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Role of Race/Ethnicity, Pre-Pregnancy BMI, and Socioeconomic Status on Risk for Large-for-gestational (LGA) Infants Born to Women with Gestational diabetes mellitus (GDM)

Anna M. Kiefer
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Role of Race/Ethnicity, Pre-Pregnancy BMI and Socioeconomic Status on Risk for Large-for-gestational (LGA) Infants Born to Women with Gestational diabetes mellitus (GDM).

Anna M. Kiefer

A Thesis Submitted to the Graduate Faculty of
GRAND VALLEY STATE UNIVERSITY

In
Partial Fulfillment of the Requirements
For the Degree of
Master of Science in Clinical Dietetics

December 2017
Abstract

Background Fetal macrosomia occurs in approximately 10% of all pregnancies taking place in the United States. Babies born LGA are placed at a greater risk for shoulder dystocia, perinatal trauma, cesarean section, jaundice, hypoglycemia, and neonatal intensive care admission. Even more, the long-term impacts are severe and include increased risk of becoming overweight or obese and developing type 2 diabetes later in life. Women with gestational diabetes mellitus (GDM) have higher rates of delivering macrosomic offspring due to insulin resistance taking place beyond what is normal during a pregnancy. Additionally, maternal obesity, socioeconomic status, and race/ethnicity have been associated with maternal and fetal risk during pregnancy.

Objectives This study sought to ascertain the role that race/ethnicity, income level, and pre-pregnancy BMI has on the risk for delivering a LGA infant when women are diagnosed with gestational diabetes mellitus.

Subjects Women diagnosed with gestational diabetes mellitus that gave birth at Spectrum Health Butterworth Hospital between January 1, 2010 and December 31, 2016.

Methods Eligible participants’ age, race/ethnicity, form of insurance, zip code, pre-pregnancy BMI, diagnosis of LGA/macrosomia, shoulder dystocia, and form of delivery were obtained through retrospective chart reviews to investigate the association of interest. Zip codes were utilized to create rounded estimated household incomes based on census data.

Analyses Means ± standard deviations were used to describe continuous characteristics and frequencies were used to describe discrete characteristics in this sample. Cross tabulations and
confidence intervals of proportions were used to determine any significant relationship among or within the categorical variables. Logistic regression was performed to estimate the odds of delivering a LGA or macrosomic newborn using demographic characteristics of the mother.

**Results** The overall prevalence of macrosomia in this patient population was 11.8%. Rates of shoulder dystocia were significantly higher in babies born LGA when compared to those born of normal or smaller size in this cohort. When age, pre-pregnancy BMI, race/ethnicity, and annual income were considered together in a logistic regression model, the odds of delivering a LGA baby was 10.7 times greater for those with Medicaid/Medicare. This study also discovered a decreased likelihood of African American and Hispanic women of having a large baby when compared to Caucasian women.

**Conclusion** Shoulder dystocia takes place more often in babies born LGA than those that were of normal or smaller size. Women with government funded health insurance are at an increased likelihood of having an LGA baby, while Hispanic and African American race/ethnicity places women at a decreased likelihood. Future studies are warranted to identify the existence and extent of confounding variables. Additionally, more research is needed on the social determinants of health, including prenatal care adequacy, paternal race/ethnicity, social support, and WIC participation.
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<td>Large-for-gestational age</td>
</tr>
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<td>GDM</td>
<td>Gestational diabetes mellitus</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>OGTT</td>
<td>Oral glucose tolerance test</td>
</tr>
<tr>
<td>ADA</td>
<td>American Diabetes Association</td>
</tr>
<tr>
<td>GLT</td>
<td>Glucose loading test</td>
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<td>OBGYN</td>
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**Introduction**

Large-for-gestational age (LGA) is defined as a birth weight greater than the 90\textsuperscript{th} percentile for age based on gestation. Using a national reference based on single live births in the United States, infants born at 40 weeks’ gestation at the 90\textsuperscript{th} percentile would have a birth weight equal to or greater than 4000 grams.\textsuperscript{1} Fetal macrosomia is commonly used as a synonym for LGA and is defined as a birth weight greater than 4,000 grams irrespective of gestational age.\textsuperscript{2} Macrosomia occurs in more than 10% of all pregnancies in the United States.\textsuperscript{3} These births are correlated with major problems during labor including shoulder dystocia, perinatal trauma, cesarean section, and admission to neonatal intensive care units.\textsuperscript{4} Additionally, LGA infants experience an increased long-term risk of becoming overweight or obese and developing type 2 diabetes later in life.\textsuperscript{5,6}

It is estimated that 12% of newborns to normoglycemic women and 15-45% of newborns of women with gestational diabetes mellitus (GDM) are born LGA.\textsuperscript{7} The increased risk in mothers with GDM can be attributed to the insulin resistance of the mother beyond what normally takes place during pregnancy. The exacerbated insulin resistance leads to a persistent hyperglycemic state. In GDM, higher levels of blood glucose pass through the placenta into fetal circulation. From the second trimester onwards, the fetal pancreas responds by increasing their secretion of insulin, resulting in hyperinsulinemia.\textsuperscript{7} Together, the hyperinsulinemia and hyperglycemia result in higher fat and protein stores and thereby, accelerated fetal growth.\textsuperscript{8}

