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Racial /Ethnic Differences Metabolic Profiles of American Women Diagnosed Diabetes Mellitus

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Racial/Ethnic Differences in Metabolic Profiles of American Women With Diagnosed Diabetes Mellitus

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ABSTRACT

Background: Evidence suggests that gestational diabetes mellitus (GDM) is associated with various metabolic conditions including elevated cholesterol, low HDL, elevated LDL, elevated triglycerides and obesity. However, comparative data on the association between GDM and various metabolic conditions across racial/ethnic groups are rare. This study focuses on differences in metabolic profiles among pregnant Non-Hispanic (NH) Whites, NH-Blacks, Mexican-Americans and women of other races/ethnicities with prediabetes and diabetes.

Method: Available data from the 1999 to 2010 survey waves of the National Health and Nutrition Examination Survey (NHANES) was used for this study. NHANES uses a stratified multistage probability sample of the civilian non-institutionalized population of the US chosen from a broad range of age groups and racial/ethnic backgrounds. Descriptive statistics were used to describe demographic variables, metabolic profiles across prediabetes/diabetes status. Univariate and multivariate logistic regression analyses were then used to determine the association between metabolic variables and prediabetes/diabetes across race/ethnicity.

Results: The study population (n=1417) consisted NH-Whites (N=620), NH-Blacks (N=219), Mexican-Americans (N=420), and "Other" races (N=168). Individuals with high LDL levels were significantly more likely to be diagnosed with GDM when compared to those with low LDL in both the crude (OR= 3.47, 95% CI= 1.90-6.33) and adjusted (OR= 2.81, 95% CI= 1.17-6.75) models. Individuals with high triglycerides levels were significantly more likely to be diagnosed with GDM when compared with individuals with low triglycerides in both the crude (OR= 2.44,95% CI= 1.36-4.38), and adjusted (OR= 1.30, 95% CI= 0.56-3.01) models. Individuals who are overweight/obese were significantly more likely to be diagnosed with GDM when compared with individuals normal weight both the crude (OR= 3.13, 95% CI= 1.28-7.64), and adjusted (OR= 2.44, 95% CI= 1.02-5.86) models. NH-Whites with elevated LDL and increased BMI are significantly more likely to be diagnosed with GDM; NH-Blacks with elevated triglycerides and increased BMI are significantly more likely to be diagnosed with GDM; Mexican-Americans with elevated triglycerides and increased BMI were significantly more likely to be diagnosed with GDM; Individuals of "Other" races with elevated LDL were significantly more likely to be diagnosed with GDM

Conclusion: With the exception of non-Hispanic Whites, pregnant American women with higher levels of cholesterols, high triglycerides, increased body mass index (25 kg/m^2 or greater), and less than high school education were found to be at greater risks of diabetes. The result of this analysis suggests that healthcare professionals should be more aggressive in controlling these metabolic abnormalities in pregnant women. Early intervention prior to pregnancy may help delay the onset of prediabetes/diabetes. Empowerment of pregnant women in the management of their diabetes may also be critical in averting the detrimental effect of these metabolic abnormalities.

APPROVAL PAGE

Racial/Ethnic Differences in Metabolic Profiles of American Women With Diagnosed Diabetes Mellitus

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Date: December 17, 2013

DEDICATION

This thesis is dedicated to God and to my family.

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TABLE OF CONTENTS

List of Tables

Chapter I

Introduction

1.1 Background

Diabetes mellitus (DM) is a metabolic disorder of multiple etiologies. It is characterized by chronic hyperglycemia with disturbances of carbohydrates, fat, and protein metabolism. The American Diabetes Association defines DM as a chronic illness that requires continuing medical care and ongoing patient self-management, education, and support to prevent acute complications and to reduce the risk of long-term complications (*American Diabetes Association (ADA), 201*3b). This disorder results from defects in insulin secretion, insulin action, or both. Untreated, DM can be fatal. It carries an extensive burden (in the US, it affects 25.6 million people aged 25 years and older, affects 12.6 million females age 20 years and older; costs over $174 billion in healthcare cost), and its incidence and prevalence is rapidly increasing worldwide (*Centers for Disease Control & Prevention (CDC), 2011; ADA, 2013a*). Chronic diabetes is associated with long-term damage, dysfunction, and multiple organ failure, especially the eyes, kidneys, nerves, heart, and blood vessels (ADA*, 2010*). There are different types of DM. However, the three most common types are: 1) Type 1 DM, characterized by lack of insulin production; 2) Type 2 DM, characterized by the inability of the pancreas to produce insulin; and, 3) Gestational DM, with onset during pregnancy.

Type 1 DM, found usually in children and young adults, was previously known as insulin-dependent diabetes mellitus (IDDM), or juvenile-onset diabetes mellitus. Characterized by

lack of insulin production, it manifests following the destruction of the pancreatic beta cells by the body's immune system; the pancreatic beta cells are the only cells in the body that secretes insulin. Type 1 DM account for approximately 5% of all diagnosed cases of diabetes (*CDC, 2011; ADA, 2010*).

Type 2 DM, previously known as non-insulin diabetes mellitus (NIDDM), or adult-onset diabetes mellitus, is usually associated with older age, obesity, family history of diabetes, history of gestational diabetes, impaired glucose metabolism, physical inactivity, and race/ethnicity *(Lowe et al, 2012).* It is characterized by lack of insulin production, and begins as insulin re-sistance. This type of diabetes account for approximately 90% to 95% of all diagnosed cases of diabetes *(Leibson et al, 2001; Ferrara, 2007).*

African-Americans, Hispanic Americans, and American Indians are particularly at high risk for Type 2 DM and its complications (*CDC, 2011*). The long-term complications include:

- Retinopathy
- nephropathy leading to renal failure
- peripheral neuropathy leading to foot ulcers
- amputations, and Charcot joints
- autonomic neuropathy leading to gastrointestinal
- genitourinary
- cardiovascular disease
- sexual dysfunction
- atherosclerotic
- peripheral arterial disease
- cerebrovascular disease

- and hypertension.

Pathologic and functional changes in target organs, without any clinical symptoms, may be present for a long time before diabetes is detected (*ADA, 2010*).

Gestational diabetes mellitus (GDM) is a form of glucose intolerance diagnosed for the first time during pregnancy. GDM accounts for 90% of cases of DM in pregnancy, while preexisting Type 2 DM accounts for 8% of such cases (*Saldana et al 2003; Black et al, 2013*). GDM is a major medical complication of pregnancy. If untreated, the would-be mother and yet-to-be-born child are likely to suffer morbidity and mortality (*Seshiah et al, 2008; Kwik et al, 2007*). Complications of DM in pregnancy include risk of preeclampsia, preterm birth, stillbirth, C-section complications, birth defects, spontaneous abortion, and macrosomia. 3% to 5% of pregnancies are complicated by GDM (*Makgoba et al, 2011*).

Macrosomia is defined as birth weight above 90^{th} percentile for gestational age or greater than 4000g (*Kwik et al, 2007; Moore & Smith, 2013*). Infants of women with preexisting DM experience double the risk of serious injury at birth, triple the likelihood of cesarean section delivery, and quadruple the incidence of newborn intensive care unit admission (*Moore & Smith, 2013*). The newborn is likely to suffer other complications, such as transient hypoglycemia and hypocalcemia. If untreated, GDM carries a long-term sequelae for both mother and child: the mother is at risk for future type 2 diabetes, and the child is at risk for future obesity, insulin resistance, and type 2 diabetes (*Dornhorst & Frost, 2003*).

On the other hand, pregnancy can cause elevation of fasting plasma glucose, and results in fetal macrosomia, large for gestational age. African-American, Hispanic, Native American, and Asian women have higher prevalence of gestational diabetes than white women. Complica-

tions of GDM differ among the various races/ethnicities: African-American women have lower rates of macrosomia despite similar levels of glycemic control; on the other hand, Hispanic women, even with aggressive management, have higher rates of macrosomia and birth injury than women of other ethnicities (*Moore & Smith, 2013*).

