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Pregnancy outcomes in women with sickle cell disease in California

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Abstract

Adverse pregnancy outcomes occur frequently in women with sickle cell disease (SCD) across the globe. In the United States, Black women experience disproportionately worse maternal health outcomes than all other racial groups. To better understand how social determinants of health impact SCD maternal morbidity, we used California's Department of Health Care Access and Information data (1991–2019) to estimate the cumulative incidence of pregnancy outcomes in Black women with and without SCD—adjusted for age, insurance status, and Distressed Community Index (DCI) scores. Black pregnant women with SCD were more likely to deliver at a younger age, use government insurance, and live in at-risk or distressed neighborhoods, compared to those without SCD. They also experienced higher stillbirths (26.8, 95% confidence interval [CI]: 17.5–36.1 vs. 12.4 [CI: 12.1–12.7], per 1,000 births) and inpatient maternal mortality (344.5 [CI: 337.6–682.2] vs. 6.1 [CI: 2.3–8.4], per 100,000 live births). Multivariate logistic regression models showed Black pregnant women with SCD had significantly higher odds ratios (OR) for sepsis (OR 14.89, CI: 10.81, 20.52), venous thromboembolism (OR 13.60, CI: 9.16, 20.20), and postpartum hemorrhage (OR 2.25, CI 1.79–2.82), with peak onset in the 2nd trimester, 3rd trimester, and 6 weeks postpartum, respectively. Despite adjusting for sociodemographic factors, Black women with SCD still experienced significantly worse pregnancy outcomes than those without SCD. We need additional studies to determine if early introduction to reproductive health

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O.O.A. developed the study concept. O.O.A., A.B., S.C.F., and T.W. analyzed the data. O.O.A., A.B. and S.C.F. drafted the manuscript. All authors designed the study, made revisions, and approved the final manuscript.

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education, continuation of SCD-modifying therapies during pregnancy, and increasing access to multidisciplinary perinatal care can reduce morbidity in pregnant women with SCD.

Keywords

sickle cell disease; sickle cell anemia; pregnancy; maternal health; maternal morbidity

Introduction

Public health efforts and therapeutic advancements have transformed sickle cell disease (SCD) from an inherited hemoglobin disorder with high childhood mortality to a chronic illness characterized by episodic acute complications and cumulative morbidity across the lifespan.¹ Many Americans with SCD, most of whom are of African or Hispanic ancestry,² are living well into their 40s and 50s,^{3,4} which encompasses most women's reproductive years.⁵ Pregnancy-associated endothelial activation and cytokine-mediated inflammation exacerbate the chronic hemolysis, microvascular occlusion, and hypercoagulability of SCD; when combined with the physiologic demands of pregnancy, these metabolic stressors significantly increase risks for acute disease-related and obstetrical complications in pregnant women with SCD.^{6–10} In both low and high healthcare resource settings, maternal-fetal complications such as cesarean sections (C-sections), preeclampsia/eclampsia, venous thromboembolism (VTE), cardiomyopathy, sepsis, postpartum hemorrhage, intrauterine growth restriction, small-for-gestational-age or low birthweight infants, and preterm deliveries occur more frequently in women with SCD, compared with those without SCD.^{8,11–16}

Using cross-sectional data from the Healthcare Cost and Utilization Project Nationwide Inpatient Sample (HCUP NIS, 1999–2008), investigators showed that pregnant SCD women who developed vasoocclusive crises (VOCs) at the time of delivery (82% Black) experienced higher rates of preeclampsia, eclampsia, and cardiomyopathy, compared to those without peripartum VOCs.¹⁴ Others used more recent NIS data (2012–2018) to show that pregnant women with SCD, also predominantly Black, were more likely to have severe maternal morbidity than women in the general US population or Black women without SCD.¹⁷ To create a more comprehensive picture of, and determine factors associated with, pregnancy outcomes for women with SCD, we analyzed administrative data from California over the last 30 years. While race is a social construct and not a biological risk factor for adverse health outcomes,^{18,19} we hypothesized that comparing pregnancy outcomes in Black women with and without SCD could account for any unmeasured social determinants of health associated with disparately poor maternal outcomes in Black women in the US.^{20–22} Compared to previous cross-sectional SCD pregnancy studies using NIS data, our longitudinal administrative dataset allows us to describe the cumulative incidence and time-course of common maternal complications in women with SCD.