In addition to maternal hyperglycemia, maternal obesity has a strong but independent effect on fetal macrosomia.\textsuperscript{9} Several previous studies have shown that high pre-pregnancy BMI may be associated with increased risks of maternal and neonatal outcomes including gestational diabetes mellitus (GDM), hypertensive disorders in pregnancy, cesarean delivery, large for
gestational age infant (LGA), and macrosomia.\textsuperscript{10,11} In one systematic review and meta-analysis, it was found that the odds of delivering a large for gestational age infant are increased by 142\% for obese mothers.\textsuperscript{12}

Socioeconomic disparities in birth weights (BW\textsuperscript{s}) are associated with lifelong differences in health and productivity.\textsuperscript{13} Several studies have provided evidence that the prevalence of infants born preterm and small-for-gestational age (SGA) decreases with higher socioeconomic status reflected by income, education, and employment status.\textsuperscript{14} Many of these studies do not include LGA infants in their analysis, however and thus, need further exploration.

In addition to socioeconomic status, racial/ethnic disparities in birth outcomes are widely researched and their findings documented. Non-Hispanic Black women exhibit the highest risks of low birth weight, preterm delivery, and infant mortality.\textsuperscript{15} A recent study demonstrated that infants of Non-Hispanic Black, Hispanic and Asian women had risks of adverse birth outcomes between 10\% and 210\% greater than Non-Hispanic White women.\textsuperscript{16}

While the fetal and maternal risks associated with infants born LGA are well established, gaps remain in the literature on the prevalence among sub-groups of women at high risk of adverse birth outcomes. This proposed study seeks to ascertain the role race/ethnicity, income level and pre-pregnancy BMI have on the risk of LGA infants born to women with GDM.
Literature Review

Large-for-gestational age & Related Complications

LGA birth and its associated complications during labor and delivery are the most frequent and serious forms of morbidity for infants to women with GDM. Macrosomic fetuses in diabetic pregnancies acquire central deposition of subcutaneous fat in both the abdominal and interscapular areas. This results in larger shoulder and extremity circumferences, and a decreased head-to-shoulder ratio. Significantly higher body fat and thicker upper-extremity skinfolds are also characteristic of these infants. However, because fetal head size does not increase, shoulder and abdominal girth can become augmented, making vaginal birth risks more common.\(^7\)

If the baby becomes wedged in the birth canal, labor may take more time and instrumental delivery may be necessary. As such, unplanned or emergency cesarean section are sometimes required. Mothers delivering LGA infants are at a greater risk for laceration of the vaginal tissue as well as perineal tears. Larger than normal babies can also lead to uterine atony, where the uterus muscle does not contract appropriately, thereby causing heavy bleeding.\(^7\)

The risks of a LGA birth are not limited to the mother as many fetal risks can present too. One of the most serious problems of vaginal deliveries is shoulder dystocia. It occurs when the fetal shoulders do not deliver after the head has emerged from the vaginal canal. One or both shoulders becomes impacted against the bones of the maternal pelvis. Shoulder dystocia is considered an obstetric emergency, and can lead to fetal death if the infant is not delivered expeditiously.\(^17\)

In a 2013 study conducted by Ouzounian et al, 221 cases of shoulder dystocia from a cohort of 13,277 vaginal deliveries were assessed and demonstrated that more than half (50.7\%) took place in the delivery of LGA infants.\(^18\) Furthermore, when compared side by side, infants of
diabetic mothers (both gestational and pre-gestational) have an increased risk of shoulder dystocia even with normal birthweight. The authors proposed that this could be due to the potential dysmorphic features including thicker upper extremity skinfolds, higher body fat, and broader shoulders often seen in these babies.\textsuperscript{18}

Macrosomia is also associated with excessive rates of neonatal morbidity. Macrosomic neonates have higher rates of both hypoglycemia and neonatal jaundice when compared to the infants of mothers without diabetes.\textsuperscript{7} A retrospective cohort study of women with type 2 diabetes or GDM and their singleton neonates found that the incidence of neonatal hypoglycemia was 18\% and was statistically associated with birth weight and macrosomia.\textsuperscript{19} Neonate hypoglycemia occurs as a result of the hyperinsulinemia in utero as a response to the high blood glucose levels from the mother. While less common, it can lead to serious complications including central nervous system and cardiopulmonary disorders.

**Gestational Diabetes Mellitus**

A recent study by Desisto et al. indicated that GDM prevalence is as high as 9.2\% in the United States, the highest prevalence observed in the world.\textsuperscript{20} Furthermore, these rates have increased with the steady rise of obesity and type 2 diabetes.\textsuperscript{20,21} A recent study collecting hospital discharge data from 1994 to 2004 found that rates of GDM increased by 56\% in the ten-year time frame.\textsuperscript{22} In the United States, rates of GDM are highest in Asian, non-Hispanic black, Native American, and Hispanic women and lowest in Non-Hispanic white women.\textsuperscript{23}

Risk factors associated with GDM include pre-pregnancy overweight or obesity, advanced maternal age, being from various minority race/ethnicity groups, multipara, and GDM in the previous pregnancy.\textsuperscript{24,25} Interestingly, a history of GDM is one of the most reliable risk factors concerning the development of type 2 diabetes for the mother later on.\textsuperscript{26}
Gestational diabetes mellitus is defined as glucose intolerance with an onset or diagnosis taking place during pregnancy. In a recent study evaluating 7,415 diabetic and non-diabetic mothers, the rate of LGA among DM and non-DM was 23.7% and 10.5%, respectively. The exact mechanisms behind GDM are unclear, however, the maternal and fetal-placental factors’ interaction have been studied at length.

