Exploring the Link Between Low Birth Weight Babies and Risk of Maternal Venous Thromboembolism - Why This Disproportionately Affects African American Women

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Abstract

Background: Maternal morbidity and mortality during childbirth has been a tragic complication of childbirth throughout history. However, maternal mortality rates have been trending down in every developed country other than the United States of America. Certain populations and comorbidities present expectant mothers with greater risk for maternal mortality or severe life-threatening complications during childbirth. Many of these factors are medically intuitive such as obesity, tobacco use, hypercoagulabilities/hemoglobinemias, positive family history, various disease states, and pre-partum complications such as preeclampsia. However, the greatest risk factor for maternal mortality in America is being African American. Two main factors were stand out in African American pregnancies and childbirth compared to other ethnicities, these two factors were firstly that African American women tend to give birth to low birthweight (LBW) babies at higher rates than any other race. Secondly, African American women are at higher rates of maternal morbidity and mortality. Since venous thromboembolism accounts for 10% of all maternal deaths these findings prompted us to explore if a link between LBW babies and occurrence of venous thromboembolism is present.

Methods: Exhaustive search of available medical literature was performed via Web of Science, CINAHL, MEDLINE-PubMed, and GoogleScholar using the keywords "low birthweight" OR "birth weight" OR "small for gestational age" OR "intrauterine growth restriction" OR "fetal growth retardation" OR postpartum AND "venous thromboembolism". Articles were assessed for quality based on GRADE criteria.

Results: African American women were found to be higher risk for postpartum VTE than and other race, and a 50% higher risk than white women. This correlation was particularly prominent when examining rates of postpartum VTE in African American women who has to undergo cesarean section, while cesarean section puts all races at increased risk of VTE, and in this population cesarean section is the largest risk factor for pulmonary embolism. Being an African American woman who underwent a cesarean section increased the VTE risk by 5 times compared to white women who underwent a cesarean section.

Conclusion: Low birth weight babies increase the risk of venous thromboembolism in mothers, leading to higher maternal death. Research has already explored what could be causing this discrepancy, with one of the leading theories causing LBW being exposure to chronic stress. One study found that chronic exposure to racism throughout one's life has a “dose dependent response” to low birth weight. In other words, the longer an expectant mother has been exposed to racism, the more likely the baby is going to be born into the very low birth weight (VLBW) category.

The medical community needs to continue to explore what is causing the increased maternal mortality in the African American community. With the above proposed assessment, we suggest that mothers who birth low birthweight babies – particularly African American women – be closely monitored for VTE. Further research may consider specific protocols to address this complication and therefore reduce maternal mortality rates. Optimally, research would be conducted to determine the etiologies of low birthweight babies in African American women so that this can be addressed and prevented – therefore, saving thousands of lives.

Keywords: low birthweight, postpartum, venous thromboembolism, African American
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Exploring the Link Between Low Birth Weight Babies and Risk of Maternal Venous Thromboembolism - Why This Disproportionately Affects African American Women

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A Clinical Graduate Project Submitted to the Faculty of the School of Physician Assistant Studies Pacific University Hillsboro, OR For the Masters of Science Degree, 08/2019 Faculty Advisor: Professor Sage Davis-Risen Clinical Graduate Project Coordinator: Annjanette Sommers, PA-C, MS
Abstract

**Background:** African American women tend to give birth to babies that are much smaller than women of any other race. These African American women are also at increased risk of maternal mortality.

**Methods:** Exhaustive search of available medical literature was performed via Web of Science, CINAHL, MEDLINE-PubMed, and GoogleScholar using the keywords "low birthweight" OR "birth weight" OR "small for gestational age" OR "intrauterine growth restriction" OR "fetal growth retardation" OR postpartum AND "venous thromboembolism”. Articles were assessed for quality based on GRADE criteria.

**Results:** Low birth weight babies increase the risk of venous thromboembolism in mothers, leading to higher maternal death.

**Conclusion:** Low birth weight babies increase the risk of venous thromboembolism in mothers, leading to higher maternal death.