1.2 Criteria for testing for Type 2 Diabetes Mellitus

According to the American Diabetes Association "Standards of Medical Care in Diabetes" – 2013, testing for type 2 diabetes in asymptomatic individuals should be considered in adults of any age who are overweight or obese(i.e., those with BMI $\geq$ 25 kg/m^2) and who have one or more additional risk factors for diabetes. These risk factors include:

- Physical inactivity
- First-degree relative with diabetes
- High-risk race/ethnicity (e.g., African-American, Hispanic/Latino, Native American, Asian American, Pacific Islander)
- Women who delivered a baby weighing >9 lbs. or were diagnosed with GDM
- Hypertension (greater than or equal to 140/90 mmHg or on therapy for hypertension)
- HDL cholesterol level <35 mg/dL and/or a triglyceride level >250 mg/dL
- Women with polycystic ovary syndrome
- A1C $\geq$5.7%, IGT, or IFG on previous testing
- Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
- History of CVD

In those without the risk factors, testing should begin at age 45. If the test for diabetes is normal, repeat testing in at least 3-year intervals. Appropriate tests for diabetes or prediabetes,

glycohemoglobin (HbA_1C), fasting plasma glucose (FPG), or 75-g 2-hour oral glucose tolerance test (OGTT) *(ADA, 2013b).*

1.3 Criteria for testing for Gestational Diabetes Mellitus

To diagnose GDM, the American Diabetes Association "Standards of Medical Care in Diabetes" – 2013 recommends:

- Screen for undiagnosed type 2 diabetes at the first prenatal visit in those with risk factors, using standard diagnostic criteria;
- Perform a 75-g OGTT, with plasma glucose measurement fasting and at 1- and 2-hour at 24-28 weeks of gestation in women not previously diagnosed with overt diabetes;
- The OGTT should be performed in the morning after an overnight fast of at least 8 Hours;
- The diagnosis of GDM is made when any of the following plasma glucose values are exceeded (fasting: ≥ 92 mg/dL; 1-hour: ≥ 180 mg/dL; 2-hour: ≥ 153 mg/dL);
- Screen women with GDM for persistent diabetes at 6-12 weeks postpartum, using OGTT and non-pregnancy diagnostic criteria;
- Women with a history of GDM should have lifelong screening for the development of diabetes or prediabetes at least every 3 years;
- Women with a history of GDM found to have prediabetes should receive lifestyle interventions of metformin to prevent diabetes; *(ADA, 2013b).*

1.4 Purpose of Study

Evidence suggests association between metabolic conditions (i.e. cholesterol, LDL, HDL, and triglyceride) and DM during pregnancy. However, data on the association across racial/ethnic groups is rare. This thesis will focus on a) examining differences in the metabolic profiles of pregnant women with prediabetes and diabetes; b) differences in the metabolic profiles of pregnantDM non-Hispanic Whites, non-Hispanic Blacks, and Mexican-Americans and Other races; c) the role of socioeconomic conditions in the relationship between pregnancy and DM, and d) the role of education in the relationship between pregnancy and diabetes. Additionally, this thesis will address healthy lifestyle choices, including nutrition, and physical activity.

1.5 Research Questions

1. What is the association between metabolic conditions (i.e., hypertension, BMI, cholesterol, triglyceride, LDL, and HDL) and a positive diabetes diagnosis during pregnancy?
2. Are differences in the above metabolic conditions attributable to racial/ethnic differences in the US?

Chapter II

Literature Review

2.1 Background

Several studies have been conducted on diabetic pregnancy outcomes, but very few have been conducted on diabetic pregnancy in the different racial/ethnic groups. Evidence suggests association between metabolic conditions of DM (i.e., cholesterol, HDL, LDL, triglycerides, etc.) and pregnancy. However, data on the association across racial/ethnic groups is rare.

Values for lipid levels during pregnancy and their changes with gestational age have not been studied substantially (*Wiznitzer et al, 2009*). This study will shed more light on the association between lipid levels and GDM, especially its association across racial/ethnic groups.

The cause of GDM is multifactorial. *Kwik et al, 2007* postulates that increase in estrogen and progesterone induces insulin production in the pancreas. These hormonal changes contribute to insulin resistance at the post-receptor level which results in higher blood glucose and free fatty acid levels in late pregnancy. Hyperglycemia in the mother causes fetal hyperglycemia, and hence fetal hyperinsulinemia. Insulin thus acts as a fetal growth factor, possibly resulting in macrosomia (*Kwik et al, 2007*). GDM alters the expression of placental genes related to markers and mediators of inflammation and leads to impaired fetal growth and programming, which causes several metabolic diseases (*Sisino, et al, 2013*). Women with GDM are at high risk of recurrence of gestational diabetes and of developing DM in the future (*Lawrence et al, 2008*). Women's risks of developing DM and metabolic syndrome are increased in the decade after de-

livery, while their newborn infants are at increased risk of obesity and DM in adolescence and adulthood (*Feig, 2012; Soma-Pillay, 2012; Chen et al, 2009*).

2.2 Definition of gestational diabetes mellitus (GDM)

The American Diabetes Association defines GDM as any degree of glucose intolerance with onset or first recognition during pregnancy (A*DA, 2013b; Kaaja, & Greer, 2005*). This definition is irrespective of whether or not insulin is used for treatment, or diabetes continues after pregnancy. The glucose intolerance, characterized by fasting and post-prandial hyperglycemia, usually disappears after birth (*Soma-Pillay, 2012*).

The criteria used in the diagnosis of GDM are not only designed to identify pregnant women who are at increased risk for perinatal outcomes but also to identify women who are at increased risk for the development of diabetes after pregnancy (*Metzger et al, 2008*).

GDM is associated with persistent metabolic dysfunction in women at 3 years after delivery. It occurs in 2 to 9% of pregnancies with substantial risks of maternal and perinatal complications (*Crowther et al, 2005*). These perinatal risks include macrosomia, shoulder dystocia, bone fractures, nerve palsies, hypoglycemia, and death. The infants have risks of long-term adverse health outcomes such as sustained impairment of glucose tolerance, subsequent obesity, and impaired intellectual achievement (*Makgoba et al, 2012; Crowther et al, 2005*). In the United States, the rate of gestational diabetes has increased by 122% between 1989 and 2004 (*Soma-Pillay, 2012).*

Ben-Haroush et al (2004) suggested an association between several high-risk prediabetic states, GDM, and Type 2 diabetes (*Ben-Haroush et al, 2004*). Prediabetes is a condition that includes impaired fasting glucose (IFG) and impaired glucose tolerance (IGT). Individuals whose

blood glucose levels are higher than normal but not high enough to qualify as diabetes are diagnosed as either impaired fasting glucose or impaired glucose tolerance. These individuals are at a higher risk of developing DM in the future. Pregnant women with pregestational diabetes are at increased risk for multiple complications affecting both mother and the fetus (*U.S. Preventive Services Task Force (USPSTF), 2008).*

2.3 Pregnancy and diabetes

Women who are obese, older than 25 years of age, have a family history of diabetes, have a history of previous GDM, or are of certain ethnic group (African-American, Hispanic, American Indian, or Asian) are at increased risk for developing gestational diabetes *(Barr et al, 2002; CDC, 2013*). Preconception care of diabetes can reduce the risk of congenital malformations, as the risk of malformations increases continuously with increasing maternal glycemia during the first 6-8 weeks of gestation.

If diabetes is poorly controlled before conception and during the first trimester of pregnancy among women with type 1 diabetes, major birth defects can occur in 5% to 10% of pregnancies and spontaneous abortions in 15% to 20% of pregnancies; when diabetes is poorly controlled in the second and third trimesters of pregnancy, excessively large babies (macrosomia) can result (*CDC.gov*).

