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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 Thrombosis; 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), defined as impaired glucose tolerance of variable severity with first 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 significant race predilection with an increased incidence in African American, Hispanic, Native American, and Asian/Pacific 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]. Significant fetal complications include increased risk of being Large for Gestational Age (LGA), Erb's palsy, neonatal hypoglycemia, and neonatal hypocalcemia [1,4].

Obesity, defined 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 Thrombosis(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. The 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 [14]. However, there have been conflicting literature reports regarding the synergistic effect of GDM and maternal obesity on negative feto-maternal and pregnancy outcomes [15-17].

Objectives and Methods

The objectives of our study were to investigate the comorbid effects of maternal obesity and GDM on maternal and neonatal outcomes in an inner city population. In addition, we intended to compare the different modes of treatment for GDM. The study protocol was designed and subsequently approved by the Albert Einstein Medical Center Institutional Review Board (IRB). This was a retrospective chart review study; singleton mothers with a new diagnosis of GDM and their infants born at Einstein Medical Center, Philadelphia, during a 3 year period (from January 2010 through December 2012) were included in the study. Maternal parameters included epidemiological and anthropometric variables, Estimated Gestational Age (EGA) at the time of delivery, mode of delivery, type of treatment for GDM (diet, insulin, and medications), complications of pregnancy, and other maternal comorbidities. Neonatal variables included birth weight, fetal size, fetal age, and complications of pregnancy like shoulder dystocia, respiratory distress, congenital anomalies/malformations, diagnosis of sepsis,

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

Definitions

Maternal variables: Obesity: We calculated pre-pregnancy Body Mass Index (BMI: weight in kilograms divided by the square of the height in meters). We defined 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. Those 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 defined 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 defined 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 defined as signs of preeclampsia plus seizure.

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

Oligohydramnios: Amniotic fluid 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 fifth percentile for gestational age.

Polyhydramnios: Presence of excess amniotic fluid in the uterus by ultrasound findings 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 after 42 weeks of gestation were considered preterm, term, and post-term, respectively.

Exclusion 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 differences between two or multiple groups of subjects. We used Chi-square and Fisher's Exact test to assess the differences between categorical variables. Pearson or Spearman correlation coefficients were used to assess the relationship between clinical, demographic, anthropometric, and laboratory parameters of interest. Whenever appropriate, Bonferroni correction was applied and Effect size was calculated. Descriptive data was expressed as mean SEM and statistical significance 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). The 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 difference 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 finding 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 difficulty (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 finding did not reach statistical significance (Table 2).

We stratified maternal variables by GDM treatment groups and observed that obese mothers who were on insulin were older, while those who were on glyburide were more commonly African American when compared to non-obese women. In addition, mothers managed by diet-only had higher risk for gestational hypertension (Table 3). We also stratified the infantile variables by GDM treatment groups and observed that infants of obese mothers on diet-only treatment had significantly lower mean blood glucose levels than infants of non-obese mothers, were more at risk for LGA and less for SGA (p=0.04). There was no difference in other neonatal outcomes by different types of GDM treatment (Table 4).

Next, we stratified both maternal and infantile variables by maternal obesity status and compared different GDM treatments groups in each strata (obese and non-obese). There was no significant difference in maternal and infantile variables (data not shown). In obese mothers, maternal BMI was weakly associated with peak bilirubin level; as maternal BMI increased, peak infantile bilirubin level increased (r=0.22 p=0.004, data not shown). Controlling for different modes of GDM treatment did not show any significance (data not shown). Finally, in obese group, we divided their BMI by quartile and compared different maternal and infantile variables between lower and higher BMI quartiles. Only mean bilirubin level was significantly higher in severely

