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Original Research Article

Association between gestational diabetes mellitus and risk of preeclampsia: a prospective observational case-control study in a tertiary care setting in Central India

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ABSTRACT

Background: Preeclampsia (PE) is a hypertensive disorder with significant maternal and fetal morbidity, often developing after 20 weeks of gestation. Gestational diabetes mellitus (GDM) is a common metabolic complication of pregnancy that shares pathophysiological mechanisms with PE, such as endothelial dysfunction and oxidative stress. This study aimed to assess the risk and correlation of preeclampsia in women diagnosed with GDM in a tertiary care setting in central India.
Methods: A prospective, observational, case-control study was conducted over two months in the Department of Obstetrics and Gynecology. A total of 248 pregnant women were enrolled and categorized into two equal groups: GDM and control. Data were collected on glycemic profiles, blood pressure, and incidence of preeclampsia at baseline and after eight weeks. Statistical analysis included unpaired t-tests and Pearson correlation coefficients.
Results: The incidence of preeclampsia was significantly higher in the GDM group (25.79%) compared to the control group (10.4%), with an odds ratio of 2.96 and a relative risk of 2.48. A positive correlation was observed between worsening glycemic parameters and the development of preeclampsia. The GDM group also required more pharmacological interventions, including insulin and antihypertensives.
Conclusions: GDM significantly increases the risk of preeclampsia. Early screening, close monitoring, and tailored management of GDM are essential in mitigating maternal and fetal complications associated with hypertensive disorders in pregnancy.

Keywords: Gestational diabetes mellitus, Preeclampsia, Pregnancy complications, Glycemic control, Risk assessment, Antenatal care, Insulin therapy

INTRODUCTION

Preeclampsia (PE) is a serious hypertensive disorder of pregnancy, typically occurring after 20 weeks of gestation. It is characterized by new-onset hypertension—defined by the International Society for the Study of Hypertension in Pregnancy (ISSHP) as a systolic blood pressure ≥140 mmHg or diastolic ≥90 mmHg—accompanied by proteinuria or evidence of maternal organ or uteroplacental dysfunction.[1]

Hypertensive disorders affect up to 10% of pregnancies worldwide, with preeclampsia accounting for 3–5% of cases.[2] In India, the prevalence of preeclampsia is approximately 36%, while eclampsia and gestational hypertension each contribute around 4.8%.[2] Preeclampsia is associated with significant maternal and fetal complications, including placental abruption, intrauterine growth restriction (IUGR), and preterm birth. In severe cases, it may lead to fetal demise.[3]

Gestational diabetes mellitus (GDM) refers to glucose intolerance first recognized during pregnancy.[4] It complicates approximately 4% of all pregnancies globally, although prevalence may vary between 1% and 14% depending on the population and screening protocols used. Women at high risk for GDM should be screened at their initial antenatal visit; if not diagnosed early, routine screening is recommended between 24 and 28 weeks of gestation.

Pregnancy is recognized as a diabetogenic state due to progressive insulin resistance and compensatory hyperinsulinemia. This physiological alteration is largely driven by elevated levels of estrogen and cortisol, with insulin resistance typically peaking between the 26th and 33rd weeks of gestation. This underpins the rationale for conducting GDM screening during the late second trimester. Initial management focuses on lifestyle interventions, which are often sufficient to achieve glycemic control. However, pharmacologic treatment should be initiated if glycemic targets are not met with lifestyle modifications alone.[5]

There is growing evidence that gestational hypertension and GDM share overlapping pathophysiological mechanisms, including oxidative stress, vascular endothelial dysfunction, and the release of pro-inflammatory cytokines.[6] These changes not only contribute to immediate pregnancy complications but also increase the long-term risk of maternal diabetes and cardiovascular disease.[7,8] Research has shown that women with gestational hypertension demonstrate reduced glucose tolerance, and several cohort studies have identified GDM as an independent risk factor for the development of PE.[9]

The maternal complications of GDM include an increased risk of preeclampsia, polyhydramnios, and cesarean delivery. Additionally, a prospective study has demonstrated a significant association between worsening glucose tolerance and adverse maternal outcomes. Fetal complications related to GDM include macrosomia, shoulder dystocia, neonatal jaundice, polycythemia, hypocalcemia, and increased perinatal mortality.[10]

Given these associations, there is a need for more region-specific data to better understand the interplay between GDM and PE, especially in the Indian context. To address this gap, we designed a prospective observational study to evaluate maternal and fetal outcomes among women diagnosed with GDM.

Aims and objectives

Aims and objectives of the study were to assess the risk of preeclampsia in women diagnosed with GDM, to assess the correlation between glucose metabolism and preeclampsia, to assess the incidence of preeclampsia caused by abnormal glucose metabolism during pregnancy, and to compare the incidence of preeclampsia between the different treatment modalities.

