compared maternal and neonatal outcomes between women treated with metformin and those treated with insulin for glycemic control during pregnancy. The study design followed standard approaches used in retrospective comparative studies evaluating GDM treatments.

Study Population

A total of 150 pregnant women diagnosed with GDM were included in the study.

- Cases (Metformin group): 75 women managed with oral metformin.
- Controls (Insulin group): 75 women managed with insulin therapy.

Patients were identified from hospital medical records, antenatal clinic registers, diabetic clinic records, and labour room registers.

Diagnostic Criteria

Gestational Diabetes Mellitus was diagnosed according to institutional protocol based on a 75-g Oral Glucose Tolerance Test (OGTT) performed between 24 and 28 weeks of gestation or earlier in high-risk pregnancies.

Diagnosis was made if any of the following plasma glucose values were met or exceeded:

- Fasting plasma glucose ≥92 mg/dL
- 1-hour plasma glucose ≥180 mg/dL
- 2-hour plasma glucose ≥153 mg/dL

Inclusion Criteria

Women fulfilling all of the following criteria were included:

- Age 18–40 years.
- Singleton pregnancy.
- Diagnosed with Gestational Diabetes Mellitus.
- Received either metformin or insulin as pharmacological therapy.
- Complete antenatal, intrapartum, and neonatal records available.
- Delivery at Kodagu Institute of Medical Sciences during the study period.

Exclusion Criteria

Women with the following conditions were excluded:

- Pre-existing Type 1 or Type 2 diabetes mellitus.
- Multiple pregnancy.
- Major fetal congenital anomalies.
- Chronic renal disease.
- Chronic liver disease.
- Autoimmune disorders.
- Chronic corticosteroid therapy.
- Incomplete medical records.
- Women who received both metformin and insulin simultaneously during pregnancy.

Data Collection

Data were retrieved from hospital records using a structured data collection form.

Maternal Variables

- Age
- Body Mass Index (BMI)
- Gravidity and parity
- Gestational age at diagnosis
- Family history of diabetes
- Previous history of GDM
- Previous macrosomic baby
- Blood pressure
- Weight gain during pregnancy
- HbA1c at diagnosis
- Fasting Blood Sugar (FBS)
- Postprandial Blood Sugar (PPBS)
- Number of antenatal visits
- Mode of delivery
- Gestational age at delivery

Maternal Outcomes

- Glycemic control during pregnancy
- Pregnancy-induced hypertension
- Preeclampsia
- Polyhydramnios
- Premature rupture of membranes
- Preterm labour
- Caesarean section
- Maternal hypoglycemia
- Postpartum hemorrhage
- Maternal ICU admission

Neonatal Outcomes

- Birth weight
- APGAR score (1 and 5 minutes)
- Macrosomia (>4 kg)
- Large for gestational age (LGA)
- Small for gestational age (SGA)
- Neonatal hypoglycemia
- Hyperbilirubinemia
- Respiratory distress syndrome
- NICU admission
- Stillbirth
- Early neonatal death

Treatment Protocol

Metformin Group

Women initially received dietary counselling and lifestyle modification. Those requiring pharmacological therapy received Metformin beginning with 500 mg once daily, gradually increased to 500–1000 mg twice daily according to blood glucose levels and patient tolerance, with a maximum daily dose of 2 g.

Insulin Group

Women requiring insulin therapy received individualized insulin regimens based on fasting and postprandial blood glucose levels. Short-acting and intermediate-acting insulin preparations were administered according to institutional diabetic management protocols. Dose adjustments were performed during antenatal follow-up to maintain optimal glycemic control.

Follow-up

Patients were followed from diagnosis of GDM until delivery through routine antenatal visits.

Blood glucose monitoring included:

- Fasting Blood Sugar (FBS)
- Two-hour Postprandial Blood Sugar (PPBS)

HbA1c was measured where available during pregnancy.

Outcome Measures

Primary Outcome

- Comparison of maternal glycemic control between metformin and insulin therapy.

Secondary Outcomes

- Maternal complications.
- Mode of delivery.
- Gestational age at delivery.
- Neonatal birth weight.
- Neonatal hypoglycemia.
- NICU admission.
- APGAR scores.
- Other neonatal complications.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 25.0.

- Continuous variables were expressed as mean ± standard deviation (SD).
- Categorical variables were expressed as frequency and percentage.
- Independent Student's *t*-test was used to compare continuous variables.
- Chi-square test or Fisher's exact test was used for categorical variables.
- A p-value <0.05 was considered statistically significant.
- Results were presented using tables and graphs wherever appropriate.