Screening is generally performed with oral glucose tolerance test OGTT), fasting plasma glucose (FPG), and glycohemoglobin (HbA1C). OGTT is performed after an overnight fasting with 75-gm dose of glucose; plasma glucose is measured fasting. HbA1C reflects average glycemia over an interval of several weeks (ADA*, 2010*). It is desired that HbA1C levels be as close to normal as possible (<7%) in an individual patient before conception is attempted (ADA*,*

2013b). In early pregnancy (i.e., first trimester and first half of second trimester) fasting and postprandial glucose tolerance are normally lower than in non-pregnant women, which may reflect the presence of undiagnosed preconception diabetes *(Alberti & Zimmet, 1998).*

There is a continuum of risk for adverse maternal and fetal outcomes as the maternal glucose level rises *(Ben-Haroush et al, 2004*). In order to provide the opportunity to optimize pregnancy outcome, it is desirable to detect overt diabetes in early pregnancy as early as possible, using OGTT, FPG, and HbA1C to perform this task. The recommendation to use of HBA1C to diagnose and identify people at increased risk for developing diabetes has been endorsed by the ADA because it does not require a fasting state, reflects the usual level of glycemia for a period of 3-4 months, has low intraindividual variability, and is a good predictor of diabetes-related complications (*Lowe et al, 2012*). HbA1C is significantly lower in early pregnancy and further lowered in late pregnancy when compared to age-matched nonpregnant women. The normal range of HbA1C in nonpregnant women is 4.7% - 6.3%, 4.5% - 5.7% in early pregnancy, and 4.4% – 5.6% in late pregnancy *(Ben-Haroush et al, 2004*).

In the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study (2008), in which 25,505 pregnant women at 15 centers in 9 countries underwent 75-gm of oral glucose tolerance testing at 24-32 weeks of gestation, risks of some adverse outcomes were low when FPG was ≤ 4.4 mmol/l (80 mg/dl) ((*Metzger, et al, 2008*; *ADA, 2010*). Five to ten percent of women with GDM have the risk of developing Type 2 DM after delivery, while the probability of developing diabetes ranges between 20% to 50% in women with GDM in the 5 to 10 years following pregnancy (*Zhang et al, 2009; Lindsay, 2009).*

2.4 Burden of Gestational Diabetes Mellitus

The prevalence of GDM increases with increasing maternal age, rising from 1.3% of pregnancies in women younger than age 21 to 8.7% of pregnancies of women older than age 35 (*Lindsay, 2009*). Prepregnancy obesity is associated with the development of GDM, as 65% to 75% of women with GDM are obese (*Black, et al, 2013*).

According to the U.S. Preventive Services Task Force, the current prevalence of gestational diabetes in the United States ranges from 1% to 9% *(USPSTF, 2008).* The reason for this increased prevalence includes the rise in obesity, rise in maternal age, and changes in lifestyles (*Feig, 2012; Lie et al, 2013*). GDM is associated with an economic burden on the US government. In the United States, significant economic burdens are associated with prediabetes and GDM. Timothy et al, (2010) wrote that nearly fifty-seven million adults have prediabetes, a condition associated with $25 billion annually in higher medical cost. Additionally, gestational diabetes affects 4.5 percent of all pregnancies (180,000 cases in 2007) at an associated cost of $636 million (*Timothy et al, 2010*). Of this total cost, about 36% is paid by government programs (primarily Medicaid), 56% by private insurance, and 8% by self-pay and charity care (*Chen, et al, 2009*). Indirect costs associated with GDM include increased time off from work or school, psychological stress, and reduced performance by offspring in school (*Chen et al, 2009).*

GDM significantly increases the rates of in-hospital admission for cesarean delivery, preeclampsia, ecclampsia, and other maternal complications of pregnancy. It is also associated with a statistically significant increase in newborns' ambulatory visits for macrosomia, or birthweight above the 90th percentile, endocrine and metabolic disturbances, labor and delivery

on the newborn *(Timothy et al, 2010*), as well as neonatal intensive care unit admission (*Zhang et al, 2009*).

2.5 Diagnosing Gestational Diabetes Mellitus

Healthy pregnant women have low HbA1C, particularly in the first half of their pregnancy. For the prevention of congenital malformations and macrosomia, it is desirable that HbA1C in pregnant women be below 5% in the first trimester, and below 6% in the third trimester. Most screening is conducted between 24 and 28 weeks' gestation; there is little evidence about the value of earlier screening (*Barr et al, 2002; Radder & Roosmalen, 2005*). GDM is also diagnosed in early pregnancy when one or more of the following values are true: fasting plasma glucose (FPG) is ≥ 5.1 mmol/l (92 mg/dl); 1-hr plasma glucose ≥10.0 mmol/l (180 mg/dl); or 2-hr plasma glucose ≥8.5 mmol/l (153 mg/dl) (*ADA, 2010*). HbA1C levels vary with patient's race/ethnicity, with African-Americans having higher rates of glycation; African-Americans, with or without diabetes, have higher levels HbA1C than non-Hispanic whites when matched for FPG (A*DA, 2013*). Women with early diagnosis of GDM, especially in the first half of pregnancy, represent a high-risk subgroup, with an increased incidence of obstetric complications, recurrent GDM in subsequent pregnancies, and future development of Type 2 diabetes (*Ben-Haroush et al, 2004*).

2.6 Race/Ethnicity and Gestational Diabetes

The prevalence of GDM has increased over time with the increase of obesity. In the United States, approximately 135,000 cases of GDM are diagnosed annually. This represents 3% to 8% of all pregnancies, and varies in prevalence among different racial/ethnic groups (*Dabalea et al, 2005*). Higher prevalence is seen among Native-American, African-American, Asian, and Hispanic populations than among Non-Hispanic whites; the prevalence of GDM is two-fold higher in women of other ethnic backgrounds, than in non-Hispanic whites (*Dabalea et al,*

2005). In a New York study of gestational diabetes mellitus from 1990 – 2001, a rapid increase of GDM prevalence was seen among most racial/ethnic groups, especially among Asians, Mexicans, and non-Hispanic Black women (*Thorpe, et al, 2005; Hedderson et al, 2012*).

The two strongest independent risk factors for GDM are race/ethnicity and obesity. The overall prevalence of GDM varies by race/ethnicity, lowest among non-Hispanic Blacks and non-Hispanic Whites (4.4% and 4.5%, respectively); intermediate among Hispanic (6.8%); and highest among Asians (10.2%) (*Hedderson et al, 2012)*. Obesity is highest among African-Americans and lowest among Asians (*Hedderson et al, 2012*). Other risk factors for GDM include: maternal age ≥30, family history of DM, previous history of GDM, previous history of macrosomia, glycosuria, and obesity (*Kashinakunti et al, 2013*). Education is also a risk factor: Asian women are more educated and less likely to be overweight (BMI >25.0 kg/m^2) or obese (BMI >30.0 kg/m^2) as compared to women of other racial/ethnic groups (*Hedderson et al, 2012*).

Chapter III

Methods

3.1 Source of Data

National Health and Nutrition Examination Survey (NHANES) 1999-2010 is the source of this data for this study. NHANES studies health and nutritional status of adults and children in the United States. This 1999-2010 study is a stratified multistage probability sampling design used to select a representative sample of the civilian non-institutionalized population of the US (*CDC, 2013*). This excludes all persons in supervised care or custody in institutionalized settings, all active –duty military personnel, active-duty family members living overseas, and any other citizens residing outside the 50 States and the District of Columbia (*National Health and Nutrition Examination Survey (NHANES), 2013*).

NHANES was started in the early 1960s. Since then, it has conducted a series of surveys focusing on different population groups or health topics. The information obtained from the surveys is used in determining the prevalence of major diseases and their risk factors; it is also used in assessing nutritional status and its association with health promotion and disease prevention (*CDC, 2013).* In addition, data obtained from the surveys is used in epidemiological studies and health sciences research. Information obtained from the current survey is compared with those obtained from previous surveys to allow planners to detect the extent various health problems and their risk factors have changed in the population over time (*CDC, 2013).* In selecting participants, NHANES used a statistical process, using the most current census information, to divide the United States into communities that are further divided into neighborhoods; housing units are selected randomly from each neighborhood for interviews and for determination of eligibility for the study (*NHANES, 2013*).

Starting in 1999, NHANES began interviewing a nationally representative sample of approximately 5,000 persons each year (*NHANES, 2013*). These persons are located in counties across the US. In a single year, about 15 counties are selected out of approximately 3,000 counties in the United States (*NHANES, 2013*).

As a major program under the National Center for Health Statistics (NCHS), NHANES conducts its survey by combining health interviews and physical examinations. The interviews include demographic, socioeconomic, dietary and health-related questions; while the physical examination component includes medical, dental, and physiological measurements, as well as laboratory tests administered by highly trained medical personnel. NCHS is responsible for producing vital and health statistics for the nation (*CDC, 2013).* It is a part of the Centers for Disease Control and Prevention (CDC).