METHODS

Study design

It was a prospective, observational and a case control study.

Study site

The study was conducted in the department of obstetrics and gynecology in a tertiary care hospital in central India.

Study period

The study was conducted over a period of 2 months, from 16 October 2023 till 15 December 2023.

Inclusion criteria

Pregnant women diagnosed with GDM according to ‘Carpenter and Coustan’ criteria and preeclampsia according to the international society for the study of hypertension in pregnancy who will be undergoing antenatal examination at 24-28 weeks of gestation; pregnant women with no history of hypertension and diabetes before pregnancy who will be undergoing the antenatal examination; pregnant females with single foetus; and those who were willing to sign informed consent form were included.

Exclusion criteria

Pregnant women with history of mental illness, cardiovascular diseases, chronic diseases such as diabetes, nephropathy, coronary heart disease before pregnancy, malignancy; individuals who have multiple foetus, multiple gestation, certain risk to develop preeclampsia i.e. chronic hypertension, overt diabetes, renal or collagen vascular disease, hyperthyroidism, and smoking; and patients not willing to give informed consent were excluded.

Sample size

The total sample size was calculated to be 248 where an estimated prevalence of preeclampsia in normal pregnant females was found to be 1.5% (0.015) based on a study (3) and an estimated prevalence rate of preeclampsia in pregnant females with GDM was found to be 9.6% (0.096) based on a study pattern.[11]

Flow of study

The study was conducted after the approval of institutional ethics committee (IEC) (IGGMC/pharma/IEC/1861-62 /2023). Patients were screened by the physician and the

principal investigator in OBGY out- patient department in a tertiary care hospital in central India. The pregnant females eligible according to the inclusion and exclusion criteria after screening were informed about the study and after obtaining written informed consent were enrolled in the study. Study participants were allocated into two groups- GDM group (pregnant females diagnosed with GDM) and control group (pregnant females without GDM) in the ratio of 1:1.

The following data was collected in CRF history

Maternal age, weight, parity, oral glucose tolerance test values, gestational age at GDM diagnosis, treatment modality, glycemic profiles after diet control and/or insulin treatment, the presence or absence of preeclampsia and blood pressures. All the parameters were recorded at baseline and after 8 weeks. The results were tabulated for data analysis.

Statistical analysis

Descriptive analysis was carried out using mean and standard deviation with range for continuous variables and in terms of percentages for discontinuous variables. Unpaired t-test was used for comparison and p value was calculated. P value less than 0.05 was considered significant. Pearson formula was used to find out the correlation coefficient (R) wherever necessary.

RESULTS

A total of 248 patients were included in the study after their screening as a part of their antenatal examination by the treating physician. The mean age in years of the control group was 27.47±5.35 whereas in GDM group it was 28.04±5.16. The mean weight (in kgs) was recorded as 57.5±9.65 in control group and 59.13±9.93 in GDM group. (Figure 1).

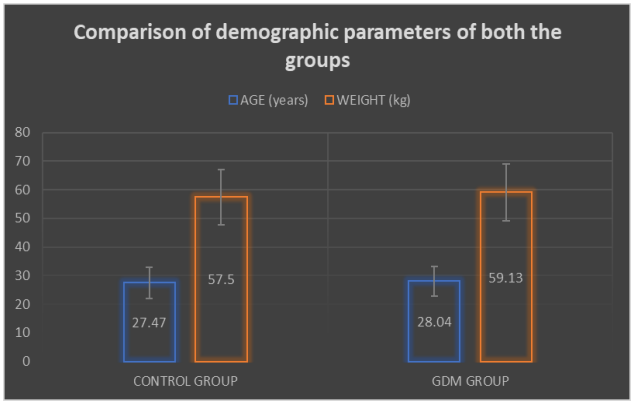

Figure 1: Comparison of demographic parameters of both the groups.

We have observed that the mean baseline glycemic profiles of GDM group was found to be considerably higher than the control group. Although no statistical significance was found (p>0.05).

After a period of 8 weeks, the mean glycemic profiles are higher in both the groups with the exception of random blood sugars. While the values of GDM group still being higher than the control group without showing any statistical significance (p>0.05).

A rise was observed in systolic as well as diastolic blood pressures in both the groups on both instances (baseline and after 8 weeks) without showing any statistical significance (p>0.05).

Relative risk (RR) was 2.48, and baseline incidence (I_1) was 0.1040=10.4%.

Incidence of preeclampsia in pregnant women with GDM (I_2) was 0.2579=25.79%.