The placenta size increases as gestational age advances and with it, there is a rise in level of estrogen, progesterone, cortisol, and placental lactogen in the maternal blood supply. Beginning at 20 to 24 weeks of gestation, this is accompanied by an increase in insulin resistance that approximate the insulin resistance observed in people with type 2 diabetics. When the mother delivers the fetus, the placental hormone production stops and the insulin resistance abates. This observation strongly suggests that these hormones dictate the difference in insulin resistance compared to what takes place in a healthy pregnancy.

Human placental lactogen increases 10-fold during the second half of pregnancy and stimulates lipolysis. This causes the mother to use free fatty acids as an alternative fuel source, thereby conserving glucose and amino acids for the fetus. In turn, the mobilization of free fatty acids interferes with the insulin-directed entry of glucose into cells. For this reason, human placental lactogen is considered an antagonist of insulin action during pregnancy.

Pedersen’s hypothesis is used to explain the pathophysiology of LGA infants. This hypothesis is based on the fact that glucose, when elevated, crosses the placenta. The maternal-derived insulin, however cannot. Consequently, in the second trimester, the fetal pancreas which has developed to secrete insulin, responds to high blood glucose. Even more, it does so in an automated manner, regardless of glucose stimulation leading to hyperinsulinemia. This
combination of hyperinsulinemia and hyperglycemia causes glucose to be stored as adipose and protein tissue.\textsuperscript{7}

Adipose tissue also plays a role in the development of GDM. This tissue produces adipocytokines, including leptin, adiponectin, tumor necrosis factor, and interleukin-6, as well as resistin, visfatin, and apelin.\textsuperscript{31,32} Adipocytokines and elevated lipid concentrations have been associated with insulin resistance in both pregnant and non-pregnant women. Evidence suggests that one or more of these components may impair insulin signaling.\textsuperscript{33}

Data from the 1991 Diabetes in Early Pregnancy Study discovered that fetal birth weight is most closely correlated with second and third-trimester postprandial blood sugar levels. This study found that when postprandial glucose values average 120 mg/dl or less, approximately 20\% of infants can be expected to be born LGA. Furthermore, if the glucose values are as high as 160 mg/dl, the rate can reach up to 35\%.\textsuperscript{34} In another study evaluating the Mediterranean population, the adjusted odds ratio associated with one standard deviation increase (7 mg/dL) in the fasting plasma glucose was 1.26 for LGA infants.\textsuperscript{35} If a woman had a fasting glucose of 157 mg/dL, her odds of having an LGA infant would be 1.26 times greater than that of a woman with a fasting glucose of 150 mg/dL. Even more, a prospective mother-offspring multiethnic cohort study of 1247 mothers (57.2\% Chinese, 25.5\% Malay, 17.3\% Indian) discovered that with each standard deviation increase in fasting glucose, there was a 1.64 increased odds ratio for LGA.\textsuperscript{36}

**Diagnosis of GDM**

Diagnosis of GDM was first proposed in 1964 to be an assay of whole blood glucose during a 3-hour oral glucose tolerance test (OGTT). Glucose levels of 90, 165, 145, and 125 mg/dl for fasting, one-hour, two-hour and three-hour post glucose load respectively, were proposed for the diagnostic thresholds. Adjustments have been made over the years based on
data from women who were diagnosed with diabetes after gestation. Spectrum Health system uses the American Diabetes Association (ADA) recommended diagnostic criteria. In this criteria, diagnosis is made if two or more of the venous plasma concentrations are met or exceeded. These are 95, 180, 155, 140 mg/dL for fasting, one hour, two hour, and three hour fasting, respectively.

In its’ most recent position statement, the ADA suggested that all pregnant women be screened for GDM between the 24th and 28th week of gestation, unless they are low risk. Low risk women include those that are younger than 25, normal pre-gestational weight, member of an ethnic group with low prevalence of diabetes, have no history of glucose intolerance and poor obstetrical outcomes, and no known diabetes in first degree relatives.

Pre-Pregnancy BMI and Risk of LGA infants

One in three adults in the U.S. are obese so it is not surprising that obesity is becoming the most common complication of pregnancy and the predominant risk factor for maternal mortality in developed countries. Women who are obese prior to pregnancy may suffer poor health before, during, and after pregnancy which may affect their birth outcomes as well as their willingness or ability to breastfeed.

