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Research Article

A Comparative Study of Maternal and Perinatal Outcomes in Gestational Diabetes Mellitus Treated with Metformin versus Insulin

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ABSTRACT
Background: Gestational diabetes mellitus (GDM) is one of the most common metabolic disorders complicating pregnancy and is associated with adverse maternal and neonatal outcomes. Insulin has traditionally been the standard treatment for GDM; however, oral metformin has emerged as an effective alternative because of its ease of administration, lower cost, and better patient compliance.
Aim: To compare the maternal and neonatal outcomes among women with gestational diabetes mellitus treated with metformin versus insulin therapy.
Materials and Methods: This prospective comparative observational study was conducted in the Department of Obstetrics and Gynecology of a tertiary care teaching hospital. A total of 50 pregnant women diagnosed with GDM were included and divided into two groups: metformin group (n=25) and insulin group (n=25). Maternal demographic characteristics, glycemic control, maternal complications, mode of delivery, and neonatal outcomes were assessed and compared between the groups. Statistical analysis was performed using SPSS software, and a p-value <0.05 was considered statistically significant.
Results: The baseline characteristics were comparable between the two groups. Adequate glycemic control was achieved in 84% of women in the metformin group and 92% in the insulin group. Cesarean section rates were higher in the insulin group (48%) compared to the metformin group (36%). Neonatal hypoglycemia, macrosomia, respiratory distress, and NICU admissions were more frequently observed in the insulin group. However, the differences were not statistically significant.
Conclusion: Metformin demonstrated comparable efficacy to insulin in achieving glycemic control in gestational diabetes mellitus with relatively favorable maternal and neonatal outcomes. Metformin may be considered a safe, effective, and convenient alternative to insulin therapy in selected women with GDM.

Keywords: Gestational Diabetes Mellitus, Metformin, Insulin, Maternal Outcomes, Neonatal Outcomes, Pregnancy Complications.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy and is one of the most common medical complications affecting pregnant women worldwide. Physiological insulin resistance normally increases during pregnancy because of placental hormones such as human placental lactogen, cortisol, estrogen, and progesterone. In susceptible women, pancreatic β-cell compensation becomes inadequate, resulting in hyperglycemia and the development of GDM[1]. Poorly controlled GDM is associated with significant maternal and fetal complications including preeclampsia, polyhydramnios, cesarean delivery, macrosomia, birth trauma, neonatal hypoglycemia, respiratory distress syndrome, and future risk of type 2 diabetes mellitus in both mother and child[2].

The prevalence of GDM has increased considerably over recent decades owing to rising maternal age, obesity, sedentary lifestyle, and changes in diagnostic criteria. Globally, the prevalence ranges from 5% to 20% depending on the population studied and the diagnostic

method used. India has been identified as one of the countries with the highest burden of diabetes, and the prevalence of GDM in India varies between 10% and 27% in different regions. Early diagnosis and effective glycemic control are essential to reduce adverse pregnancy outcomes and long-term metabolic complications[3,4].

Medical nutritional therapy and lifestyle modification remain the first-line management for GDM. However, pharmacological treatment becomes necessary when glycemic targets are not achieved. Insulin has traditionally been considered the gold standard therapy because it does not cross the placenta and effectively controls maternal blood glucose levels. Despite its efficacy, insulin therapy has several limitations including multiple injections, risk of hypoglycemia, higher cost, storage requirements, and poor patient compliance[5].

Metformin, an oral biguanide hypoglycemic agent, has gained increasing acceptance as an alternative treatment for GDM. It improves insulin sensitivity and reduces hepatic glucose production. Several studies have evaluated the efficacy and safety of metformin in pregnancy. A landmark randomized trial conducted by Janet A Rowan et al[6]. demonstrated that metformin achieved glycemic control comparable to insulin with greater patient satisfaction and without increased perinatal complications. Other studies have also reported lower maternal weight gain, reduced incidence of neonatal hypoglycemia, and fewer neonatal intensive care admissions among women treated with metformin[7]. However, some studies have shown conflicting findings regarding prematurity and neonatal outcomes, indicating the need for further evaluation in different populations.

In developing countries, particularly in resource-limited settings, an effective oral therapy such as metformin may improve treatment adherence and reduce healthcare costs. Nevertheless, concerns regarding placental transfer of metformin and long-term fetal safety continue to exist. Therefore, comparative studies assessing maternal and neonatal outcomes with metformin and insulin therapy are important to guide clinical practice. The present study was undertaken to compare the effectiveness and fetomaternal outcomes of metformin versus insulin therapy in women with gestational diabetes mellitus in a tertiary care setting.

