Is Sickle Cell Trait Pregnancy a Risk for Low Birth Weight?

Uchechi E. Okani
Texas Woman’s University

Author Note
Uchechi Okani, Doctor of Nursing Practice (DNP) student, College of Nursing, Texas Woman’s University, Dallas, Texas.

No financial support or grants were requested for this project.

Correspondence concerning this article should be addressed to Uchechi Okani, 2011 Pebble Brook Circle, McGregor, TX 76657.

Email: uokani@twu.edu
Table of Contents

Title Page..........................................................1
Table of Contents ..................................................2
Abstract..........................................................5
Introduction.......................................................6
Purpose ...........................................................7
Problem Statement..............................................7
  Research Questions .............................................11
  Research Hypotheses ..........................................11
  Null Hypotheses ...............................................12
  Pico Questions ...............................................12
Conceptual Definitions .......................................12
Operational Definitions .......................................13
Theoretical/Conceptual Framework .........................14
Review of Literature .........................................16
  Method ..........................................................16
  Evaluation of Articles ........................................17
Summary of Review of Literature .........................24
Methodology .....................................................25
  Population and Sample ......................................25
  Instrumentation .............................................27
Implementation ..................................................30
  Objective ......................................................30
# Sickle Cell Trait Pregnancy Risk

Timeline .................................................................................................................. 30

Project Requirement ............................................................................................. 32

Sources and Types of Information ........................................................................ 32

Inclusion Criteria .................................................................................................... 33

Exclusion Criteria ................................................................................................... 33

Rationale for Exclusion .......................................................................................... 34

Analysis ................................................................................................................... 34

Support site and Personnel required for the Project .............................................. 35

Evaluation .............................................................................................................. 36

Results ................................................................................................................... 38

Descriptive Analyses ............................................................................................ 38

Preliminary Analyses ............................................................................................. 41

Primary Analyses .................................................................................................. 44

Summary ................................................................................................................. 49

End Product/Deliverables ...................................................................................... 50

Discussion .............................................................................................................. 50

Conclusion ............................................................................................................. 53

References ............................................................................................................. 54

Appendix A ............................................................................................................. 60

Appendix B ............................................................................................................. 61

Appendix C ............................................................................................................. 62

Appendix D ............................................................................................................. 63

Appendix E ............................................................................................................. 66
Abstract

Low birth weight is the leading cause of death among African American infants. Controversy exists in the literature regarding the association of presence of maternal sickle cell trait (SCT) with low birth weight newborns. The purpose of this project was to determine whether African American women with SCT are more likely to have a low birth weight infant or infant classified as small for gestational age (SGA) as compared to African American women with normal hemoglobin. A retrospective chart review of 102 African American mothers (and their offspring), evenly split for genotype AS and AA profiles, who delivered between 1991 and 2011, was conducted. The groups were matched on race, gestational age, gender of baby, body mass index (BMI) of mother, and parity. Statistical analyses were conducted to examine the differences in birth weight of the infants’ in both groups. There were no differences in infants’ birth weight or birth weight centile between women with the two different genotypes.

Keywords: sickle cell anemia, sickle cell trait, small for gestational age, birth weight, birth weight centile, hemoglobinopathy, intra uterine growth restriction (IUGR)
Is Sickle Cell Trait Pregnancy a Risk for Low Birth Weight?

Approximately 8.1% of infants in the United States are born at low birth weight, with the highest incidence among African Americans (National Conference of State Legislatures [NCSL], 2011). Low birth weight babies have increased risk of heart pathologies, intestinal problems, respiratory distress, and intracranial bleeding at birth (NCSL, 2011). Lasting health problems for low birth weight babies include cerebral palsy, vision and hearing loss, learning difficulties, mental retardation, and social and emotional problems (NCSL, 2011). Sickle cell disease (SCD) is the most common hemoglobinopathy that can complicate pregnancy and is usually associated with intrauterine growth restriction (IUGR), low birth weight, and stillbirth (Tan, Seed, & Oteng-Ntim, 2008; Zack-Williams, 2007). It is estimated that SCD affects 1 of every 600 Americans of African descent (Charneski & Congdon, 2010).

Sickle cell trait (SCT) is the carrier state for sickle cell anemia (the most common type of SCD). SCT occurs in approximately 1 in every 12 African Americans in the United States (Centers for Disease Control [CDC], 2011; Randolph, 2007). SCT has long been considered a benign carrier state, but some studies have associated SCT with significantly poor pregnancy outcomes, such as low birth weight (Tsaras, Owusu-Ansah, Boateng, & Amoateng-Adjepong, 2009). Some literature suggests that placental abnormalities might play a causal role in these poor pregnancy outcomes because pregnant women with SCT were found to be at increased risk for acute ascending amniotic infection and meconium histiocytosis (Taylor et al., 2008; Tsaras et al., 2009). Placental pathologies also indicate sickling in the intervillous space and decidual vessels in patients with SCT (Taylor et al., 2008; Tsaras et al., 2009). There is conflicting evidence in the literature regarding the effect of SCT on pregnancy outcomes such as birth weight (Jans, De Jonge, & Lagro-Janssen, 2010; Tan et al., 2008).
Purpose

The purpose of this capstone project is to determine whether African American women with SCT are more likely to have a low birth weight infant or infant classified as small for gestational age (SGA) as compared to African American women with normal hemoglobin.

Problem Statement

Low birth weight is an important predictor of newborn health and survival (World Health Organization [WHO], 2011). Infants born at low birth-weight (weight less than 2500 grams at birth) or infants whose weight is classified as small for gestational age (SGA) (at or below the 10th percentile for a given gestational age) are at increased risk for neonatal distress, permanent deficits in growth and neurocognitive development, and mortality (CDC, 2008). In the United States, low birth weight and preterm births cost an estimated $26 billion every year (Mandy, 2011; NCSL, 2011; Appendix A).

Reducing the rate of poor pregnancy outcomes such as low birth weight among the African American population has been the focus of many public health initiatives in the United States (Ferré et al., 2011; Ohio Department of Health [ODH], 2011). Although there has been some decline in the U.S. over the years, infant mortality rate among African Americans has remained two-and-a-half times greater than that of the Caucasian population (16.2 and 6.2 per 1,000 live births respectively in 2008) (ODH, 2011).

Experts, over the years, in the attempt to uncover the root-cause of poor pregnancy outcomes (e.g. low birth weight and high infant mortality rate) among the African American population, have explored genetic (David & Collins, 2007) and socioeconomic factors (Debbink & Bader, 2011). In order to examine the trends in rates of low birth weight among African American infants, Ferré, Handler, Hsia, Barfield, and Collins (2011) conducted a cross-sectional
and trends study of singleton births to African American US residents from 1991 to 2004. Findings of the study showed that the rate of low birth weight among African American infants declined from 12.15% in 1991 to 11.55% in 1996. A slow decrease in low birth weight rate was also noted between 1996 (11.5%) and 2001 (11.19%). However, between 2001 and 2004, the rate of low birth weight went up from 11.19% to 11.70%. The researchers reported that both maternal socio-demographic and health-related factors were responsible for the changes in the trends observed. The researchers concluded that multiple factors need to be explored simultaneously in order to find solution to the low birth weight problem within the African American population.

Debbink and Bader (2011) conducted a study to examine the influence of racial residential segregation on the overall and specific etiological risks of low birth weight. Birth certificate information was obtained from the Michigan Department of Community Health for all the singleton births for the year 2000 in the state. The result of this inquiry showed that African American infants were more likely to be born at low birth weight compared to Caucasian infants despite the neighborhood the family’s residence. Nevertheless, this incidence was highest among the infants born to mothers in Black segregated neighborhoods. White infants born in Black segregated neighborhoods had higher rate of low birth weight than White infants born in White non-segregated and segregated neighborhoods. The researchers concluded that the odds of an infant to be born at low birth weight are higher in the black segregated neighborhoods independent of economic factors. They also noted that low birth weight was more associated with intrauterine growth restriction than preterm birth. Among the births with low birth weight, 52.9% (n=4747) were related to intrauterine growth restriction whereas 47.2% (n=4194) were related to preterm birth.
Although the effect of socioeconomic factors were evident as one explanation for the increased incidence of low birth weight in the African American population, the researchers realized that socioeconomic factors alone were not enough to explain the trend of IUGR they observed. The researchers, therefore, suggested that further investigation to physiologically explain the phenomenon, be conducted (Debbink & Bader, 2011). Better understanding of the etiology is required in order to develop proper interventions for lowering the existing high rate of low birth weight infants and high infant mortality among African Americans.

In searching for physiological answers for existing poor pregnancy outcomes and low birth weight rate among African American populations, many researchers have examined health and genetic issues such as genotypes. One of the first incidents that supported that proposition that the sickle cell trait genotype might not be as benign as had been generally presumed was the occurrence of sudden deaths in the military in 1970 (Ferster & Eichner, 2012). Within a one-year period, four African American recruits with SCT died suddenly during Army basic combat training (Ferster & Eichner, 2012). It was concluded after much investigation, that “exertional heat illness” (EHI) was the culprit (Ferster & Eichner, 2012). The result of the investigation led to enacting measures within the Army to prevent EHI occurrences in the training camps (Ferster & Eichner, 2012).

Similar concern emerged in the sports world when the number of injury and deaths of athletes with sickle cell trait increased. Sixty-three percent of non-traumatic sports deaths from 2000 to 2011 were attributed to complications of exertional sickling in sickle cell trait athletes (Jones, 2011). These occurrences led to mandatory sickle cell trait screening for all Division I athletes in the National Collegiate Athletic Association (NCAA), beginning during the 2010-2011 academic year (Jones, 2011). Today in these sports, SCT athletes are routinely identified.
and measures such as decreased intensity of exercise are in place to prevent exertional sickling episodes (Jones, 2011).

Within the healthcare community, it is well understood that the pregnancy of a woman with sickle cell anemia carries a higher risk. Whereas public awareness has increased as far as implications of exertional sickling for SCT individuals in sports and in other physically stressful conditions, the effect of sickle cell trait on outcome of pregnancy, if any, remains a subject to debate (Jans, De Jonge, & Lagro-Janssen, 2010). Over the years, studies published on this matter have provided inconsistent conclusions (Jans, De Jonge, & Lagro-Janssen, 2010). Many studies have suggested that sickle cell trait is a risk factor for poor pregnancy outcomes whereas others could not confirm the risk (Jans, De Jonge, & Lagro-Janssen, 2010). Whereas the incidence of SCD and SCT is highest among African Americans, sickle cell disease can also be found among Central Americans, Asians, and people from the Mediterranean region (Randolph, 2007). It is, therefore, important that obstetricians, midwives, and other health providers be made aware of any potential risk among SCT individuals during pregnancy.

Investigations to determine whether SCT pregnancy results in poor outcomes similar to those of SCD pregnancies are needed to further understand any relationship between SCT and low birth weight. In addition, further studies need to be performed on U.S. populations of pregnant women.

The Family health center (FHC), a network of more than 12 community clinics and home to the County Medical Education and Research Foundation (CMERF), is an ideal site to conduct an investigation on SCT and birth weight. The FHC provides primary and obstetric care to low income communities of Central Texas, among which is a large population of African American
pregnant women. The FHC has the structure, electronic database, and patient population to support any research study that will explore the effect of SCT status on pregnancy outcomes.

**Research Questions**

1. Are African American women with SCT at higher risk of having a low birth weight infant (weight at birth of less than 2500g, up to and including 2499g) compared to similar African American women with normal hemoglobin?

2. Are African American women with SCT at higher risk of having an SGA infant (birth weight at or below the 10th percentile for a given gestational age) compared to similar African American women with normal hemoglobin?

3. Is there a difference in birth weight of term infants of Africa American women with SCT (hemoglobin AS profile) as compared to similar African American women with normal hemoglobin (hemoglobin AA profile)?

**Research Hypotheses**

1. African American women with SCT are at higher risk of having a low birth weight infant (weight at birth of less than 2500g, up to and including 2499g) compared to similar African American women with normal hemoglobin.

