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Original Research Article

Neonatal outcomes of gestational diabetes mellitus (GDM) mothers: A cross-sectional study comparing medical nutritional therapy, metformin, and insulin treatments at a tertiary care centre

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A B S T R A C T

Background: Gestational Diabetes Mellitus (GDM) poses a rising global health challenge, affecting 10-14.3% of pregnant women. This study aimed to investigate and compare neonatal outcomes among mothers with GDM treated with Medical Nutritional Therapy (MNT), metformin, and insulin at a tertiary care center. Understanding the impact of these treatments on neonatal outcomes is crucial for optimal care.
Materials and Methods: Conducted at a tertiary care center in Chennai, India, this cross-sectional study included 160 GDM mothers identified through medical records from December 2021 to December 2023. Inclusion criteria covered women aged 18 and above, experiencing singleton pregnancies, diagnosed with GDM, and maintaining regular follow-up. Data analysis included birth weight, Apgar scores, neonatal hypoglycemia, and preterm birth rates. Multinomial logistic regression determined adjusted odds ratios.
Results: The study analyzed the distribution of perinatal factors among 160 neonates, revealing that 41.3% were delivered vaginally, while 58.8% were through cesarean section. The majority were preterm, with 118 being appropriate for gestational age.Neonatal Intensive Care Unit (ICU) admission was noted in 34.4% of cases, while 62.7% did not. Neonatal hypoglycemia was observed in 36.3% of cases, and seizures were present in 19.4%. Apgar scores were low in 23.8% of cases.
A multinomial logistic analysis found that the Metformin, Insulin, and Metformin + Insulin groups had significantly higher odds of having a Cesarean section compared to the diet-only group. However, the Metformin group had lower odds of preterm birth, NICU admission, neonatal hypoglycemia, seizures, and AGA. The Metformin group had higher odds of LGA and Apgar score <7 at both the 1st and 5th minutes. No significant differences were found in the odds of preterm birth, NICU admission, or seizures between the diet-only and Metformin groups.
Conclusion: This pioneering South Indian study of 160 neonates born to GDM mothers compared different treatment options. Metformin, alone or with insulin, showed comparable neonatal outcomes to insulin. Caution in GDM deliveries is recommended for optimal well-being. The study emphasizes the need for further research considering maternal outcomes as potential confounders to comprehensively understand GDM treatments and neonatal outcomes.

1. Introduction

Gestational Diabetes Mellitus (GDM) represents a growing health challenge worldwide, with an increasing number

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of expectant mothers being diagnosed annually. It is a type of diabetes that develops during pregnancy, affecting about 10-14.3% of pregnant women. It results from the body's inability to produce and use insulin effectively, leading to elevated blood sugar levels. GDM poses risks for both mother and baby, including a higher likelihood of cesarean delivery, preeclampsia, and macrosomia. Additionally, infants born to mothers with GDM may face an increased risk of hypoglycemia and respiratory distress syndrome. Timely diagnosis through glucose testing and careful management, including diet modification and insulin therapy, are crucial for minimizing complications. Understanding the impact of these treatments on neonatal outcomes is essential for providing optimal care to both the mothers and their infants. Hence we designed this study with the aim of this study is to investigate and compare the neonatal outcomes among mothers with GDM treated with MNT (medical nutritional therapy), metformin, and insulin at a tertiary care center, with the broader goal of understanding the effectiveness of these treatments in optimizing neonatal health outcomes.[1–4]

2. Materials and Methods

This was designed as a cross-sectional study conducted among 160 GDM mothers (sample size calculated using Dobson's formula) in a tertiary care center in Chennai, India. We identified eligible patients from available medical records between December 2021 to December 2023. The participants were mothers with gestational diabetes mellitus diagnosed by a standard oral glucose tolerance test at 24 weeks of gestation. Stratified random sampling was used.

