Abnormal Glucose Tolerance and Pregnancy Outcomes in Women Without Diagnosis of Gestational Diabetes

BY

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THESIS

Submitted as partial fulfillment of the requirements
for the degree of Master of Science in Clinical and Translational Science
in the Graduate College of the
University of Illinois at Chicago, 2020

Chicago, Illinois

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LIST OF ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
BMI	Body Mass Index
DM	Diabetes Mellitus
GCT	Glucose challenge test
GDM	Gestational Diabetes Mellitus
HIPAA	Health Insurance Portability and Accountability Act
IRB	Institutional Review Board
IVH	Intraventricular Hemorrhage
LGA	Large for Gestational Age
MRN	Medical Record Number
NEC	Necrotizing Enterocolitis
NICU	Neonatal Intensive Care Unit
OCC	Outpatient Clinical Center
OB/GYN	Obstetrics and Gynecology
OGTT	Oral glucose tolerance test
PHI	Protected Health Information
PI	Principal Investigator
QA/QI	Quality Assurance/Quality Improvement
RDS	Respiratory Distress Syndrome
SMFMU	Society of Maternal Fetal Medicine Unit
UIC	University of Illinois at Chicago

SUMMARY

Maternal hyperglycemia and untreated gestational diabetes mellitus (GDM) lead to adverse perinatal outcomes. There is paucity of information in pregnant women with impaired glucose tolerance without gestational diabetes. A study to determine whether there are adverse perinatal outcomes amongst groups of women who rule in for abnormal glucose tolerance, but ultimately pass the diagnostic test, compared to women who have normal glucose tolerance and women with the diagnosis of GDM was carried out via retrospective cohort approach. At the University of Illinois (UIC), 789 women were included and classified into four groups based on their degree of glucose intolerance (Group 1 being without glucose metabolism abnormality to Group 4 having diagnosis of GDM). Baseline characteristics and adverse perinatal outcomes of the four groups were compared.

A progressive, dose-dependent trend was noted, such that with increased glucose intolerance, patients were at higher risk of delivering a large-for-gestational (LGA) neonate and increased neonatal birthweight. Additionally, those without a confirmed diagnosis of GDM (though with impaired glucose tolerance not meeting GDM criteria) had similar adverse pregnancy outcomes as those with GDM. Our study shows that these screening results reflect a spectrum of glucose intolerance and these patients may require closer surveillance to improve pregnancy outcomes.

I. INTRODUCTION

A. Background

Affecting 6-9% of pregnancies in the United States, GDM continues to contribute to major causes of perinatal morbidity and mortality. Gestational diabetes mellitus is defined as an elevated blood glucose (hyperglycemia) associated with a dysfunctional metabolism of glucose during pregnancy (Hod et al., 2015). Glucose homeostasis during normal pregnancy is dependent on a physiologic insulin resistance, which favors shunting of blood glucose to the developing fetus. Insulin is required for cells to metabolize glucose. In GDM, a pathologic decreased production of insulin by the pancreatic beta cells coupled with the physiologic insulin resistance of pregnancy leads to an unregulated hyperglycemia, and thus, an abnormal glucose load on both the mother and fetus (Bozkurt et al., 2015). Those at risk for GDM include women who are obese, live a sedentary lifestyle, have a personal history of GDM, family history of diabetes, and are Hispanic, African American, Native American, or Asian (American College of Obstetricians and Gynecologists (ACOG), 2013).

B. Diagnosis of Gestational Diabetes Mellitus

Current guidelines in the US recommend screening for GDM with a two-step approach (American College of Obstetricians and Gynecologists, 2013; Coustan, 1991). Between 24-28 weeks of gestational age (WGA), a screening test, known as the 1-hour glucose challenge test (1h GCT), is administered. The patient orally consumes a 50-gram glucose solution. One hour later, a blood glucose sample is collected. If the sample is ≥ 140 mg/dl, this is considered a positive screening, and the patient goes on to the diagnostic test, known as the 3-hour oral glucose challenge test (3h OGTT). While fasting, a blood glucose sample is collected, followed by the patient receiving a 100-gram oral glucose solution load. On post-prandial hours one, two, and three, sequential blood glucose samples are also collected. Elevated blood glucose levels are considered to be ≥ 95 mg/dl, 180 mg/dl, 155 mg/dl, and 140 mg/dl for fasting, 1-hour, 2-hour, and 3-hour samples respectively. If two or more of these values are elevated, the patient is diagnosed with GDM (ACOG, 2013).

C. Clinical Implications and Significance of the Study

Maternal complications of GDM include Cesarean section, gestational hypertension, and preeclampsia. In addition, women with GDM are at a higher risk of developing diabetes mellitus (DM) later in life. Neonatal complications of GDM include macrosomia (birth weight greater than 4000 grams), LGA, weight greater than the 90th percentile for a given gestational age), shoulder dystocia, operative vaginal delivery, neonatal hypoglycemia, hyperbilirubinemia, birth trauma, and neonatal intensive care unit (NICU) admission (ACOG, 2013; Graves et al., 2015).

Women diagnosed with GDM are currently treated with interventions such as lifestyle modification, which include nutrition counseling and exercise, medications, or both, in order to prevent adverse outcomes (ACOG, 2013). However, to date, no guidelines exist on the management of women who fail to meet the criteria for GDM but who exhibit clinical signs of abnormal glucose tolerance. That is, women who screen positive on the 1h GCT, but negative on the diagnostic 3h OGTT, whether that is with zero or only one elevated value on the 3h OGTT. These women are considered to have impaired glucose tolerance. Studies (Metzger et al., 2008; Farrar et al., 2016; Landon et al., 2011; Gumus and Turhan, 2008) have shown that there is a continuous association of abnormal glucose tolerance in pregnancy and adverse pregnancy outcomes; however, these studies do not use the two-step screening and diagnostic approach used in majority of clinics in the United States, nor is their sampled population generalizable to populations who are considered high risk for GDM (Graves et al., 2015; Landon et al., 2011; Gumus and Turhan, 2008; Rehder et al., 2012). Knowledge of clear thresholds within abnormal glucose tolerance for both screening and diagnostic testing, by which to intervene or attribute higher risk for adverse pregnancy outcomes also remains unknown (Farrar et al., 2016). The paucity of knowledge on the clinical relevance of women with abnormal glucose tolerance without diagnosis of GDM, the course of their pregnancy, subsequent perinatal outcomes, and lack of distinct thresholds on which providers should intervene or assess progress should prompt further investigation.

D. <u>Objective</u>

There is paucity of information in pregnant women with impaired glucose tolerance without gestational diabetes. These groups include women who screen positive on the 1h GCT with no elevated glucose values on the 3h OGTT, and women who screen positive on the 1h GCT with only one elevated glucose value on the 3h OGTT. This study aims to determine whether there are adverse perinatal outcomes amongst these groups of women compared to women who have normal glucose tolerance (women who screen negative on the 1h GCT) and women with the diagnosis of GDM. We hypothesize that there are no differences in the pregnancy outcomes of these groups. It is our hope that this study will either validate the current practice of no intervention on women who exhibit impaired glucose tolerance or encourage the development of guidelines to address those who fail to meet the criteria of GDM but demonstrate the metabolic abnormality.

II. METHODS

A. Design

This is a retrospective cohort study of women who are screened for GDM from January to 2015 to April 2018 at the University of Illinois at Chicago (UIC), which involved a chart review of patients who were treated at UIC Medical Center. The protocol was reviewed and approved by the institutional review board (IRB #2016-1137), and consent was waived, as the patients were not treated nor contacted during the course of the study.

B. Participants

Records of women with singleton pregnancies, who were screened for GDM from January 2015 to April 2018, received all of their prenatal care at UIC, and delivered at UIC, were reviewed. Exclusion criteria were those with pre-existing diabetes mellitus, patients who received care outside of the UIC medical center, age less than 18 years, inability to complete the GCT or OGTT, multiple pregnancy, or male sex.

C. Eligibility

The study population includes pregnant women who received prenatal care and delivered at UIC medical center and who had a screening test for diabetes mellitus in pregnancy. The subjects were identified by the PI and Co-investigators using diagnostic code, ICD-10, and laboratory data. The medical record numbers, the initials and date of birth of those eligible will be written in a password encrypted protected computer, which only the PI and Co-investigator have access to.

1. Inclusion Criteria

Patients included in the study were as follows:

1. Pregnant women who underwent GDM screening with 1h GCT.
2. Patients who screened negative on 1h GCT, screened positive on 1h GCT with no elevated values on 3h OGTT, screened positive on 1h GCT with only one elevated

values on 3h OGTT, and women who were diagnosed with GDM (screened positive on 1h GCT with two or more elevated values on 3h OGTT)

3. Patients who both received prenatal care at the Outpatient Clinic Center (OCC) and delivered at the UIC medical center.