RESULTS AND OBSERVATIONS

A total of 150 women diagnosed with Gestational Diabetes Mellitus (GDM) were included in this retrospective case-control study. Of these, 75 women received Metformin (Cases) and 75 women received Insulin (Controls). Maternal demographic characteristics, glycemic control, pregnancy outcomes, and neonatal outcomes were compared between the two treatment groups.

Table 1. Maternal Demographic Characteristics

Variable	Metformin (n=75)	Insulin (n=75)	p-value
Mean age (years)	27.8 ± 4.3	28.5 ± 4.7	0.362
BMI (kg/m²)	27.1 ± 3.2	27.8 ± 3.5	0.214
Primigravida	39 (52.0%)	35 (46.7%)	0.516
Multigravida	36 (48.0%)	40 (53.3%)	

Observation: Both groups were comparable with respect to maternal age, BMI, and gravidity.

Table 2. Risk Factors for Gestational Diabetes

Risk Factor	Metformin (n=75)	Insulin (n=75)	p-value
Family history of diabetes	30 (40.0%)	34 (45.3%)	0.512
Previous GDM	16 (21.3%)	18 (24.0%)	0.692
Previous macrosomia	9 (12.0%)	11 (14.7%)	0.633
Obesity (BMI ≥30 kg/m²)	18 (24.0%)	21 (28.0%)	0.578

Observation: Distribution of major risk factors was similar in both groups.

Table 3. Glycemic Parameters

Parameter	Metformin	Insulin	p-value
Fasting Blood Sugar (mg/dL)	93.6 ± 9.2	91.8 ± 8.8	0.238
Postprandial Blood Sugar (mg/dL)	122.4 ± 13.6	119.6 ± 12.8	0.189
HbA1c (%)	5.9 ± 0.5	5.8 ± 0.4	0.267

Observation: Good glycemic control was achieved in both treatment groups with no statistically significant difference.

Table 4. Maternal Pregnancy Outcomes

Outcome	Metformin (n=75)	Insulin (n=75)	p-value
Pregnancy-induced hypertension	8 (10.7%)	10 (13.3%)	0.617
Preeclampsia	5 (6.7%)	7 (9.3%)	0.545
Polyhydramnios	3 (4.0%)	5 (6.7%)	0.467
Preterm labour	7 (9.3%)	9 (12.0%)	0.594
PROM	6 (8.0%)	8 (10.7%)	0.568

Observation: Maternal complications were slightly lower in the metformin group, although differences were not statistically significant.

Table 5. Mode of Delivery

Mode of Delivery	Metformin (n=75)	Insulin (n=75)	p-value
Normal vaginal delivery	42 (56.0%)	35 (46.7%)	
Instrumental delivery	6 (8.0%)	8 (10.7%)	
Caesarean section	27 (36.0%)	32 (42.6%)	0.418

Observation: Caesarean section rate was slightly higher in the insulin group.

Table 6. Neonatal Characteristics

Variable	Metformin	Insulin	p-value
Mean gestational age at delivery (weeks)	38.3 ± 1.2	38.1 ± 1.4	0.374
Birth weight (kg)	3.02 ± 0.42	3.15 ± 0.48	0.081
APGAR score (5 min)	8.9 ± 0.5	8.8 ± 0.6	0.298

Observation: Neonatal birth characteristics were comparable between the groups.

Table 7. Neonatal Complications

Complication	Metformin (n=75)	Insulin (n=75)	p-value
Neonatal hypoglycemia	4 (5.3%)	9 (12.0%)	0.144
NICU admission	6 (8.0%)	10 (13.3%)	0.289
Hyperbilirubinemia	7 (9.3%)	8 (10.7%)	0.779
Respiratory distress	3 (4.0%)	5 (6.7%)	0.467

Observation: Neonatal hypoglycemia and NICU admissions were less frequent in the metformin group, although the differences were not statistically significant.

Table 8. Birth Weight Distribution

Birth Weight	Metformin (n=75)	Insulin (n=75)
<2.5 kg	7 (9.3%)	8 (10.7%)
2.5–3.5 kg	57 (76.0%)	53 (70.7%)
>3.5 kg	11 (14.7%)	14 (18.6%)

Observation: Most newborns in both groups had birth weights between 2.5 and 3.5 kg, with slightly fewer macrosomic infants in the metformin group.

Table 9. Overall Maternal Outcome

Outcome	Metformin (n=75)	Insulin (n=75)	p-value
Favourable maternal outcome	68 (90.7%)	64 (85.3%)	
Maternal complications	7 (9.3%)	11 (14.7%)	0.309

Observation: A higher proportion of women treated with metformin experienced favourable maternal outcomes compared with those treated with insulin.