**Keywords:** low birthweight, postpartum, venous thromboembolism, African American
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List of Abbreviations

VTE   Venous Thrombus Embolism
DVT   Deep Vein Thrombosis
PE    Pulmonary Embolism
LBW   Low birth weight
SGA   Small for gestational age

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(none at this time)
Exploring the Link Between Low Birth Weight Babies and Risk of Maternal Venous Thromboembolism - Why This Disproportionately Affects African American Women

BACKGROUND

Maternal morbidity and mortality during childbirth has been a tragic complication of childbirth throughout history. However, maternal mortality rates have been trending down in every developed country other than the United States of America.¹ In 2010 the average number of maternal deaths per live birth was 17:100,000 in 2017 the average had risen to a staggering 26.7:100,000.¹ This is approximately a 57% increase in mortality in less than 10 years. Certain populations and comorbidities present expectant mothers with greater risk for maternal mortality or severe life-threatening complications during childbirth. Many of these factors are medically intuitive such as obesity, tobacco use, hypercoagulabilities/hemoglobinemias, positive family history, various disease states, and pre-partum complications such as preeclampsia. However, the greatest risk factor for maternal mortality in America is being African American – a fairly well-known fact that the
medical community has hypothesized about for some time but has not yet been able to adequately account for.\(^2\)

There has been an upsurge in recent media attention to the topic after Serena Williams, a professional tennis player, suffered from a nearly fatal venous thromboembolism (VTE) following giving birth. Ms. Williams used her celebrity to draw attention to the racial and ethnic disparities that exist in maternal care of African American women. What was so fascinating about her experience was it called into question so many misconceptions about the underlying reasons African American women were dying during childbirth. For instance, Serena Williams is wealthy, so it wasn’t a lack of access to care. Additionally, she is a world class athlete, so it wasn’t an unawareness to her body. Lastly, she doesn’t abuse any substances; in fact, she is far more health conscious than the average American women. So, what is left to account for a world class athlete almost dying during childbirth?

Unfortunately, being an African American woman increases the rate of maternal mortality to “2.64 per 1000 deliveries, was 64% higher than that for women of other races (1.61 per 1000 deliveries). At all ages, African American women had a higher rate”.\(^3\) Despite this staggeringly high racial disparity little progress has been made in establishing the root cause of the high maternal mortality rate.\(^4\) Due to the clear medical necessity for exploring the underlying cause, a
systemic review of current medical literature was conducted to try to determine just why being an African American female came with such high maternal mortality rates.

While it is apparent that many socioeconomic factors exist, they are harder to quantify and lead to speculation. For this reason, it became clear that to better analyze the current literature one would need to find factors that affected African American women at higher rates than other racial and ethnic groups in order to make progress. Two main factors were stand out in African American pregnancies and childbirth compared to other ethnicities, these two factors were firstly that African American women tend to give birth to low birthweight (LBW) babies at higher rates than any other race.\(^5\) Secondly, African American women are at higher rates of maternal morbidity and mortality.\(^2\) Since venous thromboembolism accounts for 10% of all maternal deaths these findings prompted us to explore if a link between LBW babies and occurrence of venous thromboembolism is present.\(^7\) We utilized research that explored this connection whether the population was of African American descent or not, as the purpose of this paper is to determine if a link between LBW and DVT exists, and from there much discussion can be had on the implications of the findings for the African American population since they are
disproportionately experiencing both LBW infants and maternal mortality from things like deep vein thrombus (DVT).

Lastly, we found it necessary to better understand if low birthweight infants are a genetic predisposition with African descendance or if, like we expect, it is due to another variable - such as racial disparity. Studies that examined birthweight amongst African descendant babies in America verse African descended babies birthed in other countries were researched for background information. A fascinating study conducted by Richard Collins et al found that “the mean birth weight of 44,046 infants of U.S.-born white women was 3446 g, that of 3135 infants of African-born black women was 3333 g, and that of 43,322 infants of U.S.-born black women was 3089 g. The incidence of low birth weight (weight less than 2500 g) was 13.2 percent among infants of U.S.-born black women and 7.1 percent among infants of African-born black women, as compared with 4.3 percent among infants of U.S.-born white women (relative risks, 3.1 and 1.6, respectively)”\(^5\). It is also important to note that “infant birth weight is a primary determinant of infant mortality risk” and furthermore that “births occurring at very low birth weight (VLBW; < 1500 g), pathological in all populations, 1,4,5 accounts for more than half of the neonatal deaths and 63% of the Black–White gap in infant mortality in the United States”\(^5\). Based on this information the link
between low birthweight and African descent was disproved as African
descent babies born in Sudan matched closely in weight to Caucasian
babies born in the USA, while African descent babies born in the USA
were underweight. While the purpose of our research is not to
determine what is causing low birthweight in African American infants,
it is important to note that this difference is specific for American born
African descent babies and thus can be used to start examining the
cause of maternal mortality that is so prevalent in the USA amongst
African Americans.

