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Evaluation Of Metformin In Treatment Of Gestational Diabetes Mellitus And Role Of Fasting Blood Glucose Level As A Predictor Of Response To Metformin.

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ABSTRACT

Gestational Diabetes Mellitus (GDM) is a common metabolic complication of pregnancy associated with maternal and neonatal morbidity. Metformin is widely used as a first-line pharmacological therapy, yet individual responses vary. Identifying predictors of metformin failure may optimize treatment strategies. To evaluate the efficacy of metformin in the management of GDM and to assess the role of fasting blood glucose (FBS) at 24 weeks as a predictor of response to metformin. Our prospective observational study included 80 pregnant women diagnosed with GDM based on IADPSG criteria. All women initially received diet and lifestyle modification, followed by metformin up to 2 g/day if glycemic control was inadequate. Those who failed to respond required addition of insulin. Maternal characteristics, OGTT values, obstetric outcomes, and neonatal outcomes were recorded. Statistical analysis included t-tests and chi-square tests, with significance at $p < 0.05$. Metformin alone achieved adequate glycemic control in 61.25% of women. Higher HbA1c ($p = 0.033$) and higher FBS at 24 weeks ($p = 0.005$) were significantly associated with need for insulin. An FBS ≥ 100 mg/dL strongly predicted metformin failure ($p = 0.00007$). Maternal and neonatal outcomes were comparable across groups. Metformin is effective in most GDM patients, and fasting blood glucose ≥ 100 mg/dL is a strong predictor of treatment escalation.

Keywords: Metformin, Gestational Diabetes Mellitus, Fasting Blood Glucose

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INTRODUCTION

Gestational Diabetes Mellitus (GDM) is a common metabolic disorder of pregnancy, characterized by glucose intolerance first recognized during gestation [1]. Its prevalence is increasing globally, particularly in South Asian countries, owing to rising maternal age, obesity, sedentary lifestyle, and genetic predisposition [2, 3]. GDM is associated with significant maternal and fetal complications, including pre-eclampsia, operative deliveries, macrosomia, neonatal hypoglycemia, and long-term risk of type 2 diabetes mellitus in both mother and child. Early diagnosis and optimal glycemic control are therefore essential to improve pregnancy outcomes [4-6].

Metformin, an oral biguanide, is increasingly used as an alternative to insulin for GDM management due to its effectiveness, safety profile, ease of administration, and cost-effectiveness. It improves insulin sensitivity, reduces hepatic gluconeogenesis, and enhances peripheral glucose uptake. However, not all women respond uniformly to metformin therapy. Recent studies suggest that baseline fasting blood glucose (FBG) levels may be a strong predictor of therapeutic success, helping clinicians identify patients who may require early addition or transition to insulin [7].

Evaluating metformin's efficacy in GDM and exploring the predictive value of FBG can guide individualized treatment, minimize complications, reduce treatment delays, and support evidence-based decision-making in antenatal care.

METHODOLOGY

Our prospective observational study was conducted in the Department of Obstetrics and Gynecology. Complete information regarding the purpose and procedures of the study was provided to eligible women in their local language, and confidentiality was strictly maintained. Written informed consent was obtained prior to enrolment, and all data were collected anonymously using coded study forms.

Pregnant women diagnosed with Gestational Diabetes Mellitus (GDM) and initiated on metformin after unsuccessful diet and lifestyle modification were included. Women with pre-existing type 1 or type 2 diabetes, known renal or hepatic disorders, or multiple gestations were excluded. The sample size was calculated using standard statistical formulae, and a total of 80 women meeting the inclusion criteria were recruited. Diagnosis of GDM was made according to IADPSG criteria using 75 g OGTT between 24–28 weeks, along with first-visit screening using random blood sugar or HbA1c to exclude overt diabetes.

All enrolled participants were evaluated in the hospital's metabolic clinic and received multidisciplinary management. Metformin therapy was initiated and titrated up to a maximum daily dose of 2 g in women who did not achieve glycemic control with dietary therapy alone. Fasting and random blood glucose trends were monitored, and insulin was added when metformin monotherapy failed to maintain target glucose levels, based on clinical judgement. Obstetric assessments, ultrasound fetal biometry, and hemodynamic parameters were routinely recorded. Maternal outcomes such as mode of delivery, induction, gestational age, and obstetric complications were documented, along with neonatal outcomes including birth weight, APGAR scores, hypoglycemia, and NICU admission.

Data were collected using a pre-designed semi-structured proforma that included demographic details, obstetric history, OGTT results, HbA1c values, and therapeutic interventions. Statistical analysis was performed using SPSS version 21 and Microsoft Excel 2007. Quantitative data were expressed as mean \pm standard deviation and compared using the Student's t-test or the Mann-Whitney U test depending on distribution characteristics. Categorical variables were analyzed using Chi-square or exact tests where applicable. A p-value <0.05 was considered statistically significant for all analyses.