2. Exclusion Criteria

Patients excluded from the study were as follows:

1. Patients with pre-existing diabetes mellitus (type 1 or 2)
2. Patients with age less than 18 years
3. Patients who received prenatal care and/or delivered outside UIC medical center
4. Patients who were unable to complete the 1h GCT or 3h OGTT
5. Patients with multiple gestation pregnancy (twins, triplets, etc.)
6. Patients of male sex

3. Excluded or Vulnerable Populations

This study focused on pregnant women, as a retrospective chart review. It did not involve intervention, nor was there direct contact with study participants. Males were excluded.

D. Subject Enrollment

This was a retrospective, cohort study (IRB approved, #2016-1137) involving a chart review of patients who were treated at UIC medical center.

1. Informed Consent

Consent was waived, as no patients were treated or contacted during the course of the study.

2. Subject Confidentiality

The confidentiality of participants was safeguarded by the use of subject identification numbers (ID #) rather than identifiers. Identifiable information was kept in a separate, password protected file on the PI's computer. The link was be kept in a third locked file separate from the data. Any identifiable information will only be accessible to the PI. Care was taken in the presentation of data not to include any potentially identifying information. Data was be entered into Research Electronic Data Capture (REDCAP) and IBM SPSS for analysis without subject identifiers.

E. Group Categorization

Women with a negative screening test, or a 1h GCT that was < 140 mg/dl were in Group 1. Women with a positive screening test (GCT ≥ 140 mg/dl) and a negative diagnostic test, 3h OGTT, of zero elevated values on the OGTT (zero elevated values of ≥ 95, 180, 155, or 140 mg/dl on the fasting, 1-hour, 2-hour, or 3-hour blood draws, respectively) were in Group 2. Women with a positive 1h GCT and a negative diagnostic test, 3h OGTT, of only one elevated value on the OGTT were in Group 3. Women with a positive 1h GCT and a positive diagnostic test, that is, two or more elevated values on the 3h OGTT, were considered having GDM, were in Group 4.

F. Outcomes

The primary outcome is LGA status. Neonatal secondary outcomes include birth weight, presence of shoulder dystocia, hypoglycemia, NICU admission, and composite neonatal outcomes. Maternal secondary outcomes include preeclampsia, preterm birth, primary Cesarean section, and 3rd or 4th degree perineal laceration.

G. Statistical Analysis

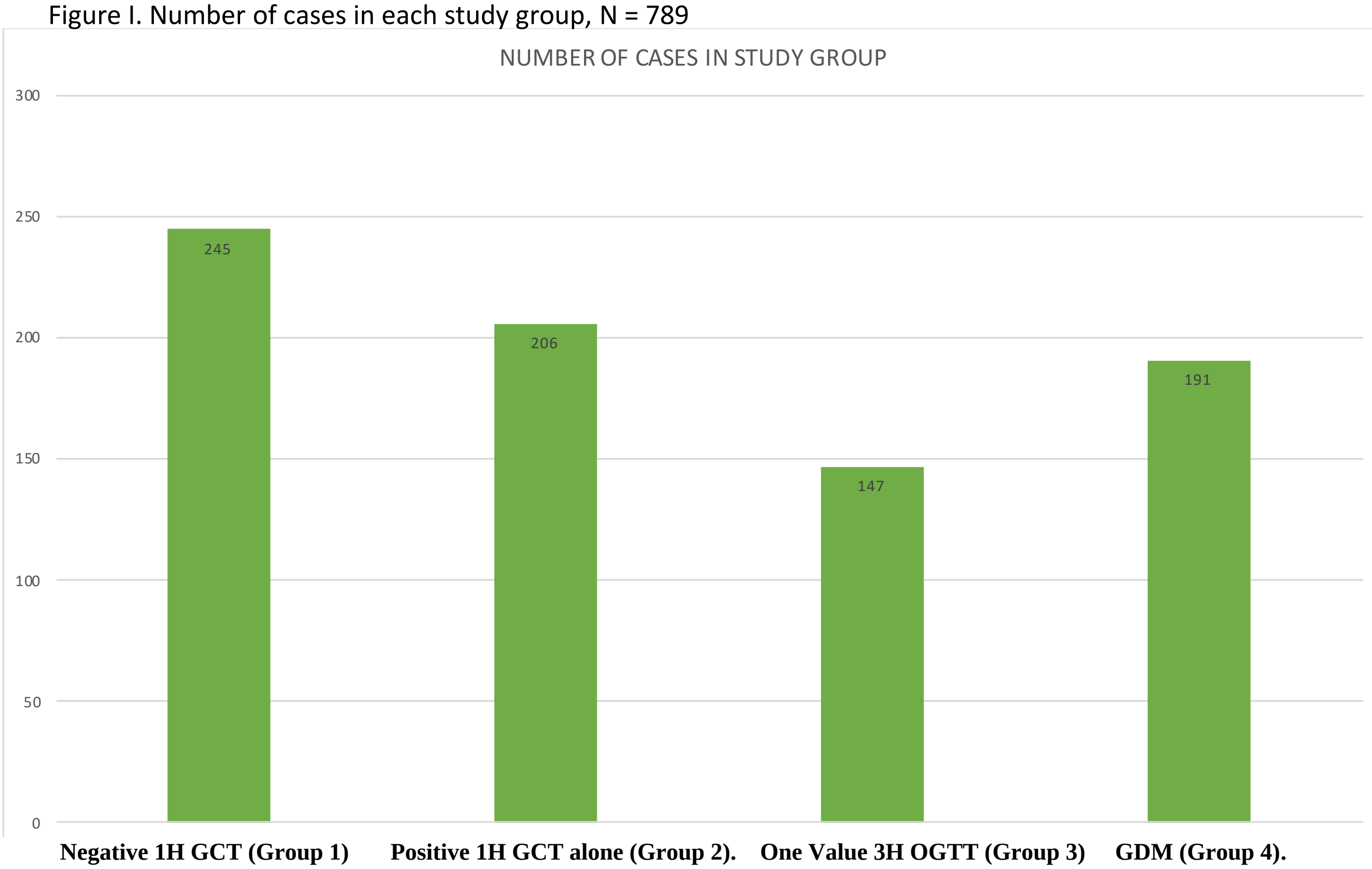
The extracted variables were entered directly into the Research Electronic Data Capture (REDCAP) software for data management hosted by the University of Illinois at Chicago (CCTS; UL1TR002003). Data analysis was performed using IBM SPSS version 24 (IBM Corp, Armonk, NY, USA) software. Frequency tables were generated; mean with two standard deviations were calculated. Comparison of categorical data was done using Chi-Square with Yates correlation or Fischer exact test. Bivariate and multivariate regression was performed to test for covariance and confounding variables, comparing all groups in the analysis as well as comparing each group-pair. Relative risks and 95% confidence intervals were calculated, with a p value less than 0.05 chosen for statistical significant level, without adjustment for multiple comparisons. Group-pairs were compared as follows: group 1 was compared to group 2 (G1 vs G2), group 3 (G1 vs G3), and group 4 (G1 vs G4); group 2 was compared to group 3 (G2 vs G3) and group 4 (G2 vs G4); and group 3 was compared to group 4 (G3 vs G4), for a total of six comparison group-pairs.

III. RESULTS

A. Total Cases in Study

Of the deliveries occurring from January 2015 to April 2018, 789 met the inclusion criteria (Figure I). 245 were classified as being in Group 1 (negative screening test, or a 1h GCT that is < 140 mg/dl). 206 were classified as being in Group 2 (positive 1h GCT and a negative diagnostic test with zero elevated values on the 3h OGTT). 147 were classified as being in Group 3 (positive 1h GCT and a negative diagnostic test with one elevated values on the 3h OGTT). 191 were classified as being in Group 4 (diagnosed with GDM).

Figure I. Number of cases in each study group, N = 789



B. Baseline Characteristics

Using one-way ANOVA, Chi-square and Fisher exact tests (Table I), age, weight at first prenatal visit, BMI, total weight gain in pregnancy, and the gestational age (GA) at which patients underwent the 1-hour GCT screening differed significantly between the four groups (p value: <0.001, 0.001, <0.001, 0.001, and 0.001, respectively). Race/ethnicity, presence of chronic hypertension (cHTN) and presence of asthma differed significantly between the four groups (p value: <0.001, 0.001, and 0.024, respectively). Gravidity, parity, tobacco use, alcohol use, drug use, history of preeclampsia, presence of renal disease, and presence of systemic lupus erythematosus did not differ between the four groups.

C. Outcomes and Comparisons of Group-Pairs

The relative risk of developing categorical outcomes was calculated for each of the comparison group-pairs. Student's t-test assessed difference in risk of developing continuous primary and secondary outcomes.