NHANES conducted the 1999-2010 interviews in respondents' homes by trained interviewers using the Computer-Assisted Personal Interviewing (CAPI) system. Interview questions on reproductive health including menstrual history, pregnancy history, lactation, oral contraceptive and hormone replacement therapy use, were asked (*CDC, 2013).* The interviews were conducted in-person with an interviewer in English or Spanish, as selected by survey participants, or with translators as requested (*CDC, 2013).* Also, many of NHANES interviewers are bilingual. Information collected from participants is kept in strict confidence.

The 1999-2010 health measurements were performed in specially-designed and equipped mobile centers that travel to locations throughout the country (*CDC, 2013).* As in past health examination surveys, NHANES collects data on the prevalence of chronic disease conditions in the population. Through the survey, estimates for previously undiagnosed conditions as well as those known and reported by respondents are produced (*CDC, 2013).* Such information is of a particu-

lar strength to the NHANES program. Data collected from such surveys indicates that undiagnosed diabetes is a significant problem in the United States. To this end, government and private agencies have intensified efforts to increase public awareness, especially among minority populations (*NHANES, 2013*). NHANES is designed to sample larger numbers of certain subgroups of particular interest to public health. Oversampling is done to increase reliability and precision of estimates of health status indicators for the population subgroups. For the 2007-2010 administration of NHANES, all Hispanic persons were oversampled, rather than just Mexican-American Hispanic persons (*NHANES, 2013)*

NHANES also uses data collected in surveys to assess nutritional status and its association with health promotion and disease prevention. The NHANES data also used in epidemiological studies and health sciences research, which helps to develop sound public health policy, direct and design health programs and services, and expand the health knowledge for the nation. Survey findings are also the basis for national standards for such measurements as height, weight, and blood pressure *(CDC, 2013).*

3.2 Inclusion and Exclusion Eligibility Criteria

Individuals were included in the study if laboratory test results for pregnancy were positive. Females 20 – 44 years of age were eligible to participate. For this study, however, females 18 – 45 years of age were included. Patients who had prediabetes and diabetes were combined to increase the sample size.

3.3 Variables

3.3.a Demographic variables

The demographic variables included in this study were age, race/ethnicity, education, and household income. Age: this is the respondent's age (in years) at screening interview. Respond-

ent's actual or imputed date of birth was used in the calculation (*CDC, 2013).* NHANES reported ages 1 to 79 for survey participants. If the year of birth is missing, or not given, NHANES computed it as the year of screening interview minus the age in years provided by the respondent during the screening interview (*CDC, 2013).* In my study, women ages 18 years to 45 years are included.

Race/ethnicity: This variable is derived from responses to the survey questions on race. The different races reported on NHANES survey are non-Hispanic whites, non-Hispanic blacks, Mexican-American (as self-identified), other Hispanics (as self-identified), and other races (self-identified) (*CDC, 2013).* Missing values were eliminated. Four categories for these variables: non-Hispanic white, non-Hispanic black, Mexican-American, and "Other" races [which include other Hispanics and participants from other races (including multi-racial)] were used in this study.

Education: This is for adults 20 years and older. This is the highest level of education completed or highest degree received. NHANES categorized this into: less than 9^{th} grade education, 9-11^{th} grade education (which includes 12^{th} grade and no diploma), High school graduate/GED or equivalent, some college (or associate degree), and college graduate or above (*CDC, 2013).*

Income: this is the estimated total annual household income, reported in dollars. Family income was used if the household is comprised of only a single family. If more than one family resided in the household, income data by each family interviewed was used (*CDC, 2013).* However, some respondents refused to provide their income information, while others had little or no knowledge of family income (*CDC, 2013).*

3.3.b Other variables

Reproductive questions asked during the interview included: 1) "Are you pregnant now?" 2) "During pregnancy, told you have diabetes?" (*CDC, 2013)*. Diabetes questions included: "Doctor told you have diabetes?", "Ever told you have prediabetes?", "Taking insulin now?", and Take diabetic pills to lower blood sugar?" (*CDC, 2013).*

Pregnancy status: this is at time of exam. Women between the ages 20 years and 44 years at the time of the mobile examination centers examination were included (*CDC, 2013)*. Pregnant women who were outside of this range were not reported due to disclosure concerns (*CDC, 2013).* Values included in the survey report are from urine pregnancy test and self-reported pregnancy status (*CDC, 2013).*

BMI: body mass index, reported in Kg/m^2. The 2009-2010 data were reviewed for unusual and erroneous values (*CDC, 2013).* Values that were above the 99^{th} percentile or below the 1^{st} percentile were flagged for review; if determined to be unrealistic, they were deleted from the file (*CDC, 2013).* Blood pressure: systolic and diastolic blood pressure measurements (in mmHg). Prior to taking blood pressure measurements, participants rested quietly in a sitting position for 5 minutes, after which 3 consecutive blood pressure readings were obtained (*CDC, 2013).*

Three of the diabetes measures used in assessing diabetes mellitus include fasting plasma blood glucose (FPG), oral glucose tolerance test (OGTT), and glycohemoglobin (HbA1C). OGTT was added to the laboratory protocol in 2005 (*NHANES, 2013*). A fasting glucose test was performed on all participants after a 9-hour fast (*NHANES, 2013*). Participants were required to drink a calibrated dose of Trutol (75 grams of glucose) after the initial venipuncture, and to have a second venipuncture 2 hours after consuming the Trutol (*NHANES, 2013*). Exclusion criteria

include hemophilia and chemotherapy safety exclusions, fasting less than 9 hours, taking insulin or oral hypoglycemic agents, refusing phlebotomy, and not taking the entire Trutol solution within the allotted time (*NHANES, 2013*). Glycohemoglobin: (HbA1C), reported in percentage (%). Fasting plasma glucose (FPG), reported in mg/dL. It is measured in the morning examination session only. 2-hour glucose tolerant test: (OGTT), reported in mg/dL. It is measured in the morning examination session only.

Data on blood lipid levels are essential in monitoring the status of hyperlipidemia. Duration of fasting (≥ 8.5 hours) and the time of the day of the venipuncture were recorded (*NHANES, 2013*). Lipid measurement is used to screen for atherosclerotic risk as well as lipid and lipoprotein metabolic disorders (*NHANES, 2013*). The lipid and lipoprotein variables measured include:

Total cholesterol, measured in mg/dL

HDL cholesterol, measured in mg/dL

LDL cholesterol, measured in mg/dL

Triglyceride, measured in mg/dL. Elevated triglyceride measurements are associated with diabetes mellitus and other diseases (*NHANES, 2013).*

3.3.c Definition of terms

Glycohemoglobin (HbA1C): This reflects the average blood glucose over a 2-3 month period. It has been used to evaluate the treatment of diagnosed diabetes mellitus (*Hjellestad et al, 2013*). A value ≥6.5% is used for the diagnosis of DM (ADA, *2013c; WHO, 2013*). Fasting plasma blood glucose: Used in the diagnosis of DM. defined as fasting plasma glucose ≥126 mg/dl (ADA*, 2013b; Hjellestad et al, 2013*). Oral glucose tolerance test: Level of ≥200mg/dl is one of the criteria used in the diagnosis of DM (*Hjellestad et al, 2013*; ADA*, 2013b).*

Hypertension: defined as blood pressure ≥140/90 mmHg, or taking antihypertensive medications (*Ong et al, 2007*). The goal is to reduce blood pressure levels <140/90 mmHg and lower in those with diabetes (*Lenfant et al, 2003*). Diabetes: Defined as random plasma glucose >200 mg/dl, and HbA1c >2 standard deviation above the laboratory mean (*Barr et al, 2002*). Prediabetes: Diagnosed when FPG is 100 mg/dl-125mg/dl (impaired fasting glucose), or 2-h plasma glucose in the 75-g OGTT is 140 mg/dl-199 mg/dl (impaired glucose tolerance), or HbA1c is 5.7%-6.4%. These individuals have increased risk for developing diabetes (ADA, *2013b*). Gestational diabetes mellitus (GDM): Defined as glucose intolerance that is first detected during pregnancy. It has variable severity: in some women, homeostasis is restored shortly after delivery, while others remain at high risk for the development of type 2 DM in the future (*Bellamy et al, 2009; Schmidt et al, 2001*). GDM is diagnosed when: FPG ≥92 mg/dl, OGTT (1-h plasma glucose) ≥180 mg/dl, or OGTT (2-h plasma glucose) ≥153mg/dl (ADA, *2013b*).

