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# Maternal Obesity, Maternal Gestational Diabetes Mellitus, and Maternal and Neonatal Outcomes

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## Abstract

We aimed to investigate the co-morbid effects of maternal obesity, Gestational Diabetes Mellitus (GDM), and GDM treatment options on maternal and neonatal outcomes in an inner-city population. This is a retrospective chart review study of singleton mothers with new diagnosis of GDM and their infants during a 3-year period. During the study period, 356 women ages 13-48 years with GDM gave birth to 180 males and 175 females. Majority of mothers were African American (50.8%) and had Medicaid insurance (75.8%). Obese mothers constituted 48.3% of the study population, had a higher prevalence of pregnancy induced hypertension/preeclampsia, more commonly were managed with medication and delivered by C-section than non-obese mothers. Infants of obese GDM mothers had significantly higher mean birth weight, lower mean blood glucose, and were less at risk for Small for Gestational Age (SGA). In obese mothers, heaviest mothers had infants with higher bilirubin levels than less heavy mothers. We also observed a high rate of feeding difficulty in infants of GDM mothers (12.4%). Our study emphasizes the burden of maternal obesity as a major risk factor for both maternal and neonatal poor outcomes in the context of GDM and calls for further prospective and interventional research.

**Keywords:** Gestational diabetes mellitus; Maternal obesity; Pregnancy outcome; Infants of mothers with gestational diabetes

**Abbreviations:** AFI: Amniotic Fluid Index; AGA: Appropriate for Gestational Age; BMI: Body Mass Index; CDC: Center for Disease Control and Prevention; DVT: Deep Venus rombosis; EGA: Estimated Gestational Age; GDM: Gestational Diabetes Mellitus; IRB: Institutional Review Board; LGA: Large for Gestational Age; NICU: Neonatal Intensive Care Unit; OGTT: Oral Glucose Tolerance Test; PIH: Pregnancy Induced Hypertension; SGA: Small for Gestational Age

## Introduction

Gestational Diabetes Mellitus (GDM), de ned as impaired glucose tolerance of variable severity with rst onset during pregnancy, is one of the most common medical complications of pregnancy. It is estimated that 1-14% of pregnancies are complicated by GDM, with a prevalence as high as 9.2% based on a report by Centers for Disease Control and Prevention (CDC) [1,2]. Epidemiologic studies have found a signi cant race predilection with an increased incidence in African American, Hispanic, Native American, and Asian/Paci c Islanders as compared to Non-Hispanic White populations [3]. Pregnancies complicated by GDM have well-known maternal complications including increased risk of shoulder dystocia, preeclampsia, polyhydramnios, fetal macrosomia and primary cesarean section [1,3]. Signi cant fetal complications include increased risk of being Large for Gestational Age (LGA), Erb's palsy, neonatal hypoglycemia, and neonatal hypocalcemia [1,4].

Obesity, de ned as an adult with Body Mass Index (BMI) greater than 30, is present in over one third (35.8%) of all United States (US) women [5]. Recent data implies that more than half of women during the pregnancy period are overweight/obese [5,6]. Similar to the prevalence of GDM, certain ethnic groups like non-Hispanic Blacks and Hispanics, have higher age-adjusted rates of obesity [7]. Obesity in pregnancy has been associated with multiple negative maternal health outcomes including gestational hypertension, preeclampsia, GDM, thrombosis, preterm delivery, cesarean section with increased postoperative complications i.e. wound infection/ Deep Venous rombosis(DVT), and postpartum endometritis as wel1 as negative neonatal outcomes including congenital anomalies, macrosomia, and birth injury [1,4,8-13].

A body of literature has shown that GDM and maternal obesity are independently associated with adverse maternal and neonatal outcomes. Both conditions share common metabolic characteristics including increased insulin resistance, hyperglycemia and hyperinsulinemia. e landmark observational study of hyperglycemia and adverse pregnancy outcome (HAPO) demonstrated increased odds of adverse pregnancy outcomes with GDM and obesity combined than either risk factor alone

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feeding di culties, admission to Neonatal Intensive Care Unit(NICU), as well as laboratory variables such as bilirubin, hemoglobin, calcium, and glucose levels.