RESULTS

Table 1: Predictive Role of Fasting Blood Glucose (FBS) ≥ 100 mg/dL at 24 Weeks FBS and Escalation of Therapy (Metformin “Failure”)

Treatment group	FBS <100 mg/dL	FBS ≥ 100 mg/dL	Total	Interpretation
Diet + exercise (n=18)	18 (100%)	0 (0%)	18	No high-FBS patients in diet-only group
Metformin only (n=49)	43 (87.75%)	6 (12.24%)	49	Minority required higher FBS
Metformin + insulin (n=13)	5 (38.46%)	8 (61.53%)	13	Majority had FBS ≥ 100 mg/dL

Chi-square p = 0.00007 (highly statistically significant).

FBS ≥ 100 mg/dL strongly associated with need for **insulin addition** (metformin failure).

Table 2: FBS and Neonatal Birth Weight (>3500 g)

(Groups II + III combined)

Birth weight category	FBS <100 mg/dL	FBS ≥ 100 mg/dL	Total	p-value
<3500 g (n = 48)	39 (81.25%)	9 (18.75%)	48	
≥ 3500 g (n = 14)	9 (64.28%)	5 (35.71%)	14	0.274

Higher proportion of babies ≥ 3500 g in FBS ≥ 100 mg/dL group, **but not statistically significant.**

DISCUSSION

In this prospective observational study involving 80 pregnant women with gestational diabetes mellitus (GDM), the clinical efficacy of metformin and the predictive value of fasting blood glucose (FBS) levels at 24 weeks were evaluated. The demographic characteristics of the study population were consistent with global evidence showing increased GDM risk with advancing maternal age. The mean age in our cohort was 33.6 years, with the majority falling in the 31–35-year age group, reflecting the contemporary trend of delayed childbearing. More than half of the participants were primigravidae, aligning with studies that suggest increasing GDM rates even in first pregnancies. The BMI distribution indicated that most women were in the overweight category (24.5–30 kg/m²), which is an established risk factor for GDM [8].

A significant finding was the large proportion (73/80; 91.25%) who met the diagnostic threshold based on fasting glucose alone, highlighting the importance of FBS as a sensitive early diagnostic marker. The HbA1c levels were below 6% in all women, confirming that these were true GDM cases rather than overt pre-existing diabetes.

Metformin was the most frequently used pharmacological therapy (61.25%), reflecting current clinical practice favouring metformin as a first-line agent after lifestyle modification. Only 16.25% required supplementary insulin. The comparison between the metformin-only and metformin-plus-insulin groups revealed several key differences. The mean HbA1c was significantly higher in the metformin-plus-insulin group (5.6% vs 5.426%), suggesting that subtle differences in early glycemic control influence treatment requirements. More importantly, the FBS at 24 weeks emerged as the strongest determinant of therapeutic escalation. Women requiring insulin had significantly higher FBS values (103 mg/dL vs 95.75 mg/dL, p = 0.005). This reinforces the concept that fasting hyperglycemia reflects greater hepatic insulin resistance, which may be inadequately controlled by metformin alone.

The analysis using an FBS cut-off of 100 mg/dL further strengthened this observation. More than 60% of women with FBS ≥ 100 mg/dL required insulin, compared to only 12.24% in the metformin-only group, demonstrating a highly significant association (p = 0.00007). Hence, an FBS threshold of 100 mg/dL at diagnosis may be a reliable predictor of metformin failure and could guide early therapeutic decisions.

Maternal and fetal outcomes were comparable across treatment groups. There were no significant differences in preterm delivery rates, mode of delivery, birth weight, Apgar scores, neonatal hypoglycemia, or NICU admissions. This suggests that metformin is as safe and effective as insulin in

appropriately selected women. Notably, no cases of macrosomia (>4 kg) were observed, and only a small proportion (17.5%) had birth weights >3500 g. The third-trimester abdominal circumference percentile also did not differ significantly between groups, supporting the adequacy of glycemic control with metformin in most cases [9-11].

Overall, our study highlights the strong predictive value of fasting blood glucose levels at 24 weeks in determining response to metformin. Early identification of women at risk of metformin failure can allow earlier initiation of insulin and potentially improve perinatal outcomes. Metformin remains an effective, safe, and suitable first-line therapy for a majority of GDM patients.

CONCLUSION

Metformin is effective in most GDM patients, and fasting blood glucose ≥ 100 mg/dL is a strong predictor of treatment escalation.

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