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RESEARCH ARTICLE**Impact of Medical Nutrition Therapy, Metformin, and Insulin on Neonatal Outcomes in Gestational Diabetes Mellitus: A Cross-Sectional Study**Amanda Salvatore^{1*} | Jamie Tsao² | Thomas Jefferson³**Abstract**

Gestational diabetes mellitus (GDM) is associated with increased risks of adverse neonatal outcomes. This cross-sectional study aimed to evaluate and compare the effects of medical nutrition therapy (MNT), metformin, and insulin on neonatal outcomes in pregnancies complicated by GDM. Conducted at a tertiary care hospital, the study included pregnant women diagnosed with GDM who were managed with one of the three interventions based on glycemic control needs and clinical assessment. Neonatal outcomes assessed included birth weight, incidence of macrosomia, neonatal hypoglycemia, NICU admission, Apgar scores, and mode of delivery. Statistical analysis revealed that MNT was associated with the lowest incidence of adverse neonatal outcomes, while insulin-treated mothers had a higher frequency of macrosomia and NICU admissions. Metformin showed a favorable safety profile, with neonatal outcomes comparable to MNT and better than insulin in certain parameters. These findings suggest that MNT remains an effective first-line management strategy, while metformin may be a viable alternative to insulin in selected GDM cases with fewer neonatal complications.

Key words: Gestational diabetes mellitus, Medical nutrition therapy, Metformin, Insulin, Neonatal outcomes, Cross-sectional study

1 | INTRODUCTION

Gestational diabetes mellitus is a significant cause of morbidity and mortality in neonates, as well as illness in mothers, and complicates numerous pregnancies. The classic definition of gestational diabetes mellitus is "hyperglycemia of varying severity with onset or first recognition during pregnancy" (1). It is anticipated that the revised diagnostic criteria will result in an increase in the incidence due to the increased detection, as the overall incidence of 3-7 percent has progressively increased over time (2). The incidence

in Iran is currently estimated 10.2%. The patient's risk of gestational diabetes mellitus increases as insulin sensitivity decreases during the course of a typical pregnancy. Gestational diabetes mellitus is distinguished by maternal hyperglycemia, which elevates the quantity of glucose that is transferred to the embryo. Thereby increasing the likelihood of neonatal mortality, trauma during birth, and shoulder dystocia. A number of newborn metabolic problems, including respiratory distress syndrome, hypomagnesemia, hypoglycemia, polycythemia, hypocalcemia, and an increased long-term risk of diabetes mellitus and obesity in the kid, may

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also be brought on by hyperinsulinemia (3, 4).

Maternal conditions include preeclampsia, hypertension, the need for a cesarean section, and a higher risk of developing diabetes mellitus are also associated with gestational diabetes mellitus. Treating hyperglycemia in women with gestational diabetes mellitus has been shown in prospective randomized studies to potentially avoid adverse neonatal outcomes (5, 6). The main line of treatment for this is guidance on diet and exercise, however women often need further therapy (20% to 60%). For a long time, pregnant women with hyperglycemia have been treated with insulin. Though many pregnant women find this treatment choice problematic due to increased appetite and weight gain, it is still the recommended therapy in many circumstances. These challenges also stem from the difficulty of providing medication that requires many daily injections. Moreover, around 71% of pregnant women who take insulin experience hypoglycemia (7, 8).

Recent research indicates that an oral hypoglycemic drug may have improved maternal and fetal outcomes while simultaneously increasing patient acceptability. Alternatively to insulin, oral metformin is an effective treatment for gestational diabetes. Metformin enhances insulin sensitivity and reduces postprandial and fasting plasma glucose. It is not linked to hypoglycemia or excessive weight gain (9, 10). Although metformin crosses the placenta, there is no proof that it harms the developing fetus or raises the risk of severe defects. Metformin has been administered to pregnant women, although it is unknown whether this medication, like insulin, may reduce adverse perinatal outcomes and complicate the pregnancy (11, 12).

The results of earlier studies comparing the effects of insulin and metformin on glycemic management, pregnancy, and neonatal outcomes have been conflicting. Specific pregnancy-related complications and neonatal outcomes, including neonatal hypoglycemia, newborn hyperbilirubinemia, short-for-gestational-age neonates, and early labor, were demonstrated to differ substantially between the metformin and insulin groups. Additionally, other investigations discovered that the variations lacked statistical significance (13, 14). Examining the outcomes

of newborns delivered to mothers with gestational diabetes mellitus is the goal of this study. Insulin, metformin, and medical nutritional treatment were evaluated in a cross-sectional study.

2 | METHODOLOGY

This was a cross-sectional study of 60 GDM moms in the Obstetrics and Gynecology Department at ANMMCH in Gaya, Bihar, India for one year. The women had gestational diabetes mellitus, which was identified at 24 weeks of gestation using a routine oral glucose tolerance test. The method used was stratified random sampling.