Pregnant women with GDM have 2.48 times higher risk of developing preeclampsia compared to normal pregnant women. The incidence of preeclampsia in the GDM group is 25.79%, whereas in the control group, it is 10.4%. The odds ratio of 2.96 reflects a strong association between GDM and the risk of preeclampsia, but the relative risk of 2.48 gives a better understanding of the actual increased risk in the population (Table 1).

Table 1: Incidence of preeclampsia in both the groups.

Variables	Preecla-mpsia present	Preeclamp-sia not present	Odds ratio
GDM group (n=124)	32	92	2.96
Control group (n=124)	13	111	

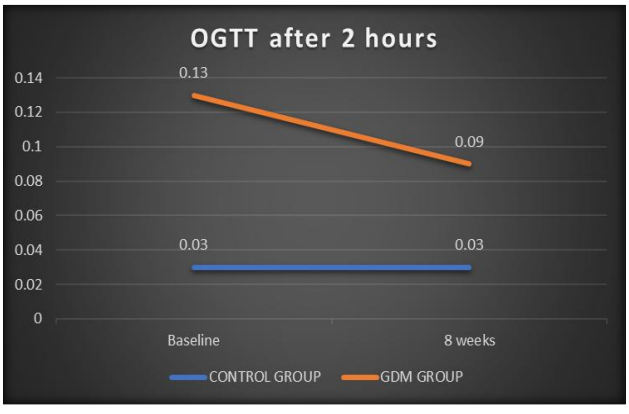

Figure 2: Comparison of OGTT after 2 hours in both groups.

There was a positive correlation seen with sugar levels and preeclampsia (Table 3).

Table 2: Comprehensive overview of medications commonly prescribed within our hospital setting.

Drugs	Control group	GDM group
Tab. Labetalol 100 mg	10	25
Inj. Insulin IM	0	47
Tab. Nicardipine 10 mg	3	8
Inj. Lasix 10 mg	5	1
Inj. $MgSO_4$ IM	2	0
Tab. Bisoprolol 10 mg	1	0
Tab. Ecosprin 75/150 mg	1	1

Table 3: Correlation coefficient (R) using Pearson formula.

Variables	Control group		GDM group	
	Baseline	8 weeks	Baseline	8 weeks
OGTT (1 hour)	0.04	0.05	0.35	0.06
OGTT (2 hour)	0.03	0.03	0.138	0.09
FBS	0.13	0.12	0.07	0.1
PPBS	0.11	0.15	0.06	0.04
RBS	0.01	0.02	0.128	0.03

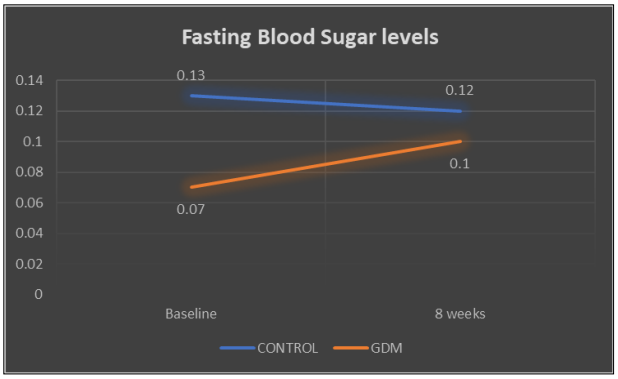

Figure 3: Comparison of fasting blood sugar levels in both groups.

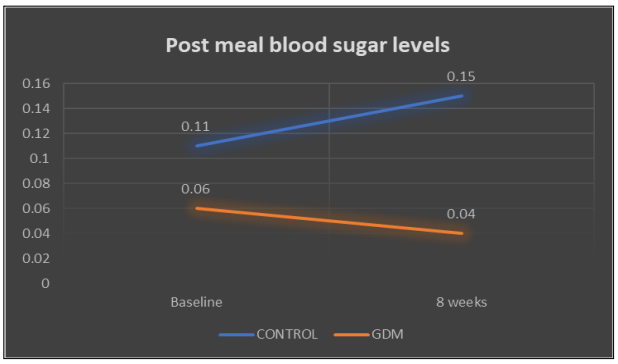

Figure 4: Comparison of post-meal blood sugar levels in both groups.

DISCUSSION

This study aimed to assess the risk of preeclampsia (PE) in pregnant women diagnosed with GDM, examine correlation between glucose metabolism and preeclampsia, and evaluate treatment modalities. The findings present important insights into maternal health during pregnancy, particularly in relation to the increasing prevalence of GDM and associated hypertensive disorders.