Methods

Databases

We conducted this retrospective observational cohort study using de-identified patient records from the Patient Discharge Data (PDD) and the Emergency Department Utilization (EDU) databases, both obtained from the California Department of Health Care Access and Information (CA HCAI). Since July 1990, the State of California has required that all non-federal inpatient facilities record up to 25 diagnoses and 21 procedures for each hospital encounter using codes from the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM). CA HCAI adopted the 10th revision of these diagnostic and procedural codes (ICD-10-CM) on 10/1/2015. Similarly, all emergency departments (ED) associated with non-federal hospitals have reported encounter diagnoses into the EDU database since 2005. In addition to patient characteristics such as age, sex, race/ethnicity, residential zip-code, and type of health insurance recorded with each encounter, CA HCAI uses a record linkage number (RLN)—an encrypted form of the social security number—that allows serial tracking of an individual over multiple encounters. We included CA HCAI data from 1991–2019 in this study.

Patient Selection Criteria

We identified SCD cases using SCD-specific ICD-9/10-CM codes (Supplemental Table 1) from hospitalizations and ED visits recorded in the California PDD and EDU databases. Cases met at least 1 of the following criteria: (i) 2 different encounters with a SCD code in the principal position/diagnosis, (ii) 1 encounter with SCD as principal diagnosis and 2 more encounters with SCD as a secondary diagnosis, or (iii) 3 separate encounters with SCD in any secondary position. This algorithm combines stringent case definitions from our previous work^{23–27} and broader criteria used by our colleagues^{28–30} to arrive at similar number of SCD cases from hospital and ED discharge data sources reported in a recent external validation study.³¹ Further, we only included SCD females of reproductive potential, which we defined as those between ages 10–45 years. We chose this age range because it (i) encompasses the average ages at menarche and menopause in the US,^{5,32,33} and (ii) excludes expectant females at extremes of age, who may experience more pregnancy-related complications.^{34–37}

We identified all SCD females with *at least* 1 in-hospital delivery in the PDD or EDU using viable and non-viable pregnancy-specific ICD-9/10-CM codes from 1991–2019 (Supplemental Table 1). Per the American College of Obstetricians and Gynecologists (ACOG) criteria, we defined non-viable pregnancies as those with gestational age < 22 weeks, while viable pregnancies exceeded 22 weeks gestational age.³⁸ Although the CA HCAI dataset allows us to follow health outcomes in the same person over time, we analyzed peripartum outcomes during the first delivery only to eliminate repeated measures from multiparous women and the potential for increased maternal morbidity with higher parity.^{39,40} Of the group of SCD women with at least 1 in-hospital delivery, 88% self-identified as Black (Supplemental Figure 1). We compared peripartum outcomes between this cohort of Black pregnant women with SCD and *all* Black women without SCD, ages 10–45 years, with *at least* 1 in-hospital delivery over the 30-year study period. This study

was approved by the California Health and Human Services Agency’s Committee for the Protection of Human Subjects and the University of California, Davis, Human Research Protections Program.

Exposure/Outcomes

Our primary study endpoints were peripartum outcomes from the first hospitalization with an ICD-9/10-CM delivery code (Supplemental Table 1). A delivery code captures the end of a pregnancy, while pregnancy-codes denote any time during gestation. Peripartum outcomes of interest included non-viable vs viable pregnancy, stillbirth vs livebirth, mode of delivery (C-section vs vaginal), and inpatient maternal mortality. We defined inpatient maternal mortality as any woman’s death following a livebirth within the same hospital encounter. To further identify obstetric and SCD complications occurring during a woman’s first viable pregnancy, we ascertained ICD-9/10-CM codes for pregnancy-related outcomes that occurred in the 40 weeks prior to, and up to 6 weeks after, the delivery discharge date. Pregnancy-associated outcomes of interest included pre-eclampsia/eclampsia, preterm delivery, gestational diabetes, C-section, post-partum hemorrhage, sepsis, and venous thromboembolism (deep vein thrombosis and/or pulmonary embolism). Hospital admissions or ED visits for VOCs or pneumonia/acute chest syndrome (PNA/ACS) (defined by specific ICD-9/10-CM codes) were also ascertained during that same period. VOCs were defined as any admission with a code for “SCD with crisis.” PNA/ACS was defined as any of the following: (i) admission with pneumonia in the principal diagnostic position, (ii) SCD code in the principal position with pneumonia in the second position, or (iii) ACS in any diagnostic position of the hospital encounter from 2003–2019 (of note, specific ACS codes were only available in the PDD/EDU after 2003).