1. Group 1 Compared to Group 2

Group 2 (positive 1h GCT, no values on 3h OGTT) was compared to Group 1 (negative 1h GCT), with Group 1 as the reference group (Table II). Group 2 was more likely to give birth to an LGA neonate (RR 1.07, 95% CI 1.02-1.11, p = 0.002) and was more likely to have a neonate with greater birthweight (3245.3 $\pm$ 587.1 g vs 3099.8 $\pm$ 571.0 g, p = 0.008) than Group 1. The mean maternal age was higher in Group 2 compared to Group 1 (30.2 $\pm$ 6.3 years vs 27.4 $\pm$ 6.0, p < 0.0001) and BMI was higher in Group 2, compared to Group 1 as well (30.3 $\pm$ 7.8 kg/m^2 vs 28.6 $\pm$ 7.9 kg/m^2, p = 0.023). In terms of preterm birth, Group 1 was more likely to deliver a neonate prior to 37 weeks of gestation compared to Group 2 (6.0% vs 1.4%, p = 0.017). Regarding secondary neonatal outcomes of gestational age (GA) at delivery, presence of shoulder dystocia at birth, 5-minute APGAR < 7, mean umbilical artery (UA) pH, NICU admission, mean stay in

NICU, presence of neonatal hypoglycemia, presence of neonatal hyperbilirubinemia, and presence of respiratory distress syndrome; these did not differ between Group 1 and Group 2. Secondary maternal outcomes of initial weight, gestational weight gain, presence of preeclampsia, primary Cesarean section, vaginal delivery, operative vaginal delivery, and presence 3rd or 4th degree laceration did not differ between Group 1 and Group 2.

2. **Group 1 Compared to Group 3**

Group 3 (positive 1h GCT with one value on 3h OGTT) was compared to Group 1, with Group 1 as the reference group (Table III). Group 3 was more likely to give birth to an LGA neonate (RR 1.06, 95% CI 1.01-1.12, $p = 0.003$) and was more likely to have a neonate with a greater birthweight (3278.7 ± 546.6 g vs 3099.8 ± 571.0 g, $p = 0.002$) than Group 1. Maternal age, initial weight, and BMI was greater in Group 3 than in Group 1 (31.7 ± 5.7 years vs 27.4 ± 6.0 years, $p < 0.001$; 187.6 ± 64.4 lbs vs 169.1 ± 50.3 lbs, p 0.002; and 32.6 ± 9.3 kg/m^2 vs 28.6 ± 7.9 kg/m^2, p <0.001, respectively). Regarding the other secondary neonatal and maternal outcomes, there were no differences between the two groups.

3. Group 1 Compared to Group 4

Group 4 (GDM) was compared to Group 1, with Group 1 as the reference group (Table IV). Group 4 was more likely to give birth to an LGA neonate (RR 1.10, 95% CI 1.05-1.16, $p < 0.001$) and was more likely to have a neonate with a greater birthweight (3228.0 ± 650.8 g vs 3099.8 ± 571.0 g, $p = 0.028$) than Group 1. Group 4 was also more likely to have a neonate with a lower UA pH at birth (7.25 ± 0.08 vs 7.27 ± 0.07, $p = 0.022$). Maternal age, Initial weight, and BMI was greater in Group 4 than in Group 1 (32.2 ± 5.5 years vs 27.4 ± 6.0 years, $p < 0.001$; 186.5 ± 54.5 lbs vs 169.1 ± 50.3 lbs, p 0.001; 32.7 ± 8.8 kg/m^2 vs 28.6 ± 7.9 kg/m^2, and p <0.001, respectively). Group 4, however, had a reduced gestational weight gain compared to Group 1 (17.9 ± 17.4 lbs vs 23.3 $\pm$ 16.5 lbs, p = 0.001). Regarding the other secondary neonatal and maternal outcomes, there were no differences between the two groups.

4. <u>Group 2 Compared to Group 3</u>

Group 3 was compared to Group 2, with Group 2 as the reference group (Table V). There were no differences between the groups in likelihood of delivering an LGA neonate, nor were their differences in neonatal birthweight. There were no differences between the groups in the other secondary neonatal outcomes. Patients in Group 3 were older and had a greater BMI than Group 2 (31.7 $\pm$ 5.7 years vs 30.2 $\pm$ 6.3 years, p = 0.022; 32.6 $\pm$ 9.3 kg/m^2 vs 30.3 $\pm$ 7.8 kg/m^2, p = 0.013, respectively). The likelihood of preterm birth was also higher in Group 3 compared to Group 2 (6.1% vs 1.4%, p = 0.032). No differences occurred between the groups in the other secondary maternal outcomes.

5. <u>Group 2 Compared to Group 4</u>

Group 4 was compared to Group 2, with Group 2 as the reference group (Table VI). There were no differences between the groups in likelihood of delivering an LGA neonate, nor were their differences in neonatal birthweight. Group 4 delivered at an earlier gestational age (GA) than Group 2 (38.1 $\pm$ 2.1 weeks vs 38.5 $\pm$ 2.0 weeks, p = 0.002). Group 4 was older, had a greater BMI, and a greater likelihood of delivering preterm compared to Group 2 (32.2 $\pm$ 5.5 years vs 30.2 $\pm$ 6.3 years, p = 0.001; 32.7 $\pm$ 8.8 kg/m^2 vs 30.3 $\pm$ 7.8 kg/m^2, p = 0.005; 6.2% vs 1.4%, p = 0.016, respectively). Gestational weight gain in Group 4 was less than that of Group 2 (17.9 $\pm$ 17.4 lbs vs 23.6 $\pm$ 18.4 lbs, p = 0.001). There were no differences between the groups in the other secondary neonatal and maternal outcomes.

6. <u>Group 3 Compared to Group 4</u>

Group 4 was compared to Group 3, with Group 3 as the reference group (Table VII). There were no differences between the two groups in likelihood of delivering an LGA neonate, nor were their differences in neonatal birthweight. There were also no differences between the groups, in terms of secondary maternal and neonatal outcomes.

D. Multiple Logistic Regression, LGA vs All Groups

A binomial logistic regression was performed to determine the effect of study group on the likelihood of developing an LGA neonate, controlling for covariates, which included age, race, BMI, weight gained in pregnancy, GA at the 1h GCT, presence of chronic hypertension, and presence of asthma (Table VIII). The logistic regression model was statistically significant, X^2 (13) = 59.554, p <0.0005. The model explained 19.7% (Nagelkerke R^2) of the variance in LGA and correctly classified 93.6% of the cases. After controlling for confounding variables, the likelihood of developing an LGA neonate increased as the severity of glucose intolerance increased. With Group 1 as the reference group, the risk of developing LGA was 3.93 (95% CI 1.05 – 14.64), 4.40 (95% CI 1.12 – 17.20), and 6.24 (95% CI 1.70 – 22.94) times higher in Group 2, Group 3, and Group 4, respectively.

E. Multiple Logistic Regression, LGA vs Group-Pairs

A binomial logistic regression was also performed to determine the effect of the study group-pairs on the likelihood of developing an LGA neonate, controlling for covariates (Table IX). Each logistic regression model was statistically significant. Group 2 was 5.30 (95% CI 1.34 – 20.92) times more likely to deliver an LGA neonate than Group 1; Group 3 was 5.281 (95% CI 1.10 – 25.32) times more likely to deliver an LGA neonate than Group 1; and Group 4 was 6.71 (95% CI 1.61 – 27.92) times more likely to deliver an LGA neonate than Group 1. When comparing Group 3 to Group 2, Group 4 to Group 2, and Group 4 to Group 3, there was no greater risk of developing an LGA infant as glucose intolerance increased (RR 0.946, 95% CI 0.397 – 2.26; RR 1.53, 95% CI 0.72 – 3.29; and RR 1.37, 95% CI 0.61 – 3.09, respectively).

F. Multiple Linear Regression, Birthweight vs All Groups

Multiple linear regression was run to determine the effect of study group status on neonatal birthweight, while controlling for covariates (Table X). All assumptions were met. The full model of age, race, BMI, weight gained in pregnancy, GA at the 1h GCT, presence of chronic hypertension, presence of asthma, and study group (Model 2) was statistically significant, $R^2 = 0.136$, $F(11,752) = 10.734$, $p<0.0005$, adjusted $R^2 = 0.123$. For every one unit increase in study group ascending from Group 1 to Group 4, the neonatal birthweight increased by 38.225g (95% CI 3.28 – 73.18g, $p<0.05$).

G. Multiple Linear Regression, Birthweight vs Group-Pairs

Multiple linear regression was then analyzed for each group-pair run to determine the effect of group-pair status on neonatal birthweight, while controlling for covariates (Table XI). All assumptions were met. When comparing Group 3 to Group 1, there was an increase in birthweight of 147.30g (95% CI 16.30 – 278.30g). For all other comparison group-pairs, there was no significant differences in birthweight.

H. Multiple Linear Regression, 1h GCT vs All Groups

One-way ANOVA was run to compare means of the values of the screening 1h GCT (Table XII). The mean (SD) 1h GCT values for each group were 104.84 mg/dl (16.97 mg/dl), 151.48 mg/dl (19.51 mg/dl), 158.06 mg/dl (15.03 mg/dl), and 165.60 mg/dl (20.80 mg/dl) for Group 1, Group 2, Group 3, and Group 4, respectively. Differences between each group was significant, with a p value of <0.001. Multiple regression then was run to determine the effect of study group status on the value of 1h GCT, while controlling for covariates (Table XII). All assumptions were met. The model was statistically significant. For every one unit increase in study group ascending from Group 1 to Group 4, the 1-hr GCT value increased by 17.67mg/dl (95% CI 16.37 – 18.97mg/dl).