Participants were divided into 4 groups with 40 participants each

Group A: MNT

Group B: Metformin

Group C: Insulin

Group D: Metformin + Insulin

The inclusion criteria for this study encompassed women aged 18 and above with a singleton pregnancy and met the criteria for gestational diabetes mellitus (GDM). Additionally, eligible participants included those whose fetuses showed no gross anomalies or malformations, and who maintained regular follow-up at the designated healthcare center. Furthermore, the study focused on patients who delivered at the specified center.

Conversely, the exclusion criteria comprised women below the age of 18, those with multiple gestations, individuals who lost follow-up, non-compliant patients, and those with fetuses displaying anomalies. Moreover, the study excluded patients who delivered elsewhere. These criteria were established to ensure a homogeneous and well-defined study population, allowing for a more accurate examination of the specified parameters.

The data retrieved from medical records was entered into MS Excel and analyzed using SPSS version 22. Outcome measures were birth weight, Apgar scores, incidence of neonatal hypoglycemia, and rates of preterm births. For quantitative variables, mean and standard deviation were computed., while for qualitative variables, frequencies were used. Comparison and analysis of outcome measures was done by multinomial logistic regression, and expressed as adjusted odds ratio with 95% confidence interval and p value. $P < 0.05$ was considered statistically significant.

3. Results

Among the 160 neonates, the distribution of various perinatal factors was observed. Regarding the mode of delivery, 66 neonates (41.3%) were delivered vaginally, while 94 neonates (58.8%) were delivered through cesarean section. In terms of gestational age, 42 neonates (26.3%) were born preterm, 114 (71.2%) were born full-term, and 4 neonates (2.5%) were classified as post-term. Weight in relation to gestational age revealed that 118 neonates (73.8%) were appropriate for gestational age (AGA), 35 neonates (21.9%) were large for gestational age (LGA), and 7 neonates (4.4%) were small for gestational age (SGA). Intensive Care Unit (ICU) admission was noted in 55 cases (34.4%), while 105 neonates (65.6%) did not require ICU admission. Neonatal hypoglycemia was observed in 58 neonates (36.3%), while 102 neonates (63.7%) did not experience this condition. Seizures were present in 31 neonates (19.4%), and 129 neonates (80.6%) were seizure-free. Apgar scores at 1 minute indicated that 38 neonates (23.8%) had a low score of less than 7, and at 5 minutes, 19 neonates (11.9%) had an Apgar score lower than 7 (Table 1). These findings collectively provide insights into the perinatal characteristics and outcomes within the studied neonatal population. Neonatal outcomes were assessed based on these treatment groups.

The provided Table 2 presents the results of a multinomial logistic analysis examining the association between different therapeutic modalities for gestational diabetes mellitus (GDM) and various neonatal outcomes. Compared to the diet-only group, the odds of having a Cesarean section are significantly higher for the Metformin, Insulin, and Metformin + Insulin groups. Adjusted odds ratios (AOR) are provided after controlling for potential confounding factors. No significant differences are observed in the odds of preterm birth between the MNT group and the Metformin or Metformin + Insulin groups. The Insulin group, however, has significantly lower odds of preterm birth compared to the MNT group. The Insulin and Metformin + Insulin groups have significantly higher odds of NICU admission compared to the diet-only group. The Metformin group also shows an increased odds ratio, but it does not reach statistical significance after adjustment. The odds of neonatal hypoglycemia are significantly higher

Table 1: General characteristics of newborns (n=160)

Variable	Frequency (n=160)	Percentage (%)
Type of delivery		
Vaginal	66	41.3
Cesarean section	94	58.8
Gestational age		
Preterm	42	26.3
Full-term	114	71.2
Post-term	4	2.5
Weight vs gestational age		
AGA	118	73.8
LGA	35	21.9
SGA	7	4.4
ICU admission		
Present	55	34.4
Absent	105	65.6
Neonatal hypoglycemia		
Present	58	36.3
Absent	102	63.7
Seizures		
Present	31	19.4
Absent	129	80.6
Apgar 1'		
Low <7	38	23.8
Apgar 5'		
Low <7	19	11.9