Covariate Descriptions

We defined the “first pregnancy” as the first encounter in the PDD/EDU with a viable or non-viable delivery code. Age at first delivery was the age at discharge for the patients’ first delivery encounter. We used the Elixhauser comorbidity index during the delivery encounter to determine the number of comorbidities for each patient.⁴¹ We excluded “Blood loss anemia” from the comorbidities list as we were concerned about its validity in SCD patients. We categorized the number of comorbidities into 0, 1–2, and 3 and the delivery era into 3 decades (1991–1999, 2000–2009, 2010–2019). Health insurance type at delivery is available in the PDD and EDU, and labeled as Medicare, Medi-Cal, other government, self-pay, private insurance, and unknown. Lastly, we included the Distressed Communities Index (DCI), which compares the economic well-being of communities across the US using a weighted average of 7 populations-based metrics derived from zip code level data, then normalizes that value into a single summary statistic (or DCI score) ranging from 0–100.⁴² We assigned each woman’s DCI score based on her residential zip code at time of delivery as reported in the PDD or EDU, then categorized them into 1 of 5 predefined economic groups: prosperous (0–20), comfortable (21–40), mid-tier (41–60), at-risk (61–80), and distressed (81–100).

Statistical analysis

For pregnant women with SCD, we used paired *t*-tests to compare the number of PDD/EDU encounters for VOCs or PNA/ACS before and during their first pregnancy, over an equal duration of observation. We used χ^2 tests to compare the characteristics of Black pregnant women with and without SCD; and unpaired *t*-tests to compare their mean DCI scores. We also calculated rates of maternal mortality per 100,000 livebirths and stillbirths per 1,000 births. We then used multivariable logistic regression models to analyze risk factors associated with each peripartum outcome—adjusted for age, comorbidities, era, type of health insurance, and DCI score—at the time of delivery. Since C-sections are often indicated for obstetrical complications, we further adjusted the C-section logistic regression model for all peripartum complications. Postpartum hemorrhage models were adjusted for VTE, pre-eclampsia/eclampsia, and C-section delivery because concurrent anticoagulation (typically initiated for VTE treatment), placental vasculopathy associated with pre-eclampsia/eclampsia,⁷ and C-sections could all be associated with higher bleeding rates. We used the cumulative incidence function to determine the timing of 3 common peripartum outcomes: sepsis, VTE, and postpartum hemorrhage. Pregnancy-related sepsis and VTE were ascertained from the assumed conception date of 40 weeks prior to the delivery discharge date. Postpartum hemorrhage was evaluated from delivery date up to time of postpartum hemorrhage diagnosis codes or 6 weeks post-delivery discharge, whichever occurred first. We performed all analyses using SAS 9.4 software and all between-group differences to be significant if *p*-values < 0.05.

Results

We identified 4,972 women with SCD from the PDD/ED databases from 1991–2019, with 4,174 women between the ages of 10–45 years. Of these, 1,656 women accounted for a total of 3,764 pregnancies (median=2, range=1–15), which we further categorized into viable and non-viable births, per ACOG criteria.³⁸ Non-viable pregnancies had the following outcomes: 41.7% spontaneous abortion, 20.6% elective termination, 16.5% missed abortion, 11.5% ectopic pregnancies, 7.3% unspecified abortion, and 2.3% other (Supplemental Figure 2). Women with SCD were hospitalized for acute VOCs or ACS for a mean frequency of 1.31 times during pregnancy compared with 0.88 times in the 46-week period preceding their first pregnancy, for a difference in means of 0.43 (*p*-value <0.00001) and 95% confidence interval (CI) (0.33, 0.53). Women with SCD had a progressively increasing risk of acute VOCs throughout their pregnancy with cumulative incidence rate of 14.3% (95% CI: 12.5, 16.1) at the end of the 1st trimester rising to 35.4% (95% CI: 33.0, 37.9) at delivery (Supplemental Figure 3A). PNA/ACS cumulative incidence rates increased from 1.7% (95% CI: 1.2, 2.5) at the end of the 2nd trimester/beginning of the 3rd trimester to 4.2% (95% CI: 3.2, 5.3) at delivery (Supplemental Figure 3B).