One explanation for the link between birth weight outcomes and maternal weight is the fetal origins hypothesis, similar to the Pedersen hypothesis formulated in 1954. The fetal origins hypothesis posits that pre-pregnancy obesity causes greater concentrations of glucose and fatty acids to be delivered to the developing fetus. The resulting increase in fetal insulin accelerates fetal growth and leads to high birth weight. Consistent with this hypothesis, it has been shown that women who are overweight or obese at the start of their pregnancy are at increased risks for LGA infant and macrosomia.
In one Chinese study, the odds of delivery of LGA for overweight or obese pregnant women were 2 and 3.8 times greater than normal weight women, respectively.\textsuperscript{40} In another study, researchers analyzed data for 276,436 deliveries in 23 developing countries throughout the world. Higher maternal age (20-34 years), body-mass index, and presence of diabetes were associated with significantly increased risk of macrosomia. In all regions, maternal BMI of 35 kg/m\(^2\) or greater had substantially higher odds for delivering a macrosomic infant than did those with a BMI less than 30 kg/m\(^2\).\textsuperscript{41} The results of these studies suggest that primary prevention of overweight/obesity in women of childbearing age may be an important strategy to reduce the number of LGA newborns, and consequently, the long-term public health burden of obesity.

Role of Sociodemographic & Socioeconomic Factors on Prenatal Risk

There is a large body of evidence illustrating the link between socioeconomic status and birth risk. Socioeconomic disparities in birth outcomes are pervasive and take place at both the individual and community level. A prospective cohort study in Canada used information from maternal questionnaires and medical records and found significant associations between lower socioeconomic status and increased risk of macrosomia with higher pre-pregnancy BMI at both the individual and neighborhood level. The neighborhoods were distinguished by census data and closely resemble U.S. zip codes.\textsuperscript{42} Another study using data for 28,722 live births in Shaanxi, China from 2010-2013 discovered that rates of LGA were higher in those of low socioeconomic status.\textsuperscript{43}

While countless studies have examined the association between low socioeconomic status and low birth weight, preterm deliveries, and infant death is extensive, there lacks an analysis of low-socioeconomic status and risk of delivering an LGA infant.
**Race/Ethnicity & Poor Outcomes**

To explain the disparities that exist in birth outcomes using the weathering hypothesis proposal of cumulative experiences of social inequality and racism, studies have suggested that chronic stress associated with everyday interpersonal and institutional racism may have an impact on birth outcomes of minorities. Recent data has showed that non-Hispanic Black and Hispanic women experience the highest likelihood of having a low birth weight (LBW) or preterm infant. These groups of women also have the highest rates of infant and maternal mortality.\(^{16}\)

Unfortunately, few studies have evaluated if risk of LGA infants to women with GDM varies by race/ethnicity or by income level. Studying such disparities is important from a public health standpoint to develop individualized approaches for managing GDM. In doing so, risks to mothers and their infants could both be improved.

As previously mentioned, incidence of GDM is highest in Asian and non-black Hispanic women and lowest in African American and white women.\(^{23}\) These disparities are surprising given that obesity, the strongest known risk factor for GDM, is highest in African Americans and lowest in Asians.\(^{44}\)

There remains conflicting research on the racial and ethnic disparities in risk for macrosomia to women with GDM. A retrospective cohort study found that among Hawaiian women with GDM, the highest prevalence of macrosomia was in white women (14.5%), while the lowest was in Filipina women (5.3%).\(^{45}\) Another study evaluating a wider range of racial/ethnic groups found that the highest risk of LGA were infants born to non-Hispanic black women (17.2%), followed by those to Pacific Islander (16.2%), Hispanic (14.5%), non-Hispanic
white (13.1%), Asian Indian (12.8%), Filipino (11.6%), and other Asian (9.6-11.1%) women. These findings were consistent with another California study that demonstrated highest rates of LGA newborns to African American women (25.1%), lowest rates in Asian women (13.9%), and intermediate among Hispanic (17.9%), white (16.4%), and Filipina women (15.3%). In most racial and ethnic groups, the highest increased risk of LGA newborns was to women with class II obesity. Furthermore, African American and Asian women in that BMI category had a four-fold increased risk of LGA newborns compared to women in the same racial and ethnic group but of normal weight.

Contrary to these findings, a 2017 retrospective cohort analysis of births in Texas between 2006 and 2011 found that the risk of GDM increased as BMI increased for all racial/ethnic groups but that the rate of LGA was lowest in the non-Hispanic Blacks and Asians compared to Whites and Hispanics.

These studies suggest that the perinatal outcomes in women with GDM differ by race/ethnic group. Together, they demonstrate the need for additional research so further evidence can support the identification of different counseling techniques for women. Because being overweight and obese are risk factors for both developing gestational diabetes mellitus as well as independently for having an infant born LGA, it is likely the rates of both will increase. Even more, the increased rate of GDM and LGA will likely draw the attention of health care practitioners, thereby requiring uniform diagnostic measures. In addressing the role of race/ethnicity and socioeconomic status on the risk of LGA infants born to women diagnosed with GDM, this study could better direct public health interventions. Because the health of mothers and their infants is indicative of the future health of communities, it is crucial that the health care system understand the disparities at play.
Methods and Materials

Design
This study was a retrospective chart review.

