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EFFICACY OF METFORMIN IN MAINTAINING EUGLYCEMIA IN PATIENTS WITH GESTATIONAL DIABETES MELLITUS

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Abstract

Objective:

To determine the efficacy of metformin in maintaining euglycemia in patients with gestational diabetes mellitus (GDM).

Methodology:

This descriptive study was conducted at the Department of Medicine, Jinnah Postgraduate Medical Centre from 1st July 2024 to 31st December 2024. A total of 189 pregnant women aged 18–40 years diagnosed with GDM were enrolled through non-probability consecutive sampling. GDM was confirmed using a 75 g oral glucose tolerance test according to ADA criteria. Metformin was initiated at 500 mg daily and titrated up to 2500 mg as required. Fasting blood glucose was reassessed after two weeks. Euglycemia (60–110 mg/dl) was labeled as treatment efficacy. Data were analyzed using SPSS version 25.

Results:

The mean age of participants was 29.4 ± 4.8 years, and mean gestational age was 24.1 ± 5.2 weeks. Euglycemia was achieved in 163 (86.2%) patients. Stratification by age and BMI showed no statistically significant association with efficacy ($p > 0.05$).

Conclusion:

Metformin is an effective and well-tolerated option for achieving glycemic control in GDM and may be considered a suitable first-line pharmacological therapy with appropriate monitoring.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as glucose intolerance first recognized during pregnancy and represents one of the most common metabolic complications of gestation [1]. Its global prevalence has increased considerably over the past two decades due to rising maternal age, obesity, sedentary lifestyle, and changes in diagnostic criteria. The reported frequency varies widely depending on the population studied and the screening strategies employed, ranging from 5% to over 20% in certain high-risk groups [2]. In South Asian populations, the burden is particularly significant due to higher baseline insulin resistance and genetic predisposition.

Uncontrolled GDM is associated with substantial maternal, fetal, and neonatal morbidity. Maternal complications include pregnancy-induced hypertension, polyhydramnios, increased operative delivery rates, and long-term risk of developing type 2 diabetes mellitus. Fetal and neonatal complications include macrosomia, shoulder dystocia, respiratory distress syndrome,

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neonatal hypoglycemia, polycythemia, hypocalcemia, and increased risk of metabolic disorders later in life [3]. These adverse outcomes highlight the importance of achieving and maintaining optimal glycemic control during pregnancy.

Traditionally, insulin has been considered the gold standard for pharmacological management of GDM when lifestyle modifications fail to achieve glycemic targets. Although effective, insulin therapy requires injections, frequent glucose monitoring, dose titration, refrigeration, and carries the risk of hypoglycemia and weight gain, which may affect patient compliance [4]. In resource-limited settings, these challenges can compromise adherence and accessibility.

Metformin, a second-generation biguanide, has emerged as an alternative therapeutic option in GDM. It primarily acts by decreasing hepatic gluconeogenesis, improving peripheral insulin sensitivity, and enhancing glucose uptake in skeletal muscle. Additionally, metformin favorably influences lipid metabolism by reducing triglycerides and low-density lipoprotein cholesterol while modestly increasing high-density lipoprotein levels [5]. Its oral route of administration, lower cost, and better patient acceptability make it particularly attractive in developing countries.

A major concern regarding metformin use in pregnancy is its ability to cross the placenta. However, multiple studies have demonstrated that metformin does not appear to increase the risk of congenital anomalies or adverse perinatal outcomes when compared to insulin therapy [6]. Moreover, unlike sulfonylureas, metformin does not stimulate fetal pancreatic insulin secretion and therefore carries a lower risk of fetal hyperinsulinemia and neonatal hypoglycemia [7].

Clinical trials and observational studies have reported high rates of glycemic control with metformin therapy in women with GDM. Reported efficacy ranges between 80% and 95% in achieving target glycemic levels, although a subset of patients may require supplemental insulin to maintain optimal control [1,7]. Meta-analyses have further supported its comparable efficacy and safety profile relative to insulin, particularly in mild to moderate GDM [8].

Despite the growing body of international evidence, data from local populations remain limited. Differences in ethnicity, dietary patterns, socioeconomic status, and healthcare accessibility may influence therapeutic response and treatment adherence. Therefore, evaluating the efficacy of metformin in maintaining euglycemia among women with GDM in our local setting is essential to inform clinical practice and optimize management strategies.

Given the increasing prevalence of GDM and the practical advantages of metformin, there is a need to generate local evidence regarding its effectiveness in achieving glycemic control. Such data will assist obstetricians and physicians in making evidence-based decisions and provide better counseling to pregnant women diagnosed with GDM.

Objective

To determine the efficacy of metformin in maintaining euglycemia in patients with gestational diabetes mellitus.

METHODOLOGY

Study Design and Setting

This descriptive study was conducted at the Department of Medicine, Jinnah Postgraduate Medical Centre (JPMC), Karachi.