Of the 1,438 women with SCD who had at least 1 delivery during the study period, 1260 (88%) self-identified as Black. We compared their pregnancy outcomes with 469,018 Black women without SCD of similar age, who also had at least 1 delivery. A significantly higher proportion of Black women with SCD delivered at younger age, compared with Black women without SCD (Supplemental Figure 4). Most pregnant Black women in this study did

not have comorbidities at the time of their first delivery (comorbidity score = 0 in 65.8% with SCD vs. 80.2% without SCD). While most Black women had Medi-Cal insurance at delivery, a higher proportion of women with SCD had Medicare (Table 1). A significantly higher proportion of Black women with SCD lived in distressed neighborhoods (18.3% vs. 16.1%, p -value=0.0316), compared with those without SCD (Table 1).

Black women with SCD were more likely to undergo a C-section during their first delivery, compared to those without SCD (40% vs. 29%, p -value<0.0001) (Table 2). While the median length of stay after a C-section was similar between Black women with and without SCD, the interquartile ranges were wider for the SCD subgroup. Univariate analyses showed Black women with SCD had higher rates of stillbirth, inpatient maternal mortality, and adverse peripartum outcomes (except gestational diabetes), compared to those without SCD (Table 2). In the multivariate logistic regression models, Black women with SCD had higher odds of experiencing adverse peripartum outcomes compared to those without SCD, most strikingly for sepsis and VTE (Figure 1). The cumulative incidence of sepsis increased from 0.5% (95% CI: 0.2, 1.0) by the end of the 1st trimester to 3.4% (95% CI: 2.5, 4.5) at the end of the postpartum period, while the cumulative incidence of VTE increased from 0.3% (95% CI: 0.1, 0.8) at the end of the 2nd trimester to 2.1% (95% CI: 1.5, 3.1) at the end of the postpartum period in Black women with SCD (Figure 2). In contrast, Black women without SCD had significantly low risk for sepsis (0.2%; 95% CI: 0.2, 0.2) and VTE (0.15%; 95% CI: 0.1, 0.1) throughout their pregnancy. Postpartum hemorrhage was twice as likely in women with SCD (5.6%; 95% CI: 4.5–7.0), compared to those without SCD (2.6%; 95% CI: 2.5–2.6). Using ICD-10-CM codes (available from 10/1/2015 and onwards), we determined that women with SCD delivered at a median gestational age of 38 weeks, compared with 39 weeks for women without SCD. In a sensitivity analysis, we regenerated cumulative incidence curves for sepsis and VTE based on these revised gestational periods, with similar results to our prior analysis using 40 weeks gestational age (Supplemental Figure 5).

Discussion

In this study, we described pregnancy-related outcomes for women with SCD across the socio-economically diverse state of CA from 1991–2019. We used longitudinal data to determine the cumulative risks of common peripartum outcomes in Black women with and without SCD, after adjusting for clinical risk factors, type of health insurance, and DCI scores at the time of delivery. Our main study findings were (i) frequency of acute care visits for VOCs and PNA/ACS increased during pregnancy for all women with SCD, compared to their pre-pregnant baseline; (ii) Black pregnant women with SCD experienced higher rates of peripartum complications, including C-sections, stillbirth, and maternal mortality, compared with Black women without SCD; and (iii) cumulative incidence rates for sepsis, VTE, and postpartum hemorrhage significantly differed between Black pregnant women with and without SCD. Despite advances in SCD and obstetrical care in the US, these results show worse peripartum outcomes in Black women with SCD, even after accounting for relevant clinical and sociodemographic factors.