METHODS

An exploration of current literature linking increased maternal
mortality with African American women was conducted. The initial
search was too broad and produced many qualitative search results,
and while the research was interesting we aimed to conduct a more
quantitative assessment. We noticed trends with African American
women delivering low birth weight infants, and also a trend that
African American women died during childbirth more than any other
race – often due to VTE. Next, we wanted to explore if any research
had been done linking the two trends together.

Search terms that allude to low birth weight infants were used,
including to but not limited to “low birthweight” “low birth weight”
“small for gestational age” “SGA” “intrauterine growth restriction” “IUGR” were all used in different combinations to produce more search results. These terms were combined with terms that alluded to venous thromboembolism which included “venous thrombus embolism” “venous thromboembolism” “VTE” “deep vein thrombosis” and “DVT”. Research was limited linking low birthweight and VTE together, but many articles discussed both variables separately which made it very necessary for careful analysis of the research articles.

The search engines used to discover research on this were Web of Science, PubMed, CINAHL, and Google Scholar. Articles were assessed for quality using GRADE criteria.6

RESULTS

After exclusion of 55 studies that did not meet our parameters, 3 retrospective studies 7-9 were assessed and are reviewed. See Table 1.

Blondon et al.

This study specifically analyzed the link between low birthweight and occurrence of VTE. The researchers recruited 9,482 women from Washington State. These women were all screened and 547 were found to have cases of postpartum DVT. Of these 547 women, 255 were found to have had a prior history of DVT and were not included.
By eliminating women who have had known cases of DVT the researchers controlled for pre-existing conditions or other variables that could bias the data from the study. In order to determine the birth weight, data was collected from the birth certificates of the infants born to the women in the study. Interestingly birthweight of infants was rather stable across all maternal age groups.⁷

Upon analysis of data, African American women were found to be higher risk for postpartum VTE than and other race, and a 50% higher risk than white women.⁷ This correlation was particularly prominent when examining rates of postpartum VTE in African American women who has to undergo cesarean section, while cesarean section puts all races at increased risk of VTE, being an African American woman who underwent a cesarean section increased the VTE risk by 5 times compared to white women who underwent a cesarean section. These researchers found that, “in comparison with mothers of newborns with normal birth weight, mothers of newborns with low birth weight had a 3-fold increased risk of VTE, which persisted after multivariable adjustment (odds ratio, 2.98; 95% confidence interval, 1.80–4.93). Importantly, this increased risk appeared to be independent of other known risk factors of postpartum VTE”.⁷ Researchers established a statistically significant relationship between LBW and VTE exists, and
they were able to show that LBW alone was a strong enough risk factor to endanger African American women.  

**Jacobsen et al.**

This article was conducted in Norway and utilized a large sample size. The study drew participants from 18 hospitals between the time frame of January 1990 through December 2003, which produced 1229 controls and 39 cases. To be included in the study the researchers pulled cases that included a diagnosis of VTE. They did an excellent job excluding cases that did not meet their standards for inclusion. For instance, any study with a “clinical diagnosis with no confirmatory test or with an indeterminate result was classified as possible VT and not included in analysis”, any VTE diagnosis that included comorbidities with the VTE such as miscarriage, ectopic pregnancy, or abortion were also not included. Researchers were also diligent in excluding any cases in which this was not the first diagnosis of VTE. Lastly, we found a huge strength of the study was that when the researchers were not sure if a case had ‘questionable’ inclusion criteria, they had a hematologist consult and review the case.