I. Multiple Linear Regression, 1h GCT vs Group-Pairs

Multiple regression was then run for each group-pair to determine the effect of each group-pair status on 1h GCT value, while controlling for covariates (Table XIII). All assumptions were met and all models were statistically significant. When comparing Group 2 to Group 1 (as reference), there was an increase in 1h GCT value of 45.41 mg/dl (95% CI 42.40 – 48.41 mg/dl). When comparing Group 3 to Group 1 (as reference), there was an increase in 1h GCT value of 49.52 mg/dl (95% CI 45.78 – 53.26 mg/dl). Comparing Group 4 to Group 1 (as reference), there was an increase in 1h GCT value of 56.15 mg/dl (95% CI 52.28 – 60.02 mg/dl). Comparing Group 3 to Group 2 (as reference), there was an increase in GCT value of 3.83 mg/dl (95% CI 0.750 – 6.90 mg/dl). Comparing Group 4 to Group 2 (as reference), there was an increase in GCT value of 11.69 mg/dl (95% CI 8.37 – 15.01 mg/dl). Lastly, comparing Group 4 to Group 3 (as reference), there was an increase in GCT value of 7.78 mg/dl (95% CI 3.93 – 11.64 mg/dl).

TABLE I
BASELINE CHARACTERISTICS

	Group 1 [a]	Group 2 [b]	Group 3 [c]	Group 4 [d]	p value
Age (y), m (SD)	27.4 (6.0)	30.2 (6.3)	31.7 (5.7)	32.2 (5.5)	**<0.001**
Weight (lbs), m (SD)	169.1 (50.3)	176.7 (51.1)	187.6 (64.4)	186.5 (54.6)	**0.001**
BMI (kg/m2), m (SD)	28.6 (7.9)	30.3 (7.8)	32.6 (9.3)	32.7 (8.8)	**<0.001**
Total Weight Gain (lbs), m (SD)	23.3 (16.5)	23.6 (18.4)	20.1 (14.0)	17.9 (17.4)	**0.001**
GA at 1hr GCT (wks), m (SD)	25.4 (6.3)	28.1 (15.1)	24.2 (7.3)	25.4 (11.1)	**0.001**
Gravidity, n (%)					0.584
1 to 2	125 (50.8)	103 (51.9)	68 (46.3)	88 (45.1)	
3 to 4	76 (30.1)	66 (31.7)	43 (29.3)	70 (35.9)	
5 to 6	27 (11.0)	28 (13.5)	27 (18.4)	28 (14.4)	
7 or greater	18 (7.3)	11 (5.3)	9 (6.1)	9 (4.6)	
Parity, n (%)					0.701
0	85 (34.6)	77 (37.0)	49 (33.3)	64 (32.8)	
1 to 2	121 (49.2)	95 (45.7)	72 (49.0)	91 (46.7)	
3 to 4	30 (12.2)	29 (13.9)	19 (13.0)	36 (18.5)	
5 or greater	10 (4.1)	7 (3.4)	7 (4.8)	4 (2.1)	
Race/Ethnicity, n (%)					**<0.001**
Black	155 (63.0)	69 (33.2)	54 (36.7)	62 (31.8)	
Hispanic	14 (5.7)	25 (12.0)	22 (15.0)	29 (14.9)	
White	4 (1.6)	36 (17.3)	30 (20.4)	34 (17.4)	
Asian	48 (19.5)	16 (7.7)	16 (10.9)	28 (14.4)	
Other	25 (10.2)	62 (29.8)	25 (17.0)	41 (21.0)	
Tobacco Use, n (%)	41 (16.7)	34 (16.3)	24 (16.3)	39 (20.1)	0.719
Alcohol Use, n (%)	50 (20.8)	49 (24.0)	30 (20.7)	54 (28.4)	0.243
Drug Use, n (%)	25 (10.6)	16 (8.0)	10 (6.9)	11 (5.8)	0.295
Chronic Hypertension, n (%)	13 (5.3)	15 (7.2)	24 (16.3)	26 (10.5)	**0.001**
History of Preeclampsia, n (%)	13 (5.3)	20 (9.7)	12 (8.2)	19 (9.7)	0.259
Asthma, n (%)	40 (16.2)	19 (9.2)	19 (12.9)	15 (7.7)	**0.024**
Renal Disease, n (%)	2 (0.8)	1 (0.5)	2 (1.4)	6 (3.1)	0.115
Systemic Lupus Erythematosus, n (%)	1 (0.4)	1 (0.5)	1 (0.7)	1 (0.5)	0.987

[a] Negative GCT
[b] Positive GCT, no values elevated on OGTT
[c] Positive GCT, one elevated value on OGTT
[d] GDM

TABLE II

PRIMARY AND SECONDARY OUTCOMES OF GROUP-PAIR 1 AND 2

PRIMARY OUTCOME:	**Group 2**	**Group 1** (REF)	**RR (95% CI)**	**p value**
LGA, n (%)	16 (7.7)	4 (1.6)	1.07 (1.02-1.11)	**0.002**
SECONDARY NEONATAL OUTCOME:				
Birthweight (g), m (SD)	3245.3 (587.1)	3099.8 (571.0)		**0.008**
GA at delivery (wks), m(SD)	38.5 (2.0)	38.6 (2.1)		0.606
Shoulder Dystocia, n (%)	2 (1.5)	4 (2.3)	0.99 (0.96-1.02)	0.699
5min APGAR < 7, n (%)	1 (0.5)	1 (0.4)	0.85 (0.05-13.43)	0.905
Mean UA pH, m (SD)	7.26 (0.08)	7.27 (0.07)		0.453
NICU Admission, n (%)	49 (23.7)	58 (23.7)	1 (0.90-1.11)	1
Mean NICU stay (d), m (SD)	11.7 (14.2)	12.3 (15.7)		0.849
Neonatal Hypoglycemia, n (%)	14 (15.6)	16 (19.0)	0.96 (0.84-1.10)	0.542
Neonatal Hyperbilirubinemia, n (%)	39 (19.6)	40 (16.3)	1.04 (0.95-1.14)	0.37
RDS, n (%)	22 (10.6)	15 (6.1)	1.05 (0.99-1.11)	0.082
SECONDARY MATERNAL OUTCOME:				
Mean Maternal Age (y), m (SD)	30.2 (6.3)	27.4 (6.0)		**<0.001**
Mean Initial Weight (lbs), m (SD)	176.7 (51.1)	169.1 (50.3)		0.111
Mean BMI (kg/m2), m (SD)	30.3 (7.8)	28.6 (7.9)		**0.023**
Mean Gestational Weight Gain (lbs), m (SD)	23.6 (18.4)	23.3 (16.5)		0.85
Preterm Birth, n (%)	3 (1.4)	14 (6.0)		**0.017**
Preeclampsia, n (%)	26 (12.5)	24 (9.8)	1.03 (0.97-1.10)	0.352
Primary C-section, n (%)	39 (22.3)	37 (17.5)	1.06 (0.96-1.18)	0.234
Vaginal Delivery, n (%)	131 (63.0)	169 (68.7)	0.85 (0.65-1.09)	0.2
Operative Vaginal Delivery, n (%)	5 (3.7)	6 (3.4)	1 (0.96-1.05)	0.907
3rd or 4th Degree Laceration, n (%)	6 (8.0)	9 (8.8)	0.99 (0.91-1.08)	0.846

TABLE III

PRIMARY AND SECONDARY OUTCOMES OF GROUP-PAIR 1 AND 3

PRIMARY OUTCOME:	**Group 3**	**Group 1** (REF)	**RR (95% CI)**	**p value**
LGA, n (%)	11 (7.5)	4 (1.6)	1.06 (1.01-1.12)	**0.003**
SECONDARY NEONATAL OUTCOME:				
Birthweight (g), m (SD)	3278.7 (546.6)	3099.8 (571.0)		**0.002**
GA at delivery (wks), m (SD)	38.4 (1.6)	38.6 (2.1)		0.101
Shoulder Dystocia, n (%)	0 (0)	4 (2.3)	0.98 (0.96-1.00)	0.137
5min APGAR < 7, n (%)	1 (0.7)	1 (0.4)	1 (0.99-1.02)	0.712
Mean UA pH, m (SD)	7.26 (0.08)	7.27 (0.07)		0.206
NICU Admission, n (%)	37 (25.5)	58 (23.7)	1.03 (0.91-1.15)	0.682
Mean NICU stay (d), m (SD)	11.8 (23.1)	12.3 (15.7)		0.909
Neonatal Hypoglycemia, n (%)	8 (11.9)	16 (19.0)	0.92 (0.80-1.05)	0.235
Neonatal Hyperbilirubinemia, n (%)	34 (24.1)	40 (16.3)	1.1 (0.99-1.23)	0.61
RDS, n (%)	17 (11.6)	15 (6.1)	1.06 (0.99-1.14)	0.055
SECONDARY MATERNAL OUTCOME:				
Mean Maternal Age (y), m (SD)	31.7 (5.7)	27.4 (6.0)		**<0.001**
Mean Initial Weight (lbs), m (SD)	187.6 (64.4)	169.1 (50.3)		**0.002**
Mean BMI (kg/m2), m (SD)	32.6 (9.3)	28.6 (7.9)		**<0.001**
Mean Gestational Weight Gain (lbs), m (SD)	20.1 (14.0)	23.3 (16.5)		0.053
Preterm Birth	9 (6.1)	14 (6.0)		0.861
Preeclampsia, n (%)	20 (13.6)	24 (9.8)	1.05 (0.97-1.13)	0.242
Primary C-section, n (%)	26 (21.1)	37 (17.5)	1.05 (0.94-1.17)	0.405
Vaginal Delivery, n (%)	93 (63.3)	169 (68.7)	0.85 (0.64-1.13)	0.269
Operative Vaginal Delivery, n (%)	4 (4.1)	6 (3.4)	1 (0.96-1.06)	0.77
3rd or 4th Degree Laceration, n (%)	3 (5.9)	9 (8.8)	0.97 (0.88-1.06)	0.524