Body Mass Index (BMI): This is a simple index of weight-for-height used commonly to classify underweight, overweight, and obesity in adults. It is defined as weight in kilograms divided by the square of the height in meters (kg/m^2) (*WHO, 2006*). It is classified as: underweight (<18.5 kg/m^2), normal weight (18.5 kg/m^2 -24.99 kg/m^2) , overweight (25 kg/m^2-29.99 kg/m^2), and obese (≥30 kg/m^2) (*WHO, 2006*).

Desirebale total cholesterol level is <200 mg/dl; borderline high is 200 mg/dl-239 mg/dl; and high is ≥240 mg/dl *(National Cholesterol Education Program (NCEP) 2001).* HDL cholesterol is considered low at levels ≤40 mg/dl; high at ≥60 mg/dl *(NCEP, 2001).* Optimal LDL cholesterol is <100 mg/dl; high at 160 mg/dl-189 mg/dl; very high ≥190 mg/dl *(NCEP, 2001).* Nor-

mal triglyceride is <150 mg/dl; borderline high at 150 mg/dl-199 mg/dl; high 200 mg/dl-499 mg/dl; very high ≥400 mg/dl *(NCEP, 2001).*

3.3.d Statistical Method

Statistical Analysis System 9.2 version (SAS 9.2) was used in setting and analyzing data, including the mean, standard deviation, odds ratio, confidence intervals, and p-values. $P<0.05$ was used to establish statistical significance. Descriptive statistics were derived for the demographic variables using SAS 9.2. SAS 9.2 version was also used to run univariate logistic regression analysis to determine the association between metabolic variables (BMI, cholesterol, LDL, HDL, triglyceride, hypertension) among pregnant diabetic women.

Logistic regression analysis was used to determine the likelihood of being diagnosed with DM, provided the patient has the metabolic conditions. It was also used to determine the likelyhood of being diagnosed with GDM stratified by race/ethnicity, age, income, and education.

Chapter IV

Results

4.1 Descriptive Statistics

The sample size for the study is 1417, of which 114 (9.3%) were diagnosed with diabetes. Table 1 shows the demographic characteristics of the sample. Among the respondents (N=1417), approximately 39% (n= 616) were between ages 18-25 years, 687 (48.9%) were between ages 26-35 years, while 110 (1.6%) are between ages 36-45 years. Non-Hispanic whites made up the majority racial/ethnic group (52.9%), followed non-Hispanic blacks (15.6%) and Mexican-Americans (16%), and 168 (15.5%) represent "Other" racial groups. Nearly 22% had less than high school education, 20% were high school graduates, and 58% had at least some college education.

Table 1: Demographic Characteristics in the General Population (N=1417)

Variable	N	% (SE)
Diabetes		
Yes	114	9.3
No	1303	90.7
Race/Ethnicity		
NH Whites	620	52.9
NH Blacks	219	15.6
Mex-Americans	420	16.0
Others	168	15.5
Age (years)		
18-25	616	39.5
26-35	687	48.9
36-45	110	11.6
Education		
<HS	395	21.6
HS Graduate	300	20.1
At least College	667	58.3

In Table 2, majority of the respondents were overweight (66.9%). A total of 127 (9.0%) had hypertension, 619 (39.1%) had elevated total cholesterol, 397 (25.7%) had elevated low den-

sity lipoprotein (LDL), 1028 (68.15%) had low high density lipoprotein (HDL), while 359 (20.96%) had elevated triglycerides. The mean levels of total cholesterol, LDL, HDL, Triglycerides, and BMI are also shown in Table 3.

Table 2: Metabolic Profile in the General Population

Variable	N	% (SE)
BMI		
Underweight	124	7.4
Normal	359	25.8
Overweight	934	66.9
Hypertension		
Yes	127	9.0
No	1290	91.0
Total Cholesterol		
Low	798	61.9
Elevated	619	39.1
HDL		
Low	1028	68.2
Elevated	389	31.9
LDL		
Low	1020	74.4
Elevated	397	25.7
Triglycerides		
Low	1058	79.1
Elevated	359	21.0

Table 3: Mean levels of metabolic factors among pregnant women

Variable	N	Mean (SE)	95% CI
Total cholesterol	986	212.6 (2.7)	207.2-217.9
HDL	450	67.0 (1.1)	65.8-69.2
LDL	596	114.8 (2.1)	110.6-118.9
TG	640	160.3 (4.6)	151.0-170.0
BMI	1315	29.1 (0.3)	28.5-29.7

Tables 4 show the mean values for metabolic conditions stratified across diabetes status. As shown there were statistically significant differences between pregnant diabetic women and pregnant non-diabetic women in terms of mean total cholesterol level [(210 vs. 221) (p<0.0001)]; mean LDL cholesterol [(105 vs.122) (P<0.0001)]; mean HDL cholesterol [(62 vs. 69) (P<0.0001)]; mean triglyceride level [(190.4 vs. 178.4) (P<0.0001)]; and mean BMI [(32.3 vs. 28.7) (P<0.0001)];

Table 4: Metabolic Profile by Diabetes Diagnosis Among Pregnant Women

Diabetes Diagnosis					
Variable	**Yes**		**No**		**P-value**
	n	Mean (SD)	n	Mean (SD)	
Total Cholesterol (mg/dL)	97	210.0 (53.2)	889	221.4 (50.3)	<0.0001
LDL Cholesterol (mg/dL)	88	104.7 (35.9)	508	122.0 (40.1)	<0.0001
HDL Cholesterol (mg/dL)	56	61.7 (16.2)	394	69.4 (16.8)	<0.0001
Triglycerides (mg/dL)	101	190.4 (102.2)	539	178.4 (86.6)	<0.0001
Avg. BMI (kg/m^2)	110	32.3 (8.3)	1205	28.7 (6.5)	<0.0001

Table 5 shows proportions of pregnant diabetic versus pregnant non-diabetic women in the population across various demographic and metabolic variables. Only about 40% of pregnant diabetic women had at least some college education, when compared to 60% of those who have not been diagnosed with diabetes (p=0.0294). Similarly, 86.9% of pregnant diabetic women were overweight/obese when compared to 64.8% of pregnant non-diabetic women (p<0.0001) as were 51.0% of pregnant diabetic women with elevated levels of LDL versus 23% of non-diabetic pregnant women (p=0.0001); and 36.9% of pregnant diabetic women with elevated levels of tri-glyceride versus 19.3% of non-diabetic pregnant women (p=0.0036). There were no significant associations between diabetes and race/ethnicity (p=0.1423), age levels (p=0.7074), hypertension diagnosis (p=0.6312), HDL levels (p=0.1169), or total cholesterol levels (p=0.9183).

Table 5: Demographic and metabolic variables by diabetes diagnosis among pregnant women

Variable	Yes		No		P-value
	N	% (SE)	N	% (SE)	
Education					
Less than High School	37	36.0 (7.6)	358	20.1 (1.7)	
HS Grad	30	24.0 (6.8)	270	19.7 (1.8)	0.0294
At least college	43	39.9 (7.2)	624	60.2 (2.1)	
Race/Ethnicity					
NH White	45	45.6 (7.0)	575	53.6 (2.6)	
NH Blacks	14	12.2 (3.6)	205	16.0 (1.8)	0.1423
Mexican-American	39	23.5 (4.9)	371	15.2 (1.4)	
"Other" Races	16	18.7 (5.7)	152	15.2 (2.0)	
Age (years)					
18-25	43	44.1 (7.9)	573	39.0 (2.1)	
26-35	51	42.8 (7.8)	636	49.6 (2.6)	0.7074
36-45	19	13.1 (3.3)	91	11.5 (1.9)	
Hypertension (mmHg)					
Yes	13	10.9 (4.5)	114	8.82 (1.4)	0.6312
No	101	89.1 (4.5)	1189	91.2 (1.4)	

Table 5 (continued): Demographic and metabolic variables by diabetes diagnosis among pregnant women