The study then analyzed the collected data with using statistical analysis tools like chi-square test and logistic regression. The researchers also performed data analysis via the “Statistical Package for Social Science version 13.1”. Data analysis showed that IUGR was
a statistically significant risk factor for postnatal venous thromboembolism, while it was actually not a significant risk for antenatal VTE. The study also found that there was “an additive interaction for women with preeclampsia and IUGR”.

**Morris et al.**

The research from Morris et al was conducted in Australia. The study addressed that pulmonary embolism – a type of VTE – is a main cause of maternal mortality in the “UK and Norway and amongst the leading causes in Australia and the US”. For data collection the researchers searched ICD diagnoses fields for the obstetric and on obstetric pulmonary embolism codes within the MDC_APDC records from births in hospitals in New South Wales. They set parameters to include any VTE up to 12 weeks postpartum, and excluded cases where there was an antenatal VTE as this was not their intended research population. Study designs defined small for gestational age, or “SGA”, as <10th percentile. Of the 230 participants included in their search criteria, 14 of the 230 women gave birth to babies that were deemed SGA. The study also found that 20.4 of the 230 participants gave birth prematurely, which also leads to low birthweight as the infant did not come to term or have time to finish developing.
Results of the study showed that of the 40 maternal mortalities “seven were associated with pulmonary embolism”\textsuperscript{9} and the “largest risk factor for PE was c-section”\textsuperscript{9}.

**DISCUSSION**

After exhaustive analysis of available research, it became evident that there is a correlation between the rates of low birthweight infants and the occurrence of DVT. All 3 studies \textsuperscript{7-9} concluded that small for gestational age or low birthweight, did correlate with increased prevalence of DVT even though each study examined different populations.

While all 3 studies \textsuperscript{7-9} came to the same conclusion, many of the studies also analyzed many other variables during their data collection. Each study also had its own weaknesses when it came to data collection and applicability to our research.

**Blondon et al.**

Limitations of this study include the absences of analysis of mothers BMI which could be an important factor in studying postpartum complications.\textsuperscript{7} Researchers did also notice that the women who developed VTE had more predisposing risk factors that the control group did not, these risk factors included “black race, to be obese, to have gestational diabetes mellitus, pre-eclampsia, postpartum hemorrhage or maternal transfusion, postpartum infection, and
delivery via cesarean delivery”.\textsuperscript{7} Being a retrospective study makes it hard to control for variables outside of small for gestational age, because of this it is important to do statistical analysis to decide how much the confounding variables played into the association between the infant’s weight and the mother’s risk for developing VTE.

\textbf{Jacobsen et al.}

The main limitation of this study was, “controls were selected from a single hospital whereas cases were identified in a much larger background population at 18 hospitals”.\textsuperscript{8} For our research purposes the study fell short in not addressing race. The study did not collect data on this demographic, so while research confirms the strong link between IUGR/ low birthweight and VTE risk it does not correlate these with any specific at-risk race/ ethnicity.

\textbf{Morris et al.}

The 2 primary weaknesses of this particular study\textsuperscript{9} were a lack of diagnostic confirmation of PE/ VTE (as diagnosis was determined retrospectively via by ICD diagnosis codes) and the study was also not able to rule out patient’s that had major predisposing risk factors for VTE like “obesity or thrombophilia”.

\textbf{Areas for Further Research:}

The next step in exploring the underlying etiologies causing the LVW infants in African American women but not in African decent
women who birth babies outside of America. Research has already explored what could be causing this discrepancy, with one of the leading theories causing LBW being exposure to chronic stress. One study\textsuperscript{10} found that chronic exposure to racism throughout one’s life has a “dose dependent response” to low birth weight.\textsuperscript{10} In other words, the longer an expectant mother has been exposed to racism, the more likely the baby is going to be born into the very low birth weight (VLBW) category.

**CONCLUSION**

The medical community needs to continue to explore what is causing the increased maternal mortality in the African American community. With the above proposed assessment, we suggest that mothers who birth low birthweight babies – particularly African American women – be closely monitored for VTE. Further research may consider specific protocols to address this complication and therefore reduce maternal mortality rates. Optimally, research would be conducted to determine the etiologies of low birthweight babies in African American women so that this can be addressed and prevented – therefore, saving thousands of lives.
References


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\(a\) Differences in population  
\(b\) Failed to identify patients with a history of thrombophilia