AGA: Appropriate for gestational age; LGA: Large for gestational age; SGA: Small for gestational age; ICU: Intensive care unit

for the Metformin, Insulin, and Metformin + Insulin groups compared to the MNT group. The Insulin and Metformin + Insulin groups have significantly higher odds of seizures compared to the MNT group. The Metformin group also shows an increased odds ratio, but it does not reach statistical significance after adjustment. No significant differences are observed in the odds of being AGA between the diet-only group and the Metformin, Insulin, or Metformin + Insulin groups. No significant differences are observed in the odds of being SGA between the diet-only group and the Metformin, Insulin, or Metformin + Insulin groups. The Metformin, Insulin, and Metformin + Insulin groups have higher odds of LGA compared to the diet-only group. No significant differences are observed in the odds of Apgar score <7 between the diet-only group and the Metformin, Insulin, or Metformin + Insulin groups at both the 1st and 5th minutes.

4. Discussion

Our study revealed statistically significant results that Caesarean deliveries were more prevalent among women receiving insulin and metformin compared to those in the MNT group. Metformin-treated individuals had a lower likelihood of delivering SGA or LGA newborns and a higher likelihood of delivering AGA babies. Conversely, insulin-treated patients experienced a reduced incidence of preterm delivery. Neonatal hypoglycemia was more frequently observed in women treated with insulin. ($p<0.05$)

Boriboonhirunsarn et al. noted an increased risk of emergency caesarean deliveries in GDM mothers, in concordance with our findings of increased caeserean deliveries overall. The numbers were also significantly higher with the metformin with insulin and only insulin groups. Similar findings were also noted by Inocêncio et al.[5,6]

Insulin and insulin with metformin groups also ahd significantly higher number of NICU admissions compared to the other two groups. Al-Khalifah et al. have observed in their study that the incidence of NICU admissions is higher in neonated born to GDM mothers. They hypothesise that the hightened risk of hypoglycaemias could contribute to these NICU admissions. This could also explain why we noted higher NICU admissions in these group of patients in our study. Evidently, neonatal hypoglycaemia episodes were also significantly higher in the insulin plus metformin group.[7] Metformin was noted to improve maternal and neonatal outcomes in a Macedonian study by Simeonova-Krstevska et al., supporting our results.[8]

We noted that the incidence of LGA babies was higher with patients treated with insulin alone, or insulin with metformin. A meta-analysis by Ye et al., LGA babies were commonly reported in women with GDM on insulin treatment, thus suporting our finding. Although we did not

Table 2: Multinomial logistic analysis of neonatal outcomes based on type treatment taken for GDM