Variables		Total n=356	Obese Mothers n=172 (48.3)	Non-obese Mothers n=184 (51.7)	p-value
Age (year)		29.99 ± 0.33	30.06 ± 0.48	29.94 ± 0.47	NS
Pre-Pregnancy Weight (kg)		81.02 ± 1.31	97.32 ± 1.77	65.82 ± 1.00	0
Pre-Pregnancy Height (cm)		160.71 ± 0.63	160.73 ± 0.98	160.69 ± 0.81	NS
Pre-Pregnancy BMI		30.68 ± 0.41	36.49 ± 0.51	25.19 ± 0.27	0
Insurance	Medicaid	270 (75.8)	131 (76.2)	139 (75.5)	
	Medicare	7 (2)	5 (2.9)	2 (1.1)	NS
	Private	61 (17.1)	32 (18.6)	29 (15.8)	
	Other/Unknown	18 (5.1)	4 (2.3)*	14 (7.6)	
Race	African American	181 (50.8)	99 (57.6)*	82 (44.6)	0
	Asian	34 (9.6)	7 (4.1)*	27 (14.7)	
	Caucasian	42 (11.8)	24 (14)	18 (9.8)	
	Hispanic	63 (17.7)	33 (19.2)	30 (16.3)	
	Mixed	2 (0.86)	1 (0.6)	1 (0.5)	
	Other/Unknown	34 (9.6)	8 (4.7)*	26 (14.1)	
Type of Delivery	SVD	196 (55.1)	84 (48.8)*	112 (60.9)	0.03
	CS	156 (43.8)	87 (50.6)*	69 (37.5)	
	Vacuum	3 (0.8)	1 (0.6)	2 (1.1)	
	Forceps	1 (0.3)	0	1 (0.5)	
Oligohydramnios		20 (5.6)	12 (7)	8 (4.3)	NS
Polyhydramnios		20 (5.6)	9 (5.2)	11 (6)	NS
Preeclampsia		63 (17.7)	38 (22.1)	25 (13.6)	0.036
Gestational Hypertension		65 (18.3)	40 (23.3)	25 (13.6)	0.018
Chorioamnionitis		12 (3.4)	2 (1.2)	10 (5.4)	0.033
GDM Treatment	Diet Only	251 (70.5)	109 (63.4)*	142 (77.2)	0.017
	Insulin	20 (5.6)	13 (13)	7 (3.8)	
	Metformin	2 (0.6)	2 (1.2)	0	
	Glyburide	82 (23)	47 (27.3)	35 (19)	
	Insulin+Glyburide	1 (0.3)	1 (0.6)	0	

Mean ± SEM; n: number (percent);*Statistically significant between groups.

Table 1: Maternal variables by maternal obesity status.

Variables		Total (n=356)	Obese Mothers (n=172)	Non-Obese Mothers (n=184)	p-value
Gestational Week		38.02 ± 0.10	37.96 ± 0.15	38.08 ± 0.15	NS
Birth Weight (gr)		3320 ± 0.03	3393.50 ± 46.81	3251.46 ± 47.81	0.035
Birth Length (cm)		50.09 ± 0.17	50.32 ± 0.23	49.87 ± 0.25	NS
Head Circumference (cm)		33.87 ± 0.11	34.05 ± 0.16	33.70 ± 0.14	NS
Mean Blood Glucose (mg/dL)		70.03 ± 0.66	68.21 ± 0.94	71.71 ± 0.92	0.008
Peak Bilirubin (mg/dL)		7.46 ± 0.18	7.64 ± 0.26	7.29 ± 0.25	NS
Hemoglobin (mg/dL)		17.08 ± 0.21	17.01 ± 0.29	17.14 ± 0.30	NS
Hematocrit (%)		50.22 ± 0.68	50.02 ± 0.89	50.38 ± 1.00	Ns
calcium (mg/dL)		8.87 ± 0.13	8.85 ± 0.19	8.88 ± 0.18	NS
Gender	Female	175 (49.3)	83 (48.3)	92 (50)	NS
	Male	180 (50.7)	88 (51.2)	92 (50)	
Fetal Size	AGA	263 (73.9)	122 (70.9)	141 (76.6)	0.026
	SGA	8 (2.2)	1 (0.6)*	7 (3.8)	
	LGA	84 (23.6)	48 (27.9)	36 (19.6)	
Fetal Age	Term	291 (81.7)	139 (80.8)	152 (82.6)	NS
	Pre-term	59 (16.6)	29 (16.9)	30 (16.3)	
	Post-term	4 (1.1)	3 (1.7)	1 (0.5)	
NICU Admission		78 (21.9)	38 (22.1)	40 (21.7)	NS
Intubation		9 (2.5)	6 (3.5)	3 (1.6)	NS
Phototherapy		24 (6.7)	10 (5.8)	14 (7.6)	NS
Shoulder Dystocia		7 (2)	4 (2.3)	3 (1.6)	NS
Birth Trauma		14 (3.9)	6 (3.5)	8 (4.3)	NS
Malformation/Anomaly		59 (16.6)	23 (13.4)	36 (19.6)	NS

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: Infants characteristics by maternal obesity status.