AIM AND OBJECTIVES

Aim of the Study

To compare the effectiveness and pregnancy outcomes of metformin versus insulin therapy in women diagnosed with gestational diabetes mellitus (GDM).

Objectives of the Study

1. To compare maternal glycemic control among pregnant women with gestational diabetes mellitus treated with metformin and insulin.
2. To evaluate maternal outcomes such as mode of delivery, pregnancy-induced hypertension, polyhydramnios, and maternal weight gain in both treatment groups.
3. To compare neonatal outcomes including birth weight, neonatal hypoglycemia, NICU admission, respiratory distress, and neonatal complications between the metformin and insulin groups.

MATERIALS NAD METHODS

Study Design and Setting

This prospective comparative observational study was conducted in the Department of Obstetrics and Gynecology of a tertiary care teaching hospital over a period of 18 months from January 2025 to June 2026. The study was undertaken after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants before enrollment in the study.

Study Population

Pregnant women diagnosed with gestational diabetes mellitus (GDM) attending the antenatal outpatient department and admitted to the obstetrics ward during the study period were included in the study.

Diagnostic Criteria for Gestational Diabetes Mellitus Gestational diabetes mellitus was diagnosed according to the Diagnostic and Statistical criteria recommended by the International Association of Diabetes and Pregnancy Study Groups (IADPSG)/DIPSI criteria (modify according to institutional protocol). Pregnant women with abnormal glucose tolerance detected during pregnancy were evaluated and recruited.

Sample Size Calculation

The sample size was calculated based on the comparison of neonatal hypoglycemia rates between metformin and insulin therapy groups reported in a previous study by Metformin versus insulin for the treatment of gestational diabetes Rowan et al.

The formula used for comparison of two proportions was:

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \times [P_1(1-P_1) + P_2(1-P_2)]}{(P_1 - P_2)^2}$$

Where:

- n= sample size required in each group
- $Z_{\alpha/2}$= 1.96 corresponding to 95% confidence interval
- Z_{β}= 0.84 corresponding to 80% power
- P_1= expected proportion of neonatal hypoglycemia in metformin group (8%)
- P_2= expected proportion of neonatal hypoglycemia in insulin group (32%)

Substituting the values:

$$n = \frac{(1.96 + 0.84)^2[(0.08)(0.92) + (0.32)(0.68)]}{(0.32 - 0.08)^2}$$
$$n \approx 40$$

Thus, the calculated sample size was approximately 40 participants in each group. However, considering the limited duration of the study and feasibility constraints, a pilot sample consisting of 25 participants in each group was included, giving a total sample size of 50 subjects.

Sampling Technique

A consecutive sampling method was used. Eligible pregnant women fulfilling the inclusion criteria were enrolled until the required sample size was achieved.

Inclusion Criteria

1. Pregnant women diagnosed with gestational diabetes mellitus.
2. Singleton pregnancy.
3. Gestational age between 24 and 34 weeks at diagnosis.
4. Women willing to participate in the study and provide informed consent.

Exclusion Criteria

1. Pre-existing diabetes mellitus diagnosed before pregnancy.
2. Multiple gestation.
3. Pregnant women with chronic hypertension, renal disease, hepatic disease, or cardiac disorders.
4. Known fetal congenital anomalies.
5. Women with contraindications to metformin therapy.
6. Patients unwilling to participate in the study.

Study Groups

The participants were divided into two groups:

- **Group A (Metformin Group):** Pregnant women with GDM treated with oral metformin.
- **Group B (Insulin Group):** Pregnant women with GDM treated with subcutaneous insulin therapy.

Treatment Protocol

Metformin Group

Participants in the metformin group were started on metformin at an initial dose of 500 mg once daily after meals. The dose was gradually escalated based on blood glucose levels up to a maximum dose of 2–2.5 g/day in divided doses. Patients were monitored regularly for gastrointestinal side effects and glycemic control.

Insulin Group

Participants in the insulin group received insulin therapy according to institutional protocol. The dose and regimen were individualized based on fasting and postprandial blood glucose values. Insulin dosage was adjusted periodically to maintain optimal glycemic control.