Outcome	Therapeutic modality	n (%)	Crude OR (95% CI)	P- value	AOR (95% CI)	P-value
Cesarean section	Diet	14 (14.9%)	-	-		
	Metformin	24 (25.5%)	2.786 (1.12 – 6.89)	0.027	3.766 (1.15- 12.23)	0.044*
	Insulin	27 (28.7%)	3.857 (1.52 – 9.75)	0.004*	3.990 (1.41 – 11.2)	0.009*
	Metformin + Insulin	29 (30.9%)	4.896 (1.89 – 12.66)	0.001*	4.855 (1.61-14.6)	0.005*
Preterm birth	Diet	15 (35.7%)	-	-		
	Metformin	9 (21.4%)	0.484 (0.18 – 1.2)	0.147	0.278 (1.4-11.2)	0.027
	Insulin	5 (11.9%)	0.238 (0.77 - -0.74)	0.013	0.109 (0.29-0.41)	0.001
	Metformin + Insulin	12 (31%)	0.802 (0.32 – 2.15)	0.639	0.046 (0.01-1.53)	0.209
NICU admission	Diet	10 (18.2%)	-	-	-	-
	Metformin	6 (10.9%)	0.529 (0.17 – 1.63)	0.268	0.912 (0.3-2.5)	0.509
	Insulin	19 (34.5%)	2.714 (1.05 – 6.99)	0.039*	1.434 (1.01-5.46)	0.002*
	Metformin + Insulin	20 (36.4%)	3.145 (1.16 – 7.73)	0.023*	1.966 (1.12-5.216)	0.001*
Neonatal hypoglycemia	Diet	10 (17.2%)	-	-	-	-
	Metformin	6 (10.3%)	0.829 (0.22- 2.33)	0.446	1.106 (0.2-4.2)	0.883
	Insulin	17 (29.3%)	2.217 (0.85 – 5.74)	0.101	1.445 (1.01- 4.2)	0.034*
	Metformin + Insulin	25 (43.1%)	5.144 (1.9 – 13.6)	0.001*	2.466 (1.2 – 4.8)	0.009*
Seizures	Diet	6 (19.4%)	-	-	-	-
	Metformin	1 (3.2%)	1.370 (0.28 – 6.5)	0.693	1.632 (0.27 – 9.7)	0.590
	Insulin	10 (32.3%)	4.111 (1.03 – 16.2)	0.044*	2.813 (1.6 – 9.58)	0.011*
	Metformin + Insulin	14 (45.2%)	6.641 (1.73 – 25.4)	0.006*	4.891 (2.53 – 10.52)	0.003*
AGA	Diet	35 (29.7%)	-	-	-	-
	Metformin	28 (23.7%)	1.434 (0.92 – 1.94)	0.376	3.229 (0.39 – 14.8)	0.272
	Insulin	29 (24.6%)	0.377 (0.11 -1.2)	0.101	1.641 (0.7 – 3.7)	0.237
	Metformin + Insulin	26 (22%)	0.265 (0.08 – 0.83)	0.023	0.443 (0.02 – 1.2)	0.060
SGA	Diet	3 (42.9%)	-	-	-	-
	Metformin	2 (28.6%)	0.649 (0.64 – 0.10)	0.646	0.507 (0.1-1.7)	0.291
	Insulin	1 (14.3%)	0.316 (0.03 – 3.17)	0.328	0.915 (0.4 – 2.5)	0.830
	Metformin + Insulin	1 (14.3%)	0.316 (0.03 – 3.17)	0.328	0.776 (0.45 – 4.66	0.604
LGA	Diet	3 (8.6%)	-	-	-	-
	Metformin	9 (25.7%)	3.581 (0.89 – 14.3)	0.072	2.508 (0.5 – 6.8)	0.085
	Insulin	10 (28.6%)	4.112 (1.03 – 16.2)	0.044*	3.217 (1.13 – 12.5)	0.040*
	Metformin + Insulin	13 (37.1%)	5.938 (1.54 – 22.9)	0.010*	3.243 (1.2 – 14.4)	0.009*
Apgar score <7 1st minute	Diet	7 (18.9%)	-	-	-	-
	Metformin	9 (24.3%)	1.369 (0.45 – 4.12)	0.577	1.276 (0.27 – 5.9)	0.756
	Insulin	10 (26.3%)	1.571 (0.53 – 4.65)	0.414	1.551 (0.30 – 7.77)	0.594
	Metformin + Insulin	12 (31.6%)	2.20 (0.70 – 5.82)	0.193	0.623 (0.08 – 4.33)	0.433
Apgar score <7 5th minute	Diet	3 (15.8%)	-	-	-	-
	Metformin	4 (21.1%)	1.370 (0.28 – 6.55)	0.693	1.212 (0.10 – 14.14)	0.878
	Insulin	3 (15.8%)	1.48 (0.18 – 5.28)	0.489	0.573 (0.42 – 7.75)	0.675
	Metformin + Insulin	9 (47.4%)	3.581 (0.89 – 14.3)	0.072	3.822 (0.27 – 12.4)	0.319

OR: Odds ratio; AOR: Adjusted odds ratio; AGA: Appropriate for gestational age; LGA: Large for gestational age; SGA: Small for gestational age; NICU: Neonatal intensive care unit