TABLE IV

PRIMARY AND SECONDARY OUTCOMES OF GROUP-PAIR 1 AND 4

PRIMARY OUTCOME:	Group 4	Group 1 (REF)	RR (95% CI)	p value
LGA, n (%)	21 (10.8)	4 (1.6)	1.10 (1.05-1.16)	**<0.001**
SECONDARY NEONATAL OUTCOME:				
Birthweight (g), m (SD)	3228.0 (650.8)	3099.8 (571.0)		**0.028**
GA at delivery (wks), m (SD)	38.1 (2.1)	38.6 (2.1)		**0.001**
Shoulder Dystocia, n (%)	5 (4.3)	4 (2.3)	1.02 (0.98-1.07)	0.492
5min APGAR < 7, n (%)	5 (2.6)	1 (0.4)	1.02 (1.00-1.05)	0.052
Mean UA pH, m (SD)	7.25 (0.08)	7.27 (0.07)		**0.022**
NICU Admission, n (%)	60 (31.3)	58 (23.7)	1.11 (0.99-1.25)	0.077
Mean NICU stay (d), m (SD)	12.6 (24.7)	12.3 (15.7)		0.943
Neonatal Hypoglycemia, n (%)	43 (22.6)	16 (19.0)	1.05 (0.92-1.19)	0.506
Neonatal Hyperbilirubinemia, n (%)	43 (22.9)	40 (16.3)	1.09 (0.99-1.19)	0.086
RDS, n (%)	31 (15.9)	15 (6.1)	1.12 (1.04-1.20)	**0.001**
SECONDARY MATERNAL OUTCOME:				
Mean Maternal Age (y), m (SD)	32.2 (5.5)	27.4 (6.0)		**<0.001**
Mean Initial Weight (lbs), m (SD)	186.5 (54.5)	169.1 (50.3)		**0.001**
Mean BMI (kg/m2), m (SD)	32.7 (8.8)	28.6 (7.9)		**<0.001**
Mean Gestational Weight Gain (lbs), m (SD)	17.9 (17.4)	23.3 (16.5)		**0.001**
Preterm Birth	12 (6.2)	14 (6.0)		0.838
Preeclampsia, n (%)	21 (10.8)	24 (9.8)	1.01 (0.95-1.08)	0.727
Primary C-section, n (%)	33 (21.4)	37 (17.5)	1.05 (0.95-1.17)	0.34
Vaginal Delivery, n (%)	117 (60.0)	169 (68.7)	0.78 (0.61-1.00)	0.57
Operative Vaginal Delivery, n (%)	4 (3.3)	6 (3.4)	1.00 (0.96-1.04)	1
3rd or 4th Degree Laceration, n (%)	5 (7.7)	9 (8.8)	0.99 (0.90-1.08)	0.797

TABLE V

PRIMARY AND SECONDARY OUTCOMES OF GROUP-PAIR 2 AND 3

PRIMARY OUTCOME:	Group 3	Group 2 (REF)	RR (95% CI)	p value
LGA, n (%)	11 (7.5)	16 (7.7)	1.00 (0.94-1.06)	0.931
SECONDARY NEONATAL OUTCOME:				
Birthweight (g), m (SD)	3278.7 (546.6)	3245.3 (587.1)		0.587
GA at delivery (wks), m (SD)	38.4 (1.6)	38.5 (2.0)		0.215
Shoulder Dystocia, n (%)	0 (0)	2 (1.5)	0.99 (0.97-1.01)	0.513
5min APGAR < 7, n (%)	1 (0.7)	1 (0.5)	1.00 (0.99-1.02)	0.805
Mean UA pH, m (SD)	7.26 (0.08)	7.26 (0.08)		0.619
NICU Admission, n (%)	37 (25.5)	49 (23.7)	1.03 (0.91-1.16)	0.692
Mean NICU stay (d), m (SD)	11.8 (23.1)	11.7 (14.2)		0.98
Neonatal Hypoglycemia, n (%)	8 (11.9)	14 (15.6)	0.96 (0.85-1.09)	0.519
Neonatal Hyperbilirubinemia, n (%)	34 (24.1)	39 (19.6)	1.06 (0.94-1.19)	0.318
RDS, n (%)	17 (11.6)	22 (10.6)	1.01 (0.94-1.09)	0.769
SECONDARY MATERNAL OUTCOME:				
Mean Maternal Age (y), m (SD)	31.7 (5.7)	30.2 (6.3)		**0.022**
Mean Initial Weight (lbs), m (SD)	187.6 (64.4)	176.7 (51.1)		0.077
Mean BMI (kg/m2), m (SD)	32.6 (9.3)	30.3 (7.8)		**0.013**
Mean Gestational Weight Gain (lbs), m (SD)	20.1 (14.0)	23.6 (18.4)		0.054
Preterm Birth	9 (6.1)	3 (1.4)	1.05 (1.01-1.10)	**0.032**
Preeclampsia, n (%)	24 (9.8)	26 (12.5)	1.01 (0.93-1.10)	0.76
Primary C-section, n (%)	37 (17.5)	39 (22.3)	0.99 (0.87-1.11)	0.813
Vaginal Delivery, n (%)	169 (68.7)	131 (63.0)	1.01 (0.76-1.33)	0.956
Operative Vaginal Delivery, n (%)	6 (3.4)	5 (3.7)	1.01 (0.95-1.06)	1
3rd or 4th Degree Laceration, n (%)	9 (8.8)	6 (8.0)	0.98 (0.89-1.77)	0.738

TABLE VI

PRIMARY AND SECONDARY OUTCOMES OF GROUP-PAIR 2 AND 4

PRIMARY OUTCOME:	Group 4	Group 2 (REF)	RR (95% CI)	p value
LGA, n (%)	21 (10.8)	16 (7.7)	1.03 (0.97-1.01)	0.292
SECONDARY NEONATAL OUTCOME:				
Birthweight (g), m (SD)	3228.0 (650.8)	3245.3 (587.1)		0.779
GA at delivery (wks), m (SD)	38.1 (2.1)	38.5 (2.0)		**0.002**
Shoulder Dystocia, n (%)	5 (4.3)	2 (1.5)	1.03 (0.99-1.08)	0.255
5min APGAR < 7, n (%)	5 (2.6)	1 (0.5)	1.02 (1.00-1.05)	0.112
Mean UA pH, m (SD)	7.25 (0.08)	7.26 (0.08)		0.172
NICU Admission, n (%)	60 (31.3)	49 (23.7)	1.11 (0.98-1.25)	0.09
Mean NICU stay (d), m (SD)	12.6 (24.7)	11.7 (14.2)		0.835
Neonatal Hypoglycemia, n (%)	43 (22.6)	14 (15.6)	1.09 (0.97-1.23)	0.17
Neonatal Hyperbilirubinemia, n (%)	43 (22.9)	39 (19.6)	1.04 (0.94-1.16)	0.431
RDS, n (%)	31 (15.9)	22 (10.6)	1.06 (0.99-1.15)	0.114
SECONDARY MATERNAL OUTCOME:				
Mean Maternal Age (y), m (SD)	32.2 (5.5)	30.2 (6.3)		**0.001**
Mean Initial Weight (lbs), m (SD)	186.5 (54.5)	176.7 (51.1)		0.066
Mean BMI (kg/m2), m (SD)	32.7 (8.8)	30.3 (7.8)		**0.005**
Mean Gestational Weight Gain (lbs), m (SD)	17.9 (17.4)	23.6 (18.4)		**0.001**
Preterm Birth	12 (6.2)	3 (1.4)	1.05 (1.01-1.09)	**0.016**
Preeclampsia, n (%)	21 (10.8)	26 (12.5)	0.98 (0.91-1.05)	0.589
Primary C-section, n (%)	33 (21.4)	39 (22.3)	0.99 (0.88-1.11)	0.851
Vaginal Delivery, n (%)	117 (60.0)	131 (63.0)	0.93 (0.72-1.19)	0.539
Operative Vaginal Delivery, n (%)	4 (3.3)	5 (3.7)	1.00 (0.95-1.04)	1
3rd or 4th Degree Laceration, n (%)	5 (7.7)	6 (8.0)	1.00 (0.91-1.10)	1