2. African American women with SCT are at higher risk of having an SGA infant (birth weight at or below the 10th percentile for a given gestational age) compared to similar African American women with normal hemoglobin.

3. There is a difference in birth weight of term infants of Africa American women with SCT (hemoglobin AS profile) as compared to similar African American women with normal hemoglobin (hemoglobin AA profile).
Null Hypotheses

1. African American women with SCT are not at higher risk of having a low birth weight infant (weight at birth of less than 2500g, up to and including 2499g) compared to similar African American women with normal hemoglobin.

2. African American women with SCT are not at higher risk of having an SGA infant (birth weight at or below the 10th percentile for a given gestational age) compared to similar African American women with normal hemoglobin.

3. There is no difference in birth weight of term infants of African American women with SCT (hemoglobin AS profile) as compared to similar African American women with normal hemoglobin (hemoglobin AA profile).

PICO Questions

1. Among African Americans, are pregnant women with SCT at a higher risk of having low birth weight infants (weight at birth of less than 2500g, up to and including 2499g) compared to similar women with normal hemoglobin?

2. Among African Americans, are pregnant women with SCT at a higher risk of having an SGA infant (birth weight at or below the 10th percentile for a given gestational age) compared to similar women with normal hemoglobin?

3. Among African Americans, is there a difference in birth weight of term infants of women with SCT as compared to similar women with normal hemoglobin?

Conceptual Definitions

- Low birth weight is a term used to describe a weight at birth of less than 2500g (up to and including 2499g), irrespective of gestational age (WHO, 2011).
- Term birth refers to a birth that occurs between 37 and 0/7ths and 42 weeks of gestation.
• Preterm birth refers to a birth that occurs before 37 weeks of gestation (Lockwood, 2011).

• Post term birth refers to a birth that occurs after 42 weeks of gestation.

• Small for gestational age (SGA) is a term used to describe a baby with a birth weight at or below the 10th percentile for a given gestational age (CDC, 2008).

• Sickle cell disease (SCD) is an inherited hemoglobinopathy and is associated with the following three conditions:
  o Sickle cell anemia (HBSS)
  o Sickle cell hemoglobin C disease (HbSC)
  o Sickle cell B-thalassemia (HbSBthal) (Zack-Williams, 2007).

• Sickle cell trait (SCT) is the carrier for sickle cell anemia (SCA) and is not a disease or illness (Zack-Williams, 2007). SCT is a heterozygous condition in which the individual has one beta (A) globin gene and one beta (S) globin gene, resulting in the production of the hemoglobin (AS) profile (Zack-Williams, 2007).

• Normal hemoglobin is an AA profile as determined by sickle cell test or hemoglobin electrophoresis test.

**Operational Definitions**

• Birth weight is the weight of the baby recorded in grams in the clinic’s electronic medical record, which was obtained within an hour of birth using the neonatal scale.

• Low birth weight is any weight of a baby less than 2500g (up to and including 2499g) recorded in grams in the clinic’s electronic medical record, which was obtained within an hour of birth using the neonatal scale.

• Term birth is any birth that occurred between 37 and 0/7ths and 42 weeks of gestation, recorded in the clinic’s electronic medical record.
• Preterm birth is any birth with a gestation age less than 37 weeks, recorded in the clinic’s electronic medical record.

• Post term birth is any birth with a gestation age more than 42 weeks, recorded in the clinic’s electronic medical record.

• Small for gestational age (SGA) is any birth weight at or below the 10th percentile for a given gestational age using the birth weight centile calculator (Appendix C).

• Sickle cell trait is the laboratory result of “hemoglobin AS” recorded in the clinic’s electronic medical record, which was obtained from hemoglobin electrophoresis test.

• Normal hemoglobin is the laboratory result of “hemoglobin AA” recorded in the clinic’s electronic medical record, which was obtained from a negative sickle cell test result or hemoglobin electrophoresis.

**Theoretical/Conceptual Framework**

Vaso-occlusive phenomena and hemolysis are the clinical hallmarks of SCD (Randolph, 2007; Vichinsky, 2010). The pathogenesis of vaso-occlusion in SCD is not fully understood, but Hb S polymerization and sickling of red blood cells (RBCs) and other factors play a major role in this process (Randolph, 2007). Several interrelated processes important to the pathophysiology of sickle cell vaso-occlusion have been identified and include the following:

• Interaction of the leukocyte with the endothelium resulting from inflammation which impedes micro-vascular flow thereby leading to sickling (Randolph, 2007; Steinberg, 2011).

• Activation of platelets, coagulation, and endothelial cells by activated macrophage tissue (Randolph, 2007; Steinberg, 2011).
Clinical dehydration or activation of endothelial cells and platelets may elevate levels of thrombospondin or von Willebrand factor to mediate red cell adhesion to the endothelium (Randolph, 2007; Steinberg, 2011).

Regional hypoxia may induce the expression of endothelial cell P-selectin to enhance the adhesion of sickle cells as well as heterocellular interactions with platelets and neutrophils (Randolph, 2007; Steinberg, 2011).

The pathophysiology of sickle cell hemolysis and vaso-occlusion contributes to compromised placental blood flow associated with pregnancy of SCD women (Vichinsky, 2011). Significant fetal complications in pregnancies of women with sickle cell disease (SCD) such as spontaneous abortion, intrauterine growth restriction, fetal death in utero, and low birth weight have been associated with compromised placental blood flow (Vichinsky, 2011; Yu, et al., 2009).

Though these poor pregnancy outcomes are more common with SCD compared with sickle cell trait, similar processes of compromised placental blood flow have been observed by researchers, which could be responsible for some fetal complications seen in SCT pregnancies (Tsaras et al., 2009).

Determination of any difference in birth weight between infants born to SCT mothers and those born to mothers with normal hemoglobin will be helpful in determining if there is presence of compromised placental blood flow in SCT pregnancies (Tan, Khanapure, & Oteng-Ntim, 2008). If it is established that there is a significantly higher incidence of low birth weight in infants born to SCT mothers than for women with normal hemoglobin, primary prevention interventions such as pre-conception health care assessments for SCT women could be implemented to prevent fetal growth restriction, diagnose fetal growth restriction earlier in this
pathological process, and improve overall pregnancy outcomes for SCT women (Brown, et al., 1972; Tan, Khanapure, & Oteng-Ntim, 2008)

Closer monitoring and more frequent prenatal clinic visits for SCT pregnant women could be recommended, which would facilitate early detection of any sign of intrauterine growth restriction (Tan, Khanapure, & Oteng-Ntim, 2008). Secondary prevention interventions, such as treatment of prenatal maternal infections and other health conditions such as hypertension, would also be encouraged to prevent significant damage to fetal well-being (Brooks, 2011).

Review of Literature

The review of literature for this study was done through a search of different academic databases. This literature review contains strategies used by the principal investigator in obtaining research studies and articles pertaining to the research question. It examined findings from studies about sickle cell trait pregnancy outcomes, low birth weight, infants classified as SGA, and the effects of sickle cell pregnancy on birth weight and birth weight centile.

Methods

Sources. Extensive search of databases using various search terms related to outcomes of SCT pregnancies and effect on birth weight was conducted through the Texas Woman’s University (TWU) Libraries Resources Online for medicine and health-related databases. The databases searched include: CINAHL Plus with Full Text, MEDLINE, MEDLINE Plus with Full Text, SPORTDiscus with Full Text, Cochrane Library, PubMed, Health Source: Consumer Edition, and Health Source: Nursing/Academic Edition. A total of 10 Web-based databases were searched for publications in English, from 2006 through 2012. Very few articles were identified within this 6-year period; therefore the search was carried out without restriction by publication date. Several prospective and retrospective cohort studies were obtained from MEDLINE and
CINALHL databases. Finally, a comprehensive search of the internet was done using the Google search engine. Subject directories especially MEDLINE and HEALTHFINDER were also searched. The password-protected UPTODATE online database was also searched.

**Search Terms.** Broad search terms were used in order to ensure that key articles were not missed. Key search terms include: “sickle cell”, “low birth weight and sickle cell trait”, “sickle cell trait and pregnancy”, “sickle cell anemia and pregnancy outcomes”, “hemoglobinopathy and birth weight”, “small for gestational age and sickle cell trait”, “IUGR and sickle cell”, “low birth weight and African Americans”, and “pregnancy outcomes and sickle cell trait”.

**Evaluation of Articles**

Many articles were identified, and the most relevant articles were chosen based on how they addressed the question of this inquiry. The following are the eligibility criteria for articles included in this review:

- The focus of the study was on outcomes of pregnancy related to SCT.
- The study reported specifically on pregnancy outcomes such as birth weight or SGA in SCT and or SCD pregnancies.
- Issues of low birth weight and other poor pregnancy outcomes among the African American population were addressed.
- The majority of participants in the study were of African descent.
- A generous sample size was used for the study.
- The type of study was considered with higher consideration given to experimental studies and lower consideration to observational studies.
There were very few recent studies conducted on the SCT and birth weight in the United States therefore, studies dating more than 10 years and studies conducted in Europe, the Middle East, and Africa were considered.

Overall, 44 articles were initially identified from which 11 were selected for meeting the inclusion criteria. One research article investigated the effects of SCD on pregnancy outcomes, 4 research studies associated SCT with low birth weight and or SGA, and 6 research studies found no evidence to substantiate increased risk associated with SCT pregnancy.

**Low Birth Weight and SCD**

Yu and colleagues (2009) conducted a prospective study to determine the outcome of pregnancies of SCD women. Seventy one SCD pregnancies were followed over a 6-year period. Findings from the investigation indicated that 18% of infants experienced reduced growth velocity with measurement crossing below the 10th centile. Other fetal outcomes reported in the study include preterm delivery and fetal demise due to placental abruption. The maternal outcomes reported include sickle crisis requiring hospital admission (47%), anemia requiring blood transfusion (24%), urinary tract infection, pre-eclampsia, increased risk of caesarean section, and a higher rate of induction of labor. Though the study was not specifically related to SCT pregnancies, this exploration of pregnancy outcomes associated with maternal SCD provided basic knowledge that could relate SCT pregnancy outcomes.

**No Association of SCT with Low Birth Weight and SGA**

Several studies have directly investigated outcomes associated with SCT pregnancy in an attempt to provide explanations for causes of increasing low birth weight rates among African Americans. One such study was done by Tan, Seed, and Oteng-Ntim (2008). Tan and colleagues conducted this study to investigate the birth weights of babies born to sickle cell trait mothers as
compared to birth weight of infants born to women with normal hemoglobin. Their analyses of the birth weights showed a lower mean birth weight in the SCT pregnancies than in the control pregnancies. However, the difference was not significant enough to conclude that SCT was a risk for SGA. Majority of participants in this study were African and Afro-Caribbean women. The study was retrospective and was conducted on 505 SCT deliveries and 16,320 deliveries with normal hemoglobin. The records of these deliveries were collected from a London hospital between 2000 and 2005 and were obtained through the hospital’s electronic database. Findings from the study showed that the mean birth weight of SCT pregnancies was significantly lower by 57 grams but there was no difference in the mean birth weight centile between the control group and the SCT group. Strengths of this study include the generous sample size, the focus on the race (Black) of the majority of participants, the specific concentration on SCT pregnancies, birth weight centile, birth weight, and the use of a control group with normal hemoglobin.

Another study with similar result was conducted by Adeyemi, Adediran, Kuti, Owolabi, and Durosimi, (2006) to determine the outcomes of SCT pregnancies. This prospective study was carried out in a West African Teaching Hospital between 2003 and 2005 over a 24 month period. Analysis of findings indicated no significant difference in pregnancy outcomes between women with SCT and women with normal hemoglobin. An interesting finding of this African study is that pregnant women with SCT had a lower incidence of malaria (25.7% compared to 34.8% in the control group), which made the authors hypothesize that SCT may confer resistance to malaria in pregnancy. Despite the malaria disadvantage on the part of women with normal hemoglobin, intrauterine growth restriction occurred in 2.4% of pregnancies with SCT compared with 1.9% in the control group. A limitation of this study is that while it concluded that SCT poses no additional risk to women in pregnancy, it did not take into consideration the advantage
of the lower incidence of malaria among SCT women when calculating the significance of the difference in the birth weights of the groups. Strengths of this African study include the generous sample size (420 cases, 210 with SCT and 210 with normal hemoglobin), the race of the participants (all Black), the prospective, analytical study design, and specific concentration on SCT pregnancy outcomes and birth weight.