Maternal Variables		Obese Mothers	Non-obese Mothers	p-value
Age (year)		mean ± SEM (n)	mean ± SEM (n)	
Diet only		29.98 ± 0.64 (109)	29.65 ± 0.53 (142)	NS
Insulin		32.46 ± 1.07 (13)	25.86 ± 2.12 (17)	0.006
Metformin		25 ± 1 (2)		-
Glyburide		29.75 ± 0.87 (47)	31.91 ± 1.07 (35)	NS
Insulin+Glyburide		33 (1)		-
Pre-Pregnancy Weight (kg)				
Diet only		97.51 ± 2.25 (106)	65.94 ± 1.20 (138)	0
Insulin		95.10 ± 4.65 (12)	66.64 ± 3.22 (7)	0
Metformin		105.7 ± 10.2 (2)		-
Glyburide		96.05 ± 3.49 (46)	65.17 ± 1.87 (34)	0
Insulin+Glyburide		145 (1)		-
Pre-Pregnancy Height (cm)				
Diet only		159.61 ± 1.42 (106)	160.94 ± 1.01 (140)	NS
Insulin		164.69 ± 2.52 (13)	159.29 ± 2.35 (7)	NS
Metformin		159.5 ± 5.5 (2)		-
Glyburide		161.83 ± 1.07 (46)	159.97 ± 1.02 (34)	NS
Insulin+Glyburide		180 (1)		-
Pre-Pregnancy BMI (kg/cm^2)				
Diet only		36.53 ± 0.63 (108)	24.99 ± 0.31 (138)	0
Insulin		35.17 ± 1.26 (12)	26.33 ± 1.20 (7)	0
Metformin		41.55 ± 1.35 (2)		-
Glyburide		36.32 ± 1.08 (46)	25.73 ± 0.55 (34)	0
Insulin+Glyburide		45 (1)		-
Insurance				
Diet only	Medicaid	85	107	NS
	Medicare	3	2	
	Private	17	20	
	Other/Unknown	4	13	
Insulin	Medicaid	10	6	NS
	Medicare	0	0	
	Private	3	1	
	Other/Unknown	0	0	
Metformin	Medicaid	2	2	NS
	Medicare	0	0	
	Private	0	0	
	Other/Unknown	0	0	
Glyburide	Medicaid	33	26	NS
	Medicare	2	0	
	Private	12	8	
	Other/Unknown	0	1	
Insulin+Glyburide	Medicaid	1	1	NS
	Medicare	0	0	
	Private	0	0	
	Other/Unknown	0	0	
Race				

Diet-Only	Asian	4*	18	0.004
	African American	56	65	
	Caucasian	17	13	
	Hispanic	24	21	
	Mixed	1	1	
	Other/Unknown	7*	24	
Insulin	Asian	0	0	NS
	African American	9	5	
	Caucasian	2	0	
	Hispanic	2	2	
	Mixed	0	0	
	Other/Unknown	0	0	
Metformin	Asian	0	0	NS
	African American	2	2	
	Caucasian	0	0	
	Hispanic	0	0	
	Mixed	0	0	
	Other/Unknown	0	0	
Glyburide	Asian	3*	9	0.027
	African American	31*	12	
	Caucasian	5	5	
	Hispanic	7	7	
	Mixed	0	0	
	Other/Unknown	1	2	
Insulin+ Glyburide	Asian	0	0	NS
	African American	1	1	
	Caucasian	0	0	
	Hispanic	0	0	
	Mixed	0	0	
	Other/Unknown	0	0	
Type of Delivery				
Diet-only	SVD	58	90	NS
	CS	50	49	
	Vacuum	1	2	
	Forceps	0	1	
Insulin	SVD	4	2	NS
	CS	9	5	
	Vacuum	0	0	
	Forceps	0	0	
Metformin	SVD	0	0	NS
	CS	2	2	
	Vacuum	0	0	
	Forceps	0	0	
Glyburide	SVD	22	20	NS
	CS	25	15	
	Vacuum	0	0	
	Forceps	0	0	
Insulin+Glyburide	SVD	0	0	NS
	CS	2	2	
	Vacuum	0	0	
	Forceps	0	0	
Oligohydramnios		n=12	n=8	
Diet only		5	6	NS
Insulin		0	0	-
Metformin		0	0	-
Glyburide		7	2	NS
Insulin+Glyburide		0	0	-
Polyhydramnios		n=9	n=11	