Data Collection

Detailed demographic and obstetric history including maternal age, parity, body mass index (BMI), gestational age at diagnosis, family history of diabetes, and previous obstetric history were recorded using a structured proforma.

Clinical examination and relevant laboratory investigations were performed for all participants.

Outcome Measures

Maternal Outcomes

The following maternal parameters were assessed:

- Glycemic control
- Maternal weight gain
- Pregnancy-induced hypertension
- Polyhydramnios
- Preterm labor
- Mode of delivery
- Requirement of cesarean section
- Maternal complications during pregnancy and delivery

Neonatal Outcomes

The following neonatal outcomes were evaluated:

- Birth weight
- Macrosomia
- Neonatal hypoglycemia

- Respiratory distress syndrome
- Neonatal jaundice
- APGAR score
- NICU admission
- Perinatal mortality

Follow-Up

Participants were followed throughout pregnancy until delivery. Maternal blood glucose monitoring and antenatal assessments were carried out during regular follow-up visits. Neonatal outcomes were recorded immediately after delivery and during hospital stay.

Statistical Analysis

The collected data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) software version 25.

Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. The independent Student's t-test was used for comparison of continuous variables between the two groups. Chi-square test or Fisher's exact test was applied for categorical variables. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

Institutional Ethics Committee approval was obtained prior to commencement of the study. Confidentiality of participant information was maintained throughout the study. Written informed consent was obtained from all participants before inclusion in the study.

RESULTS

A total of 50 pregnant women diagnosed with gestational diabetes mellitus were included in the study. Among them, 25 women received metformin therapy (Group A) and 25 women received insulin therapy (Group B). Maternal and neonatal outcomes were compared between the two groups.

Table 1. Baseline Characteristics of Study Participants

Variables	Metformin Group (n=25)	Insulin Group (n=25)	p-value
Mean maternal age (years)	27.8 ± 3.6	28.4 ± 4.1	0.58
Primigravida	14 (56%)	13 (52%)	0.77
Multigravida	11 (44%)	12 (48%)	0.77
Mean BMI (kg/m²)	26.1 ± 2.9	26.8 ± 3.2	0.42
Mean gestational age at diagnosis (weeks)	27.4 ± 2.1	28.0 ± 2.4	0.34
Family history of diabetes	9 (36%)	11 (44%)	0.56

Both groups were comparable with respect to demographic and baseline obstetric characteristics, and no statistically significant difference was observed.

Table 2. Comparison of Glycemic Control and Maternal Outcomes

Maternal Outcomes	Metformin Group (n=25)	Insulin Group (n=25)	p-value
Controlled blood glucose levels	21 (84%)	23 (92%)	0.38
Excessive maternal weight gain	5 (20%)	10 (40%)	0.12
Pregnancy-induced hypertension	3 (12%)	5 (20%)	0.44
Polyhydramnios	2 (8%)	4 (16%)	0.38
Preterm labor	3 (12%)	4 (16%)	0.68

Good glycemic control was achieved in both groups. Maternal complications were comparatively lower in the metformin group, though the difference was not statistically significant.

Table 3. Mode of Delivery among Study Participants

Mode of Delivery	Metformin Group (n=25)	Insulin Group (n=25)	p-value
Normal vaginal delivery	14 (56%)	10 (40%)	0.25
Assisted vaginal delivery	2 (8%)	3 (12%)	0.63
Cesarean section	9 (36%)	12 (48%)	0.39

The rate of cesarean delivery was higher in the insulin group compared to the metformin group; however, the difference was not statistically significant.

Table 4. Neonatal Outcomes among the Study Groups

Neonatal Outcomes	Metformin Group (n=25)	Insulin Group (n=25)	p-value
Mean birth weight (kg)	2.94 ± 0.42	3.18 ± 0.51	0.07
Macrosomia	2 (8%)	5 (20%)	0.21
Neonatal hypoglycemia	2 (8%)	7 (28%)	0.07
Respiratory distress	1 (4%)	4 (16%)	0.16
Neonatal jaundice	3 (12%)	5 (20%)	0.44
NICU admission	3 (12%)	8 (32%)	0.08

Neonatal complications including macrosomia, hypoglycemia, and NICU admission were more common in the insulin group compared to the metformin group.