Earlier in 2003, before the findings of the research of Adeyemi and colleagues were published, Abdulsalam, Bashour, Monem, and Hamadeh (2003) conducted a prospective cohort study to examine the pregnancy outcomes of women with SCT between 2000 and 2002. Ninety-eight pregnant SCT women and 402 women with normal hemoglobin were enrolled in the study. Participants were followed up and data were collected throughout pregnancy up till 40 days after pregnancy. The findings showed no significant difference in pregnancy outcomes between the women with SCT and those with normal hemoglobin. Strengths of this study include the generous sample size, use of a control group, and a prospective study design. The limitations of the study include the fact these findings are now 10 years old, and this research was conducted with a population of Palestinian refugee women in four different locations who may have encountered environmental factors capable of affecting their pregnancy outcomes.

To further investigate the hypothesis that carriers of hemoglobinopathies are not in any greater risk of poor pregnancy outcomes than the general population, Jans, De Jonge, and Lagro-Janssen (2010) conducted a systematic review focused on the maternal and perinatal outcomes of carriers of hemoglobinopathies. They searched major databases such as Cochrane Library, Medline, EMBASE, and CINAHL databases for publications in English, French, German, Spanish, and Dutch. A total of 46 studies were assessed. The findings from this systematic review pertaining to sickle cell trait pregnancy indicated that sickle cell trait pregnancy was
associated with a low risk of premature birth, lower newborn Apgar scores, and increased perinatal mortality rate. In addition, no significant effects were found for low birth weight, high blood pressure, or growth retardation. However, a risk for anemia, asymptomatic bacteriuria, and subsequent risk of pyelonephritis were detected among pregnant women with sickle cell trait. These researchers also suggested that hemoglobinopathy carriers be followed more frequently during pregnancy to assess these conditions.

Taylor and colleagues (2008) conducted a retrospective study in which data from 131 African Americans with SCT were analyzed. Findings from the study revealed 8.13% of the participants experienced intrauterine fetal deaths, 10.6% of the infants were classified as IUGR, and there was one neonatal death among the SCT population. In addition, there was evidence of acute ascending amniotic fluid infection from placental pathology in 50% of the specimens, and 92% of placentas showed evidence of meconium histiocytes. Evidence of sickling in the decidual vessels and intervillous spaces of all examined placentas were also identified. Placental infarction was associated with the sickled vasculature of the placentas in 40% of the fetal demises, whereas retro-placental hemorrhage was present in 10% of the fetal demises. Some of the acknowledged limitations of this study are the design (retrospective), and that most of the patients were socioeconomically disadvantaged. However these limitations do not override the significance of placental pathologies discovered in the SCT population. The finding of this study intensifies the question of how much placental insufficiency could be attributed to the SCT status.

A more dated study on the same subject of outcomes of sickle cell trait pregnancies was conducted by Blattner, Dar, Harold, and Nitowsky (1997). This study was prospective and was conducted in a prenatal clinic with the objective to evaluate pregnancy outcomes in women with
sickle cell trait compared with pregnancy outcomes in women with normal hemoglobin. A group of 85 women with SCT was compared with a control group of 85 women with normal hemoglobin. Participants were matched for race, age, sex of offspring, and parity. The findings of the study showed no significant difference in the birth weight of infants born to the mothers in the two different groups. Additionally, the rate of pregnancy complications was not significantly different in both groups; no complications such as hemolytic episodes or painful crises were recorded among the group of women with SCT.

**Association of SCT with Low Birth Weight**

One of the earliest studies about sickle cell trait pregnancy outcomes was done in 1972. Brown, Merkow, Weiner, and Khajezadeh (1972) conducted a retrospective study to test the hypothesis that SCT in pregnant African American women may be contributory to lower birth weight which is responsible for higher infant mortality rate among African Americans. The investigators compared the number of live fetuses, stillbirths, premature births, abortions, and the birth weight of infants between African American mothers with sickle cell trait and African American mothers with normal hemoglobin. No significant difference was found in the number of live fetuses, stillbirths, premature births, and abortions between the two groups. However, the mean birth weight of babies born to African American mothers with normal hemoglobin was significantly higher (3.2kg or 7.02 lb.) than the mean birth weight of infants born to the group of African American mothers with sickle cell trait (2.7kg or 5.94 lb.) with pooled standard error of 0.29 ($t = 3.35; \ p < .01$). The investigators suspected that lack of oxygenation to the developing fetus may be the cause of this discrepancy in birth weight. The conclusion was that sickle cell trait is a pathological genetic state that requires particular attention in the immediate post-partum
period. However, the researchers also suggested that further studies be carried out to better explain the low birth weight phenomenon.

To overcome some of the limitations that may be posed by a retrospective study, Larrabee and Monga (1997) conducted one of the first prospective studies that investigated outcomes of SCT pregnancy, and this research is repeatedly referenced in current literature (including Tsaras, et al. [2009] and Vichinsky [2011]). The study enrolled 1584 women (including 162 women with SCT and the rest with normal hemoglobin). Outcome data were collected for various factors including pre-eclampsia, gestational age at delivery, and birth weight. The Mann-Whitney U test, chi square analysis, student t-test, and Fisher’s exact tests were used for statistical analysis. Results of the study indicated a statistically significant decrease in gestational age at delivery (36.7 +/- 2.7 vs. 37.7 +/- 3.0 weeks, p<0.0001) and birth weight (3082 +/- 591 vs 3369 +/- 573 gm, p<0.0001) in SCT women than in the control group (Larrabee & Monga, 1997). This was one of the studies that sparked further investigations into this subject.

A similar finding was obtained from a later study done by Tan, Khanapure, and Oteng-Ntim (2008). The authors assessed the incidence of SGA in SCT pregnancies, and their analysis of study findings showed a significant SGA rate in pregnancies with SCT despite exclusion of cases with identified pregnancy complications. A total of 471 SCT deliveries in a London hospital between 2001 and 2005 were analyzed. Of the 471 SCT pregnancies analyzed, 16.8% had SGA babies compared to 10% in the general population. Complications affecting birth weight such as pre-eclampsia, eclampsia, and gestational diabetes were detected in 51 cases, which were later excluded from analysis. The exclusion of these 51 cases lowered the SGA rate among the SCT pregnancies to 14.8%, which was still significantly higher than that of the general population (p <= 0.05). One major limitation of this study is the absence of a control
group. The authors of this later study recommended that a study comparing the birth weight of SCT pregnancies with pregnancies without hemoglobinopathy be conducted for confirmation of this risk. Strengths of this study include the generous sample size, the focus on Black participants, and specific concentration on SCT pregnancies and birth weight.

Another study that continues to contribute to the controversy surrounding pregnancies complicated by maternal SCT was conducted by Balgir, (2007) in the Orissa state of India. The aim of this prospective study was to investigate the cause of the high infant mortality rate in Orissa, India and the association of infant mortality to different genotypes. Information from couples with hemoglobinopathies was compared to those of couples with normal hemoglobin. Hemoglobinopathies were confirmed by lab tests. Detailed reproductive histories such as number of conceptions, abortions, and miscarriages were collected from all the couples. Out of a total of 128 couples studied, 51 were thalassemia carriers, 54 were carriers of sickle cell disease, and 16 were carriers of sickle cell/thalassemia. Analysis of the findings indicated that infant mortality rate (per 1000 births) was higher among sickle cell trait (75.9), thalassemia (184.2), and sickle cell/thalassemia (70.2) couples, compared to couples with normal hemoglobin. The study concluded that hemoglobinopathy was a reason for high infant mortality rate in the state of Orissa. The investigators suggested that hemoglobinopathy carriers avoid marriages with mates with hemoglobinopathies in order to reduce the rate of “reproductive wastage” (still birth, miscarriages, and neonatal deaths) and to promote better health of subsequent generations.

**Summary of Review of Literature**

Whereas in this literature review there are many studies that addressed the question of SCT as a risk factor for low birth weight newborns, there is no consistency in the findings that would assist with a conclusive answer to the question. Even when some authors, such as Tan,
participated in two of the studies reviewed, the outcomes of the investigations were different and conflicting. Many of the studies reviewed were conducted in countries outside the United States, whose participants experience pregnancy under different conditions than those of African Americans mothers in United States. Some of the studies did not address confounding variables, some of the results were obtained over 10 years ago, and some studies did not use a control group.

This literature review failed to bring closure to the controversy about the impact of SCT pregnancy on birth weight and hence the need for this current study. This current study compared SCT pregnancies with a control group with normal hemoglobin. The control group was matched for ethnicity to the SCT mothers for maternal BMI, gestation age, parity, and infant’s gender. This current study also controlled for confounders such as diabetes, hypertension, alcohol use, smoking, and drug use.

**Methodology**

**Population and Sample.**

The current study is a retrospective chart review of a convenience sample of African American (AA) women conducted at a Family Health Center in Central Texas. The family health center is made up of 12 satellite clinics in a network. Screening for sickle cell anemia is routinely offered to all pregnant African American mothers registered for obstetric care in all the 12 health clinics. Records of pregnant patients who attended the 12 community clinics in the network are contained in the same electronic database. At the beginning of this chart review, medical record numbers of 101 African American women with sickle cell trait, who received prenatal care from the health center, from year 2000 to 2010 were identified (Appendix A). The medical record number was the sole identifying data that was initially collected. By searching these records for
required information, 23 cases were eliminated because the corresponding offspring records were either incomplete or not available in the electronic database. Out of the 78 sickle cell trait records left, 14 were excluded for maternal age below 18 years. From the remaining 64 records, 15 more records were excluded for one or more of the following reasons: smoking, drug use, and alcohol use during pregnancy; complications of pregnancy such as uncontrolled hypertension and diabetes; missing lab result confirming genotype; and multiple pregnancies. Only 49 SCT records met the inclusion criteria for the study from year 2000 to 2010. Because of the need for more records, a request to go beyond 2000 and 2010 was sent to the Institutional Review Boards (IRBs) of the Health Center and Texas Woman’s University (TWU) (Appendices I, J, & L). The request was granted by the two IRBs for the chart review to cover the period from 1991 to 2011 (Appendices J & M).

From the expanded time-period, 5 more records of SCT pregnancies meeting the inclusion criteria were selected. This addition brought the total number of SCT records that met the inclusion criteria to 54. At this point of review, the focus shifted from selecting SCT records to selecting records of women with normal hemoglobin for the control group. A total of 64 records of African American pregnancies with normal hemoglobin and corresponding offspring records were selected for the control group. This number brought the total participants’ count to 118 (54 + 64). From this total number, 51 pairs, one from each group (hemoglobin AA and AS), were matched on race, gestation age, gender of baby, BMI of mother, and parity. The maximum number of cases required for this study was 100 (50 for each group). The sample size was determined by power analysis. A G* Power 3.1.2 analysis was conducted to determine the sample size required to conduct all planned analyses. The sample size required to detect a moderate effect size \( w = .30 \) in the logistic regression, an alpha = .05, and power = .80 is 88
African American mothers. The sample size of 100 African American mothers who have either SCT or normal hemoglobin was chosen to account for potential outlier data and was considered adequate for all analyses.

Once the entirety of the study data was collected and verified, medical record numbers were removed, leaving only de-identified data for further analysis by the researchers. Data was stored in a password-protected Excel file. The anonymous, de-identified data file was later imported into Statistics Package for the Social Science (SPSS) for analyses. Paper-based records were kept to a minimum and were stored in a secure locked location, accessible only to study staff. Computer files were accessible only to study staff and were universally password protected. The study staff members all signed confidentiality agreements regarding the protection of identifiable health information prior to accessing study information. The chart reviews were conducted in a private, Health Insurance Portability and Accountability Act (HIPPA)-compliant setting.