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)	38.07 ± 0.18 (142)	NS
Insulin	37.08 ± 0.75 (13)	37.14 ± 0.51 (7)	NS
Metformin	38 ± 1 (2)		-
Glyburide	38.04 ± 0.23 (47)	38.29 ± 0.25 (35)	NS
Insulin+Glyburide	39 (1)		-
Birth Weight (gr)			
Diet only	3345.31 ± 58.70 (108)	3200 ± 54.62 (142)	NS
Insulin	3388 ± 171.19 (13)	3392.86 ± 381.82 (7)	NS
Metformin	4450 ± 170 (2)		-
Glyburide	3460.66 ± 87.53 (47)	3431.20 ± 89.12 (35)	NS
Insulin+Glyburide	3400 (1)		-
Birth Length (cm)			
Diet only	50.14 ± 0.29 (105)	49.63 ± 0.31 (139)	NS
Insulin	50.04 ± 0.80 (13)	48.86 ± 1.16 (7)	NS
Metformin	52 ± 1 (2)		-
Glyburide	50.72 ± 0.44 (47)	51.04 ± 0.34 (34)	NS
Insulin+Glyburide	51 (1)		-
Head Circumference (cm)			
Diet only	34.02 ± 0.19 (105)	33.64 ± 0.17 (139)	NS
Insulin	33.97 ± 1.26 (13)	33.57 ± 0.64 (7)	NS
Metformin	35.88 ± 1.13 (2)		-
Glyburide	34.03 ± 0.38 (47)	34.00 ± 0.33 (33)	NS
Insulin+Glyburide	35.5 (1)		-
Mean Blood Glucose (mg/dL)			
Diet only	69.52 ± 1.24 (102)	72.87 ± 1.06 (135)	0.04
Insulin	65.13 ± 2.91 (13)	74.78 ± 5.55 (7)	NS
Metformin	59.65 ± 7.85 (2)		-
Glyburide	66.42 ± 1.63 (46)	66.59 ± 1.74 (35)	NS
Insulin+Glyburide	74.75 (1)		-

Peak Bilirubin (mg/dL)			
Diet only	7.49 ± 0.32 (107)	7.09 ± 0.28 (139)	NS
Insulin	7.79 ± 0.90 (13)	7.42 ± 0.71 (6)	NS
Metformin	9.55 ± 3.65 (2)		-
Glyburide	7.94 ± 0.54 (47)	8.04 ± 0.65 (35)	NS
Insulin+Glyburide	3.70 (1)		-
Hemoglobin (mg/dL)			
Diet only	16.88 ± 0.35 (42)	16.76 ± 0.32 (63)	NS
Insulin	16.82 ± 1.27 (5)	16.87 ± 2.05 (3)	NS
Metformin	17.3 ± 0.9 (2)		-
Glyburide	17.46 ± 0.68 (13)	18.89 ± 0.61 (14)	NS
Insulin+Glyburide			-
Hematocrit (%)			
Diet only	49.52 ± 1.06 (42)	49.24 ± 1.12 (63)	NS
Insulin	48.82 ± 3.56 (5)	50.63 ± 7.08 (3)	NS
Metformin	55.05 ± 1.95 (2)		-
Glyburide	51.34 ± 2.11 (13)	55.41 ± 1.94 (14)	NS
Insulin+Glyburide			-
Calcium (mg/dL)			
Diet only	8.81 ± 0.22 (12)	8.86 ± 0.22 (17)	NS
Insulin	9.25 ± 0.35 (2)	8.90 (1)	NS
Metformin			-
Glyburide	8.78 ± 0.49 (5)	8.98 ± 0.41 (4)	NS
Insulin+Glyburide			-
Gender		n=171	n=184
Diet-only	Male	56	70
	Female	52	72
Insulin	Male	7	4
	Female	6	3
Metformin	Male	2	0
	Female	0	0
Glyburide	Male	23	18
	Female	24	17
Insulin+	Male	0	0
Glyburide	Female	1	0
Fetal Size		n=171	n=184
	AGA	78	111
Diet-only	SGA	1	7
	LGA	29	24
	AGA	8	5
Insulin	SGA	0	0
	LGA	5	2
	AGA	0	0
Metformin	SGA	0	0
	LGA	2	0
	AGA	35	25
Glyburide	SGA	0	0
	LGA	12	10
Insulin+	AGA	1	0
Glyburide	SGA	0	0
	LGA	0	0
Fetal Age		n=171	n=183
	Term	86	114
Diet-only	Pre-term	19	26
	Post-term	3	1
	Term	9	5
Insulin	Pre-term	4	2
	Post-term	0	0