There was a statistically significant difference in mean rates of acute care visits for VOCs and PNA/ACS in primigravid women with SCD, compared to their immediate non-

pregnant baseline. The cumulative incidence rates for VOCs increased as the pregnancy progressed, while PNA/ACS risk rose during the 3rd trimester up to 6 weeks postpartum. Investigators from the Cooperative Study of Sickle Cell Disease (CSSCD) studied maternal-fetal outcomes in a prospective cohort of 297 women with 445 pregnancies, recruited from SCD centers across the US between 1979–1981.¹⁶ They found that women with sickle cell anemia (HbSS genotype) enrolled in CSSCD experienced similar VOC rates before, during, and after the first and subsequent pregnancies. Differences between our results and these CSSCD findings likely stem from our study cohort comprising a sizeable proportion of compound heterozygote SCD women with varying susceptibility to complications, though SCD genotype is inaccurately coded in our administrative dataset.⁴³ Our findings of increased VOCs and PNA/ACS during pregnancy are more consistent with a contemporary prospective cohort study of 99 pregnant women with SCD (HbSS 41%, HbSC 59%) followed at a tertiary center in Accra, Ghana.⁴⁴ The investigators compared the frequency of acute SCD complications during pregnancy to the postnatal period (> 6 weeks through 52 weeks after delivery),⁴⁴ while we chose the time prior to the first pregnancy for comparison. It is also possible that current SCD-modifying therapies have improved survival for women with severe SCD, who may then experience more disease-related complications during pregnancy in our contemporary study cohort, compared to women with homozygous SCD enrolled in the CSSCD over 40 years ago. Whether acute care utilization in women with SCD returns to their baseline prenatal frequency after delivery remains unknown; further, caring for a newborn likely confounds health care utilization rates after delivery.

Although maternal age at first delivery has trended upwards in the general US population over time,⁴⁵ we found that Black women with SCD were younger than those without SCD at their first delivery. This could be due to higher rates of unplanned pregnancies in adolescents with SCD, which highlights the importance of incorporating reproductive health education and genetic counseling into comprehensive care for all pre-pubertal children living with SCD.^{46–49} Subfertility and premature ovarian failure in women with SCD could also account for lower pregnancy rates with older age; thus, studies on fertility preservation and non-gonadotoxic therapies for SCD should remain a high research priority.^{10,46,50} Lastly, cumulative end-organ damage and decreased median survival may prematurely truncate the reproductive lifespan of women living with SCD.^{3,4} Of note, we studied the interaction between SCD and delivery era (in decades) for all peripartum outcomes. Preterm delivery rates significantly differed between Black women with and without SCD from 1991–1999 to 2000–2009, but not in 2010–2019. All other peripartum complications did not significantly change over the 3 decades included in this study duration.

Primary C-section rates increased in Black women with SCD across each 10-year era of our study, though this increase did not significantly differ from that of primigravid Black women without SCD. Since 1966, C-section rates have steadily risen in women of all ages and from all racial/ethnic groups across the US, but remain highest in non-Hispanic Black women older than 35 years of age.^{51,52} Outside of medical necessity, higher C-section rates may also be attributed to expectant women's preferences due to their perceived innocuity of the procedure, short-term postpartum benefits, or obstetricians' recommendations due to their concerns over litigations for adverse maternal-infant outcomes.^{51,53} We suspect that higher C-sections in Black pregnant women with SCD, compared with those without SCD of

similar age, health insurance status, and DCI scores, likely reflects medical necessity given their increased peripartum morbidity.

The overall number of in-hospital maternal deaths in our study cohort was low, similar to findings from the more recent NIS study.¹⁷ Despite these small absolute events, we found a striking difference in inpatient maternal mortality rates between Black pregnant women with and without SCD during their first deliveries. Maternal mortality rates have steadily risen in the US since 2005 and it remains highest for non-Hispanic Black women at 49 per 100,000 livebirths, compared with overall mortality of 29 per 100,000 livebirths for all women.^{22,54,55} Black pregnant women in the US disproportionately experience adverse peripartum outcomes even after adjusting for maternal age, socioeconomic status, educational attainment, comorbidities, gestational age, or prenatal care, which suggests other factors such as systemic racism and limited access to maternal-fetal specialists contribute to this disparity.^{56–58} Others showed similar maternal mortality rates in women with and without SCD, after adjusting for healthcare resource settings¹³ and instituting multidisciplinary perinatal care.⁵⁹ Investigating how predictors for adverse maternal morbidity and mortality in the general population,^{22,60} frequency of SCD-related complications, or higher obstetrical morbidity^{44,59,61} contribute to increased mortality in pregnant women with SCD remains an important area for research.