Subject Selection
The researcher completed a retrospective chart review of 754 women using electronic medical records (EMR). These records were selected for study from a large Midwest urban hospital for dates of service between January 1, 2010 to December 31, 2016. Following chart selection, the researcher used an Honest Broker System to de-identify and enter relevant data into a password protected Excel Extraction Tool Spreadsheet. All identifiable data were stored on a secure drive only accessible at the healthcare organization. Statistical analysis was completed in October 2017.

Inclusion criteria
Mothers with an ICD 9/10 codes for Gestational diabetes mellitus (Code: O24.41, O24.41, O24.410, O24.410, O24.414, O24.414, O24.415, O24.419, O24.419, 648.0, 648.00, 648.00, 648.01, 648.01, 648.03, 648.03, 648.03) using the hospital’s electronic medical record database were included in this study. Of these women, those with infants diagnosed with LGA (ICD-9/10 Code:656.601, 036.60X0, 036.63X0, O66.2) or macrosomia (ICD-9/10 Code: 766.0, 766.1, P08.0, P08.1) were identified. Participants were selected with the following criteria: Pregnant women with Gestational diabetes mellitus diagnosis taking place during their pregnancy.

Exclusion criteria
Exclusion criteria included any mothers younger than 18 years of age at delivery, any births that did not result in a live birth, and any multifetal pregnancies. Due to the study design, consent for participation was not necessary and participants were not compensated.
**Sample Size: Statistical Considerations**

Necessary minimum sample size was calculated using *An Introduction to Categorical Data Analysis* textbook by Agresti, 1996. Within the text, a logistic regression calculation was found to calculate sample size based off prior research. A probability of having a LGA baby was derived from the prior research using 0.16, a power of 0.90, alpha of 0.05, three predictors in the model and a correlation estimate of 0.50 for the variables within the model. This calculated to an estimation of 825 patients. The sample size available from the designated hospital between 2010-2016 was 754.
Figure 1. Sample Size Determination

Gestational Diabetes Patients 2010-2016
N=991

Patient Delivered a Baby 2010-2017
N=799

Removed Still Born Births
N=779

Removed Multiple Pregnancies
N=754

Normal Weight Babies
N=665

LGA Babies
N=89
**Data Management**

Data detailing the mother’s age at delivery, race and ethnicity as well as pre-pregnancy BMI were collected from the medical record. Race and ethnicity was stratified into four groups: Caucasian, African American, Hispanic and Other. Pre-pregnancy BMI was calculated by pre-pregnancy weight (kg) divided by height (m^2). The BMI categories were based on the World Health Organization International Classification of adult underweight, overweight, and obesity according to BMI.

- Underweight: <18.5,
- Normal: 18.5-24.99
- Overweight: 25-29.99
- Obese Class I:30-34.99
- Obese Class II:35-29.99
- Obese Class III:>= 40

Additionally, the mother’s primary, secondary, and tertiary insurance form were collected as a means to represent socioeconomic status. Both median and average income were estimated using the mother’s zip code and census data. The offspring’s medical charts were evaluated for LGA and macrosomia diagnoses as well as diagnosis of shoulder dystocia. Form of delivery (i.e, vaginal versus cesarean section) was also recorded. The table below (Table 1) highlights the data descriptions.
## Table 1: Data Description

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
<th>Formats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Record ID</td>
<td>Randomly Assigned Record ID that goes from 1-754</td>
<td></td>
</tr>
<tr>
<td>Diagnosis Year</td>
<td>This is the year that the Diagnosis of Gestation Diabetes Occurred</td>
<td></td>
</tr>
<tr>
<td>Delivery Year</td>
<td>This is the year the mother delivered the baby</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>Age of the mother at delivery</td>
<td></td>
</tr>
<tr>
<td>Racial/Ethnic Group</td>
<td>Race/ethnicity of the mother</td>
<td>1=White, 2= Black or African American, 3= Hispanic, 4=Other</td>
</tr>
<tr>
<td>Primary Insurance Group</td>
<td>Primary Insurance of the Mother at delivery</td>
<td>0=NA, 1=Commerical/Private, 2=Medicare, 3=Medicaid</td>
</tr>
<tr>
<td>Median Income Rounded</td>
<td>Median income rounded up and comes from the zip code of the Mother at delivery and cross referenced with census estimates</td>
<td></td>
</tr>
<tr>
<td>Median Income Group</td>
<td>Grouping created based off the rounded Median income</td>
<td>1=&lt;40,000, 2=40,000-45,000, 3=46,000-49,000, 4=50,000-59,000</td>
</tr>
<tr>
<td>Average Income Rounded</td>
<td>Average Income rounded up and comes from the zip code of the mother at delivery and cross referenced with census estimates</td>
<td></td>
</tr>
<tr>
<td>Average Income Group</td>
<td>Grouping created based off the rounded Average Income</td>
<td>1=&lt;50,000, 2=50,000-55,000, 3=56,000-65,000, 4=66,000-75,000, 5=76,000+</td>
</tr>
<tr>
<td>Macrosomia</td>
<td>If baby or Mother had LGA/Macrosomia diagnosis codes on their records</td>
<td>0=No, 1=Yes</td>
</tr>
<tr>
<td>Shoulder Dystocia</td>
<td>If Mother had a Shoulder Dystocia diagnosis code on their record</td>
<td>0=No, 1=Yes</td>
</tr>
<tr>
<td>Cesarean Section</td>
<td>Surgical procedure listed as Cesarean Section</td>
<td>0=No, 1=Yes</td>
</tr>
<tr>
<td>BMI Result Year</td>
<td>Result of the BMI year</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>Pre-pregnancy BMI value</td>
<td></td>
</tr>
<tr>
<td>Days Prior to Delivery</td>
<td>Number of days prior to delivery that the pre-pregnancy BMI was captured</td>
<td></td>
</tr>
</tbody>
</table>
Statistical Analysis