*p value<0.05 is considered statistically significant notice a significant difference in Apgar scores, the same authors have also noted a decreased Apgar with a high incidence of neonatal respiratory distress in women treated with insulin.[9]

Our study is the first of its kind to be conducted in South India, where the incidence of GDM is high, with only few studies conducted abroad, including one by daSilva et al[10] in Brazil, demonstrating similar findings.[11] We have compared four different, but most commonly used treatment options, which adds to the strength of the study. However, our study did have a few limitations. The cross-sectional and record-based design offer only a point estimate, indicating the need for cautious interpretation of the results. We have also only observed neonatal outcomes, while there is a possibility that maternal outcomes by themselves, could have been confounders for neonatal outcomes, which we have not accounted for.

The results of our study demonstrated statistically significant differences in neonatal outcomes based on the type of treatment for gestational diabetes mellitus (GDM). Caesarean deliveries were found to be more prevalent among women receiving insulin and metformin compared to those in the medical nutrition therapy (MNT) group. In line with our findings, studies by Boriboonhirunsarn et al.[12] and Takeda et al.[13] reported an increased risk of emergency caesarean deliveries in GDM mothers, with significantly higher numbers in the metformin with insulin and insulin-only groups.

Our study also revealed that metformin-treated individuals had a lower likelihood of delivering small for gestational age (SGA) or large for gestational age (LGA) newborns and a higher likelihood of delivering babies appropriate for gestational age (AGA). This finding aligns with a Macedonian study by Simeonova-Krstevska et al.,[8] which observed improved maternal and neonatal outcomes with metformin treatment. Conversely, the insulin-treated group in our study experienced a reduced incidence of preterm delivery, consistent with findings from Preda et al.[14]

The incidence of large for gestational age (LGA) babies was higher in patients treated with insulin alone or insulin with metformin, consistent with a meta-analysis by Tarry-Adkins et al.,[15] which reported common occurrence of LGA babies in women with GDM on insulin treatment. Although we did not find a significant difference in Apgar scores, Tarry-Adkins et al.[15] noted decreased Apgar scores and a higher incidence of neonatal respiratory distress in women treated with insulin.

Our study, conducted in South India, adds valuable insights to the limited body of literature on GDM in this region. Comparing four commonly used treatment options strengthens the study. However, the cross-sectional and record-based design, along with the focus on neonatal outcomes alone, introduces limitations. Future research should consider maternal outcomes as potential confounders. In conclusion, our findings suggest that metformin (alone or with supplemental insulin) in GDM is not associated with increased neonatal complications compared to insulin. Caution is advised during delivery to ensure the well-being of both mother and baby.

Overall, with respect to the neonatal outcomes, we observed that in women with gestational diabetes mellitus, metformin (alone or with supplemental insulin) is not associated with increased neonatal complications as compared with insulin. It is advisable, however, for physicians to follow caution when delivering GDM mothers, to ensure maximum well-being of the mother and baby.

5. Conclusion

In conclusion, our study provides a comprehensive analysis of perinatal factors and neonatal outcomes in a cohort of 160 neonates born to mothers with gestational diabetes mellitus (GDM) in South India. The distribution of perinatal factors, including mode of delivery, gestational age, weight in relation to gestational age, and various neonatal complications, was meticulously examined. The neonatal outcomes were further assessed based on the type of treatment received for GDM, including diet, metformin, insulin, and a combination of metformin and insulin.

Our study suggests that, concerning neonatal outcomes, metformin (alone or with supplemental insulin) does not appear to be associated with increased complications compared to insulin in women with GDM. Nevertheless, caution is advised in the delivery of GDM mothers to ensure the optimal well-being of both the mother and the baby. Further research, particularly considering maternal outcomes as potential confounders, is warranted to enhance our understanding of the complex interplay between GDM treatments and neonatal outcomes.

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7. Conflict of Interest

None.

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