## De nitions

**Maternal variables:** Obesity: We calculated pre-pregnancy Body Mass Index (BMI: weight in kilograms divided by the square of the height in meters). We de ned obesity as pre-pregnancy BMI of equal to or greater than 30, while a BMI of less than 30 was considered as non-obese.

**Gestational diabetes mellitus:** In our center, we followed a 2-step approach for the diagnosis of GDM. ose with a level equal to or greater than 130 mg/dl in a one-hour screening Oral Glucose Tolerance Test (OGTT) at 24 to 28 weeks of gestation underwent a three-hour OGTT. GDM was de ned as any two abnormal levels (higher than 95, 180, 155, and 140 mg/dL at fasting, one hour, two hours, and three hours, consecutively).

**Pregnancy induced hypertension (PIH):** Gestational hypertension was de ned as any systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg in a previously normotensive pregnant woman at ≥20 weeks of gestation without any sign of proteinuria, edema, or new signs of end-organ dysfunction. Presence of proteinuria and or edema was an indication for preeclampsia, while eclampsia was de ned as signs of preeclampsia plus seizure.

**Chorioamnionitis:** Bacterial infection of the fetal amnion and chorion membranes de ned by the presence of maternal fever (intrapartum temperature ≥100.4°F or ≥38°C), signi cant maternal tachycardia (>120 beats/min), fetal tachycardia (>160-180 beats/min), purulent or foul-smelling amniotic uid or vaginal discharge, uterine tenderness, and maternal leukocytosis (total blood leukocyte count >14,000-18,000 cells/µL).

**Oligohydramnios:** Amniotic uid volume less than expected for gestational age was detected by ultrasound examination that shows an Amniotic Fluid Index (AFI) of less than 5 cm or less than the h percentile for gestational age.

**Polyhydramnios:** Presence of excess amniotic uid in the uterus by ultrasound ndings of deepest vertical amniotic pool more than 8 cm or an AFI more than 95th percentile for the corresponding gestational age.

### Infantile variables

**Fetal Size:** An infant was considered SGA (Small for Gestational Age) if the birth weight was less than 10th percentile for gestational age; LGA (Large for Gestational Age) if the birth weight was more than 90th percentile for gestational age; and birth weight between 10th and 90th percentile for gestational age was considered AGA (Appropriate for Gestational Age).

**Fetal Age:** Infant born prior to 37 weeks of gestation, between 37 to 42 weeks of gestation, and a er 42 weeks of gestation were considered preterm, term, and post-term, respectively.

**E clusion Criteria:** Mothers with a history of pre-gestational diabetes (Type 1 or 2 Diabetes Mellitus) and those with a history of GDM in previous pregnancies were excluded from the study. In addition, we excluded those with twin and /or multiple fetal gestation and infants known to have fetal anomalies.

### Statistics

Descriptive data, Student's t-test and Analysis of variance (ANOVA) were used to determine di erences between two or multiple groups of subjects. We used Chi-square and Fisher's Exact test to assess the di erences between categorical variables. Pearson or Spearman correlation coe cients were used to assess the relationship between clinical, demographic, anthropometric, and laboratory parameters of interest. Whenever appropriate, Bonferroni correction was applied and E ect size was calculated. Descriptive data was expressed as mean SEM and statistical signi cance was inferred with a P value of less than 0.05.

## Results

During the study period 356 women ages 13 to 48 years (mean 29.99 ± 0.33 yrs) with the diagnosis of GDM gave birth to 180 males and 175 female infants. As shown in Table 1, 48.3% of participants were obese (n=172, mean BMI of 36.49 ± 0.51 kg/m2), while non-obese mothers constituted 51.7% of mothers (n=184, mean BMI of 25.19 ± 0.27 kg/m2). e majority of mothers had Medicaid insurance (75.8%), was African American (50.8%), and gave birth by SVD (55.1%). Preeclampsia and gestational hypertension were the most common observed maternal complication of GDM in this study group (17.7% and 18.3%, respectively). We did not observe any di erence between obese and non-obese mothers in regard to their age, insurance type, and occurrence of oligo/hydramnios, but maternal obesity was more prevalent in African American females with GDM. Obese mothers with GDM were more commonly managed with medication than diet-only, had a higher prevalence of PIH, and more commonly gave birth by C-section than non-obese mothers with GDM. Conversely, we observed more chorioamnionitis in non-obese mothers than obese mothers with GDM (Table 1).