TABLE VII

PRIMARY AND SECONDARY OUTCOMES OF GROUP-PAIR GROUP 3 AND 4

PRIMARY OUTCOME:	Group 4	Group 3 (REF)	RR (95% CI)	p value
LGA, n (%)	21 (10.8)	11 (7.5)	1.04 (0.97-1.10)	0.302
SECONDARY NEONATAL OUTCOME:				
Birthweight (g), m (SD)	3228.0 (650.8)	3278.7 (546.6)		0.446
GA at delivery (wks), m (SD)	38.1 (2.1)	38.4 (1.6)		0.097
Shoulder Dystocia, n (%)	5 (4.3)	0 (0)	1.05 (1.00-1.09)	0.066
5min APGAR < 7, n (%)	5 (2.6)	1 (0.7)	1.02 (0.99-1.05)	0.242
Mean UA pH, m (SD)	7.25 (0.08)	7.26 (0.08)		0.444
NICU Admission, n (%)	60 (31.3)	37 (25.5)	1.08 (0.95-1.24)	0.25
Mean NICU stay (d), m (SD)	12.6 (24.7)	11.8 (23.1)		0.885
Neonatal Hypoglycemia, n (%)	43 (22.6)	8 (11.9)	1.14 (1.00-1.28)	0.059
Neonatal Hyperbilirubinemia, n (%)	43 (22.9)	34 (24.1)	0.98 (0.87-1.11)	0.792
RDS, n (%)	31 (15.9)	17 (11.6)	1.05 (0.97-1.14)	0.253
SECONDARY MATERNAL OUTCOME:				
Mean Maternal Age (y), m (SD)	32.2 (5.5)	27.4 (6.0)		0.391
Mean Initial Weight (lbs), m (SD)	186.5 (54.5)	169.1 (50.3)		0.856
Mean BMI (kg/m2), m (SD)	32.7 (8.8)	28.6 (7.9)		0.952
Mean Gestational Weight Gain (lbs), m (SD)	17.9 (17.4)	23.3 (16.5)		0.2
Preterm Birth	12 (6.2)	9 (6.1)	1.00 (0.95-1.06)	0.99
Preeclampsia, n (%)	21 (10.8)	24 (9.8)	0.97 (0.89-1.05)	0.424
Primary C-section, n (%)	33 (21.4)	37 (17.5)	1.00 (0.89-1.14)	0.953
Vaginal Delivery, n (%)	117 (60.0)	169 (68.7)	0.92 (0.70-1.21)	0.539
Operative Vaginal Delivery, n (%)	4 (3.3)	6 (3.4)	0.99 (0.94-1.05)	1
3rd or 4th Degree Laceration, n (%)	5 (7.7)	9 (8.8)	1.02 (0.92-1.13)	1

TABLE VIII

MULTIPLE LOGISTIC REGRESSION, LGA VS ALL GROUPS

	B	SE	Wald	df	p value	RR	95% CI
Constant	-7.826	1.655	22.358	1	0.0005	-	-
Group 1 (ref)			7.819	3	0.05	1	
Group 2	1.368	0.671	4.151	1	0.042	3.928	1.053 - 14.644
Group 3	1.481	0.696	4.523	1	0.033	4.396	1.123 - 17.202
Group 4	1.831	0.664	7.591	1	0.006	6.237	1.696 - 22.937

TABLE IX

MULTIPLE LOGISTIC REGRESSION, LGA VS GROUP-PAIRS[a]

	RR of LGA	95% CI	p value
Group 2 compared to Group 1 (REF)	5.294	1.34 - 20.92	**0.013**
Group 3 compared to Group 1 (REF)	5.281	1.101 - 25.319	**0.037**
Group 4 compared to Group 1 (REF)	6.708	1.612 - 27.921	**0.009**
Group 3 compared to Group 2 (REF)	0.946	0.397 - 2.255	0.901
Group 4 compared to Group 2 (REF)	1.532	0.714 - 3.286	0.273
Group 4 compared to Group 3 (REF)	1.368	0.605 - 3.094	0.452

[a] Covariates controlled (age, race, initial BMI, total weight gain in pregnancy, gestational age at GCT, cHTN, asthma)

TABLE X

MULTIPLE LINEAR REGRESSION, BIRTHWEIGHT VS ALL GROUPS

Variable	B (95% CI)	Sebeta	b	B	SEbeta	b
Constant	2312.45**	143.19		2294.43**	143.09	
Age	-0.66	3.188	-0.008	-2.106	3.251	-0.024
BMI	18.236**	2.571	0.284	17.41**	2.593	0.271
Weight Gained	8.133**	1.147	0.253	8.305**	1.147	0.258
GA at 1h GCT	4.262*	1.825	0.081	4.449*	1.822	0.084
Afr American						
White	227.84**	60.548	0.141	197.132*	62.074	0.122
Hispanic	146.5*	63.718	0.085	124.5	64.386	0.072
Asian	184.404*	63.444	0.117	171.14*	63.593	0.108
Other	168.849*	52.784	0.123	151.51*	53.273	0.11
Chronic HTN	-192.72*	67.768	-0.104	-199.7*	67.68	-0.108
Asthma	-141.731*	60.387	-0.083	135.612*	60.31	-0.079
Study Group				38.225 (3.275 - 73.175) *	17.803	0.081

*p < 0.005, ** < 0.001

TABLE XI

MULTIPLE LINEAR REGRESSION, BIRTHWEIGHT VS GROUP-PAIRS[a]

	B (95% CI)	SEbeta	beta	p value
Group 2 compared to Group 1 (REF)	40.65 (-70.16 - 151.46)	56.38	0.037	0.471
Group 3 compared to Group 1 (REF)	147.30 (16.30 - 278.30)	66.62	0.13	**0.028**
Group 4 compared to Group 1 (REF)	99.14 (-20.68 - 218.95)	60.95	0.09	0.105
Group 3 compared to Group 2 (REF)	82.51 (-33.12 - 198.13)	58.78	0.075	0.161
Group 4 compared to Group 2 (REF)	65.23 (-41.25 - 171.71)	54.15	0.06	0.229
Group 4 compared to Group 3 (REF)	- 35.19 (-150.37 -79.98)	58.54	-0.032	0.548

[a] Covariates controlled (age, race, initial BMI, total weight gain in pregnancy, gestational age at GCT, cHTN, asthma)

TABLE XII

MULTIPLE LINEAR REGRESSION, 1H GCT VS ALL GROUPS[a]

	Group 1	Group 2	Group 3	Group 4	p value
1h GCT value (mg/dl), m(SD)	104.8 (17.0)	151.5 (19.5)	158.1 (15.0)	165.6 (20.8)	**<0.001**
	B (95% CI)	**Sebeta**	**beta**	p value	
Study Group	17.7 (16.4 - 19.0)	0.663	0.657	**<0.001**	

[a] Covariates controlled (age, race, initial BMI, total weight gain in pregnancy, gestational age at GCT, cHTN, asthma)

TABLE XIII

MULTIPLE LINEAR REGRESSION, 1H GCT VS GROUP-PAIRS[a]

	B (95% CI)	SEbeta	beta	p value
Group 2 compared to Group 1 (REF)	45.41 (42.40 - 48.41)	1.53	0.765	**<0.001**
Group 3 compared to Group 1 (REF)	49.52 (45.78 - 53.26)	1.9	0.789	**<0.001**
Group 4 compared to Group 1 (REF)	56.15 (52.28 - 60.02)	1.97	0.786	**<0.001**
Group 3 compared to Group 2 (REF)	3.83 (0.750 - 6.90)	1.56	0.105	**0.015**
Group 4 compared to Group 2 (REF)	11.69 (8.37 - 15.01)	1.69	0.275	**<0.001**
Group 4 compared to Group 3 (REF)	7.78 (3.93 - 11.64)	1.96	0.206	**<0.001**

[a] Covariates controlled (age, race, initial BMI, total weight gain in pregnancy, gestational age at GCT, cHTN, asthma)

IV. DISCUSSION

A. Principal Findings

Our study shows that with increased severity of abnormal glucose tolerance, risk for development of an LGA neonate and a neonate of greater birthweight increased. In addition, our study shows that there are differences in the screening 1h GCT value between each of the four study groups, indicating that both the screening data as well as perinatal outcomes differ between these groups. However, this relationship does not exist between Groups 3 and 4. While there are differences in the 1h GCT value between Group 3 and Group 4, there are no differences in outcomes between these two groups. This suggests that although Group 3 is not diagnosed with GDM, patients with this severity of glucose tolerance have very similar outcomes to those that were diagnosed with GDM. In agreement with the HAPO study[6], our study confirms that the risk of developing an LGA neonate and increased birth weight was associated with the severity of glucose tolerance in a dose-response manner. When comparing group-pair outcomes of LGA and birthweight for the group-pairs G2 v G1, G3 v G1, and G4 v G1, the relationship remained, even after controlling for confounders. The severity of maternal glycemia on the screening 1h GCT increased with each group. This relationship held also after controlling for confounding variables. The incidence of LGA and increased birthweight was significantly associated with group status, as the severity of impaired glucose tolerance increased from Group 1 to Group 4.