**Instrumentation.**

The main instruments utilized for this study were the codebook and the sickle cell test and or electrophoresis lab test results. The test results dictated which group each participant was assigned to.

**Codebook.** The codebook (Appendix F) was the major instrument used in this chart review. The codebook described the items that were collected from the research subjects’ charts in the database. Items listed in the codebook (e.g. birth weight and gestational age) were important variables needed for statistical analysis in order to answer the research questions. The codebook contains the summary of the instructions that were used to convert the information obtained from each subject’s chart into SPSS compatible format. Research assistants helping
with data collection were able to obtain similar data from each participant’s record by following the instructions contained in the codebook.

Each data item in the codebook was given a unique variable name that clearly identified the information this item represents (e.g. “weight” as the variable name for maternal weight at initial prenatal visit). Each item in the codebook was also assigned a numerical code before the data was entered into SPSS. The first variable in the codebook is the identification number (ID), which is a unique number that identified each subject. Another item in the codebook is the maternal age at birth of baby, with the SPSS variable name as “Age”. Other variables in the codebook include body mass index, maternal genotype, infant’s gestation at delivery, baby’s gender, birth weight, birth-weight centile, “Matchup” etc. “Matchup” is the variable name for the pairs of matched participants from the two different groups. Each matched pair is assigned the same “Matchup” number which is different from other “Matchup” numbers. Pairs are matched on race, gestation age, gender, BMI, and parity.

The codebook instructions made the process of creating a data file and data entry process efficient. The use of codebook also enabled data files created in the Excel spreadsheet to be set up in conformity with SPSS recommendations for easy transport later to SPSS.

**Lab Tests.** Sickle cell test and hemoglobin electrophoresis were the most common tests used for routine clinical purposes, to screen and diagnose sickle cell disease. The classic sickle cell test or “sickle cell prep” (using sodium metabisulfite or dithionite) and turbidity tests only detect the presence of sickle hemoglobin (Hb S) but not the other hemoglobins (Hb A, Hb A₂, Hb S, Hb D, Hb C, and Hb F). Therefore, these tests do not differentiate sickle cell disease from sickle cell trait (Quinn & Packman, 2010; Randolph, 2007). Hemoglobin electrophoresis separates the different hemoglobin and is the confirmatory test for SCT and SCD (Quinn &
Packman, 2010; Randolph, 2007). In 1949, Pauling showed that when Hb SS is electrophoresed, the SS hemoglobin it migrates differently than Hb AA (Randolph, 2007). This difference was shown to be caused by an amino acid substitution in the globin chain (Randolph, 2007). Pauling was able to use the electrophoresis method to clearly distinguish heterozygous sickle cell trait (Hb AS) from the homozygous state (Hb SS) (Randolph, 2007).

The United States Preventive Services Task Force (USPSTF) recommends that all newborns be tested for sickle cell disease (USPSTF, 2007). Testing is also recommended for high-risk individuals such as African Americans, and couples who may be carriers of SCT and who are planning to have children. People who test positive for SCD or SCT are encouraged to get genetic counseling before deciding to have children.

The sickle cell test, by detecting Hb S, is positive in sickle cell disease and sickle cell trait (without differentiating the two), but negative in patients with normal hemoglobin (Hb AA). Sickle cell trait is diagnosed by detecting the presence of the Hb S and Hb A on hemoglobin electrophoresis (Randolph, 2007). On electrophoresis, sickle cell trait has approximately 40% of Hb S and 60% or more of Hb A (Randolph, 2007). In patients with sickle cell disease, electrophoresis shows no Hb A, and Hb S is usually greater than 80% (Randolph, 2007).

There are factors that may interfere with sickle cell test and electrophoresis results, and the factors are as follows:

- Blood transfusion in the past 4 months which may cause a false-negative result on both tests due to normal hemoglobin from the blood donor.

- Age of infants under 6 months which may cause false-negative results due to the presence of more hemoglobin F (Fetal hemoglobin) in the blood.
Hemoglobin electrophoresis is simple and inexpensive; it is very reliable in diagnosing sickle cell anemia (Hb SS) and sickle cell trait (Hb AS) when done properly. However, there are other forms of mutant hemoglobins that are not electrophoretically sensitive (Benz, 2010). Most diagnostic laboratories in recent years concurrently use high-performance liquid chromatography (HPLC) and iso-electric focusing in order to identify those hemoglobin that are electrophoretically silent (Benz, 2010; Quinn & Packman, 2010).

This chart review relied on the sickle cell test results to identify participants assigned to the control group. Every participant with a negative sickle cell test result was qualified for inclusion (provided other inclusion criteria are met). However, participants with positive sickle cell test result were required to have a confirmatory hemoglobin electrophoresis test result confirming SCT status before the participant was qualified for inclusion to the SCT group.

Implementation

Objective

The main objective for this study was to determine whether African American mothers with SCT are at increased risk of having a low-birth weight infant compared to African American mothers with normal hemoglobin. This finding could determine if African American women with SCT should be targeted for pre-conception care and enhanced prenatal care.

Timeline

This study was started in November 2011 and ended in March 2012. The following timeline activities represent the actual points that occurred for this project.

1. A retrospective chart review project proposal was drafted and approval from the members of the capstone committee was obtained by October 2011.
2. The retrospective chart review proposal form and consent form for the Family Health Center’s IRB was submitted for approval by October 2011. The study was granted approval with waiver of consent by the Health Center’s IRB on October 27, 2011 (Appendix H).

3. A study proposal form and copy of approval from the health center’s IRB were sent to the Texas Woman’s University (TWU) IRB for a dual IRB approval on November 11, 2011 (Appendix O).

4. An approval from the TWU IRB was granted for the study on December 5, 2011 (Appendix K). The study was granted an expedited approval from both IRBs.

5. Deliveries between 2000 and 2010 in the health center’s electronic database were searched to identify SCT deliveries and deliveries with normal hemoglobin (controls), starting in early December 2011, with assistance of research assistants, a professional practice mentor, a research advisor, and the health center’s records department staff. Selected records, especially those of SCT mothers were not enough for the planned analyses.

6. A request to expand chart review time-period in order to obtain adequate sample size was submitted to the Health center’s IRB on the 23rd of January 2012 (Appendices I & J).

7. Approval for the modification was received from the Health Center’s IRB on the 30th January 2012 (Appendix J).

8. A request to expand chart review time-period in order to obtain adequate sample size together with a copy of the approval for the modification from the Health Center’s IRB were submitted to the TWU IRB on the 30th of January 2012 (Appendix L).
9. An expedited approval for the modification was granted by the TWU IRB on 30th of January 2012 (Appendix M).

10. The expanded chart review continued until a total of 118 records of African American women, together with their corresponding offspring were selected by end of February 2012.

11. Data analysis was started by end of February 2012.


13. The defense of the capstone project is expected take place in second week of March 2011.

14. The completed project is expected to be bound and submitted to the capstone chair and committee by April 2012.

15. An article for journal publication is expected to be submitted for consideration by May 2011.

**Project Requirements**

**Sources and Types of Information**

This retrospective chart review required approval from both the health center and TWU Institutional Review Boards (IRBs) before initiation of the project. The source of information was solely from the Health Center’s electronic database. All deliveries between 1991 and 2011 by African American Women with SCT and normal hemoglobin were identified in the health center’s in-house electronic database. The information in the database was accessed using assigned individual secret passcodes. Information stored in the database was entered by physicians, obstetricians, advanced practice nurses and other authorized staff involved with the deliveries.
Information such as the mother’s age, weight at initial prenatal visit, ethnicity, estimated date of delivery was calculated using the last menstrual period (LMP) or ultrasound, method of delivery, infant’s gestation at delivery, gender, and birth weight were recorded (Appendix N). The birth weight centile was calculated using the birth weight centile calculator which considers the child’s gender, gestational age and birth weight (Appendix C). Single baby deliveries between 24 and 42 completed weeks were included. Direct identifiers, such as names and email addresses, were not collected. Information recorded did not contain data that could identify the subjects. The only identifiable information was the medical record number (MRNs). In order to de-identify the MRN, certain numbers that make up the MRNs were uniformly replaced by letters that only the research staff understood. No linking list of any sort that could enable someone to look up a code number assigned to a subject and determine the identification of that subject was kept.

**Inclusion Criteria**

The delivery records reviewed were those of women 18 years old and above. The records were of subjects identified as African American (Non-Hispanic Black), with SCT (HbAS) or normal hemoglobin profile (HbAA). The gestation age selected were those between 24 and 42 completed weeks at delivery. The deliveries were those that occurred between 1991 and 2011.

**Exclusion Criteria**

The cases that were excluded were those with maternal age at birth below 18 years, gestation age below 24 completed weeks and above 42 completed weeks, non-African Americans, and deliveries with obvious complications of pregnancy (as mentioned above). Other hemoglobinopathies, including HBSS, HbSC, HbSBthal, and the carrier states of HbSC and HbSBthal, were excluded. Cases with incomplete records and lab tests were also excluded. Cases
missing any of the parameters used for calculating birth-weight centile (such as gestation age and infant’s gender) were also excluded.

**Rationale for Exclusion**

- Maternal age at birth below 18 years (Escartín et al., 2011) and gestation age below 24 weeks and above 42 completed weeks were excluded because these conditions affect birth weight.
- Non-African American pregnancies were excluded because the study was an investigation of the African American population.
- Deliveries with obvious complications of pregnancy, as noted above, were excluded because those conditions also affect birth weight. Drug and alcohol use during pregnancy has been associated with low birth weight (Horton, 2011). Women with gestational diabetes mellitus (GDM) are prone to having large babies (Fadl, Östlund, Magnuson, & Hanson, 2010).
- Other hemoglobinopathies were excluded because they may affect birth weight ((Jans, De Jonge, & Lagro-Janssen, 2010) and because they are not the focus of this investigation.

**Analysis**

- The information from selected cases was entered into the SPSS data set. Daily data quality checks were conducted to ensure accuracy of entries.
- Low birth weight was defined as all birth weights of less than 2500g (up to and including 2499g), irrespective of gestational age.
- SGA was defined as a birth weight at or below the 10th percentile for a given gestational age and was calculated using the 10th percentile of birth weight calculator (Table A2).
• Term birth was defined as a birth that occurred between 37 and 0/7ths and 42 weeks of gestation.

• Statistical analysis comparing the data from SCT women and women with normal haemoglobin were performed using the SPSS Statistics software and the assistance of a statistician.

**Support Site and Personnel Required for the Project**

The personnel required for this project, other than the principal investigator, included 3 research assistants (undergraduate pre-med students) who are volunteers at the health center, records department’s staff, and the principal investigator’s clinical practice mentor, who is a staff of the Family Health Center – the study site.

The project site was the private offices, library, and records department of the Family Health Center. The health center is home for the County Medical Education and Research Foundation (CMERF). The CMERF has been actively involved in clinical research for over thirty years. There is strong community support of the organization and its mission, which includes ongoing research. The co-investigator in this study has several years of research experience, including multiple published works and has presented research at regional and international forums.

The research staff involved in the study underwent and passed (with certificate) the online training by National Institute of Health (INH) for protecting the rights of human research participants. They understand their obligation to protect the rights and welfare of human research participants by adhering to applicable federal, state, and local regulations governing clinical research. The research assistants signed confidentiality agreement with the Health center’s administrator to uphold their obligation to protect the welfare of the participants.
Evaluation

To determine if SCT pregnancy is a risk factor for low birth weight among African Americans, the birth weight of babies born to the selected African American women with SCT were compared with the birth weight of babies born to the African American women with normal hemoglobin. Data exploration was conducted at the end of data collection and once data was entered into SPSS. Data exploration involved testing assumptions, such as the normalcy of the data. Outliers and missing variables were accounted for by removing outlier cases and removing participants with excessive missing data. Upon completion of the data exploration, descriptive analyses were conducted. Categorical variables were analyzed through frequencies and percentages. Continuous variables were analyzed with means and standard deviations.