Study Duration

The study was carried out over a period of six months, from 1st July 2024 to 31st December 2024.

Sample Size and Sampling Technique

The sample size was calculated using the WHO sample size calculator, taking the anticipated efficacy of metformin in gestational diabetes mellitus as 85.7%, margin of error 5%, and confidence level 95%. The calculated sample size was 189 patients. A non-probability consecutive sampling technique was employed.

Inclusion and Exclusion Criteria

Women aged 18 to 40 years, with gestational age between 11 and 32 weeks, parity 0–4, and diagnosed with gestational diabetes mellitus as per operational definition were included in the study.

Patients with pre-gestational use of metformin, multiple pregnancies, known hypersensitivity to

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metformin, prior history of lactic acidosis, chronic kidney disease (eGFR <60 ml/min/1.73 m²), chronic liver disease (coarse liver parenchyma on ultrasound), or history of congenital anomalies in previous pregnancies were excluded.

Data Collection Procedure

After obtaining approval from the institutional research review board, patients fulfilling the inclusion criteria were enrolled from the outpatient department of Medicine, JPMC. Informed written consent was obtained from all participants after explaining the purpose, risks, and benefits of the study.

Baseline demographic and clinical data including age, gestational age, parity, residence, education, profession, and socioeconomic status were recorded. Pre-pregnancy weight and height were noted from medical records, and body mass index (BMI) was calculated using the formula: weight (kg)/height (m²). BMI was categorized as underweight (<18.5 kg/m²), normal (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), and obese (≥30 kg/m²).

Gestational diabetes mellitus was confirmed using a 75 g oral glucose tolerance test (OGTT) according to American Diabetes Association (ADA) criteria 2011. Metformin was initiated at a dose of 500 mg once daily, administered 15 minutes before breakfast. Blood glucose levels were assessed after one week. If two or more glucose readings were found deranged, the dose was increased to twice daily and subsequently titrated up to a maximum of 2500 mg per day according to glycemic response.

Liver function tests (ALT/AST) and renal function tests (serum creatinine and urea) were measured at baseline and monitored monthly to detect adverse effects. Routine antenatal care was continued for all patients. Home glucose monitoring was performed biweekly using a seven-point blood glucose profile to assess compliance.

After two weeks of treatment, patients were re-evaluated, and a repeat 75 g OGTT was performed. Achievement of fasting blood glucose between 60–110 mg/dl was labeled as euglycemia. Efficacy was defined as attainment of euglycemia after two weeks of treatment.

Data Analysis

Data were entered and analyzed using IBM SPSS version 25. Quantitative variables such as age, gestational age, BMI, and fasting blood glucose levels were expressed as mean ± standard deviation or median (IQR) after assessment of normality using the Shapiro–Wilk test. Qualitative variables such as parity, residence, education, socioeconomic status, and efficacy were presented as frequencies and percentages.

Efficacy was stratified with respect to age, gestational age, BMI, and parity to control for potential effect modifiers. Post-stratification Chi-square test or Fisher's exact test was applied where appropriate. A p-value ≤0.05 was considered statistically significant.

RESULTS

A total of 189 patients diagnosed with gestational diabetes mellitus were included in the study. The mean age of participants was 29.4 ± 4.8 years, while the mean gestational age at enrollment was 24.1 ± 5.2 weeks. The mean pre-pregnancy BMI was 27.6 ± 3.9 kg/m². Majority of women were multigravida (58.7%) and 64.0% belonged to urban areas. Detailed baseline characteristics are presented in **Table 1**.

Table 1: Baseline Characteristics of Study Participants (n = 189)

Variable	Value
Age (years), Mean ± SD	29.4 ± 4.8
Gestational Age (weeks), Mean ± SD	24.1 ± 5.2
BMI (kg/m²), Mean ± SD	27.6 ± 3.9
Primigravida	78 (41.3%)
Multigravida (Parity 1–4)	111 (58.7%)
Urban Residence	121 (64.0%)
Rural Residence	68 (36.0%)

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After two weeks of metformin therapy, 163 patients (86.2%) achieved euglycemia, whereas 26 patients (13.8%) failed to achieve glycemic control. Overall efficacy results are summarized in **Table 2**.

Table 2: Overall Efficacy of Metformin (n = 189)

Outcome	Frequency (n)	Percentage (%)
Achieved Euglycemia	163	86.2
Did Not Achieve Euglycemia	26	13.8

Stratification of efficacy with respect to age group showed comparable response across all categories. The highest efficacy was observed in women aged 26–32 years (86.8%), followed by 18–25 years (86.5%) and 33–40 years (84.8%). Chi-square test showed no statistically significant association between age and treatment efficacy ($\chi^2 = 0.12$, $p = 0.94$). These findings are presented in **Table 3**.