B. Results

With regards to the demographic data of the participants, there was an increase in age, BMI, and total weight during pregnancy that correlated with severity of abnormal glucose tolerance. This was expected, as we know that major risk factors for developing GDM include advanced age, weight greater than ideal body weight as well as greater than average weight gain in gestation. African American patients outnumbered all other race/ethnicity groups in each study group, which is consistent with the patient population that is served at the University of Illinois Hospital. Gravidity and parity did not differ between study groups.

When comparing Group 2 to Group 1, Group 3 to Group 1, and Group 4 to Group 1 on primary and secondary outcomes, LGA status and birthweight increased in a dose-dependent manner. When comparing age, BMI, and total weight gain in pregnancy between each group-pair, the group with the more impaired glucose tolerance tended to be older, weigh more, and gained the most weight. However, some of these patterns did not hold for each group-pair. For example, when comparing Group 4 to Group 1 and Group 4 to Group 2, Group 4 had a mean less total gestation weight gain than Group 1 and Group 2. This is likely due to the fact that women diagnosed with GDM (Group 4), were counseled on diet and lifestyle modifications, which could have translated into less weight gain than the negative screening group (Group 1) or the positive screen group with negative OGTT (Group 2). When comparing perinatal outcomes between Group 3 and Group 4, there were no significant differences. This could imply that Groups 3 and 4 are quite similar, and that their level abnormal glucose tolerance leads to similar implications, both maternally and for the neonate. This observation was also noted when analyzing the logistic regression, with the dependent variable as LGA and the independent variable as each study group-pair. A dose-dependent response in relative risk (RR) was demonstrated when analyzing all study groups in terms of the outcome of LGA (Group 1 (ref): 1.00, Group 2: 3.93, Group 3: 4.40, Group 4: 6.24); however, when comparing group-pairs, no difference in RR was observed between group-pair G3 v G2, G4 v G2, or G4 v G3. Again, when comparing these groups to the negative screening group (Group 1), it is clear that maternal hyperglycemia plays a role in the development of LGA and birthweight; however, when comparing severity of hyperglycemia between the groups with more severe glucose intolerance, the relationship becomes less concrete, after controlling for confounding variables. In terms of birthweight, with increased severity of glucose intolerance, birthweight increased by 38.23g for each unit increase in group assignment, as demonstrated by the multiple regression analysis which considered all groups as the independent variable. When analyzing multiple regression for each group-pair, there was a significant difference in birthweight for Group 3 compared to Group 1 (p 0.028). There was no difference when comparing group-pair Group 4 to Group 1. As mentioned before, women diagnosed with GDM (Group 4), tend to be counseled and treated with lifestyle and diet modifications in addition to medications. They also are induced at 39 weeks for labor, given their medical condition. This could be a reason why Group 4 had neonates that had a birthweight that did not differ from Group 1. Our study highlights an important observation; Group 3 is a potential group of women that could benefit from counseling on diet on lifestyle changes, which could potentially lead to neonates who have birthweights and weight-for-gestational age similar to those of the negative screening group (Group 1).

C. Clinical Implications

There is presently no recommendation on treating women who fail to meet the criteria for diagnosis of GDM but demonstrate abnormal glucose tolerance. An important clinical implication of our study is to offer early intervention (i.e. diet and lifestyle modification, medication, and 3rd trimester growth ultrasound) on these groups of women (Groups 2 and 3). Our study demonstrates that Group 4 (GDM) gained less gestational weight and also had neonates that weighed less than those in other groups; given that both of these outcomes increase risks associated with GDM, early interventions may reduce the risks of LGA, increased birthweight, and other adverse perinatal outcomes in women who have abnormal glucose tolerance.

D. Strengths and Limitations

A strength of the study is that it is one of the only studies that investigates glucose intolerance with the use of the two-step approach of diagnosing GDM[3,4] with the 1h GCT and 3h OGTT compared to the one-step approach used in the HAPO study[6] (2h, 75-gram OGTT), making this more generalizable to high-risk populations in the United States. This study also has relatively larger sample sizes than other studies and is the first to analyze differences in 1h GCT values between each study group.

This study is not without limitations. This was a retrospective cohort study in a single institution. It does not provide enough evidence to universally recommend interventions/treatment in women with abnormal glucose tolerance, not diagnosed with GDM. Nonetheless, the outcomes of this study provide evidence that counseling and intervention in women with abnormal glucose tolerance, especially those with only one elevated value on the 3h OGTT, could be helpful in a case-by-case basis in preventing perinatal adverse outcomes, namely LGA neonates and neonates with elevated birthweight compared to average. Prospective cohort studies which focus on providing intervention to these groups with impaired glucose tolerance and assessing their perinatal outcomes compared to both negative screening and GDM groups is warranted.

V. CONCLUSION

Our study shows that the severity of glucose impairment in pregnancy increases the risk of LGA and increased birthweight in a dose-response manner. After controlling for confounders, this relationship remains significant. The results also show that these screening results reflect a spectrum of glucose intolerance in a high-risk population, as related to both the primary and secondary outcomes, and that these outcomes are similar to those of other important studies, including the HAPO study[5,8-10]. Patients with an abnormal 1h GCT, and patients with an abnormal 1h GCT in addition to one elevated value on 3h GTT can suffer similar adverse pregnancy outcomes as those with GDM. Negative long-term implications on both the neonate and the mother can result from LGA status, including higher risk for GDM in future pregnancy, shoulder dystocia, greater risk for cardiovascular disease, and others. Our study shows that these 1h GCT screening results reflect a spectrum of glucose intolerance and these patients who are not diagnosed with GDM may require closer surveillance, such as lifestyle and/or diet modification, 3rd trimester ultrasound, or medications to improve pregnancy outcomes.

CITED LITERATURE

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Rehder P, Pereira B, Silva J. The prognostic value of a normal oral glucose tolerance test in pregnant women who tested positive at screening: a validation study. *Diabetology Metabolic Syndrome*. 2012;4(1):1–5.

VITA

TIFFANY NICOLE JONES, MD

PRESENT ACADEMIC RANK

Johns Hopkins Hospital, Department of Gynecology and Obstetrics *July 2018 – present*
Resident Physician, Postgraduate-Year Three
Chief of Education

EDUCATION

University of Illinois at Chicago, College of Medicine *August 2013 – May 2018*
Doctor of Medicine

University of Illinois at Chicago, School of Public Health *August 2014 – May 2018*
Master of Science – Clinical and Translational Science

University of Wisconsin – Madison *June 2008 – December 2012*
Bachelor of Science: Genetics, Global Health, cum laude

PUBLICATIONS AND ABSTRACTS

Jones T, Smith AJ, Miao D, Fader AN. Minimally invasive radical hysterectomy for cervical cancer: A systematic review and meta-analysis. Oral presentation, presented at the Mid-Atlantic Gynecologic Oncology Society. 2020, Oct. 24.

Jones T, Smith AJ, Miao D, Fader AN. Minimally invasive radical hysterectomy for cervical cancer: A systematic review and meta-analysis. Submitted for review. 2020, September.

Jones, T. and Gaillard, S. "Chemotherapy, Antineoplastic, and Radiation Therapy." *The Johns Hopkins Manual of Gynecology and Obstetrics*. 6th edition.

Enakpene, C, DiGiovanni, L, **Jones, T**, et al. Cervical cerclage for singleton pregnant patients on vaginal progesterone with progressive cervical shortening. *American Journal of Obstetrics & Gynecology*. 2018;219(4):397e1-e10.

Enakpene, C, **Jones, T**, Marshalla, M et al. Predictors of cervical cerclage success in the prevention of spontaneous preterm birth. *Obstetrics & Gynecology.* 2018;131:132S. DOI: 10. 1097/01.AOG.0000533552.43445.84

Enakpene, **Jones, T**, C, Della Torre, et al. Abnormal glucose tolerance and pregnancy outcomes in women without diagnosis of gestational diabetes mellitus. *Obstetrics & Gynecology*. 2018;131:36S. DOI: 10. 1097/01.AOG.0000532963.62149.e5

Enakpene C, Marshalla M, **Jones T** et al. To stitch or not to stitch in singleton pregnancy with progressively shortening incidental extreme short cervix on vaginal progesterone. *American Journal of Obstetrics & Gynecology*. 2018;218(1):S72-3. DOI: doi.org/10.1016/j.ajog.2017.10.511

Hoskins K, Sidani A, **Jones T** et al. Detection of PIK3CA mutations in cell-free plasma DNA from women with early breast cancer. *Cancer Research.* 2015; 75(9). DOI: 10.1158/1538- 7445.SABCS14-P3-06-42, Poster Session Abstract.