Furthermore, preliminary analyses were conducted to determine any potential relationships between demographic variables (e.g., baby’s gender and baby’s gestational age). Specifically, crosstabulations with Pearson chi square analyses were conducted to examine the relationships between categorical variables (e.g., gender, multiple births). Analyses of variance (ANOVAs) were conducted to determine if there are any potentially significant relationships between demographic categorical variables (e.g., gender) and continuous variables (e.g., gestational age). Finally, preliminary analyses included Pearson Product Moment correlations between any continuous variables. Non-parametric analyses were conducted if it is determined that the data is non-normal.

The first research question, which asks if African American women with SCT are at greater risk of having a low birth weight infant compared to similar African American women with normal hemoglobin, was analyzed with a logistic regression. For this analysis, the predictor variable was SCT status (SCT or normal hemoglobin) and the outcome variable was low birth
weight, defined as weight at birth of less than 2500g versus 2500g and higher. A logistic regression determines as the more appropriate analyses because the outcome measure is dichotomous.

The second research question, which asks if African American women with SCT are at higher risk of having an SGA infant, compared to similar African American women with normal hemoglobin was analyzed with a separate logistic regression. For this particular analysis, the predictor variable was SCT status and the outcome variable was percentile weight. As with the first research question, a logistic regression is the most appropriate analyses as the outcome measure is a two level measure. Furthermore, the risk of having a low birth weight baby because of SCT status is best assessed with a logistic regression used to predict the probability, or risk, of an occurrence of an event (e.g., having a low birth weight baby).

Finally, two crosstabulation with Pearson chi square analyses were conducted to analyze the third research question, which asks if there is a difference between the birth weights of term infants of African American women with SCT compared to similar African American women with normal hemoglobin. Because the birth weight variables are dichotomous variables, crosstabulations are more appropriate analyses for the third research question. Crosstabulations with Pearson chi square analyses test the relationships between categorical variables (e.g., SCT status and birth weight variables).

A G* Power 3.1.2 was conducted to determine the sample size required to conduct all planned analyses. The sample size required to detect a moderate effect size ($w = .30$) in the logistic regression, an alpha = .05, and power = .80 is 88 African American mothers. A generous sample size of 100 African American mothers who have either SCT or normal hemoglobin was considered adequate for all analyses in order to account for potential outlier data.
Results

The purpose of the project was to determine whether African American women with SCT (i.e., hemoglobin AS profile) are more likely to have a low birth weight infants and/or infants classified as small for gestational age (SGA) compared to African American women with normal hemoglobin (i.e., hemoglobin AA profile). It was expected that women with SCT would, indeed, be more likely to have low birth weight infants (i.e., less than 2500 grams) and infants at or below the tenth percentile for birth weight. Furthermore, this issue was examined overall and with a specific focus on term infants.

Descriptive Analyses

The sample for the current study included 118 African American women, together with their corresponding offspring. Sixteen cases were removed from the sample, as their data was not matched for demographic information. Therefore, the final sample size included 102 cases. As shown in Table 1, there were 47 male infants (46.1%) and 55 female infants (53.9%). The majority of the pregnancies were full term (94.1%), with only 5.9% of deliveries occurring preterm. In terms of parity, the majority of mothers had given birth zero (33.3%), one (32.4%), or two (23.5%) times prior to the current delivery, with a few participants exceeding those numbers. Specifically, 6.9% of mothers had given birth three times before the current delivery, 1.0% of mothers had given birth four times before the current delivery, and 2.9% of mothers had given birth five times before the current delivery. The sample was evenly split for genotype, with 50.0% of mothers having a hemoglobin AS profile and 50.0% of mothers having a hemoglobin AA profile. Only 4.9% of offspring were low birth weight babies. Furthermore, only 15.7% of infants were at or below the 10th percentile for birth weight.
Table 1

*Frequencies and Percentages of Categorical Variables*

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>47</td>
<td>46.1</td>
</tr>
<tr>
<td>Female</td>
<td>55</td>
<td>53.9</td>
</tr>
<tr>
<td><strong>Term of Pregnancy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre Term</td>
<td>6</td>
<td>5.9</td>
</tr>
<tr>
<td>Term</td>
<td>96</td>
<td>94.1</td>
</tr>
<tr>
<td><strong>Parity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 Previous Pregnancies</td>
<td>34</td>
<td>33.3</td>
</tr>
<tr>
<td>1 Previous Pregnancy</td>
<td>33</td>
<td>32.4</td>
</tr>
<tr>
<td>2 Previous Pregnancies</td>
<td>24</td>
<td>23.5</td>
</tr>
<tr>
<td>3 Previous Pregnancies</td>
<td>7</td>
<td>6.9</td>
</tr>
<tr>
<td>4 Previous Pregnancies</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>5 Previous Pregnancies</td>
<td>3</td>
<td>2.9</td>
</tr>
<tr>
<td><strong>Genotype</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sickle Cell Trait (AS)</td>
<td>51</td>
<td>50</td>
</tr>
<tr>
<td>Normal Hemoglobin (AA)</td>
<td>51</td>
<td>50</td>
</tr>
<tr>
<td><strong>Low Birth Weight</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>97</td>
<td>95.1</td>
</tr>
<tr>
<td>Yes</td>
<td>5</td>
<td>4.9</td>
</tr>
<tr>
<td><strong>Centile</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below or at 10th Percentile</td>
<td>16</td>
<td>15.7</td>
</tr>
<tr>
<td>Above 10th Percentile</td>
<td>86</td>
<td>84.3</td>
</tr>
</tbody>
</table>

*Note.* Frequencies not equaling 102 reflect missing data.

As shown in Table 2, infants’ birth weight in grams ranged between 2211 g and 4252 g, with an average of 3186.58 g ($SD = 422.13$). Maternal body mass index (BMI) ranged between
17.07 and 46.60 with an average of 28.49 (SD = 6.82). Gestational age ranged between 35 weeks and 41 weeks with an average of 39 weeks (M = 38.58, SD = 1.24).

Table 2

Means and Standard Deviations of Continuous Variables

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Weight</td>
<td>102</td>
<td>3186.58</td>
<td>422.13</td>
<td>2211.00</td>
<td>4252.00</td>
</tr>
<tr>
<td>BMI</td>
<td>102</td>
<td>28.49</td>
<td>6.82</td>
<td>17.07</td>
<td>46.60</td>
</tr>
<tr>
<td>Gestational Age</td>
<td>102</td>
<td>38.58</td>
<td>1.24</td>
<td>35.00</td>
<td>41.00</td>
</tr>
</tbody>
</table>

Preliminary Analyses

A series of analyses were conducted in order to uncover potential relationships between the variables. The preliminary analyses were used to determine which, if any, variables to include as covariates for analyses pertaining to the research questions. More specifically, crosstab analyses with Pearson’s chi-square ($\chi^2$) tests and Cramer’s V test were conducted to examine relationships between the categorical demographic and independent variables (i.e., infant’s gender, mother’s genotype, term, centile, parity, and low birth weight). Analyses of variance (ANOVAs) were used to test the effects of each categorical independent variable on the continuous variables (i.e., mother’s BMI, gestational age, and birth weight). Pearson’s product moment correlations were conducted to examine the relationship between the continuous demographic variables.
Crosstabulations. Separate crosstabulations with Pearson’s chi-square ($\chi^2$) tests are used to determine whether or not a significant relationship exists between the categorical independent variables. Cramer’s $V$ tests are used to determine the strength of the relationship between the variables.

The first set of crosstabulations examined the relationship between mother’s genotype and the variables that were not addressed in the primary analyses, infants’ gender and term. There was no significant relationship between genotype and the variables gender or term of pregnancy, all $ps$ ns.

For the remaining crosstabulations, genotype was removed, as the variable was more closely scrutinized when addressing the research questions (in primary analyses). Thus, the remaining crosstab analyses focused on the relationships between infants’ gender, term, centile, parity, and low birth rate. Beginning with low birth rate, as anticipated, there was a significant relationship between low birth weight and centile, $\chi^2(1) = 28.26, p < .001$, Cramer’s $V = .53$. A greater proportion low birth weight infants were at or below the 10$^{th}$ percentile for birth weight (100.0%) compared to infants who were not low birth weight (11.3%). There was no significant relationship between low birth rate and the variables gender, term of pregnancy, or parity, all $ps$ ns.

For term of pregnancy, there was no significant relationship between term of pregnancy and the variables gender, centile, low birth weight, or parity. For centile, as expected and mentioned previously, there was a significant relationship between centile and low birth weight, $\chi^2(1) = 28.26, p < .001$, Cramer’s $V = .53$. A greater proportion of infants who were above the 10$^{th}$ percentile for birth weight were not low birth weight babies (100.0%) compared to infants who were at or below the 10$^{th}$ percentile for birth weight (68.8%). There was no significant
relationship between centile and gender, term of pregnancy, or parity, all ps ns. For gender, there was no significant relationship between gender and the variables term of pregnancy, centile, low birth weight, or parity, all ps ns. Finally, for parity, there was no significant relationship between parity and the variables gender, pregnancy, birth weight, or centile, all ps ns.

**Analyses of variance.** The next step in preliminary analyses included a series of one-way ANOVAs to test the effects of each categorical independent variable on the continuous independent variables. Beginning with BMI, five separate one-way ANOVAs tested the effect of gender, term of pregnancy, parity, genotype, and centile on BMI. There were no significant differences in BMI, all ps ns. For gestational age, five separate one-way ANOVAs tested the effect of gender, term of pregnancy, parity, genotype, and centile on gestational age. As anticipated, there was a significant effect of pregnancy term on gestational age, \( F(1, 100) = 44.97, p < .001, \eta^2 = .310 \), in that preterm infants had a shorter gestational age (\( M = 35.83, SD = .41 \)) compared to full term infants (\( M = 38.75, SD = 1.06 \)). There were no significant differences in gestational age for gender, parity, genotype, or centile, all ps ns.

For birth weight, five separate one-way ANOVAs tested the effect of gender, term of pregnancy, parity, genotype, and centile on infants’ birth weight. As expected, there was a significant effect of term on birth weight, in that preterm infants were lighter in weight in grams (\( M = 2858.33, SD = 393.37 \)) than full term infants (\( M = 3207.09, SD = 417.22 \)), \( F(1, 100) = 3.97, p = .049, \eta^2 = .04 \). Also as anticipated, there was a significant effect of centile on birth weight, with infants at or below the 10\(^{th} \) percentile for birth weight having lower birth weights in grams (\( M = 2599.31, SD = 177.08 \)) compared to infants above the 10\(^{th} \) percentile for birth weight in grams (\( M = 3295.84, SD = 359.45 \)), \( F(1, 100) = 57.15, p < .001, \eta^2 = .36 \). There were no significant differences in birth weight for gender, parity, or genotype, all ps ns.
Correlations. The final step in preliminary analyses involved examining the relationship between the continuous independent variables (i.e., birth weight, BMI, and gestational age) with Pearson’s product moment correlations. As expected, there was a significant positive relationship between gestational age and birth weight, $r = .452$, $p < .001$, indicating that infants who had a higher gestational age tended to have a higher birth weights. There was no significant relationship between mother’s BMI and birth weight or gestational age, all $ps ns$.

Primary Analyses

Primary analyses focused on the research questions and hypothesis. More specifically, a series of logistic regression analyses were used to predict risk of having a lower birth weight (i.e., low birth weight and centile) from genotype for the full sample and for term infants alone. An analysis of variance (ANOVA) was used to examine potential difference in birth weight by genotype. Pearson’s chi-square ($\chi^2$) tests and Cramer’s $V$ tests were conducted to examine relationships between centile, low birth weight, and SCT status.

Because there were unequal sample sizes for low birth weight as well as centile, additional analyses were conducted on a subset of the full sample of infants that were not low birth weight. That is, because there were only five infants who were categorized as low birth weight, a random sample of equivalent normal weight infants were selected and nonparametric analyses were conducted comparing this sample to the low birth weight infants. Nonparametric approaches included Mann-Whitney $U$ tests for research question 1 and research question 3 and crosstabs with Pearson chi-square ($\chi^2$) tests for research question 2. Findings from the follow-up analyses were consistent with findings for the full sample. Therefore, the focus on the findings will be on the full sample of infants below.