Women who met the criteria for gestational diabetes mellitus (GDM) and were 18 years of age or older and pregnant with a singleton were eligible to participate in this research. Participants were also eligible if the fetus had frequent follow-up visits at the assigned healthcare facility and no evident anomalies or malformations. Additionally, the research concentrated on women who gave delivery at the approved facility. Patients who were noncompliant, had multiple gestations, missed follow-up, were women under the age of 18, or had malformed fetuses were all omitted. Furthermore, individuals who had deliveries elsewhere were excluded from the study.

3 | RESULTS

In a study of 60 patients, 43.33% were full-term, 36.67% preterm, and 20% post-term. Among 43.33% of women were suitable for gestational age, 23.33% were small for gestational age, and 33.33% were big for gestational age based on weight vs gestational age. The mode of delivery was split between vaginal (56.67%) and cesarean section (43.33%). ICU admission was necessary for 36.67% of the newborns, while 63.33% did not require ICU care. Neonatal hypoglycemia occurred in 30% of cases, and 26.67% experienced seizures. The Apgar score at 1 minute was low (<7) in 63.33% of the infants, while 31.67% had a low Apgar score at 5 minutes.

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Table 1. Characteristics of infants (n=60)

Variable	Frequency (n=60)	Percentage (%)
Gestational age		
Post-term	12	20.00
Full-term	26	43.33
Preterm	22	36.67
Weight vs gestational age		
SGA	14	23.33
AGA	26	43.33
LGA	20	33.33
Type of delivery		
Cesarean section	26	43.33
Vaginal	34	56.67
ICU admission		
Absent	38	63.33
Present	22	36.67
Neonatal hypoglycemia		
Absent	42	70.00
Present	18	30.00
Seizures		
Absent	44	73.33
Present	16	26.67
Apgar 1'		
Low <7	38	63.33
Apgar 5'		
Low <7	19	31.67

Neonatal hypoglycemia was more frequent in the Metformin + Insulin group (11.67%), with the highest adjusted odds ratio (AOR) of 2.366. Preterm birth was least frequent in the Insulin group (3.33%), with an AOR of 0.102. Cesarean sections were more common in those on Metformin + Insulin (18.33%), with the highest AOR of 4.755. Seizures were also more frequent in the Metformin + Insulin group (10%), with an AOR of 3.691. NICU admissions were more common in the Metformin + Insulin group (13.33%), although the AOR was only 1.966. Large for gestational age (LGA) infants were most frequent in the

Metformin + Insulin group (16.67%), with an AOR of 3.243, while small for gestational age (SGA) outcomes were not strongly influenced by treatment. Apgar scores <7 at 1 minute were most frequent in the Metformin + Insulin group (23.33%), but the AOR was lower at 0.623. Similarly, Apgar scores <7 at 5 minutes were most common in the Metformin + Insulin group (11.67%), with an AOR of 2.622. Overall, the Metformin + Insulin group showed the most elevated risk for various neonatal complications.

4 | DISCUSSION

Metformin use in pregnant women have garnered significant attention recently and transplacental translocation is the principal concern associated with metformin therapy in individuals with gestational diabetes mellitus (GDM). Research indicates that metformin traverses the placenta, and after delivery, its concentration in the umbilical cord may exceed 50% of maternal levels. The chance of delivering AGA newborns increased with metformin

medication, whereas the risk of delivering SGA or LGA neonates decreased. On the other hand, those receiving insulin had a decreased chance of preterm delivery. Women receiving insulin treatment were more likely to have neonatal hypoglycemia. In line with our findings of a greater overall rate of caesarean deliveries, Boriboonhirunsarn et al. observed that mothers with GDM had a higher risk of emergency cesarean deliveries. The values were likewise considerably higher in the metformin and insulin groups. Inocência et al. reported simi-

Table 2. Multinomial logistic analysis of newborn outcomes according to the kind of GDM therapy received.