Multiple studies show increased maternal morbidity in SCD,^{11,12,62} yet few have investigated the timing of these peripartum complications to aid with appropriate monitoring or interventions.⁴⁴ We found that in Black women with SCD, sepsis risk steadily increased throughout pregnancy into the postpartum period. The significantly higher rates of sepsis in Black pregnant women with SCD compared to those without SCD may be due, in part, to additive immunocompromise from their underlying SCD and physiologic changes of pregnancy.⁶³ VTE risk for Black women with SCD mainly increased in the 3rd trimester up to 6-weeks postpartum. Our group and others previously showed increased VTE risks in SCD in general,^{25,26,64} which is likely further exacerbated by the hypercoagulable state of pregnancy. Postpartum hemorrhage remained twice as high in Black women with SCD compared to those without SCD up to 6 weeks post-delivery, even after adjusting for VTE during pregnancy (a proxy for likely anticoagulation use), preeclampsia/eclampsia (possible underlying vasculopathy and/or aspirin use), and C-section history. The etiology for increased postpartum hemorrhage in women with SCD remains unclear. Additional studies are required to determine if targeted interventions like prophylactic antimicrobials, anticoagulation, or antifibrinolytics can reduce these common complications in pregnant women with SCD.

An expert panel of multidisciplinary clinical investigators, health analysts, epidemiologists, research biologists, policy makers, and community-based advocates convened by the Centers for Disease Control and Prevention (CDC) and the Foundation for Women and Girls with Blood Disorders, laid out a framework for future research priorities, funding mechanisms, and healthcare policies geared towards improving female reproductive health across the SCD lifespan.⁴⁶ Their broad review of complications spanning menarche to menopause highlighted the need for better understanding of timely interventions that can mitigate adverse maternal-fetal outcomes in SCD. Others have demonstrated that implementing

cost-effective multidisciplinary interventions early in antenatal care can significantly reduce maternal mortality rates in pregnant women with SCD.^{59,61,65} Our study partly address this knowledge gap by highlighting when sepsis, VTE, and postpartum hemorrhage are most likely to occur in pregnant women with SCD.

There are limitations to this study. The CA HCAI dataset only includes emergency department and inpatient discharge diagnostic and procedural codes, so women who solely received antenatal care as an outpatient or delivered outside of California were not included. However, we have no reason to suspect these detection and migration biases would significantly differ between pregnant women with and without SCD. We lacked accurate laboratory data on SCD genotype,¹⁶ pharmacy records on antimicrobial and anticoagulation prescriptions and refills, and use of disease-modifying interventions during pregnancy; e.g., hydroxyurea⁶⁶ or prophylactic red blood cell transfusions,⁶⁷ which may have modified peripartum outcomes in our study cohort. Since women with SCD have potentially higher mortality risks from disease-related complications, we limited our maternal mortality analyses to inpatient deaths only. Thus, our maternal mortality rates cannot be directly compared with CDC data, which include all-cause mortality in pregnant women from the time of delivery through their first postpartum year. Study strengths include the large sample size, longitudinal follow-up for each woman, ability to ascertain the time-course of complications, and comparison to a large, contemporaneous population-based group of Black pregnant women without SCD. Since 99% of US births occur in a hospital setting,⁴⁵ our findings are likely generalizable to most women living with SCD in California and across the country.