Research question and hypothesis 1. The first research question asked, “Are African
American women with SCT at higher risk of having a low birth weight infant (weight at birth of less than 2500g, up to and including 2499g) compared to similar African American women with normal hemoglobin?” It was hypothesized that African American women with SCT are at higher risk of having a low birth weight infant (weight at birth of less than 2500g, up to and including 2499g) compared to similar African American women with normal hemoglobin. This research question and hypothesis were examined in two ways.

First, logistic regression analysis was conducted to predict the risk of giving birth to a low birth weight infants from genotype (i.e., SCT status). As shown in Table 3, the overall model was not significant, \( \chi^2(1) = 0.21, p = .645, pseudo R^2 = .006 \). Furthermore, genotype was not a significant predictor of low birth weight (Odds Ratio = .65, \( p = .649 \)). Therefore, the logistic regression analysis did not provide support for the hypothesis that African American women with SCT are at higher risk of having low birth weight infants.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>B</th>
<th>SE</th>
<th>Wald</th>
<th>df</th>
<th>p</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype</td>
<td>-.426</td>
<td>.94</td>
<td>.21</td>
<td>1</td>
<td>.649</td>
<td>.653</td>
</tr>
</tbody>
</table>

Note. \( \chi^2 (1) = .21, p = .645, pseudo R^2 = .006 \)
Second, a one-way analysis of variance (ANOVA) was also conducted to examine if genotype (i.e., SCT status) had an effect on birth weight. As shown in Table 4, genotype did not have a significant effect on birth weight, indicating no differences in infants’ birth weight between African American women with SCT or normal hemoglobin, $F(1, 100) = .13, p = .722, \eta^2 = .001$. This further supported that that there were no significant differences in birth weight based on genotype.

Table 4

<table>
<thead>
<tr>
<th>Genotype</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sickle Cell Trait (AA)</td>
<td>51</td>
<td>3171.63</td>
<td>423.05</td>
<td>.13</td>
<td>.722</td>
</tr>
<tr>
<td>Normal Hemoglobin (AS)</td>
<td>51</td>
<td>3201.53</td>
<td>424.87</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Research question and hypothesis 2.** The second research question asked, “Are African American women with SCT at higher risk of having an SGA infant (birth weight at or below the 10th percentile for a given gestational age) compared to similar African American women with normal hemoglobin?” It was expected that that African American women with SCT are at higher risk of having an SGA infant (birth weight at or below the 10th percentile for a given gestational age) compared to similar African American women with normal hemoglobin. To examine this research question and hypothesis, logistic regression analyses was conducted to predict the risk of having a smaller birth centile from genotype (i.e., SCT status). As shown in Table 5, the overall model was not significant, $\chi^2(1) < .001, p = 1.000, \text{pseudo } R^2 < .001$. Furthermore,
genotype was not a significant predictor of centile (*Odds Ratio* = 1.00, *p* > .999). Therefore, the logistic regression analysis did not provide support for the hypothesis that African American women with SCT are at higher risk for having SGA infants compared to similar African American women with normal hemoglobin. An ANOVA was not conducted for the second research question because the dependent variable ‘centile’ was dichotomous; therefore, a logistic regression was the only appropriate statistic to use.

---

**Table 5**

*Logistic Regression Predicting Risk of Having SGA Infant from SCT Status*

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>SE</th>
<th>Wald</th>
<th>df</th>
<th><em>p</em></th>
<th><em>Odds Ratio</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype</td>
<td>.000</td>
<td>.55</td>
<td>.00</td>
<td>1</td>
<td>&gt; .999</td>
<td>1.000</td>
</tr>
</tbody>
</table>

*Note. Χ² (1) = .00, *p* > .999, pseudo *R*² = .000*

**Research question and hypothesis 3.** The third research question asked: “Is there a difference in birth weight of term infants of Africa American women with SCT (hemoglobin AS profile) as compared to similar African American women with normal hemoglobin (hemoglobin AA profile)?” It was predicted that there would be a difference in birth weight of term infants of Africa American women with SCT (hemoglobin AS profile) as compared to similar African American women with normal hemoglobin (hemoglobin AA profile). Examination of this final research question and hypothesis involved three steps, and for all three steps analyses focused on full term infants (37th to 42nd week).

First, a one-way ANOVA was conducted to test the effect of genotype (i.e., SCT status) on the weight of full term infants. As shown in Table 6, genotype did not have a significant
effect on birth weight for full term infants, indicating no significant difference in the birth weight of infants for mothers with different genotypes (i.e., hemoglobin AS or AA profiles), $F(1, 94) = .001, p = .970, \eta^2 < .001$. Therefore, this did not support the hypothesis that there would be differences in birth weight of term infants for African American women with SCT as compared to similar African American women with normal hemoglobin.

Table 6

Means and Standard Deviations of Infants’ Weight at Term by SCT Status

<table>
<thead>
<tr>
<th>Genotype</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sickle Cell Trait (AA)</td>
<td>47</td>
<td>3208.74</td>
<td>404.61</td>
<td>.00</td>
<td>.97</td>
</tr>
<tr>
<td>Normal Hemoglobin (AS)</td>
<td>49</td>
<td>3205.51</td>
<td>433.15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Second, a crosstabulation with Pearson chi-square was conducted to examine the relationship between genotype and centile (at or below the 10th percentile versus above the 10th percentile). As shown in Table 7, there was no significant relationship between genotype and centile, $X^2 (1) = .04, p = .847$, Cramer’s $V = .020$. Thus, this also did not provide support for the hypothesis that there would be an association between the birth weights of term infants and mothers’ genotype.

Finally, a crosstabulation with Pearson chi-square was conducted to examine the relationship between genotype and low birth weight. Also as shown in Table 7, there was no significant relationship between genotype and low birth weight, $X^2 (1) = .96, p = .328$, Cramer’s $V = .100$. This provided a final piece of information to indicate that there were no differences in
birth weight of term infants for African American women with a hemoglobin AS profile compared to a hemoglobin AA profile.

Table 7

Frequencies and Percentages of Centile Weight and Low Birth Weight by SCT Status

<table>
<thead>
<tr>
<th>Centile</th>
<th>Sickle Cell Trait (AA)</th>
<th>Normal Hemoglobin (AS)</th>
<th>$\chi^2$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below or at 10th Percentile</td>
<td>7 14.9</td>
<td>8 16.3</td>
<td>.04</td>
<td>.847</td>
</tr>
<tr>
<td>Above 10th Percentile</td>
<td>40 85.1</td>
<td>41 83.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Low Birth Weight

<table>
<thead>
<tr>
<th></th>
<th>Sickle Cell Trait (AA)</th>
<th>Normal Hemoglobin (AS)</th>
<th>$\chi^2$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>46 97.9</td>
<td>46 93.9</td>
<td>.96</td>
<td>.328</td>
</tr>
<tr>
<td>Yes</td>
<td>1 2.1</td>
<td>3 6.1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Summary

The current research examined whether African American women with SCT (i.e., hemoglobin AS profile) were more likely to have low birth weight infants and/or infants classified as small for gestational age (SGA) compared to African American women with normal hemoglobin (i.e., hemoglobin AA profile). Overall, there were no differences in birth weight for the two genotypes. More specifically, there was no support for the first hypothesis that African American women with SCT would be at greater risk of having low birth weight (i.e., birth weight less than 2500g) infants compared to similar African American women with normal hemoglobin. In fact, there were no differences in infants’ birth weight between women with the two different genotypes. Furthermore, there was also no support for the second hypothesis that
African American women with SCT would be at higher risk of having SGA infants (i.e., birth weight at or below the 10th percentile given gestational age) compared to similar African American women with normal hemoglobin. Finally, there were no significant differences between the genotypes for term infants’ birth weight or centile.

**End Products/ Deliverables**

The site of this study is the headquarters for a network of 12 community clinics in a central Texas county. It is home to the only Family Medicine Residency Program in the county and home for the County Medical Education and Research Foundation (CMERF). This research supports the organization’s main mission which includes ongoing research. The results of this chart review have been presented to the research site. It is the author’s assumption that the challenges encountered during the chart review process (such as data entry errors in the system) will cause the agency’s directors to take proper actions towards system’s quality improvement. The results of this project will serve as the impetus for further research on this topic by the institution. It is also the author’s assumption that the results of this investigation will be useful for education of health providers and will also affect the way that health care is provided to the health center’s SCT patients.

**Discussion**

The study’s hypotheses and research questions were addressed with the analyses described earlier. The first current study’s research questions sought to explore whether African American women with SCT are at higher risk of having a low birth weight infant (weight at birth of less than 2500g, up to and including 2499g) compared to similar African American women with normal hemoglobin. The first hypothesis predicted that African American women with SCT are at higher risk of having a low birth weight infant compared to similar African American
women with normal hemoglobin. The first null hypothesis predicted that African American women with SCT are not at higher risk of having a low birth weight infant compared to similar African American women with normal hemoglobin. The hypothesis was rejected (null hypothesis accepted) by the findings of this study as the logistic regression analysis ($\chi^2(1) = 0.21, p = .645$, pseudo $R^2 = .006$) and a one-way ANOVA analysis ($F(1, 100) = .13, p = .722$, $\eta^2 = .001$) did not provide support for the hypothesis.

The second research question of the current study sought to explore whether African American women with SCT are at higher risk of having an SGA infant (birth weight at or below the 10th percentile for a given gestational age) compared to similar African American women with normal hemoglobin. Again, the hypothesis was rejected (null hypothesis accepted) by the findings of this study as the logistic regression analysis ($\chi^2(1) < .001, p = 1.000$, pseudo $R^2 < .001$) did not provide support for the hypothesis.

The third research question of the current study sought to explore whether there is a difference in birth weight of term infants of Africa American women with SCT (hemoglobin AS profile) as compared to similar African American women with normal hemoglobin (hemoglobin AA profile). Once more, the hypothesis was rejected (null hypothesis accepted) by the findings of this study as the one-way ANOVA analysis ($F(1, 100) = .13, p = .722$, $\eta^2 = .001$) did not provide support for the hypothesis. Also, a crosstabulation with Pearson chi-square showed no significant relationship between genotype and centile ($\chi^2 (1) = .04, p = .847$, Cramer’s $V = .020$) and no significant relationship between genotype and low birth weight, $\chi^2 (1) = .96, p = .328$, Cramer’s $V = .100$.

This result indicates that there were no differences in birth weight of term infants for the African American women with hemoglobin AS profile compared to hemoglobin AA profile.
The current study suggests that SCT pregnancy is not a risk for low birth weight, having an infant classified as SGA, or having any significant difference in birth weight compared to pregnancy of women with normal hemoglobin, among the African Americans.

The outcome of pregnancy in women with SCT has continued to generate conflicting results in different populations. The study lends credence to the general belief that sickle cell trait is not a pathologic state. These study findings agree with several study findings suggesting that SCT pregnancies are not predisposed to any higher rate of low birth weight or SGA babies. The finding of this study is similar to findings of the study done by Tan, T. L., Seed, P., and Oteng-Ntim, E. (2008) which concluded that SCT was not a risk for SGA because there was no significant difference in the mean birth weights of babies born to sickle cell trait women when compared to birth weight of infants born to women with normal hemoglobin. The results were similar despite the fact that unlike in this current study, Tan and colleagues did not account for smoking as a confounder (Tan, Seed, & Oteng-Ntim, 2008).

The findings of this study did not uncover the tendencies in the SCT pregnant women to have lighter babies as reported in the study by Brown, Merkow, Weiner, and Khajezadeh, (1972). One way that this current study improved upon previous study designs was in excluding women with major complications of pregnancy and other confounders from review. It is possible that excluding all possible confounders and complications from review may be the reason for low number of low birth weight babies and SGA babies (5 or 4.9% and 16 or 15.69% respectively) analyzed.