Statistical analysis of de-identified data was performed by the researcher with the help of members of the Statistics Consulting Center at Grand Valley State University. Data was analyzed with SPSS 20. Descriptive/summary statistics were obtained for all data collected. Quantitative data was expressed as a means +/- standard deviation and qualitative data is expressed as a frequency (percentage). Cross-tabulations were used along with confidence intervals of proportions with 95% confidence intervals for all categorical variables. Binary logistic regression was used to estimate the odds of delivering an LGA or macrosomic newborn using demographic characteristics of the mother. Significance was assessed at the 0.05 level.

Ethical Considerations

Institutional review and approval

To ensure that the basic rights and welfare of the research participants are protected, the protocol for this study was submitted to the Spectrum Research Review Committee online, for evaluation and approval. They determined that this study is not considered to be human research because it does not meet the definition of human subjects as defined by DHHS or FDA regulations. A waiver of HIPAA authorization was made.
Results

Of the 754 charts selected by a diagnosis of Gestational diabetes mellitus during pregnancy, 89 women delivered a baby described by LGA or macrosomia (11.8%). The form of delivery was denoted as a cesarean section in 341 cases (45.2%) compared to 413 women (54.8%) that delivered their babies vaginally. Shoulder dystocia occurred in just 12 of the total number of deliveries (1.6%). Compared to offspring that did not have the complication of shoulder dystocia, those that did were more likely to have been born LGA in that pregnancy (33%, CI 0.13-0.60).

The mothers’ ages ranged from 19 to 50 years of age, with a mean age of 31.15 years (± 5.739 years). There was no significant difference in the risk of macrosomia by age group, with all groups experiencing macrosomia rates of approximately 10%. The patients’ race/ethnicity was categorized into one of four groups: Caucasian, African American, Hispanic, and Other. Hispanic mothers had the highest rates of LGA, however, this was not significantly greater than the rates of the other groupings. In fact, there was no significant difference between any of the race/ethnic categories. Additionally, there remained no significant difference in risk by race when the women were grouped into non-Caucasian and Caucasian descriptions.

Average household income determined by the zip code of the mother using Census data varied widely, with a minimum of $27,000 and a maximum of $167,000. The mean income was $61,980.11 (± $16,177.82). Primary insurance form was also reviewed as an indicator for socioeconomic status. The majority of study participants received their insurance through commercial/employer based insurance (89%). Rates of macrosomia were similar in the commercial and government funded insurance groups at 11% and 13%, respectively. Regardless,
neither average income nor form of insurance as proxies demonstrated significantly different rates of LGA deliveries.

Pre-pregnancy BMI was only gathered from 142 mothers. The average BMI from this sample size was 34.42 (+/- 8.9). Only 8.5% of the women with pre-pregnancy BMI values gathered were of normal weight, whereas 23.9% of mothers were overweight, and 66.9% were obese. Although the rate of macrosomia was highest among normal weight mothers at 25%, there was also no difference in macrosomia risk by pre-pregnancy BMI. See Table 2 for complete results of the analyses by maternal characteristics and macrosomia.

Finally, binary logistic regression was performed as a means to approximate the role of maternal demographics on one’s risk for having a baby born LGA. The results indicate that Medicare/Medicaid insurance forms produced the greatest odds ratio (10.7, 95% CI 1.7-68). This signifies that women having Medicare/Medicaid insurance in this study were placed at a 10.7 times greater odds of delivering an infant that was large when compared to women with commercial insurance.