Conclusion

In this large retrospective cohort study of pregnant women with their first deliveries occurring in the hospital, we found higher rates for maternal morbidity and inpatient maternal mortality in Black women with SCD, compared to those without SCD, despite adjusting for age, insurance status, and other sociodemographic factors at the time of delivery. Our results should not dissuade women with SCD who desire parenthood; rather, it is important to note that most pregnancies in women with SCD resulted in live births. Our data emphasizes the need for integrating reproductive health counseling into the care of girls and women with SCD, so they can make informed reproductive decisions. Our results highlight the importance of multidisciplinary perinatal care, ongoing studies to target SCD modification, and increased public health efforts to reduce disparities in pregnancy-related outcomes for women with SCD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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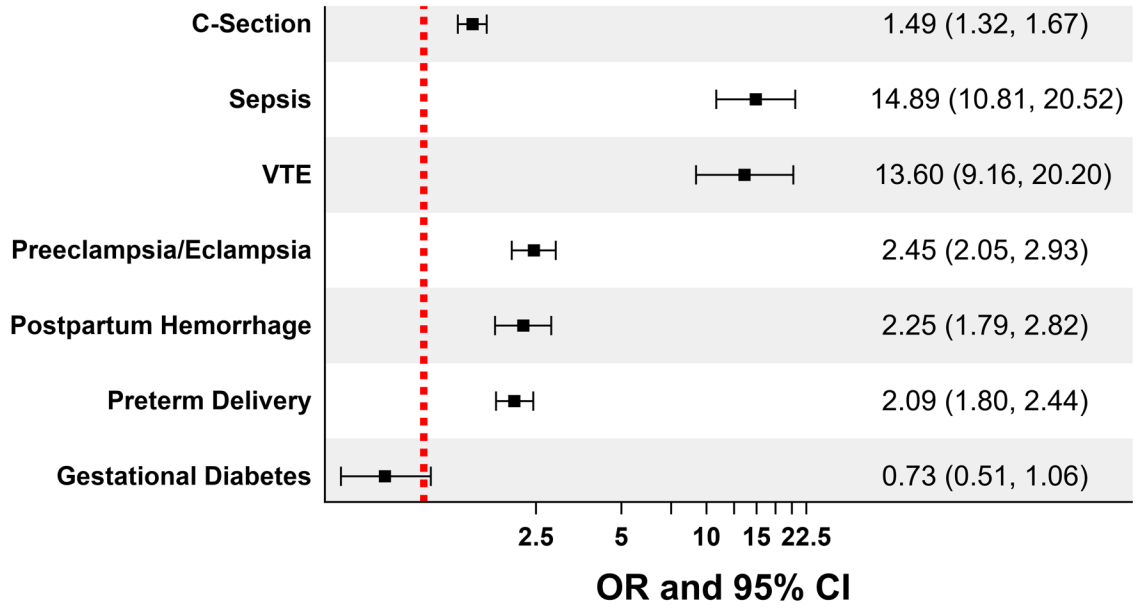


Figure 1. Peripartum outcomes adjusted for complications, comorbidities, and sociodemographic factors in Black pregnant women with SCD (compared with those without SCD) in California, during their 1st pregnancy (1991–2019)

Footnote:

OR- Odds Ratio; CI- Confidence Interval; SCD- Sickle cell disease; C-section-Cesarean section; VTE- Venous thromboembolism

All models were adjusted for age, era, comorbidities, health insurance and Distressed Communities Index scores at the time of delivery

C-Section model was further adjusted for all peripartum complications

Postpartum hemorrhage model was further adjusted for C-section, VTE, and preeclampsia/eclampsia

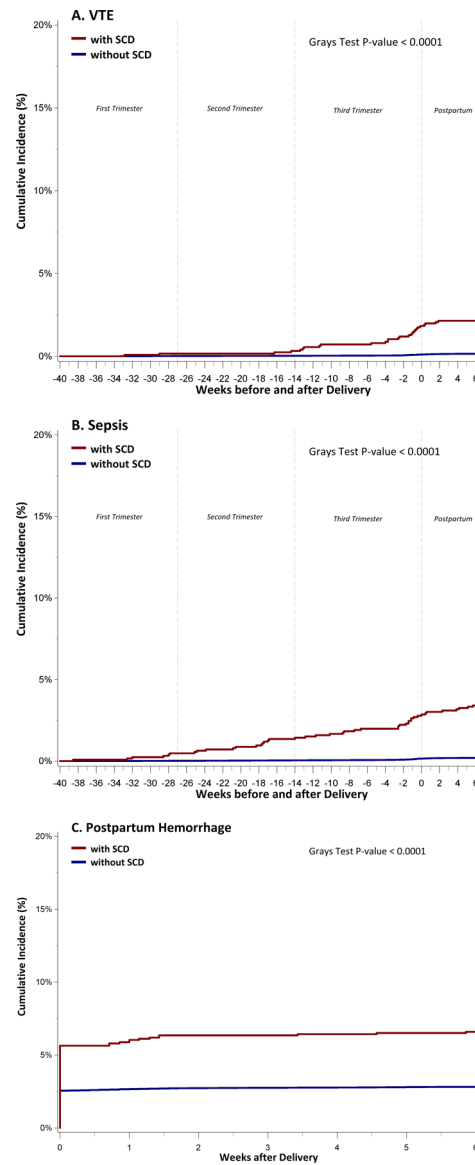


Figure 2. Cumulative incidence of sepsis(A), VTE (B), and Postpartum hemorrhage (C) among Black women with and without SCD in California, during their 1st pregnancy (1991–2019)