The results in Table 1 indicate that pregnant women with GDM have a significantly higher incidence of preeclampsia (25.79%) compared to those without GDM (10.4%). This correlation is underscored by an odds ratio of 2.96 and a relative risk of 2.48, emphasizing the elevated risk associated with GDM. Yang et al conducted a study on the relationship between GDM and preeclampsia, finding a strong correlation between elevated glucose levels and the occurrence of PE.[9] They observed that women with GDM had a higher risk of developing PE compared to those without GDM, reinforcing the findings of the current study. Zhou et al reported that blood glucose levels significantly correlate with hypertensive disorders during pregnancy, which aligns with the current findings of increased preeclampsia incidence in women diagnosed with GDM.[12] However, Gathiram et al argued that while there is a recognized association between GDM and preeclampsia, the risk factors can significantly vary based on population demographics and underlying health conditions, suggesting that the correlation may not hold consistently across different populations.[13]

Table 2 presents the different classes of medications prescribed to pregnant women in the study, including those in both the GDM and control groups. The medications highlighted include: Labetalol, Insulin, Nicardipine, Lasix, Magnesium sulfate ($MgSO_4$), Bisoprolol and Ecosprin. Labetalol was prescribed to 25 women in the GDM group compared to just 10 in the control group, indicating a significant need for intervention in the GDM cohort. This aligns with clinical guidelines that recommend aggressive management of elevated blood pressure in pregnant women, particularly those with comorbidities such as GDM.[5] McElwain et al highlighted the importance of blood pressure management in women with GDM, noting that effective antihypertensive therapy, including Labetalol, can improve outcomes for both mother and child by reducing the risk of preeclampsia and other complications related to elevated blood pressure.[14]

Insulin was exclusively given to the GDM group, with 47 patients requiring this treatment for glycemic control. This underscores the necessity of pharmacological intervention to manage GDM effectively, especially since uncontrolled diabetes can lead to adverse maternal outcomes such as hypertensive disorders and fetal complications (American Diabetes Association, 2018).[5] Gui et al performed a meta-analysis comparing metformin and insulin for the management of GDM and noted that while insulin is often

the first-line treatment, metformin offers an advantage in certain cases, pointing to the necessity of individualized treatment approaches based on patient needs.[15] Buhary et al emphasized the role of early glycemic control in improving maternal and fetal outcomes in pregnancies complicated by diabetes, which supports the findings regarding the exclusive need for insulin therapy in the GDM group.[16]

Nicardipine and Lasix showed minimal usage across both groups, which might reflect careful consideration in prescribing these medications due to potential side effects in pregnancy.

The absence of magnesium sulphate in the GDM group and minimal prescriptions in the control group suggests that severe cases of hypertension requiring this therapy might have been rare in the study population.

The differences in medication usage between the GDM and control groups reflect the heightened risk that GDM poses for developing complications like preeclampsia. This calls for tailored management protocols for women with GDM, integrating dietary interventions, monitoring, and pharmacological treatments as needed. The findings also highlight the importance of early identification and intervention to mitigate risks associated with GDM and hypertension.

The results in Table 3 indicate a positive correlation between sugar levels and preeclampsia in the GDM group, suggesting that as glycemic control worsens, the likelihood of developing preeclampsia increases. Phoswa et al reported similar outcomes, linking oxidative stress to both GDM and preeclampsia, reinforcing the hypothesis that poor glucose management exacerbates hypertensive disorders during pregnancy.[6] McElwain et al emphasized the role of endothelial dysfunction in both conditions, reaffirming the findings of this study that metabolic disturbances significantly contribute to the risk of preeclampsia in GDM patients.[14] Barden et al found divergent results, wherein they noted that while glucose intolerance is a factor in preeclampsia, other variables such as obesity and genetic factors may play a more significant role in certain demographics, prompting a need for more nuanced understanding of risk factors across populations.[17]

Figures 2-4 illustrate the glycemic control measures between the two groups. Both groups demonstrate increased blood pressure and glycemic levels over the study period, indicating a lack of significant improvement in management strategies. Malik et al highlighted that glucose intolerance and preeclampsia often coexist, and commonly used treatment strategies may need reconsideration to better manage these conditions in tandem.[2] Pankiewicz et al focused on the coexistence of GDM and preeclampsia, suggesting that effective management requires careful monitoring and interventions tailored to improve both maternal and fetal outcomes.[18] Fang et al presented a study suggesting different management outcomes based on the timing of intervention, arguing that some early-phase interventions may lead to better outcomes for both GDM and preeclampsia patients compared to traditional late-stage management, prompting a reevaluation of current practices.[19]

The evidence presented in this study supports the notion that both conditions are interrelated and necessitate a multifaceted approach to care during pregnancy, while also calling for further studies to disentangle the complexities of their association across diverse populations.

CONCLUSION

The study's findings underscore a significant relationship between GDM and preeclampsia, emphasizing the need for vigilant screening and management strategies. The increased incidence of preeclampsia among GDM patients warrants further investigation into tailored preventative measures and treatment modalities to mitigate risks associated with these maternal conditions.

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