ONGOING RESEARCH AND PROJECTS

Minimally invasive radical surgery compared to open approach for cervical cancer: A systematic review and meta-analysis. Anna Jo Bodurtha Smith, MD MPH MSc, Tiffany Nicole Jones, MD MS, Diana Miao MD, Amanda Fader, MD. ***Submitted.***

Systemic Review and meta-analysis of radical hysterectomy for early-stage cervical cancer – subgroup analysis by tumor histology and surgical approach. Anna Jo Bodurtha Smith, MD MPH MSc, Tiffany Nicole Jones, MD MS, Diana Miao MD, Amanda Fader, MD. ***Submitted.***

The Impact on Food Deserts on Endometrial Cancer Outcomes. Tiffany N Jones, MD MS, Kimberly Levinson, MD MPH (Principal Investigator). Retrospective cohort study which aims to determine the association between the density of food markets as well as the type of food markets (i.e. supermarkets and convenience stores) and the incidence of endometrial cancer. ***Submitted.***

Thromboprophylaxis in patients undergoing minimally invasive gynecologic surgery. Tiffany Nicoel Jones, MD MS, Bernard Morris, MD, Rebecca Stone, MD.

The trend of HSIL within the cervical cancer screening program at Johns Hopkins Hospital. Tiffany N Jones, MD MS, Anna Jo Smith, MD MPH, Mihaela Plesa, Connie Trimble MD, Lynn McDonald, DNP, RN. Retrospective study to determine whether the presence of actionable HSIL detection has changed over an 18-year period (2001-2018) within our cervical cancer screening program.

PRESENTATIONS

Oral: **Jones, T**, Miao D, Smith AJ, Fader N. Minimally invasive radical surgery compared to open approach for cervical cancer: A systematic review and meta-analysis. The Mid-Atlantic Gynecologic Oncology Society (MAGOS) Conference 2020. 2020, September.

Poster: **Jones, T**, Enakpene, C, Della Torre, M, et al. Abnormal glucose tolerance and pregnancy outcomes in women without diagnosis of gestational diabetes mellitus. The American College of Obstetricians and Gynecologists (ACOG) Conference 2018. 2018, April.

Poster: Enakpene, C, **Jones, T**, Della Torre, M et al. Predictors of cervical cerclage success in the prevention of spontaneous preterm birth. The American College of Obstetricians and Gynecologists (ACOG) Conference 2018. 2018, April.

Oral: Enakpene, C, Marshalla, M, **Jones, T**, Della Torre, M, et al. To stitch or not to stitch in singleton pregnancy with progressively shortening incidental extreme short cervix on vaginal progesterone. The Society of Maternal-Fetal Medicine Conference 2018. 2017, August.

Oral: Enakpene, C, Marshalla, M, **Jones, T**, Della Torre, M, et al. Cerclage Versus no Cerclage in Singleton Pregnancy with Progressively Shortening Incidental Extreme Short Cervix on Vaginal Progesterone. Innovative Approaches to Reduce Infant Mortality Symposium. 2017, September.

Oral: **Jones T**, Enakpene C. Master's Thesis Proposal: Abnormal glucose tolerance and pregnancy outcomes in women without diagnosis of gestational diabetes mellitus. Presented at the University of Illinois – Chicago, School of Public Health, Thesis Committee. Jan 2017.

Poster: **Jones T**, Sidani A, Hoskins K, et al. (Nov 2014). PIK3CA and breast cancer: detection in tumor and cell-free plasma DNA via ultrasensitive Digital Droplet PCR. Poster presented at the University of Illinois – Chicago, College of Medicine Research Day Conference. Nov 2014.

TEACHING EXPERIENCE

Implicit Bias and Privilege, Impact on Patient Care *Discussion Series* *May 2020 – present*

- Created curriculum for co-residents, as Chief of Education, to facilitate difficult conversations surrounding social groups and disadvantage status, to have fruitful discussion regarding the impact of bias, privilege, and institutional racism or discrimination, and its impacts on patient care

The Johns Hopkins Hospital – Department of Gynecology and Obstetrics *January 2019*
Shining Start Educator Award

- Award bestowed upon a resident physician, voted on by medical students as being the most outstanding educator on their clerkship

University of Illinois – Chicago College of Medicine *December 2017* – May 2018
OB/GYN Clerkship Tutor

- Strengthened 3rd year medical students' knowledge of OB/GYN clerkship material via small group question and answer sessions and pre-exam reviews

University of Illinois – Chicago College of Medicine *January 2015 – March 2015*
Medical Genetics Tutor

- Strengthened 1st year medical students' knowledge of medical genetics material via pre-made handouts, small group question and answer sessions, and pre-exam reviews

University of Wisconsin – Madison, Dept. of Physics *August 2011 – December 2012*
Introductory Physics Tutor

- Strengthened peers' knowledge of physics material via pre-made handouts, small group sessions, and pre-exam reviews

VOLUNTEER & LEADERSHIP EXPERIENCE

Social Justice Task Force, Department of Gynecology & Obstetrics *July 2020 – present*
Johns Hopkins Hospital

- Charged by the Department Chair as a call to action to directly address racial inequity and injustice present within the department
- Worked with a focused group of attendings, fellows, and co-residents to develop initiatives aimed at addressing implicit bias present from provider to patient standpoint, as well as partnering with several non-for-profit organizations to better serve the Baltimore community as it relates to inequity and health disparities

Chief of Education, Gynecology and Obstetrics Residency Program *May 2020 – present*
Johns Hopkins Hospital

- Coordinates resident school education and professional development experience
- Leads simulation activities for residency training including Da Vinci robot training, laparoscopic skills, shoulder dystocia, vaginal hysterectomy

COVID-19 Redeployment Program, Resident Physician *April – May 2020*
Johns Hopkins Hospital

- Selected by Program Director, Graduate Medical Education Director as one of few off-service resident physicians to serve in COVID-19 intensive care units throughout Johns Hopkins Hospital
- Provided care to critically ill COVID-19 positive patients by managing ventilators, complex co-morbidities, placing central lines and arterial lines, performing ACLS, and facilitating end-of-life discussions with patient families

Johns Hopkins Hospital House Staff Diversity Council *September 2018 – present*
Resident Mentor

- Serves as a mentor to GYN/OB interested medical students, providing opportunities for shadowing as well as giving insight/advice on application processes

Student National Medical Association *April 2014 – May 2018*
Ambassador, Volunteer, Event Planner

- Served as a liaison between UIC-COM faculty, fellow classmates and underclassmen within the organization to build mentorship and collaboration amongst all classes with the College
- Participated in community service projects as a general body member

American Medical Student Association (AMSA) Mentor *January 2014 – May 2018*

- Mentors and advises an undergraduate student with prospects of applying to medical school within the next year
- Provides mentees with tips on MCAT and application do's and don'ts

Minority Association of Pre-medical Students (MAPS) Mentor *April 2014 – May 2018*

- Mentors and advises undergraduate students of color with prospects of applying to medical school within the next year
- Educates mentees on the importance of eliminating racial-health disparities, while understanding the social epidemiology of our communities

PROFESSIONAL EXPERIENCE

University of Illinois Health – Obstetrics & Gynecology Dept. *March 2016 – May 2018*
Graduate Student Research Fellow

- Conducted clinical translational research on Gestational Diabetes Mellitus within the Division of Maternal-Fetal Medicine
- Proficient in SPSS, Research Electronic Data Capture (REDCap), Quality Control & Assurance

Medical Accelerator for Devices (MAD) Lab – University of Illinois *October 2014 – March 2015*
Medical Student Research Fellow

- Mission statement: We make abstract ideas tangible
- Researched and discussed innovative ideas in a multidisciplinary setting to develop patented medical devices/inventions

Craig Fellowship – University of Illinois – Chicago COM *February 2014 – November 2015*
Research Fellow

- Conducted research on breast cancer with Kent Hoskins, MD and Anjen Chenn MD/PhD to study mutation detection in plasma samples
- Practiced basic lab technique including digital droplet PCR, DNA extraction and experimental design

University of Wisconsin – Madison, Dept. of Physics *September 2008 – December 2012*
Research Intern

- Studied sun emission spectra data gathered from Wisconsin H-Alpha Mapper to determine solar cycle and geomagnetic field correlation with green house gas concentration and global warming

University of Wisconsin – Madison, Dept. of Medical Microbiology *May 2011 – August 2011*
Research Intern

- Studied and genetically altered proteins affecting the pathogenicity of harmful secondary metabolites produced by plant pathogen *A. flavus* and human pathogen *A. fumigatus*

AWARDS & HONORS

The Jack Johnson Maternal Fetal Medicine Award	June 2020
Howard A. Kelly Society Resident Research Award	April 2020
Shining Start Educator Award	*January 2019*
Excellence in Obstetrics & Gynecology Award, University of Illinois	*May 2018*
Best Oral Presentation, Society of Maternal Fetal Medicine Conference	*January 2018*
Craig Research Fellow, University of Illinois – College of Medicine	*February 2014 – May 2018*
Merit-based Scholarship, University of Illinois – College of Medicine	*August 2013 – May 2018*

PROFESSIONAL MEMBERSHIPS

Physician Scientist Training Program	*September 2018 – present*
American Medical Association	*March 2014 – present*
Alpha Kappa Alpha Sorority, Inc.	*May 2010 – present*
American Medical Student Association	*August 2013 – May 2018*
Student National Medical Association	*August 2013 – May 2018*
Sigma Alpha Pi Leadership Fraternity, Inc.	*April 2010 – December 2012*