When age, insurance form, average income, and pre-pregnancy BMI were adjusted for, African American and Hispanic women experienced a reduced likelihood of macrosomia. African American and Hispanic women were at a 16.7 and 20 times lower risk compared to the referent group denoted as Caucasian mothers (0.06 95% CI .01-.80, 0.05 95% CI .01-.75). See Table 3 for complete results of the logistic regression model.
<table>
<thead>
<tr>
<th>Total Births N=754</th>
<th>Births n (%)</th>
<th>Macrosomia/LGA % (95% CI*)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maternal age</strong> (n=754)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 or under</td>
<td>142 (19)</td>
<td>10 [.06-.17]</td>
</tr>
<tr>
<td>26-30</td>
<td>193 (26)</td>
<td>10 [.06-.15]</td>
</tr>
<tr>
<td>31-36</td>
<td>278 (37)</td>
<td>14 [.10-.18]</td>
</tr>
<tr>
<td>37 or above</td>
<td>141 (19)</td>
<td>10 [.06-.16]</td>
</tr>
<tr>
<td><strong>Maternal race/ethnicity</strong> (n=754)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>460 (61)</td>
<td>12 [.10-.16]</td>
</tr>
<tr>
<td>African American</td>
<td>114 (15)</td>
<td>7 [.03-.13]</td>
</tr>
<tr>
<td>Hispanic</td>
<td>124 (16)</td>
<td>15 [.09-.21]</td>
</tr>
<tr>
<td>Other</td>
<td>56 (7)</td>
<td>7 [.02-.17]</td>
</tr>
<tr>
<td><strong>Maternal BMI</strong> (n=142)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>1 (1)</td>
<td>0 [.00-.79]</td>
</tr>
<tr>
<td>Normal</td>
<td>12 (9)</td>
<td>25 [.08-.53]</td>
</tr>
<tr>
<td>Overweight/Obese</td>
<td>129 (91)</td>
<td>14 [.09-.21]</td>
</tr>
<tr>
<td><strong>Average Income Group</strong> (n=754)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than $50,000</td>
<td>37 (18)</td>
<td>15 [.10-.22]</td>
</tr>
<tr>
<td>$50-55,000</td>
<td>204 (27)</td>
<td>10 [.07-.15]</td>
</tr>
<tr>
<td>$56-65,000</td>
<td>193 (26)</td>
<td>11 [.07-.17]</td>
</tr>
<tr>
<td>$66-75,000</td>
<td>99 (13)</td>
<td>8 [.04-.15]</td>
</tr>
<tr>
<td>$76,000 or greater</td>
<td>121 (16)</td>
<td>14 [.09-.21]</td>
</tr>
<tr>
<td><strong>Primary Insurance group</strong> (n=738)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commercial/Private</td>
<td>639 (87)</td>
<td>11 [.09-.14]</td>
</tr>
<tr>
<td>Medicare/Medicaid</td>
<td>99 (13)</td>
<td>13 [.07-.21]</td>
</tr>
<tr>
<td><strong>Delivery</strong> (n=754)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal</td>
<td>413 (55)</td>
<td>12 [.09-.16]</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>341 (45)</td>
<td>11 [.08-.15]</td>
</tr>
<tr>
<td><strong>Shoulder dystocia</strong> (n=754)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12 (2)</td>
<td>33 [.14-.61]</td>
</tr>
<tr>
<td>No</td>
<td>752 (98)</td>
<td>11 [.09-.13]</td>
</tr>
</tbody>
</table>
Table 3. Factors associated with LGA/macrosomia by maternal demographics, 2010-2016.

<table>
<thead>
<tr>
<th>Maternal age</th>
<th>Odds ratio (95% CI exp β*)</th>
<th>p-value (&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 or under</td>
<td>referent</td>
<td></td>
</tr>
<tr>
<td>26-30</td>
<td>.66 (.11-3.9)</td>
<td>.652</td>
</tr>
<tr>
<td>31-36</td>
<td>1.325 (.28-6.1)</td>
<td>.718</td>
</tr>
<tr>
<td>37 or above</td>
<td>.48 (.06-3.8)</td>
<td>.488</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Maternal race/ethnicity</th>
<th>Odds ratio (95% CI exp β*)</th>
<th>p-value (&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>referent</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>.06 (.01-.80)*</td>
<td>.033*</td>
</tr>
<tr>
<td>Hispanic</td>
<td>.05 (.01-.75)*</td>
<td>.030*</td>
</tr>
<tr>
<td>Other</td>
<td>.93 (.09-9.1)</td>
<td>.947</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Maternal BMI</th>
<th>Odds ratio (95% CI exp β*)</th>
<th>p-value (&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>Normal</td>
<td>referent</td>
<td></td>
</tr>
<tr>
<td>Overweight/Obese</td>
<td>.23 (.04-1.4)</td>
<td>.115</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Average Income Group</th>
<th>Odds ratio (95% CI exp β*)</th>
<th>p-value (&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than $50,000</td>
<td>1.7 (.34-8.9)</td>
<td>.505</td>
</tr>
<tr>
<td>$50-55,000</td>
<td>referent</td>
<td></td>
</tr>
<tr>
<td>$56-65,000</td>
<td>.10 (.01-1.0)</td>
<td>.052</td>
</tr>
<tr>
<td>$66-75,000</td>
<td>.42 (.08-2.2)</td>
<td>.309</td>
</tr>
<tr>
<td>$76,000 or greater</td>
<td>1.2 (.26-5.6)</td>
<td>.807</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary Insurance group</th>
<th>Odds ratio (95% CI exp β*)</th>
<th>p-value (&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial/Private</td>
<td>referent</td>
<td></td>
</tr>
<tr>
<td>Medicare/Medicaid</td>
<td>10.7 (1.7-68)*</td>
<td>.011*</td>
</tr>
</tbody>
</table>
Discussion

The analysis found that the rate of babies born LGA to women with gestational diabetes mellitus at Butterworth Hospital between 2010-2016 was similar to overall rates of macrosomia in the United States. One previous study investigating women with gestational diabetes, however, estimated that 15-45% of newborns born to these women were LGA, indicating that this study sample’s incidence rate of 11.8% is lower than the expected value. The wide range predicted by Kamana et. al could be attributed to various maternal and environmental factors, including adequacy of prenatal care as well as whether or not women controlled their gestational diabetes with diet, insulin, or not at all. Our findings that shoulder dystocia occurs significantly more often in the delivery of LGA babies is also supported by other studies.