According to our nding in Table 2, majority of children were born AGA and at term but we observed a high rate of LGA (23.6%), pre-term delivery (16.6%) , NICU admission (21.9%), malformation/anomaly(16.6%), respiratory distress(13.2%), and feeding di culty (12.4%) in infants of mothers with GDM. Children of obese GDM mothers had higher mean birth weight and lower mean blood glucose levels and were less likely to be SGA when compared to infants of non-obese mothers. Although, obese mothers with GDM commonly gave birth to LGA infants, the nding did not reach statistical signi cance (Table 2).

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|---|---|---|---|---|
| Respiratory distress | 47 (13.2) | 24 (14) | 23 (12.5) | NS |
| Sepsis | 20 (5.6) | 6 (3.5) | 14 (7.6) | NS |
| Feeding Difficulty | 44 (12.4) | 17 (9.9) | 27 (14.7) | NS |
| Mortality | 2 (0.6) | 1 (0.6) | 1 (0.5) | NS |
| mean ± SEM; n: number (percent); *Statistically significant between group | | | | |

**Table 2:**

| | | | |
|---|---|---|---|
| Diet only | 6 | 7 | NS |
| Insulin | 1 | 0 | NS |
| Metformin | 0 | 0 | - |
| Glyburide | 2 | 4 | NS |
| Insulin+Glyburide | 0 | 0 | - |
| Preeclampsia | n=38 | n=25 | |
| Diet only | 24 | 21 | NS |
| Insulin | 3 | 0 | NS |
| Metformin | 0 | 0 | - |
| Glyburide | 11 | 4 | NS |
| Insulin+Glyburide | 0 | 0 | - |
| Gestational Hypertension | n=40 | n=25 | |
| Diet only | 23 | 17 | 0.05 |
| Insulin | 4 | 1 | NS |
| Metformin | 1 | 0 | NS |
| Glyburide | 12 | 7 | NS |
| Insulin+Glyburide | 0 | 0 | - |
| Chorioamnionitis | n=2 | n=10 | |
| Diet only | 2 | 10 | NS |
| Insulin | 0 | 0 | - |
| Metformin | 0 | 0 | - |
| Glyburide | 0 | 0 | - |
| Insulin+Glyburide | 0 | 0 | - |
| mean ± SEM (n); n: number; *Statistically significant between group | | | |

**Table 3:** Maternal variables by maternal obesity status divided by GDM treatment group.

| Variables | Obese Mothers | Non-obese Mothers | p-value |
|---|---|---|---|
| Gestational Week | mean ± SEM (n) | mean ± SEM (n) | |
| Diet only | 38.02 ± 0.19 (108) | | |
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**Citation:**

| | | | |
|---|---|---|---|
| | Term | 2 | 0 |
| Metformin | Pre-term | 0 | 0 |
| | Post-term | 0 | 0 |
| | Term | 41 | 33 |
| Glyburide | Pre-term | 6 | 1 |

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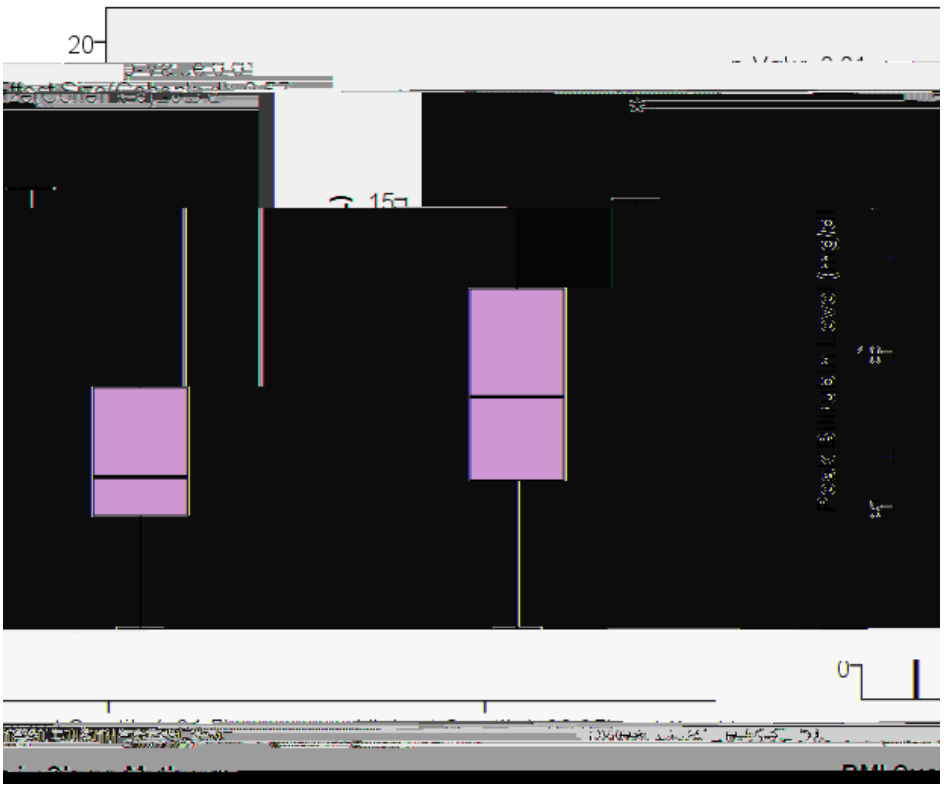