Table 3: Stratification of Efficacy by Age Group (n = 189)

Age Group (years)	Total (n)	Achieved Euglycemia n (%)	p-value
18–25	52	45 (86.5%)	
26–32	91	79 (86.8%)	
33–40	46	39 (84.8%)	0.94

Efficacy was further stratified according to BMI category. Women with normal BMI demonstrated higher treatment success compared to overweight and obese women. However, the association between BMI category and efficacy was not statistically significant ($\chi^2 = 3.21$, $p = 0.20$). The detailed comparison is shown in **Table 4**.

Table 4: Stratification of Efficacy by BMI Category (n = 189)

BMI Category	Total (n)	Achieved Euglycemia n (%)	p-value
Normal (18.5–24.9)	58	53 (91.4%)	
Overweight (25–29.9)	79	67 (84.8%)	
Obese (≥30)	52	43 (82.7%)	0.20

DISCUSSION

The present study demonstrated that metformin achieved euglycemia in 86.2% of patients with gestational diabetes mellitus (GDM) after two weeks of therapy. This high efficacy supports the growing body of evidence suggesting that metformin is an effective pharmacological alternative to insulin for glycemic control in GDM. The observed response rate in our study is comparable to previously reported efficacy ranging between 80% and 95% in various clinical trials and observational studies [9,10]. These findings reinforce the role of metformin as a practical and reliable therapeutic option in appropriately selected patients.

The mechanism underlying metformin's efficacy in GDM is primarily related to its ability to reduce hepatic gluconeogenesis and improve peripheral insulin sensitivity. Pregnancy is characterized by progressive insulin resistance due to placental hormones such as human placental lactogen and progesterone. By enhancing insulin-mediated glucose uptake and decreasing hepatic glucose production, metformin directly targets this pathophysiological mechanism [11]. This explains the substantial proportion of women achieving glycemic targets without the need for insulin supplementation.

Our results are consistent with randomized trials comparing metformin and insulin in GDM, which have demonstrated similar glycemic control between the two therapies [12]. Furthermore, meta-analyses have shown that metformin is associated with lower

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maternal weight gain and reduced incidence of neonatal hypoglycemia compared to insulin therapy [13]. These additional benefits may improve overall pregnancy outcomes and maternal satisfaction, particularly in settings where insulin administration poses practical challenges.

In the present study, stratification by age did not reveal a statistically significant association between maternal age and treatment efficacy. This finding suggests that metformin's glycemic response is relatively consistent across reproductive age groups. Similar observations have been reported in other studies where maternal age did not significantly influence treatment outcomes in GDM [14]. This uniformity enhances the generalizability of metformin use across a broad age spectrum.

Although higher efficacy was observed among women with normal BMI compared to overweight and obese categories, the association was not statistically significant. Previous studies have indicated that obesity may reduce the therapeutic response to metformin due to greater baseline insulin resistance [15,16]. However, the lack of statistical significance in our study suggests that BMI alone may not be a strong determinant of short-term glycemic response, especially within the two-week evaluation period used in this study.

The overall efficacy observed in our cohort is also aligned with findings from systematic reviews evaluating oral antidiabetic agents in pregnancy. These reviews concluded that metformin provides effective glycemic control with a safety profile comparable to insulin, particularly in mild to moderate GDM [17]. Importantly, long-term follow-up studies assessing offspring exposed to metformin in utero have not demonstrated significant adverse developmental outcomes, further supporting its safety profile [18].

One of the major advantages highlighted in previous literature is improved patient compliance with metformin due to its oral administration and lower cost compared to insulin [19]. In resource-limited healthcare settings, these factors significantly influence treatment adherence and accessibility. The high efficacy rate observed in this study may partly reflect better compliance and acceptability among participants.

Despite the favorable results, it is important to recognize that a subset of patients (13.8%) did not achieve adequate glycemic control and may require additional insulin therapy. This observation is consistent with previous studies reporting that 10–20% of women on metformin eventually require supplemental insulin to maintain optimal glycemia [20]. Therefore, careful monitoring remains essential to identify non-responders early and prevent adverse maternal and fetal outcomes.

Limitations

This study has several limitations. First, it was conducted at a single center, which may limit generalizability. Second, the descriptive study design without a comparison group (e.g., insulin-treated patients) restricts direct evaluation of comparative effectiveness. Third, glycemic control was assessed after a relatively short duration of two weeks, and long-term maternal and neonatal outcomes were not evaluated. Additionally, potential confounding variables such as dietary compliance and physical activity were not quantitatively assessed. Future multicenter randomized controlled trials with longer follow-up periods are recommended to further validate these findings.

CONCLUSION

Metformin demonstrated high efficacy in achieving and maintaining euglycemia among patients with gestational diabetes mellitus, with more than four-fifths of participants attaining adequate glycemic control within two weeks of therapy. The response was consistent across different age groups and showed no statistically significant association with BMI, indicating its broad applicability in routine clinical practice. Given its oral administration, favorable safety profile, cost-effectiveness, and patient acceptability, metformin can be considered a reliable first-line pharmacological option for selected women with gestational diabetes mellitus, with careful monitoring to identify those requiring additional insulin therapy.

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