	Term	2	0
Metformin	Pre-term	0	0
	Post-term	0	0
	Term	41	33
Glyburide	Pre-term	6	2
	Post-term	0	0
Insulin+	Term	1	0
Glyburide	Pre-term	0	0
	Post-term	0	0
NICU Admission		n=38	n=40
Diet only		5	10
Insulin		2	1
Metformin		1	0
Glyburide		3	2
Insulin+Glyburide		0	0
Intubation		n=6	n=3
Diet only		5	2
Insulin		1	0
Metformin		0	0
Glyburide		0	1
Insulin+Glyburide		0	0
Phototherapy		n=10	n=14
Diet only		7	10
Insulin		1	0
Metformin		0	0
Glyburide		2	4
Insulin+Glyburide		0	0
Shoulder Dystocia		n=4	n=3
Diet only		3	1
Insulin		1	0
Metformin		0	0
Glyburide		0	2
Insulin+Glyburide		0	0
Birth Trauma		n=6	n=8
Diet only		2	5
Insulin		1	0
Metformin		0	0
Glyburide		3	3
Insulin+Glyburide		0	0
Malformation/Anomaly		n=23	n=36
Diet only		18	30
Insulin		2	1
Metformin		0	0
Glyburide		3	5

Insulin+Glyburide	0	0
Respiratory distress	n=24	n=23
Diet only	16	18
Insulin	2	1
Metformin	1	0
Glyburide	5	4
Insulin+Glyburide	0	0
Sepsis	n=6	n=14
Diet only	5	11
Insulin	0	1
Metformin	0	0
Glyburide	1	2
Insulin+Glyburide	0	0
Feeding Difficulty	n=17	n=27
Diet only	12	23
Insulin	1	1
Metformin	1	0
Glyburide	3	3
Insulin+Glyburide	0	0
Mortality	n=1	n=1
Diet only	1	1
Insulin	0	0
Metformin	0	0
Glyburide	0	0
Insulin+Glyburide	0	0
N: number; *Statistically significant between groups		

Table 4: Infants characteristics by maternal obesity status divided by GDM treatment group.

obese mothers than those who were less obese (Figure 1).

Discussion

In the current study, we aimed to investigate the comorbid effects of obesity and gestational diabetes mellitus and its different treatment modalities on maternal and infantile outcomes in an inner city population. Previously, many researchers have examined the burden of obesity and its effect on pregnancy, while others have studied the metabolic consequences of gestational diabetes mellitus. Accordingly, there is some evidence linking these two conditions together in relation to the subsequent long term worse adverse outcome than either alone in the future generation [14,18,19]. In the management of GDM, whenever diet and exercise does not provide optimal blood glucose control, pharmacological treatment is warranted. Traditionally, insulin was the mainstay of therapy. Use of oral hypoglycemic agents in the management of GDM is a very new approach and although not approved by the US Food and Drug Administration, is widely being prescribed [20].

Previously, only one study has looked at the effect of obesity and gestational diabetes while comparing maternal and neonatal outcomes by different GDM management modalities including insulin and oral hypoglycemic agents. In that study the number of outcome variables were limited and the majority of variables were based on maternal report (16). In comparison, we examined multiple maternal and infantile variables and were able to collect clinical and laboratory values from the patient record.

In this study, we observed an increased prevalence of obesity in African American females with GDM regardless of GDM treatment, and in those on Glyburide treatment. Our finding is similar to other major studies on racial differences in obesity and in those with GDM [5,7,21,22]. Little is known about the rate, racial, and trend differences in obesity, but it is believed to be a complex issue. Genetics, lifestyle and environmental, economic, and psychosocial elements are all contributing factors in the development of obesity. The racial difference in the Glyburide group may be secondary to cultural beliefs and the increased prevalence of non-compliance with diet in African American mothers compared to other racial groups [23,24]. We also found that obese mothers more commonly were started on medication for GDM than non-obese mothers. This finding emphasizes the fact that obese mothers were not well-controlled on diet and required medication for