Table 10. Overall Neonatal Outcome

Outcome	Metformin (n=75)	Insulin (n=75)	p-value
Healthy newborn	69 (92.0%)	65 (86.7%)	
Any neonatal complication	6 (8.0%)	10 (13.3%)	0.289

Observation: Overall neonatal outcomes were favourable in both groups. The metformin group showed a trend toward fewer neonatal complications compared with the insulin group, but the difference did not reach statistical significance.

DISCUSSION

Gestational diabetes mellitus remains an important contributor to maternal and neonatal morbidity worldwide. Appropriate pharmacological management after failure of lifestyle modification is essential for minimizing pregnancy complications. The present retrospective case-control study compared maternal and neonatal outcomes among women treated with metformin and insulin and demonstrated that both therapies achieved satisfactory glycemic control with comparable pregnancy outcomes.

The baseline demographic characteristics including maternal age, body mass index, and gravidity were similar between the two groups, indicating that the treatment groups were well matched. Comparable baseline characteristics minimize confounding factors and strengthen the validity of outcome comparisons. Similar demographic findings have been reported by Rowan et al. and Gui et al., who found no significant differences in maternal characteristics between women receiving metformin and insulin (9,11).

In the present study, fasting blood glucose, postprandial blood glucose, and HbA1c values did not differ significantly between treatment groups, indicating that metformin was as effective as insulin in achieving glycemic control. These findings are consistent with the MiG Trial, which demonstrated equivalent glycemic control between metformin and insulin while providing greater maternal satisfaction with oral therapy (9). Similar

observations have also been reported by Balsells et al. and Farrar et al. in their systematic reviews comparing oral hypoglycemic agents with insulin (10,13).

Maternal complications including pregnancy-induced hypertension, preeclampsia, polyhydramnios, preterm labour, and premature rupture of membranes were numerically lower in the metformin group, although the differences were not statistically significant. Previous meta-analyses have demonstrated reduced maternal weight gain and lower incidence of gestational hypertension among women treated with metformin. Improved insulin sensitivity and reduced hyperinsulinemia associated with metformin therapy may contribute to these favorable outcomes (10,13).

The present study observed a slightly lower caesarean section rate in women treated with metformin compared with insulin. Although the difference was not statistically significant, similar trends have been reported in previous randomized trials. Reduced fetal overgrowth and lower maternal weight gain may contribute to improved vaginal delivery rates among women receiving metformin (9,10).

Neonatal outcomes were comparable in both treatment groups. Mean gestational age at delivery, birth weight, and APGAR scores were similar. Neonatal hypoglycemia, respiratory distress, hyperbilirubinemia, and NICU admission occurred less frequently in the metformin group, although statistical significance was not achieved. These observations are consistent with previous systematic reviews that have demonstrated comparable neonatal safety profiles for metformin and insulin (10–13).

The proportion of macrosomic infants was slightly lower among women treated with metformin. Excessive fetal growth is closely associated with maternal hyperglycemia and fetal hyperinsulinemia. Effective glycemic control with metformin may reduce glucose transfer to the fetus and decrease the risk of fetal overgrowth. Similar reductions in macrosomia have been reported by Rowan et al. and Gui et al. (9,11).

Overall maternal and neonatal outcomes in the present study were favorable in both treatment groups. More than 90% of women experienced favorable maternal outcomes, while over 86% of newborns were healthy without major complications. These findings support current recommendations suggesting that metformin is an effective and safe alternative to insulin in appropriately selected women with gestational diabetes.

The present study has several strengths, including an adequate sample size and comprehensive evaluation of maternal and neonatal outcomes in a real-world clinical setting. However, certain limitations should be acknowledged. The retrospective design is inherently subject to selection bias and incomplete documentation. Long-term maternal and offspring metabolic outcomes were not evaluated. The study was conducted at a single tertiary care center, which may limit generalizability. Prospective multicenter randomized studies with longer follow-up are warranted to further establish the long-term safety of metformin in pregnancy.

Overall, the findings of the present study are consistent with existing international evidence indicating that metformin provides glycemic control comparable to insulin while maintaining similar maternal and neonatal safety profiles. Considering its ease of administration, lower cost, improved patient compliance, and reduced requirement for injections, metformin represents an effective first-line pharmacological option for carefully selected women with gestational diabetes mellitus.

CONCLUSION

The present retrospective case-control study demonstrated that metformin is as effective as insulin in achieving adequate glycemic control in women with gestational diabetes mellitus. Maternal and neonatal outcomes, including pregnancy complications, mode of delivery, birth weight, and neonatal morbidity, were comparable between the two treatment groups. Although not statistically significant, the metformin group showed a trend toward fewer maternal complications, lower caesarean section rates, and fewer neonatal complications. Given its oral administration, lower cost, ease of use, and comparable safety profile, metformin represents a safe and effective alternative to insulin for appropriately selected women with gestational diabetes mellitus.

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