**Figure 1:** Comparing mean peak bilirubin level by highest and lowest BMI quartiles in obese mothers.

elevated blood glucose levels [25-27].

Similar to previously published data, we found an increased prevalence of PIH (gestational hypertension17.7% and preeclampsia 18.3%) in about one third of mothers with Gestational diabetes. Although, the pathophysiology of hypertension in GDM is not clear but glucose intolerance and insulin resistance may be responsible [28-30]. We also showed an increased risk of PIH in obese versus non-obese GDM mothers while those women managed by diet-only were more likely to have gestational hypertension. Previous researchers have consistently shown similar ndings [16,25-32]. Similar ndings apply to increased prevalence of C-section in obese versus non-obese GDM mothers (50.6% vs.37.5%). However, the nding of an increased rate of chorioamnionitis in non-obese mothers has not been previously described. It may be explained by chance or attributed to the small number of patients with the nding(12 patients). In our study, similar to the study by Joy et al, obese mothers who required management by insulin were older than non-obese mothers [16].

Neonatal outcome of all infants in the study showed high risks for being LGA, born pre-term, NICU admission, malformation/anomaly, respiratory distress, and feeding di culty. Association between neonatal birth weight and maternal gestational diabetes is a well-studied topic and recently a meta-analysis shows that GDM can be an independent factor for increased neonatal birth weight [33]. Similar to our ndings, Watson et al. showed 29% NICU admission, 47% preterm delivery, and 38% respiratory distress in infants of mothers with GDM [34]. In a prospective study, Farrell et al. reported a frequency of congenital anomalies in 1.4% of the o spring of mothers with GDM [35]. Nevertheless, our observation of high rate of feeding di culty in o spring of GDM mothers (12.4%) has not been previously described. We also observed higher mean birth weight, and lower mean blood glucose levels in infants of obese compared to non-obese mothers. Similar ndings have been previously described [14,16,26,27]. Additionally, we found fewer SGA infants in obese mothers and, similar to our ndings, Avci et al. showed a higher rate of low birth weight infants in mothers with lower BMI [36]. We also found that infants had lower mean blood glucose levels and were more likely to be LGA and less likely to be SGA if they were born to obese versus non-obese mothers in the diet – only treatment group.

Similar to other researchers, we showed a weak association between maternal BMI and peak bilirubin level in infants [16,27,37,38]. Accordingly, in infants of highly obese mothers, the mean bilirubin level was higher than in infants of less obese mothers. ese ndings further demonstrate the association between maternal obesity and neonatal hyperbilirubinemia.

e fact that strati cation of our study population by obesity status showed similar maternal and neonatal outcomes in di erent GDM treatment groups implies similar outcomes despite di ering GDM treatment modalities including oral hypoglycemic agents. ese ndings further suggest that obesity is the main factor that leads to both maternal and neonatal complication.

## Limitations

Our study has several limitations. Like any other observational retrospective study, results of the current study do not imply any causal relationship. Our sample size is small and from a single center and the

majority of our subjects were of African-American or Hispanic descent; therefore, our ndings may not be applicable to other populations. We

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