BMI (kg/m^2)					
Underweight	5	1.5 (0.7)	119	8.0 (1.5)	
Normal	13	11.7 (4.6)	346	27.2 (2.0)	
Overweight	96	86.9 (4.6)	838	64.8 (2.1)	<0.0001
Tot. Cholesterol (mg/dL)					
Low	62	61.3 (6.0)	736	62.0 (2.3)	
Elevated	52	38.7 (6.0)	567	38.1 (2.3)	0.9183
LDL (mg/dL)					
Low	69	49.1 (7.5)	951	77.0 (2.1)	
Elevated	45	51.0 (7.5)	352	23.1 (2.1)	0.0001
HDL (mg/dL)					
Low	73	59.7 (6.2)	955	69.0 (2.1)	
Elevated	41	40.3 (6.2)	348	301.0 (2.1)	0.1169
Triglycerides (mg/dL)					
Low	54	63.1 (5.6)	1004	80.7 (1.8)	0.0036
Elevated	60	36.9 (5.6)	299	19.3 (1.8)	

Table 6 shows differences in demographic and metabolic characteristics among the pregnant diabetic versus pregnant non-diabetic women stratified by race/ethnicity. Among non-Hispanic whites, significant differences in terms of education levels (p=0.0155), LDL levels (p=0.0035) and BMI (p<0.0001) were observed. For instance, pregnant women with diabetes had a higher prevalence of overweight/obese (86.9%) when compared to those who were of normal weight (11.7%). Also, pregnant women who were diabetic had a higher prevalence of elevated LDL levels (54.3%) when compared to those without diabetes (23.4%).

Among non-Hispanic blacks (Table 6), significant differences were observed in terms of education levels (p=0.0015), BMI (p<0.0001), triglyceride levels (p=0.0193), and HDL levels (p=0.0194). For instance, nearly 94% of individuals who were diagnosed with diabetes were overweight/obese when compared to 70% of those who had a negative diabetes diagnosis. Similarly, 36.9% of pregnant diabetic individuals had less than a high school education, when compared to 26.0% the non-diabetic pregnant population.

Among Mexican-Americans, significant differences among the diabetic and non-diabetic groups were observed in terms of educational levels (p=0.0102), BMI (p<0.0001) and triglyceride levels (<0.0001). Within this race/ethnic group, 93.9% of individuals with diabetes were overweight/obese compared to 69.6% of non-diabetic pregnant women. Also, over 60% of diabetic pregnant women had elevated levels of triglycerides compared to 19% of non-diabetic pregnant women. Education, blood pressure, total cholesterol, and LDL were not significantly associated with diabetic pregnancy.

Among "Other" races/ethnicities, education (P=0.0173), age (P<0.0001), LDL (P=0.0007), and low HDL (P=0.0227) were significantly associated with diabetes during pregnancy. Approximately 58% of diabetic pregnant women had less than high school education

compared to just over 25% of non-diabetic pregnant women. Within this race category, 70% percent of diabetic pregnant women have elevated LDL levels compared to 21.0% of non-diabetic pregnant women. Also, 79.9% of diabetic pregnant women had low HDL compared to 67.0% of non-diabetic pregnant women. No other significant associations were observed within this group.

Table 6: Differences in the prevalence of diabetes according to demographic and metabolic variables stratified by race/ethnicity

	NH-Whites			**NH- Blacks**			**Mexican- Americans**			**"Other" Races**		
Variables	Yes N (%SE)	No N (%SE)	P-value	Yes N (%SE)	No N (%SE)	P-value	Yes N (%)	No N (%SE)	P-value	Yes N (%SE)	No N (%SE)	P-value
Education												
<HS	6 18.5 (10.1)	57 7.3 (2.2)		4 36.9 (11.7)	63 26.0 (3.2)		19 52.4 (12.2)	199 55.2 (3.6)		8 58.1 (12.0)	39 25.1 (3.7)	
HS Grad	13 26.5 (9.6)	116 18.3 (2.2)	0.0155	6 42.8 (11.7)	48 26.3 (3.3)	0.0015	10 27.7 (10.4)	82 25.3 (3.3)	0.9726	1 1.4 (1.5)	24 12.2 (1.9)	0.0173
At least college	25 55.0 (6.9)	390 74.4 (2.8)		4 20.3 (5.0)	90 47.7 (3.9)		7 19.9 (5.6)	60 19.5 (2.8)		7 40.4 (12.2)	84 62.7 (3.3)	
Age (years)												
18-25	17 41.9 (10.7)	204 35.9 (3.2)		8 65.3 (12.5)	123 55.2 (3.7)		13 24.6 (7.1)	201 50.0 (1.9)		5 59.8 (9.5)	45 21.72 (4.09)	
26-35	23 54.1 (11.0)	322 50.3 (3.2)	0.0816	3 18.0 (10.9)	73 40.2 (3.7)	0.1762	18 55.0 (7.5)	151 44.5 (2.3)	0.0102	7 16.3 (4.1)	90 62.1 (5.3)	<0.0001
36-45	5 4.01 (2.1)	48 13.9 (2.6)		3 16.7 (10.2)	9 4.58 (1.6)		7 20.4 (8.0)	18 5.5 (1.3)		4 24.0 (7.6)	16 16.2 (2.4)	
Blood Pressure (mmHg)												
Normal	36 84.9 (3.2)	518 91.0 (1.7)	0.0678	12 75.7 (13.5)	179 87.5 (2.2)	0.2921	37 95.5 (3.3)	352 95.7 (1.3)	0.9562	16 100 (0.00)	140 91.4 (1.6)	
Hyperten-sive	9 15.1 (3.2)	57 9.0 (1.7)		2 24.3 (13.5)	26 12.5 (2.12)		2 4.5 (3.3)	19 4.4 (1.3)		0 . 	12 8.6 (1.6)	

Table 6 (continued): Differences in the prevalence of diabetes according to demographic and metabolic variables stratified by race/ethnicity

Variables	NH-Whites			NH- Blacks			Mexican- Americans			"Other" Races		
	Yes N (%SE)	No N (%SE)	P-value	Yes N (%SE	No N (%SE	P-value	Yes N (%SE)	No N (%SE)	P-value	Yes N (%SE)	No N (%SE)	P-value
BMI (kg/m^2)												
Under-	2	64		1	15		2	26		0 .	14	
weight	1.6	9.9		2.83 (0.65)	5.3		1.5	3.7			8.16	
	(0.8)	(2.3)			(1.2)		(1.0)	(1.4)			(2.6)	
Normal	8	176	<0.0001	1	50	<0.0001	1	79	<0.0001	3	41	
	11.5	30.2		2.6	23.8		4.55	26.7		26.9	21.0	
	(6.4)	(3.00)		(0.6)	(2.9)		(0.8)	(2.8)		(14.3)	(3.1)	
Overweight	35	335		12	140		36	266		13	97	
	86.8	59.9		94.6	70.9		93.9	69.6		73.1	70.8	
	(6.4)	(2.7)		(1.2)	(2.9)		(1.1)	(2.5)		(14.3)	(3.5)	
Tot. cholesterol												
Low	19	307		11	127		22	208		10	94	
	58.2	62.9		73.1	62.3		64.5	54.1		56.9 (11.9)	66.6	
	(8.0)	(3.5)	0.6206	(6.4)	(3.2)	0.1541	(8.9)	(2.4)	0.3086		(3.3)	0.4713
Elevated	26	268		3	78		17	163		6	58	
	41.8	37.1		26.9	37.8		35.5	45.9		43.0	33.9	
	(8.0)	(3.5)		(6.4)	(3.2)		(8.9)	(2.4)		(11.9)	(3.3)	
LDL												
Low	25	407		12	161		23	264		9	119	
	45.7	76.6		75.4	79.2		57.3	73.8		29.6	79.01	
	(11.0)	(2.3)	0.0035	(10.6)	(3.2)	0.7220	(9.7)	(2.6)	0.1117	(9.7)	(4.1)	0.0007
Elevated	20	168		2	44		16	107		7	33	
	54.3	23.4		24.6	20.8		42.7	26.2		70.4	21.0	
	(101.0)	(2.3)		(10.6)	(3.2)		(9.7)	(2.6)		(9.7)	(4.1)	
HDL												
Low	27	438 70.57		9 42.07	150		26	260		11	107	
	56.3	(2.91)		(11.93)	72.5		59.3	61.95 (3.28)		79.92	66.93 (3.73)	
	(7.9)		0.0722		(4.4)	0.0194	(9.1)		0.7747	(4.69)		0.0229
Elevated	18	137		5	55		13	111		5	45	
	43.7	29.4		57.9	27.5		40.7	38.1		20.08	33.07 (3.73)	
	(7.9)	(2.9)		(11.9)	(4.4)		(9.1)	(3.3)		(4.69)		
Triglycerides												
Low	20	427		10	185		16	271		8	121	
	68.5	77.8		70.3	91.0		39.3	80.7		75.1	80.0	
	(7.6)	(1.9)	0.2381	(10.6)	(2.5)	0.0193	(6.9)	(2.3)	<0.0001	(5.8)	(4.3)	0.4866
Elevated	25	148		4	20		23	100		8	31	
	31.5	22.2		29.7	9.0		60.7	19.3		24.9	20.0	
	(7.6)	(1.9)		(10.6)	(2.5)		(6.9)	(2.3)		(5.8)	(4.3)	