Another limitation of the current study is that cases in excess of the BMI limit (35) originally stated in the study proposal were selected. The explanation for exceeding the BMI in the original study proposal was that many African American mothers encountered exceeded the
BMI of 35. Because the researchers could not have acquired the desired sample size, many participants with BMIs over 35 were selected but then, were matched in both groups. Studies have shown that excess body weight in pregnancy can affect birth weight (Nohr et al., 2009; Ogbuji, 2010). Morbidly obese women tend to have a higher risk of both pre- and post-term births (Nohr et al., 2009). Before the significance of SCT genotype in contributing to low birth weight or SGA could be ultimately dismissed, more extensive prospective and randomized studies (controlling for all confounders and yet capturing more babies with low birth weight and or SGA) should be performed.

Conclusion

Sickle cell trait is not a risk factor for low birth weight and small for gestational age infants among African American women in this study. However, risk factors among sickle cell trait African American pregnant women, such as drug-use, smoking, alcohol-abuse, teenage pregnancy, diabetes, UTI, etc., need to be identified and monitored closely to prevent poor pregnancy outcomes.
References


Outcome of pregnancy in a population of Nigerian women with sickle cell trait.


Larrabee K. D., & Monga, M. (1997). Women with sickle cell trait are at increased risk for


Appendix A

SCT Participants’ Selection Process

101 sickle cell trait pregnancies were identified between year 2000 to 2010

23 were eliminated because the corresponding offspring records could not be accessed

Out of 78 sickle cell trait pregnancies with corresponding offspring records

14 were excluded for maternal age at birth of child being below 18 years

Out of 64 sickle cell trait pregnancies with corresponding offspring records and maternal age ≥ 18 at birth of child

15 were excluded for the following reasons: smoking, drug use, and alcohol use during pregnancy, complications of pregnancy such as uncontrolled hypertension, missing lab result confirming genotype, and multiple pregnancy

Out of 49 sickle cell trait pregnancies with corresponding offspring records, maternal age ≥ 18 at birth of child, and without complications of pregnancy

5 more pregnancies with corresponding offspring records, maternal age ≥ 18 at birth of child, and without complications of pregnancy were selected for the study, to be matched with control
Appendix B

Cost of Low Birth-weight and Preterm Births

Appendix C

<table>
<thead>
<tr>
<th>Gestational age, weeks</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>270</td>
<td>256</td>
</tr>
<tr>
<td>21</td>
<td>320</td>
<td>310</td>
</tr>
<tr>
<td>22</td>
<td>388</td>
<td>368</td>
</tr>
<tr>
<td>23</td>
<td>446</td>
<td>426</td>
</tr>
<tr>
<td>24</td>
<td>504</td>
<td>480</td>
</tr>
<tr>
<td>25</td>
<td>570</td>
<td>535</td>
</tr>
<tr>
<td>26</td>
<td>644</td>
<td>592</td>
</tr>
<tr>
<td>27</td>
<td>728</td>
<td>662</td>
</tr>
<tr>
<td>28</td>
<td>828</td>
<td>760</td>
</tr>
<tr>
<td>29</td>
<td>956</td>
<td>889</td>
</tr>
<tr>
<td>30</td>
<td>1117</td>
<td>1047</td>
</tr>
<tr>
<td>31</td>
<td>1308</td>
<td>1234</td>
</tr>
<tr>
<td>32</td>
<td>1521</td>
<td>1447</td>
</tr>
<tr>
<td>33</td>
<td>1751</td>
<td>1675</td>
</tr>
<tr>
<td>34</td>
<td>1985</td>
<td>1001</td>
</tr>
<tr>
<td>35</td>
<td>2205</td>
<td>2109</td>
</tr>
<tr>
<td>36</td>
<td>2407</td>
<td>2300</td>
</tr>
<tr>
<td>37</td>
<td>2596</td>
<td>2484</td>
</tr>
<tr>
<td>38</td>
<td>2769</td>
<td>2657</td>
</tr>
<tr>
<td>39</td>
<td>2908</td>
<td>2796</td>
</tr>
<tr>
<td>40</td>
<td>2986</td>
<td>2872</td>
</tr>
<tr>
<td>41</td>
<td>3007</td>
<td>2891</td>
</tr>
<tr>
<td>42</td>
<td>2998</td>
<td>2884</td>
</tr>
<tr>
<td>43</td>
<td>2977</td>
<td>2868</td>
</tr>
<tr>
<td>44</td>
<td>2953</td>
<td>2853</td>
</tr>
</tbody>
</table>

Reprinted with permission from the American College of Obstetricians and Gynecologists (Obstetrics and Gynecology, 1996; 87:163).

Source: http://www.uptodate.com
Appendix D

Overview of Research Portion of Project

Design

Retrospective chart review

Sample

- The first group of cases will comprise of African American SCT deliveries, and the second will comprise of African American deliveries with normal hemoglobin.
- Data will be collected within a 21-year study period (1991-2011) from the FHC electronic database.

Intervention

- Calculate birth weights and centiles of all deliveries.
- Compare incidence of low birth weight in SCT deliveries to incidence in the control group.

Clinical Problem

- Studies show increased incidence of poor outcomes in SCD pregnancies, including intrauterine growth retardation (resulting in low birth weight and SGA babies) and stillbirth (Zack-Williams, 2007). There is conflicting evidence in the literature in regard to the effect of SCT on birth weight (Tan et al., 2008).
- Low birth weight is an important predictor of newborn health and survival (WHO, 2011).
- SGA infants are at increased risk for neonatal distress, permanent deficits in growth and neurocognitive development, and mortality (CDC, 2008).
- The highest occurrence of SGA is among non-Hispanic African Americans in 2005 (CDC, 2008).
Research Questions

1. Are African American women with SCT at higher risk of having a low birth weight infant (weight at birth of less than 2500g, up to and including 2499g) compared to similar African American women with normal hemoglobin?

2. Are African American women with SCT at higher risk of having an SGA infant (birth weight at or below the 10th percentile for a given gestational age) compared to similar African American women with normal hemoglobin?

3. Is there a difference in birth weight of term infants of Africa American women with SCT (hemoglobin AS profile) as compared to similar African American women with normal hemoglobin (hemoglobin AA profile)?

Research Hypotheses

1. African American women with SCT are at higher risk of having a low birth weight infant (weight at birth of less than 2500g, up to and including 2499g) compared to similar African American women with normal hemoglobin.

2. African American women with SCT are at higher risk of having an SGA infant (birth weight at or below the 10th percentile for a given gestational age) compared to similar African American women with normal hemoglobin.

3. There is a difference in birth weight of term infants of Africa American women with SCT (hemoglobin AS profile) as compared to similar African American women with normal hemoglobin (hemoglobin AA profile).
Null Hypotheses

1. African American women with SCT are not at higher risk of having a low birth weight infant (weight at birth of less than 2500g, up to and including 2499g) compared to similar African American women with normal hemoglobin.

2. African American women with SCT are not at higher risk of having an SGA infant (birth weight at or below the 10th percentile for a given gestational age) compared to similar African American women with normal hemoglobin.

3. There is no difference in birth weight of term infants of Africa American women with SCT (hemoglobin AS profile) as compared to similar African American women with normal hemoglobin (hemoglobin AA profile).

PICO Questions

1. Among African Americans, are pregnant women with SCT at a higher risk of having low birth weight infants (weight at birth of less than 2500g, up to and including 2499g) compared to similar women with normal hemoglobin?

2. Among African Americans, are pregnant women with SCT at a higher risk of having an SGA infant (birth weight at or below the 10th percentile for a given gestational age) compared to similar women with normal hemoglobin?

3. Among African Americans, is there a difference in birth weight of term infants of women with SCT as compared to similar women with normal hemoglobin?

Dependent variables

Birth weight and birth weight centile

Independent variables

Sickle cell trait status with hemoglobin profile (AS) and Normal Hemoglobin profile (AA).
Appendix E

Proposed Statistical Analysis Plan

<table>
<thead>
<tr>
<th>Analysis Phases</th>
<th>Procedural Steps</th>
<th>Specifics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-analysis phase</td>
<td>Identify two groups of African American SCT delivery cases and a control delivery cases with normal hemoglobin within the 21-year study period (1991-2011) Select cases using inclusion criteria Select software package Enter data into SPSS data set Perform daily data quality checks to ensure accuracy of entries and clean data Create and document analysis files</td>
<td>SPSS Statistics GradPack 19.0 Premium software will be used Data will be entered into SPSS by hand</td>
</tr>
<tr>
<td>Preliminary assessments</td>
<td>Assess missing data Assess data quality Assess for bias Assess assumptions for inferential tests</td>
<td></td>
</tr>
<tr>
<td>Preliminary actions</td>
<td>Perform needed variable transformations and recodes Address missing value problems Perform any other peripheral analysis</td>
<td></td>
</tr>
<tr>
<td>Principal analysis</td>
<td>Perform descriptive analysis Perform bivariate inferential statistical analysis and testing for potential covariates Perform prior power analysis to determine the minimum sample size needed. Obtain assistance from statistician</td>
<td>Demographic data, e.g., age, weight, height, gestational age Discriminate function analysis</td>
</tr>
<tr>
<td>Interpretive phase</td>
<td>Integrate and synthesize analyses Perform any supplementary interpretive analysis (power analysis) Obtain assistance from statistician</td>
<td></td>
</tr>
</tbody>
</table>

## Appendix F

### Codebook

<table>
<thead>
<tr>
<th>Full Variable name</th>
<th>SPSS variable name</th>
<th>Coding instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification number</td>
<td>ID</td>
<td>Subject identification number</td>
</tr>
<tr>
<td>Body mass index</td>
<td>BMI</td>
<td>numeric</td>
</tr>
<tr>
<td>Parity (How many times patient has given birth)</td>
<td>Para</td>
<td>number</td>
</tr>
<tr>
<td>Maternal genotype (reported by sickle cell test or hemoglobin electrophoresis)</td>
<td>Genotype</td>
<td>1 = AS 2 = AA 3 = other</td>
</tr>
<tr>
<td>Infant’s gestation at delivery</td>
<td>Gestage</td>
<td>Number of completed weeks</td>
</tr>
<tr>
<td>Term birth (defined as a birth occurring between 37 and 0/7ths and 42 weeks of gestation)</td>
<td>Term</td>
<td>1 = Preterm (below 37 completed weeks) 2 = Term (between 37 and 0/7ths and 42 weeks) 3 = Post term (over 42 weeks)</td>
</tr>
<tr>
<td>Baby’s gender (male or female)</td>
<td>Gender</td>
<td>1 = male 2 = female</td>
</tr>
<tr>
<td>Birth weight</td>
<td>BW</td>
<td>In grams</td>
</tr>
<tr>
<td>Low birth weight (LBW) — BW less than 2500 g</td>
<td>LBW</td>
<td>1 = no (2500 g or more) 2= yes (less than 2500 g)</td>
</tr>
<tr>
<td>Birth weight centile (calculated using tenth percentile for birth weight chart)</td>
<td>Centile</td>
<td>1= at or below tenth percentile 2 = above the tenth percentile</td>
</tr>
<tr>
<td>Match every “AS” genotype as closely as possible to an “AA” genotype based on Gender, Parity, BMI, and Gestage. Matched pairs will have same “Matchup” number</td>
<td>Matchup</td>
<td>numeric</td>
</tr>
</tbody>
</table>
## Appendix G
### Research Questions and Statistical Tests

<table>
<thead>
<tr>
<th>Research Questions</th>
<th>Independent Variables</th>
<th>Dependent Variables</th>
<th>Statistical Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are African American women with SCT at higher risk of having a low birth weight infant (weight at birth of less than 2500g, up to and including 2499g) compared to similar African American women with normal hemoglobin?</td>
<td>(a)= Sickle cell trait status with hemoglobin profile (AS) (b)= Normal Hemoglobin profile (AA).</td>
<td>1= Birth weight 2= Birth weight centile</td>
<td>Logistic regression with SCT status (SCT versus normal hemoglobin)</td>
</tr>
<tr>
<td>Are African American women with SCT at higher risk of having an SGA infant (birth weight at or below the 10th percentile for a given gestational age) compared to similar African American women with normal hemoglobin?</td>
<td>(a)= Sickle cell trait status with hemoglobin profile (AS) (b)= Normal Hemoglobin profile (AA).</td>
<td>1= Birth weight 2= Birth weight centile</td>
<td>Logistic regression with SCT status (SCT versus normal hemoglobin)</td>
</tr>
<tr>
<td>Is there a difference in birth weight of term infants of Africa American women with SCT (hemoglobin AS profile) as compared to similar African American women with normal hemoglobin (hemoglobin AA profile)?</td>
<td>(a)= Sickle cell trait status with hemoglobin profile (AS) (b)= Normal Hemoglobin profile (AA).</td>
<td>1= Birth weight 2= Birth weight centile</td>
<td>Crosstabulation with Pearson chi square analyses</td>
</tr>
</tbody>
</table>
Appendix H

PROVIDENCE Healthcare Network

October 27, 2011

Uchechi Emegh Okari, FNP-C
Family Health Center
1600 Providence Drive
Waco, TX 76707

Dear Ms. Okari:

We are pleased to announce approval by the Institutional Review Board of your request for approval of the following study for one year at Providence Health Center effective October 27, 2011:

IS SICKLE CELL TRAIT PREGNANCY A RISK FOR LOW BIRTH WEIGHT?