Outcome	Therapeutic modality	N (%)	Crude OR	AOR
Neonatal hypoglycemia	Diet	2 (3.33%)		
	Metformin	4 (6.67%)	0.729	2.106
	Insulin	5 (8.33%)	4.207	1.425
	Metformin + Insulin	7 (11.67%)	6.124	2.366
Preterm birth	Diet	9 (15.00%)		
	Metformin	5 (8.33%)	0.484	0.228
	Insulin	2 (3.33%)	0.238	0.102
	Metformin + Insulin	6 (10.00%)	0.802	0.026
Cesarean section	Diet	2 (3.33%)		
	Metformin	6 (10.00%)	3.886	2.756
	Insulin	7 (11.67%)	1.747	2.940
	Metformin + Insulin	11 (18.33%)	5.796	4.755
Seizures	Diet	3 (5.00%)		
	Metformin	2 (3.33%)	1.270	1.532
	Insulin	5 (8.33%)	5.111	2.713
	Metformin + Insulin	6 (10.00%)	6.621	3.691
NICU admission	Diet	5 (8.33%)		
	Metformin	3 (5.00%)	0.529	0.912
	Insulin	6 (10.00%)	2.714	1.434
	Metformin + Insulin	8 (13.33%)	3.145	1.966
AGA	Diet	12 (20.00%)		
	Metformin	6 (10.00%)	1.344	4.229
	Insulin	7 (11.67%)	0.237	3.601
	Metformin + Insulin	1 (1.67%)	0.265	0.443
LGA	Diet	2 (3.33%)		
	Metformin	3 (5.00%)	2.381	2.508
	Insulin	5 (8.33%)	4.112	3.217
	Metformin + Insulin	10 (16.67%)	5.938	3.243
SGA	Diet	6 (10.00%)		
	Metformin	4 (6.67%)	0.529	0.307
	Insulin	2 (3.33%)	0.216	0.615
	Metformin + Insulin	2 (3.33%)	0.216	0.776
Apgar score <7 1st minute	Diet	6 (10.00%)		
	Metformin	7 (11.67%)	1.369	1.276
	Insulin	11 (18.33%)	1.571	1.551
	Metformin + Insulin	14 (23.33%)	2.20	0.623
Apgar score <7 5th minute	Diet	3 (5.00%)		
	Metformin	6 (10.00%)	0.570	1.212
	Insulin	3 (5.00%)	1.57	0.373
	Metformin + Insulin	7 (11.67%)	3.421	2.622

lar results (15, 16). Furthermore, compared to the other two groups, the insulin and insulin plus metformin groups had NICU admission rates that were considerably higher. The research by Al-Khalifah et al. found that babies delivered to moms with GDM had a greater incidence of NICU hospitalizations. They speculate that a possible factor in these NICU hospitalizations might be the elevated risk of hypoglycemia. This might also account for the higher number of NICU hospitalizations seen in our patient population. Apparently, the insulin plus met-

formin group had significantly more bouts of neonatal hypoglycemia (17). A Macedonian research by Simeonova-Krstevska et al. that showed metformin improved mother and newborn outcomes supports our findings (18).

Those receiving insulin with metformin or insulin alone had a higher risk of LGA babies. Our results are corroborated by Ye et al.'s meta-analysis, which shows that LGA babies are often seen in GDM patients on insulin treatment. Although there was no significant variance in Apgar scores, the same

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investigators found a lower Apgar with a higher prevalence of respiratory distress in babies in moms using insulin (19). Comparable findings have only been found in a few number of studies conducted abroad, one of which was conducted by da Silva et al. in Brazil (20). The four different but most popular therapeutic options were examined, which supports the study's conclusions. Our study, however, has several limitations.

Our study founded the statistically significant differences in 'neonatal outcomes' according to kind of therapy for gestational diabetes mellitus. In comparison to women who were undergoing medical nutrition treatment, those who were using metformin and insulin had a higher incidence of Caesarean births. Boriboonhirunsarn et al. (21) and Takeda et al. (22) conducted research that demonstrated that women with GDM were at a significantly increased risk of emergency caesarean births. The metformin plus insulin and insulin alone groups exhibited markedly higher rates. These findings are in accordance with our own. Additionally, the findings of our investigation indicated that women who utilized metformin were more probable to deliver infants that were appropriate for their gestational age and less probable to have neonates that were either too small or too large for their gestational age. On the other hand, the investigation exhibited a lower incidence of preterm birth, which is in accordance with the findings of Preda et al. Twenty-three Large for gestational age infants were more prevalent in individuals who were treated with insulin alone or insulin plus metformin. This result is consistent with a meta-analysis conducted by Tarry Adkins et al. (23), which revealed that LGA infants were frequently delivered to GDM mothers who were undergoing insulin therapy. Our research provides vital insights to the region's scant literature on GDM. A comparison of four widely used therapy choices improves the research. Nevertheless, there are disadvantages to the record-based and cross-sectional approaches as well as the narrow emphasis on neonatal outcomes. Maternal outcomes should be included as possible confounders in future studies.

5 | CONCLUSION

This research looked at perinatal variables and neonatal outcomes in 60 neonates delivered to moms who had gestational diabetes mellitus. Neonatal outcomes were assessed using GDM therapies such as diet, metformin, insulin, and their combinations. The findings reveal that metformin, whether alone or in combination with insulin, was not associated with an increase in newborn problems when compared to insulin. However, the mother's and the child's health depended on careful birth management. More research on maternal outcomes is required to have a better understanding of how GDM medications affect the outcomes of newborns.

Data Availability Statement

Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study.

Conflicts of Interest The author declares no conflicts of interest.

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