Table 7 shows results of the logistic regression analysis. Among the general sample, there was no significant difference in the odds of being diagnosed with GDM between individuals with low cholesterol levels vs. individuals with high cholesterol levels in the crude (OR= 1.03, 95% CI= 0.59-1.79) and adjusted model (OR= 0.74, OR= 0.40-1.38). Individuals with high LDL levels were significantly more likely to be diagnosed with diabetes when compared with individuals with low LDL in both the crude (OR=3.47; 95% CI=1.90-6.33), and adjusted model (OR=2.82; 95% CI=1.17-6.75).

There was no significant difference in the odds of being diagnosed with GDM between individuals with high HDL levels vs. individuals with low HDL levels in the crude model (OR= 0.66, 95% CI= 0.40-1.10) and adjusted (OR= 0.71, 95% CI= 0.43-1.19). Individuals with high triglycerides levels were significantly more likely to be diagnosed with diabetes when compared with individuals with low triglycerides in both the crude (OR= 2.44, 95% CI= 1.36-4.38), and adjusted model (OR= 1.30, 95% CI= 0.56-3.01).

There was no significant difference in the odds of being diagnosed with GDM between individuals who are underweight versus individuals with normal weight in the crude model (OR= 0.43, 95% CI= 0.13-1.43) and adjusted (OR= 0.43, 95% CI= 0.12-1.56). Individuals who are overweight/obese were significantly more likely to be diagnosed with diabetes when compared with individuals of normal weight in both the crude (OR= 3.13, 95% CI= 1.28-7.64), and adjusted model (OR= 2.44, 95% CI= 1.02-5.86).

Table 7: Associations between metabolic profile and diabetes diagnosis

Variable	OR[1] (95% CI)	OR[2] (95% CI)
Cholesterol (mg/dl)		
Low	Reference	Reference
Elevated	1.0 (0.6-1.8)	0.7 (0.4-1.4)
LDL (mg/dl)		
Low	Reference	Reference
Elevated	3.5 (1.9-6.3)	2.8 (1.2-6.8)
HDL (mg/dl)		
Low	0.7 (0.4-1.1)	0.7 (0.4-1.2)
Elevated	Reference	Reference
Triglyceride (mg/dl)		
Low	Reference	Reference
Elevated	2.4 (1.4-4.4)	1.3 (0.6-3.0)
BMI (kg/m^2)		
Underweight	0.4 (0.1-1.4)	0.4 (0.12-1.6)
Normal	Reference	Reference
Overweight	3.13 (1.3-7.6)	2.4 (1.0-5.9)

OR [1]= Crude odds ratio;
OR[2]= Adjusted odds ratio (adjusted for the effect of age, BMI, LDL, HDL, and triglyceride levels)

Tables 8 show the association between diabetes diagnosis and metabolic variables stratified by race/ethnicity. Among non-Hispanic pregnant White women, individuals with elevated LDL levels, and who were overweight/obese were significantly more likely to be diagnosed with diabetes when compared to those with low LDL levels and normal weight respectively. For instance, non-Hispanic white women with elevated LDL levels were nearly 4 times more likely to be diagnosed with diabetes when compared to those with low LDL levels in both the crude and adjusted models. No other significant associations were observed within this group.

Among non-Hispanic pregnant Black women, individuals with elevated triglycerides and who were underweight, or overweight/obese were significantly more likely to be diagnosed with diabetes when compared to those with low triglyceride levels, and who were normal weight respectively. For instance, individuals with elevated triglyceride were significantly more likely to be diagnosed with diabetes in both the crude (OR=4.27; CI=1.4 – 13.4) and adjusted (adjusted

OR=5.10; CI=1.3 – 20.7) models. Also, women who were underweight were at least 5 times more likely to be diagnosed with diabetes when compared to those who were normal weight.

Among pregnant Mexican-American women, individuals with elevated triglyceride levels were significantly more likely to be diagnosed with diabetes when compared to those with low triglyceride levels in both the crude (OR= 6.5; 95% CI=3.4 – 12.4) and adjusted (OR=7.9; 95% CI=2.7 – 22.9) models. Similarly those who were overweight were significantly more likely to be diagnosed with diabetes when compared those who were normal weight in both the crude (OR= 7.9; 95% CI=5.2 – 12.1) and adjusted (OR= 5.5; 95% CI=3.2 – 9.5).

Among pregnant women from 'Other' race ethnicities, individuals with elevated LDL were significantly more likely to be diagnosed with diabetes in both the crude (OR=8.94 95% CI= 3.0 – 27.0) and adjusted (OR=19.4; 95% CI=3.6 – 10.3.9). Also, individuals with low LDL levels were significantly more likely to be diagnosed with diabetes in the crude model (OR=1.97 95% CI= 1.0 – 3.4) but not in the adjusted model.

Table 8: Stratification of the association between diabetes diagnosis and metabolic variables into race/ethnicity.

	Non-Hispanic Whites		Non-Hispanic Blacks		Mexican-Americans		"Other" Races	
Variable	**OR[1] (95% CI)**	**OR[2] (95% CI)**	**OR[1] (95% CI)**	**OR[2] (95% CI)**	**OR[1] (95% CI)**	**OR[2] (95% CI)**	**OR[1] (95% CI)**	**OR[2] (95%CI)**
Total Cholesterol								
Low	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Elevated	1.2	1.2	0.6	0.6	0.7	0.2	1.5	1.6
	(0.6-2.7)	(0.6-2.66)	(0.1-1.2)	(0.3-1.3)	(0.3-1.5)	(0.1-0.4)	(0.5-4.1)	(0.4-5.9)
LDL								
Low	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Elevated	3.9	4.4	1.24	0.88	2.10	0.88	8.94	19.44
	(1.6-9.2)	(1.7-11.5)	(0.4-4.0)	(0.30-2.6)	(0.9-5.1)	(0.2-3.2)	(3.0-27.0)	(3.6-103.9)
HDL								
Low	0.5	0.6	0.3	0.9	0.9	2.0	2.0	1.6
	(0.2-1.0)	(0.3-1)	(0.1-0.3)	(0.3-2.6)	(0.4-1.9)	(01.0-2.0)	(1.1-3.4)	(0.7-3.9)
Elevated	3Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Triglycerides								
Low	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Elevated	1.6	0.5	4.2	5.1	6.46	7.86	1.33 (0.61-2.91)	0.30
	(0.7-3.5)	(0.2-1.2)	(1.4-3.4)	(1.3-20.7)	(3.38-12.37)	(2.70-22.86)		(0.05-1.93)
BMI								
Underweight	0.43	0.3	5.00	6.0	2.4	7.9	*	*
	(0.10-1.9)	(0.08-1.6)	(2.95-8.49)	(2.4-14.7)	(0.5-12.7)	(2.7-22.9)		
Normal	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Overweight	3.8	23.0	12.5	11.8	7.9	5.5	0.8	0.8
	(1.1-13.3)	(0.8-10.4)	(7.2-21.6)	(6.4-21.7)	(5.2-12.1)	(3.2-9.5)	(0.2-3.7)	(0.4-1.9)