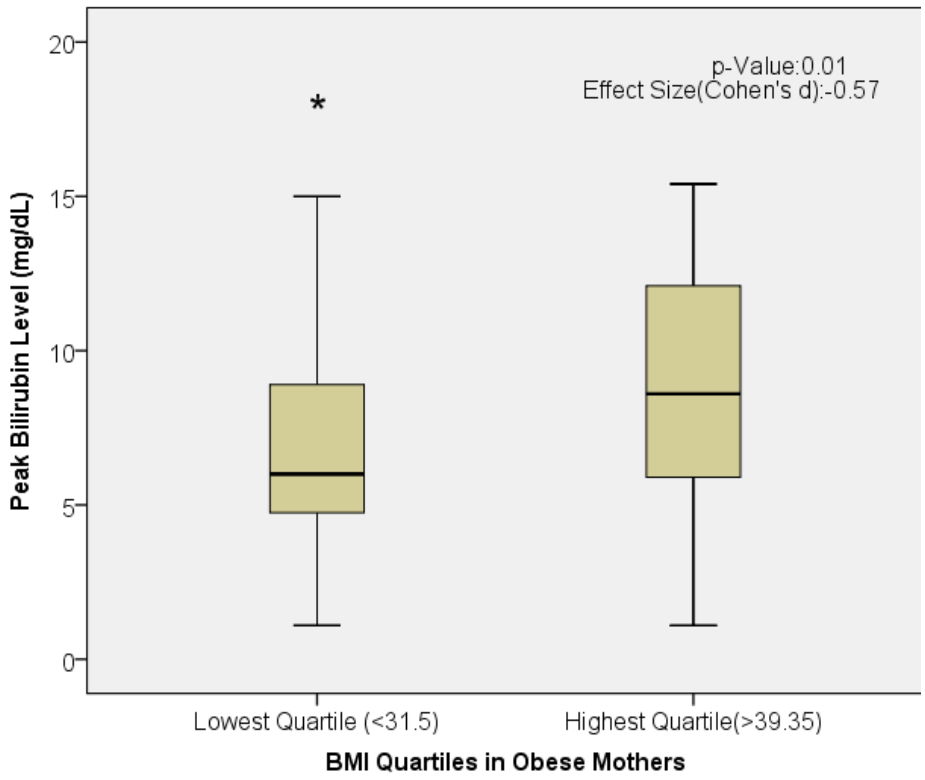

Figure 1: Comparing mean peak bilirubin level by highest and lowest BMI quartiles in obese mothers.

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 findings [16,25-32]. Similar findings apply to increased prevalence of C-section in obese versus non-obese GDM mothers (50.6% vs.37.5%). However, the finding 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 finding(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 difficulty. 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 findings, 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 offspring of mothers with GDM [35]. Nevertheless, our observation of high rate of feeding difficulty in offspring 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 findings have been previously described [14,16,26,27]. Additionally, we found fewer SGA infants in obese mothers and, similar to our findings, 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. These findings further demonstrate the association between maternal obesity and neonatal hyperbilirubinemia.

The fact that stratification of our study population by obesity status showed similar maternal and neonatal outcomes in different GDM treatment groups implies similar outcomes despite differing GDM treatment modalities including oral hypoglycemic agents. These findings 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 findings may not be applicable to other populations. We also did not include non-obese pregnant mothers without GDM for comparison. Additionally, we did not assess weight gain during pregnancy. Finally, our data does not include compliance with diet or medication and duration of medication in the management plan of GDM.

Conclusion

In conclusion, our study is another investigation that demonstrates the burden of obesity on maternal and neonatal outcomes in the context of gestational diabetes. In our study population, 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 pregnancy induced hypertension, and more commonly gave birth by C-section than non-obese mothers with GDM. About one third of GDM mothers had pregnancy induced hypertension and mothers managed by diet-only had a higher risk for gestational hypertension. We also observed a high rate of feeding difficulty in infants of GDM mothers. Infants of obese GDM mothers were significantly at risk for higher mean birth weight and lower mean blood glucose levels. There was no difference in neonatal outcome by different types of treatment for GDM with the exception of infants of obese mothers managed by diet-only who had lower mean blood glucose levels and were more likely to be LGA. Additionally, maternal obesity was associated with neonatal hyperbilirubinemia. As the prevalence of obesity continues to rise and more pregnant mothers meet the definition of obese, the complications of pregnancy outcome increase. Therefore, the development of prevention plans and optimal management strategies for obesity is a matter of priority. Our study emphasizes that maternal obesity in the context of gestational diabetes continues to be a major risk factor for both maternal and neonatal poor outcomes and calls for further prospective and interventional research.

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