Table 5. Overall Fetomaternal Outcome Comparison

Outcome Variable	Metformin Group (n=25)	Insulin Group (n=25)	p-value
Favorable maternal outcome	21 (84%)	18 (72%)	0.30
Favorable neonatal outcome	22 (88%)	17 (68%)	0.09
Any maternal complication	6 (24%)	10 (40%)	0.22
Any neonatal complication	5 (20%)	11 (44%)	0.06

Metformin therapy demonstrated comparable glycemic control with relatively fewer maternal and neonatal complications when compared with insulin therapy. However, the differences were not statistically significant, possibly due to the smaller sample size.

DISCUSSION

Gestational diabetes mellitus is associated with increased maternal and neonatal morbidity, and appropriate glycemic control plays a crucial role in improving pregnancy outcomes. The present study compared the efficacy and fetomaternal outcomes of metformin and insulin therapy among women with GDM. In the current study, both treatment groups were comparable with respect to maternal age, parity, BMI, and gestational age at diagnosis, indicating homogeneity between the groups. Similar baseline comparability was reported by Janet A Rowan et al[6]. and Gui et al.[5], who observed no significant demographic differences between metformin- and insulin-treated women with GDM.

Adequate glycemic control was achieved in the majority of women in both groups, with slightly higher control observed in the insulin group. However, the difference was not statistically significant. This finding is comparable with the randomized trial by Rowan et al.[6], which demonstrated that metformin provided glycemic control comparable to insulin therapy in women with GDM. Similar observations were also reported by Moore et al[8]. and Niromanesh et al.[9], who concluded that metformin is an effective alternative to insulin for maintaining maternal glucose levels.

In the present study, excessive maternal weight gain was lower in the metformin group compared to the insulin group. This finding correlates with previous studies that demonstrated reduced maternal weight gain with metformin therapy due to its insulin-sensitizing effect. Rowan et al[6]. reported improved maternal satisfaction and less weight gain among women receiving metformin. Reduced maternal weight gain may contribute to better pregnancy outcomes and lower operative delivery rates.

The incidence of pregnancy-induced hypertension and polyhydramnios was comparatively lower in the metformin group, although statistical significance was not achieved. Similar findings were observed in studies by Ainuddin et al.[10] and Gui et al.[5], where metformin use was associated with fewer hypertensive complications. The reduction in insulin resistance and improved metabolic profile with metformin may explain these findings.

Cesarean section rates were higher in the insulin group in the present study. Comparable findings were noted in the studies conducted by Rowan et al[6]. and Balsells et al.[7], where women receiving metformin had lower operative delivery rates. This may be related to lower fetal macrosomia and reduced maternal weight gain among women treated with metformin.

With regard to neonatal outcomes, the present study showed lower rates of macrosomia, neonatal hypoglycemia, respiratory distress, and NICU admission in the metformin group compared to the insulin group. These observations are consistent with the meta-analysis by Gui et al.[5], which reported significantly lower neonatal hypoglycemia and reduced NICU admissions among metformin-treated women. Balsells et al[7]. also demonstrated that metformin was associated with reduced neonatal complications compared to insulin therapy. The lower incidence of neonatal hypoglycemia in the metformin group may be attributed to reduced fetal hyperinsulinemia resulting from better maternal metabolic control.

Although the present study demonstrated favorable outcomes with metformin therapy, most differences between the groups were not statistically significant, possibly because of the relatively smaller sample size. Nevertheless, the findings support the growing evidence that metformin is a safe and effective alternative to insulin in selected women with gestational diabetes mellitus. Its oral administration, lower cost, ease of use, and better patient compliance make it particularly suitable in resource-limited settings.

Limitations

The study had a relatively small sample size, which may have limited the statistical significance of certain outcomes. Being a single-center study, the findings may not be generalizable to the wider population. Long-term follow-up of mothers and neonates was not performed, and therefore the long-term metabolic effects of metformin exposure during pregnancy could not be assessed.

CONCLUSION

The present study demonstrated that metformin is comparable to insulin in achieving adequate glycemic control among women with gestational diabetes mellitus. Maternal outcomes such as excessive weight gain, pregnancy-induced hypertension, and cesarean section rates were relatively lower in the metformin group. Neonatal complications including macrosomia, neonatal hypoglycemia, respiratory distress, and NICU admissions were also less frequent among women treated with metformin. Owing to its oral administration, better patient compliance, lower cost, and satisfactory fetomaternal outcomes, metformin can be considered a safe and effective alternative to insulin therapy in selected patients with gestational diabetes mellitus.

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