OR [1]= Crude odds ratio; OR[2]= Adjusted odds ratio (adjusted for the effect of age, BMI, LDL, HDL, and triglyceride levels)
*= numbers too low for analysis

Chapter V

Discussion

This study sought to determine the association between metabolic profiles and pregnancy in American women diagnosed with diabetes mellitus. American diabetic pregnant women were stratified by race/ethnicity (non-Hispanic Whites, non-Hispanic Blacks, Mexican-Americans, and "Other races") to determine the effect of the metabolic variables (total cholesterol, LDL, HDL, and triglycerides) on diabetes diagnosis. It examined the differences in the metabolic profiles of pregnant women with prediabetes and diabetes; differences in the metabolic profile of non-Hispanic Whites, non-Hispanic Blacks, and Mexican-Americans, and other races. This study shows strong association of metabolic profiles with the diagnosis of GDM. Among the NH-Whites, elevated LDL and increased BMI are significantly more associated with positive GDM diagnosis; in the NH-Black and Mexican-Americans populations, elevated triglycerides and increased BMI are significantly more associated with GDM diagnosis. In the "Other" races, elevated LDL is more significantly more associated with the diagnosis of GDM. This shows that the association between various metabolic conditions and GDM diagnosis vary according to race/ethnicity. Rosenberg et al (2005) indicated that gestational diabetes was increasing among non-White women; the prevalence of diabetes among American women continues to increase, with non-Hispanic Blacks and Hispanics more likely to be affected than non-Hispanic Whites (*Rosenberg et al, 2005).*

This study used NHANES data from 1999-2010. It is a nationally representative sample of the civilian non-institutionalized population of the US. In their study, Ziaea et al, 2006 noted

that normal human pregnancy results in a physiologic hyperlipidemia involving a gestational rise in blood triglyceride and cholesterol levels (*Ziaea et al, 2006*). However, in GDM there are increased levels of maternal total cholesterol, probably related to alterations in the expression of proteins involved in lipid and cholesterol homeostasis (*Leiva et al, 2013*). Subjects with high total cholesterol had higher preeclampsia rate: RR of 1.39 (95% CI, 1.04–1.75), and that higher levels of triglycerides are independently and significantly associated with an increased risk for adverse pregnancy outcomes (*Wiznitzer et al, 2009*). This study shows a statistically significant difference ($p<0.0001$) in the mean levels of total cholesterol, LDL, HDL, and triglycerides between gestational diabetic women and non-diabetic pregnant women. In a comparative study, Khan et al, 2013 reported mean total cholesterol and mean triglyceride significantly higher at $P<0.05$ in GDM women as compared to non-diabetic pregnant women; their LDL cholesterol and HDL cholesterol levels in GDM women were non-significantly higher than in non-diabetic women (*Khan, et al, 2013*). They found that total cholesterol was 205.81 ± 19.09 mg/dL in GDM women, compared to 194.7 ± 23.7 mg/dL in non-diabetic pregnant women; triglycerides in GDM women was 189.6 ± 20.0 mg/dL in GDM women compared to 169 ± 22.3 mg/dL in non-diabetic pregnant women. In Table 4, the mean total cholesterol in GDM women is 210 ± 53.2 mg/dL compared to 221.4 ± 50.3 mg/dL in non-diabetic pregnant women; mean triglyceride is 190.4 ± 102.2 mg/dL in GDM women compared to 178.4 ± 86.6 mg/dL in non-diabetic pregnant women.

Obesity is a significant risk factor for GDM across all racial/ethnic groups *(Golden, S.H. et al, 2012).* This statement supports my findings. My study shows significant association of BMI with GDM diagnosis ($p<0.0001$) among all racial/ethnic groups (Table 6), indicating increased risk of GDM with increasing BMI among races. This study is also supported by a previous study by Hedderson et al (2012). They found that the age-adjusted prevalence of GDM

among all racial/ethnic groups increased with increasing BMI. Across the racial/ethnic groups (Tables 6), my study shows a statistically significant (P<0.0001) relationship between obesity and diabetes diagnosis among pregnant women. Increasing BMI within the general population contributes not only to greater numbers of diabetic individuals, but also to a greater proportion of diabetic individuals who are extremely obese and, thus, to a greater proportion who are at risk of adverse outcomes (*Leibson et al, 2001).*

Socioeconomic status is also associated with increase in GDM. In my study, GDM was diagnosed more in women with high school education or less (p=0.0294) as compared to those with at least college education (Table 5). Nearly 36% of women with less than high school education were diagnosed with diabetes compared to just about 24% of those with high school education. Golden et al report that women with less than high school education had 70% greater odds of having GDM than women with at least high school education; they also reported a 7% annual increase in GDM among women with a high school education compared with a 4% annual increase among those with a college education *(Golden et al, 2012).*

Among the non-Hispanic Blacks and "Other races", my study show significant association of lower education and being diagnosed with diabetes: for non-Hispanic Blacks P=0.0246, and for "Other races" P=0.0173. A study by Hedderson et al showed that Asian women were more educated and less likely to be overweight or obese compared to women from other racial/ethnic groups (*Hedderson et al, 2012*). The number of respondents reporting income in my study was too low to run an analysis. But a study by Golden et al showed that being below the poverty limit also increased the odds of being diagnosed with GDM *(Golden et al, 2012).*

Weakness/Limitations

This is a cross-sectional study that uses secondary data from NHANES 1999-2010. Cross-sectional study does not have cause/effect relationship because it takes only a snap-shot at a point in time of the independent and outcome variables. Responses to questionnaires in NHANES 1999-2010 are self-reported. Therefore, the possibility of self-reporting biases cannot be ruled out. In addition, some of the variables received low responses. As a result, the low numbers are too small to be analyzed.

Clinical Relevance

Obesity and race/ethnicity are established risk factors GDM. In addition to these, high levels of cholesterol and triglycerides may be contributing factors for the development of GDM *(Khan et al, 2013)*. GDM alters the expression of placental genes related to markers and mediators of inflammation and leads to impaired fetal growth and programming, which causes several metabolic diseases; it can accelerate the development of cardiovascular disease (CVD) in adult life (*Sisino et al, 2013*). Women with GDM are at high risk of recurrence of gestational diabetes and of developing type 2 DM in the future (*Lawrence et al, 2008*). The risks of developing diabetes and metabolic syndrome are increased in the decade after delivery, while the newborn infants are at increased risk of developing obesity and diabetes in adolescence and adulthood (*Ferrara, 2007*). GDM plays a crucial role in the prevalence of obesity and diabetes. Other complications of GDM include macrosomia, spontaneous abortion, birth defects, cesarean section delivery, transient newborn hypoglycemia, and hypocalcmia.

Recommendations

Based on the results of my study, the medical management of pregnant women with various metabolic conditions may have to be modified dependent on the race/ethnicity of the individual. Even though recommendations have already been put forward for the screening of metabolic conditions during pregnancy, more particular attention should be paid to metabolic factors that shows significant factor according to race/ethnicity. Screening, including cholesterol and lipoprotein monitoring, should begin early in pregnancy and continued through postpartum.

Since education is an important factor in diabetes prevention, women especially non-Hispanic Blacks and Mexican-Americans, of childbearing age should be educated on the prevalence of diabetes, diabetes control, and the complications of diabetes. Lifestyle modification, including weight loss, exercise, and healthy diet, should also be stressed, as obesity is one of the greatest contributors of diabetes. The information obtained from this cross-sectional study does not show a causal relationship. Future more rigorous studies should be conducted to determine if these findings can be replicated. Future investigations is also suggested to determine the association between underweight and GDM among the NH-black women.

Conclusion

With the exception of non-Hispanic Whites, pregnant American women with higher levels of cholesterols, high triglycerides, increased body mass index (25 kg/m^2 or greater), and less than high school education were found to be at greater risks of diabetes. The result of this analysis suggests that healthcare professionals should be more aggressive in controlling these metabolic abnormalities in pregnant women. Early intervention prior to pregnancies may help to onset of prediabetes/diabetes. Empowerment of pregnant women in the management of their diabetes may also be critical in averting the detrimental effect of these metabolic abnormalities.

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Thank you, O Lord, My God. I have called on you and you have answered me. To you alone be all the glory!