Waiver of Consent has been granted for this study.

The following criteria must be adhered to during the study:

1. The committee must be informed of any changes or deviations from the submitted investigational plan within 48 hours.

2. The study is subject to annual review.

3. A copy of study findings shall be submitted to the IRB upon completion of the study along with an official letter of closure.

Should you have any further questions, please feel free to contact Keith Hopkins at 751-4840.

Sincerely,

Larry J. Davis, M.D., Chairman
Institutional Review Board

LJD/lf

www.providence.net

ASCENSION
RAIL
# Appendix I

## REQUEST FOR MODIFICATION

### Section I.

### Investigator Information

<table>
<thead>
<tr>
<th>Title is Sickle Cell Trait Pregnancy a Risk for Low Birth Weight?</th>
<th>Investigator(s) Name and Address (Include Department, Bldg., Room or mail stop number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title is Sickle Cell Trait Pregnancy a Risk for Low Birth Weight?</td>
<td>Investigator(s) Name and Address (Include Department, Bldg., Room or mail stop number)</td>
</tr>
</tbody>
</table>

| Title is Sickle Cell Trait Pregnancy a Risk for Low Birth Weight? | Investigator(s) Name and Address (Include Department, Bldg., Room or mail stop number) |

### Contact Information

<table>
<thead>
<tr>
<th>Phone</th>
<th>Fax</th>
<th>Email</th>
</tr>
</thead>
<tbody>
<tr>
<td>(254) 355-4810</td>
<td></td>
<td><a href="mailto:ukanai@yahoo.com">ukanai@yahoo.com</a></td>
</tr>
</tbody>
</table>

### Section II.

#### Type of Modification (Select ALL that apply)

- [x] Amendment
- [ ] New Procedures
- [ ] Change in Study Personnel
- [ ] Change of Site
- [x] Change in Enrollment

#### Amendment

- [ ] Add
- [ ] Delete
- [ ] Change

#### Change in Study Personnel

- [ ] Add
- [ ] Delete
- [ ] Modify

#### Change of Site

- [ ] Add
- [ ] Delete
- [ ] Modify

#### Change in Enrollment

- [ ] Increase from 100 to 200
- [ ] Decrease from 200 to 100

#### Consent Change

- [ ] New Consent
- [ ] Revised Consent

#### Advertisement

<table>
<thead>
<tr>
<th>Newspaper</th>
<th>Radio</th>
<th>Television</th>
<th>Flyer</th>
<th>Information Brochure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ad</td>
<td>Announcement</td>
<td>Station</td>
<td>Distributed</td>
<td>Distributed how</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Clinical Investigator’s Brochure

<table>
<thead>
<tr>
<th>Select</th>
<th>Addendum</th>
<th>Updated</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date:</td>
<td>Date:</td>
<td>Date:</td>
<td></td>
</tr>
</tbody>
</table>

### Funding

<table>
<thead>
<tr>
<th>Add</th>
<th>Agency Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delete</td>
<td>Agency Name</td>
</tr>
</tbody>
</table>

### Site

| List all sites this amendment applies to: |

### Other

| (e.g., Annual Report, Package Insert, General Correspondence) Describe and attach a narrative. |

---

Page 1 of 2
Appendix J

NARRATIVE: REQUESTING EXPANSION OF CHART REVIEW TIME-PERIOD TO 1991 to 2011

The purpose of this modification request is to expand the time period to be reviewed in this chart review.

This ongoing study is a chart review of African American (AA) women who gave birth between 2000 and 2010 with the Family Health Center. The charts of all African American women with sickle cell trait who delivered at 24 to 42 completed weeks of gestation together with the corresponding charts of offspring from each pregnancy have been selected and reviewed. Later these charts will be matched with charts of AA women (and their offspring) with normal hemoglobin and the data from both groups will be compared and analyzed to answer the research questions.

So far, the chart review of this originally intended population (AA women who gave birth between 2000 and 2010) has not produced enough records of women with sickle cell trait (qualified for inclusion) for the study.

A minimum of 400 records comprising 200 records of women with sickle cell trait and 200 records of women with normal hemoglobin is required.

Expanding the review time-period to include records of women who gave birth between 1991 and 2011 with the Family Health Center will most likely produce the required sample size needed to answer the research questions.
December 5, 2011

Ms. Uchechel Eunice Okani
2011 Pebble Brook Circle
McGregor, TX 76657

Dear Ms. Okani:

Re:  Is Sickle Cell Trait Pregnancy a Risk for Low Birth Weight? (Protocol #: 16890)

The above referenced study has been reviewed by the TWU Institutional Review Board (IRB) and was determined to meet requirements in regard to protection of individuals' rights and is exempt from further review.

Any modifications to this study must be submitted for review to the IRB using the Modification Request Form. Additionally, the IRB must be notified immediately of any unanticipated incidents. If you have any questions, please contact the TWU IRB. The Institutional review board is pleased to acknowledge your sense of responsibility for ethical research.

Sincerely,

Dr. Shuh-Jen Lin, Chair
Institutional Review Board - Dallas

cc. Dr. Stephanie Woods, College of Nursing - Dallas
    Dr. Peggy Mancuso, College of Nursing - Dallas
    Graduate School
Appendix L

TWU INSTITUTIONAL REVIEW BOARD (IRB)
MODIFICATION REQUEST FORM

Complete this form when you would like to request a change on an approved study. This change could be a change in the research team, data collection sites, protocol (e.g., compensation, study procedures, etc.), and/or the informed consent. Submit this signed form along with copies of any new or modified materials you describe below to the IRB. NOTE: You may not implement any changes to an IRB-approved study until your Modification Request has been approved.

PRINCIPAL INVESTIGATOR: UCHECHI EUNICE OKANI

DATE APPROVED BY IRB (most recent): December 5, 2011

TITLE OF STUDY: Is Sickle Cell Trait Pregnancy a Risk for Low Birth Weight? (Protocol #16890)

Provide a detailed description of the modification(s) requested:

REQUESTING EXPANSION OF CHART REVIEW TIME-PERIOD TO 1991-2011

The purpose of this modification request is to expand the time-period to be reviewed in this chart review.

This ongoing study is a chart review of African American (AA) women who gave birth between 2000 and 2010 with the Family Health Center. The charts of all African American women with sickle cell trait who delivered at 24 to 42 completed weeks of gestation together with the corresponding charts of offspring from each pregnancy have been selected and reviewed. Later these charts will be matched with charts of AA women (and their offspring) with normal hemoglobin. So far, the chart review of this originally intended population (AA women who gave birth between 2000 and 2010) has not produced enough records of women with sickle cell trait (qualified for inclusion) for the study.

A minimum of 400 records comprises 200 records of women with sickle cell trait and 200 records of women with normal hemoglobin is required.

Expanding the review time-period to include records of women who gave birth between 1991 and 2011 with the Family Health Center will most likely produce the required sample size needed to answer the research questions.

Provide a list of any new or modified documents materials and attach these items to this form:

(see attached Providence Healthcare Network IRB modification approval)
Appendix M

January 31, 2012

Ms. Uchechi Eunice Okani
2011 Pebble Brook Circle
McGregor, TX 76657

Re: Is Sickle Cell Trait Pregnancy a Risk for Low Birth Weight?

Ms. Okani:

Your request for modification has been reviewed by the IRB and has been approved. Any further modifications to this study must be submitted for review to the IRB using the Modification Request form. This form may be found on the IRB website. Additionally, the IRB must be notified immediately of any unanticipated incidents. If you have any questions, please contact the TWU IRB. The Institutional Review Board is pleased to acknowledge your sense of responsibility for ethical research.

Sincerely,

[Signature]

Dr. Suh-Jen Lin, Chair
Institutional Review Board - Dallas
## Appendix N

### Initial Data Collection Sheet

<table>
<thead>
<tr>
<th>De-identified MRN#</th>
<th>SPSS variable names</th>
</tr>
</thead>
<tbody>
<tr>
<td>ID# mom Initial mom</td>
<td>ID= Multiple ADD</td>
</tr>
<tr>
<td>CHILD Initial=</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Hx Birth length</td>
<td>BW= (g) LBW= Centile=</td>
</tr>
<tr>
<td></td>
<td>Gestation age (wks) Gestage Term</td>
</tr>
<tr>
<td>Birth Hx Birth weight</td>
<td></td>
</tr>
<tr>
<td>Delivery method</td>
<td>Method</td>
</tr>
<tr>
<td>Apgar score: 1m= 5m= 10m</td>
<td>Apgar</td>
</tr>
<tr>
<td>Hosp. info= Days in hosp=</td>
<td>NICU</td>
</tr>
</tbody>
</table>

| Mother Height | Height |
| Weight | Weight |
| BMI | BMI |
| BP Race | Race |
| Age | |

| LMP EDC EDD | |
| Date +ve urine preg test | |
| Genetic screen = | |
| Personal hx of G/O Diabetes= | Diabetes |
| OB Hx Para | |
| G P T | |
| Hypertension = | Hypertension Genotype |
| Diabetes = | |
| SS Trait = | |
| Other= | |

| PMHx | |
| Hypertension = | |
| Diabetes = | |
| SS Trait = | |
| Other= | |

| PSH C/Section | |
| | |

| Soc. Hx Tobacco= | Smoking |
| Quit date= | |
| Alcohol= | Alcohol |
| Quit date= | |
| Drugs= | Drugs |
| Quit date= | |

| LABS | |
| Rubella= | Disease |
| HIV= | |
| RPR= | |
| Hep B SAG= | |
| GC/Chlamydia= | Disease |
| UTI= | UTI |
| Dates= | |
| Pap smear= | Disease |
| Result= | |
| Maternal serum screen= | Defect |
Appendix O

Acknowledgement E-mail from TWU IRB

From: Lin, Suh-Jen  
Sent: Friday, November 18, 2011 10:49 AM  
To: Mancuso, Peggy; Okani, Uchechi  
Cc: Bracken, Laura  
Subject: RE: Your packet went to IRB by courier

Thanks, I received your IRB application packages.

Dr. Lin  
Chair  
Dallas IRB  
Suh-Jen Lin, PT, PhD  
Associate Professor  
School of Physical Therapy  
Presbyterian Campus  
Texas Woman's University  
8194 Walnut Hill Lane  
Dallas TX 75231

TEL: (214) 706-2461  
Fax: (214) 706-2361  
Lab: (214) 706-2472

From: Peggy Mancuso  
[mailto:peggymancuso@yahoo.com]  
Sent: Thursday, November 17, 2011 2:14 PM  
To: Okani, Uchechi  
Cc: Lin, Suh-Jen; Bracken, Laura  
Subject: Your packet went to IRB by courier

Hi Eunice -- Your packet with Dr. Wood's signature went to the IRB today. This will be for a dual review.

Peggy Mancuso, PhD, RN, CNM  
Professor and Coordinator, Doctor of Nursing Practice Program  
Texas Woman's University  
Dallas, TX  
Office: 214-689-6552, Fax: 214-689-6539