Footnote:

We assumed that all women had a gestational period of 40 weeks prior to their delivery date.
SCD- Sickle cell disease; VTE- Venous thromboembolism

Table 1:

Baseline characteristics of Black women in California, with and without sickle cell disease, during their 1st pregnancy (1991–2019)

Variables	With SCD		Without SCD		<i>p</i> -value *
	N	%	N	%	
All	1,260	100.0%	469,018	100.0%	
Comorbidities at delivery					
0	829	65.8%	376,034	80.2%	<.0001
1–2	300	23.8%	88,108	18.8%	<.0001
3	32	2.5%	4,626	1.0%	<.0001
Delivery Era					
1991–1999	612	48.6%	233,346	49.8%	0.4026
2000–2009	359	28.5%	136,059	29.0%	0.6862
2010–2019	289	22.9%	99,613	21.2%	0.1412
Health Insurance					
Medicare	73	5.8%	2,149	0.5%	<.0001
Medi-Cal	798	63.3%	245,825	52.4%	<.0001
Other Government	19	1.5%	9,892	2.1%	0.1379
Self-Pay	16	1.3%	8,814	1.9%	0.1115
Private	350	27.8%	201,171	42.9%	<.0001
Other	4	0.3%	1,080	0.2%	0.5192
Unknown	.	.	48	0.0%	0.7195
DCI Quintile					
1-Prosperous	105	8.3%	48,213	10.3%	0.0231
2-Comfortable	164	13.0%	73,061	15.6%	0.0123
3-Mid-Tier	302	24.0%	111,115	23.7%	0.8172
4-At Risk	434	34.4%	152,099	32.4%	0.127
5-Distressed	231	18.3%	75,534	16.1%	0.0316
Unknown Zip code	24	1.9%	8,996	1.9%	0.9726
DCI Distress Score					
Mean (std)	58.88 (22.82)		56.23 (23.68)		
Median (q1, q3)	63.02 (44.11, 75.25)		59.32 (38.70, 74.55)		

SCD-Sickle cell disease; DCI-Distressed Community Index; std-standard deviation; q1-quartile 1; q3-quartile 3

* χ^2 test to compare distribution of SCD vs without SCD

Table 2.

Peripartum outcomes among Black women in California, with and without sickle cell disease, during their 1st pregnancy (1991–2019)

Variables	With SCD		Without SCD		p-value *
	N	%	N	%	
All	1,260	100.0%	469,018	100.0%	
Mode of Delivery					
Vaginal	757	60.1%	333,453	71.1%	<.0001
C-Section	503	39.9%	135,565	28.9%	<.0001
Length of Delivery Admission, days median (q1, q3)					
Overall	3	(2, 5)	2	(2, 3)	<.0001
Vaginal Delivery	2	(1, 2)	2	(2, 3)	<.0001
C-Section Delivery	4	(3, 7)	4	(3, 4)	<.0001
Birth Outcome					
Live Birth	1,161	92.1%	443,081	94.5%	0.0003
Still Birth	32	2.5%	5,574	1.2%	<.0001
Maternal Complication					
Inpatient Mortality	4	0.3%	27	0.0%	<.0001
Venous Thromboembolism	27	2.1%	695	0.1%	<.0001
Sepsis	43	3.4%	917	0.2%	<.0001
Postpartum Hemorrhage	83	6.6%	13,216	2.8%	<.0001
Preeclampsia	139	11.0%	21,557	4.6%	<.0001
Preterm Delivery	205	16.3%	37,975	8.1%	<.0001
Gestational Diabetes	30	2.4%	15,672	3.3%	0.0581

SCD- Sickle cell disease; C-section-Cesarean section

* χ^2 test to compare distribution of SCD vs without SCD