Maternal characteristics including age, income level, race/ethnicity, and BMI have been associated with maternal and fetal outcomes of pregnancy. Although maternal body weight classifications of overweight/obesity have been previously linked to increased macrosomia risk, this was not supported by this study's findings. Our findings likely did not reach statistical significance due to the limited number of cases of macrosomia in women that had a pre-pregnancy BMI entered into their electronic medical record.

Prior to this study, few researchers had examined socioeconomic status's influence on risk for delivering a macrosomic baby. When average annual income was used as a proxy, no difference between groups was found, nor was there a significant odds ratio when all other categorical variables were considered. Even more, no significant difference in rates of LGA between women with commercial and government insurance was identified. On the contrary, when age, pre-pregnancy BMI, race/ethnicity, and annual income were considered together in a logistic regression model, the odds of delivering a LGA baby was 10.7 times greater for those
with Medicaid/Medicare. This finding supports the notion that mothers on government assisted health insurance experience worse perinatal outcomes as a result of Gestational diabetes mellitus.

A similar trend was identified with race/ethnicity. No difference was observed between women of Caucasian, African American, Hispanic, and Other groups when the individual effect was measured. Surprisingly, when this variable was measured with adjustment for all other maternal demographics, there was a decreased likelihood of African American and Hispanic women of having a large baby when compared to Caucasian women. Some research previously conducted has found that the odds of macrosomia among Caucasian women to be highest while others find the opposite. One reason for the ethnic variation in macrosomia rates may be due to a screening and diagnostic process that over detects glucose intolerance in certain racial/ethnic groups. The current method used to diagnose Gestational diabetes mellitus is two-fold, with a one-hour 50-gram glucose loading test (GLT) used as a screening tool first. If this value returns above a certain threshold, a three-hour 100-gram glucose tolerance test is completed, with diagnoses being made if two of the four values are high. Previous studies have suggested the need for race-specific thresholds after identifying that mean GLT values vary significantly by race. Nahum et al found that Asian women had the highest mean GLT value (134.7 mg/dL) while African American women had the lowest (116.4 mg/dL).\textsuperscript{49} In another study by Esakoff et al., they demonstrated an optimal screening threshold of 135 mg/dL for African Americans, 140 mg/dL for whites and Hispanics, and 145 mg/dL for Asians in order to achieve a 90% sensitivity and 10% false-positive rate.\textsuperscript{50}

In order to further investigate these findings, another logistic regression model was created using age, racial/ethnic group, average income group, cesarean section, and BMI to assess risk for being on Medicare/Medicaid in this patient population. Hispanic and African
American women were at a 11.5 and 13.5 times increased chance, respectively, of being beneficiaries of these forms of insurance. Due to the outcomes of this study, it is conceivable that an interaction is occurring between pre-pregnancy BMI and another variable. It is possible to distinguish pre-pregnancy BMI as one predictor because it had to be included in the logistic regression model in order for significance to be achieved.

This study is not without limitations. One such limitation is the number of women whose BMI had been gathered prior to pregnancy. In addition, the time the mother’s weight and height had been taken varied and was not a perfect reflection of their BMI immediately prior to becoming pregnant. Even more, all of the BMI’s entered were for deliveries that took place between 2011-2014, with the majority taking place in 2014. It is also important to note that just 12 women were of normal weight, while overweight/obese women accounted for 129 of the total count. This rather lopsided distribution could account for the insignificant confidence of proportions as previous studies have regularly found an increased proportion of macrosomic births with increased BMI. Because medical records with missing BMI values could not be included in the binary logistic regression, this decreased the viable sample size significantly from 754 to 142. To reiterate, this cohort is a mere snapshot and is probably not generalizable to other urban areas. Another limitation is the aggregation of multiple ethnic groups into four larger groups due to small numbers. The Other group includes diverse groups of people such as Asian, European, and African women. Finally, the retrospective study design depended on previously collected data for analysis and did not allow for any clarification of pre-existing data nor gathering of information surrounding lifestyle modification, glycemic control, medication usage, or gestational weight gain.
Conclusion

Similar to previous estimates, the rate of macrosomia among women with Gestational diabetes mellitus was 11.8%. Additionally, shoulder dystocia took place more often in babies born Large-for-gestational age than those that were of normal or smaller size. Women with government funded health insurance were placed at an increased likelihood of having an LGA baby, while Hispanic and African American women were at a decreased likelihood. Future studies should further examine what maternal factors are related to pre-pregnancy BMI. In identifying the extent of confounding variables, the individual influence of features like socioeconomic status can be considered more confidently. Even more, the lack of pre-pregnancy BMI data illustrates a potential need for closer tracking of maternal weight and/or better dissemination between obstetrician-gynecologist (OBGYN) providers and the hospital. It is clear that social determinants of health are extensive and influence one another. As such, future studies should give wider consideration to variables like prenatal care adequacy, paternal race/ethnicity, social support, and WIC participation in order to shed a better light on the risk factors for macrosomia after GDM.
References


