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Society for Maternal-Fetal Medicine Consult Series #68: Sickle cell disease in pregnancy

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Pregnant individuals with sickle cell disease have an increased risk of maternal and perinatal morbidity and mortality. However, prepregnancy counseling and multidisciplinary care can lead to favorable maternal and neonatal outcomes. In this consult series, we summarize what is known about sickle cell disease and provide guidance for sickle cell disease management during pregnancy. The following are Society for Maternal-Fetal Medicine recommendations:

1. We recommend that patients with sickle cell disease be managed by a multidisciplinary team that includes maternal-fetal medicine, hematology (ideally a hematologist specializing in sickle cell disease), genetics, pain management, and social work or behavioral health (as appropriate) starting in early pregnancy (best practice).
2. We recommend that pregnant patients with sickle cell disease receive all routinely recommended antenatal vaccinations in addition to meningococcal and pneumococcal vaccinations if due (GRADE 1A).
3. We recommend prenatal vitamins without iron unless iron deficiency is confirmed and initiation of 4 mg of folic acid for pregnant patients with sickle cell disease (GRADE 1B).
4. We recommend fetal growth surveillance every 4 weeks beginning in the 28th week of gestation (GRADE 1C).
5. For patients with uncomplicated sickle cell disease and a normally grown fetus, we suggest weekly or twice-weekly antenatal testing beginning at 32 to 34 weeks of gestation. For patients with complicated sickle cell disease (i.e., maternal hypertension, vaso-occlusive crises, fetal growth restriction, or other coexisting complication), we suggest initiating individualized antenatal testing at diagnosis or at a gestational age when delivery would be considered if results are abnormal (GRADE 2B).
6. We recommend following evidence-based guidelines for the management of chronic and acute pain during pregnancy (best practice).
7. We suggest the use of prophylactic transfusions be individualized for high-risk patients with sickle cell disease in accordance with American Society of Hematology guidelines and directed by a hematologist and maternal-fetal medicine subspecialist in shared decision-making with the patient (GRADE 2B).
8. We recommend shared decision-making occur regarding the use of hydroxyurea in pregnancy, in conjunction with a sickle cell disease specialist and maternal-fetal medicine subspecialist, accounting for the timing of use and individual disease severity (GRADE 1C).
9. We recommend that reliable contraception be offered to patients with sickle cell disease to decrease the risk of an unintended pregnancy and associated maternal and perinatal risks (GRADE 1B).

Key words: antenatal surveillance, disparities, fetal growth restriction, hemoglobinopathy, hydroxyurea, maternal morbidity, maternal mortality, pain management, perinatal outcomes, prepregnancy counseling, transfusion, vaso-occlusive crisis

Introduction

Sickle cell disease (SCD) is an autosomal recessive hemoglobinopathy and the most common inherited, clinically significant blood disorder.[1,2] Pregnant individuals with SCD have an increased risk of maternal and perinatal morbidity and mortality.[3] However, prepregnancy counseling and multidisciplinary care can lead to favorable maternal and neonatal outcomes.[4] High-level evidence to guide SCD

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management in pregnancy is sparse. This consult series presents the best available evidence to manage this complex disease process during pregnancy and outlines opportunities for research to help enhance available evidence for future advances in perinatal SCD care.

What are the pathophysiologic and epidemiologic characteristics of sickle cell disease?

SCD occurs as a result of a single amino acid change of glutamic acid to valine in the beta-globin subunit of hemoglobin.[5] In stressful environments in those with SCD, red blood cells (RBCs) polymerize into a more elongated sickle or S shape prone to hemolysis, endothelial adhesion, and subsequent vaso-occlusion.

Approximately 100,000 persons in the United States have SCD; globally, approximately 300,000 neonates are born with SCD each year.[2] SCD is particularly common among people whose ancestors came from sub-Saharan Africa; Spanish-speaking regions in the Western Hemisphere (South America, the Caribbean, and Central America); Saudi Arabia; India; and Mediterranean countries (Turkey, Greece, and Italy). In the United States, 1 in 365 neonates described as African American or Black are diagnosed with SCD.[6] Importantly, race should not be used in isolation as an assessment for genetic risk.[7] Several genotypes result in the phenotypic expression of SCD. The most common form in the United States is homozygous S or HbSS disease. Other common genotypes include the compound heterozygotes of HbS beta plus thalassemia (HbS$\beta+$), HbS beta null thalassemia (HbSβ^0), and HbSC. Although people with HbSS and HbSβ^0 often experience a more severe clinical course, individuals with all types of SCD are at risk of severe complications.[8–10]

If 2 unaffected carriers of an S allele (sickle cell trait [SCT]) produce an offspring, the offspring has a 25% chance of being unaffected (not a carrier), a 50% chance to be a carrier, and a 25% chance to have SCD.

Who should be screened for sickle cell disease?

In 1996, the US Preventive Services Task Force recommended screening for SCD in all newborns.[11] By 2006, newborn screening was required and implemented in all 50 states and the District of Columbia. However, people with SCT, thalassemia trait, or hemoglobin C disease may be unaware of their status. As recommended by the American College of Obstetricians and Gynecologists, all patients presenting for prepregnancy or prenatal care should be offered a complete blood count (CBC) with RBC indices and hemoglobin electrophoresis testing.[7] Those diagnosed with SCT or disease should have their partner undergo hemoglobinopathy evaluation to assess the risk of SCD or other hemoglobinopathies to their offspring.

How is sickle cell disease diagnosed?

The recommended laboratory techniques for detecting hemoglobinopathies are hemoglobin electrophoresis and DNA molecular testing.[7,12] Genetic testing of the beta-globin gene is the most accurate method of diagnosis, but it requires a specialized laboratory, is more expensive, and is usually reserved for special situations (i.e., conflicting protein method results). The methods that only test for the presence of sickle cells (e.g., sickle cell prep) do not detect non−S hemoglobin variants and are inadequate to distinguish between SCT, SCD, and compound heterozygous states, such as HbSC disease.[13] There are many expanded carrier screening panels that evaluate for hemoglobinopathies; however, the preferred tests for the diagnosis of SCD or trait are a CBC with RBC indices and a hemoglobin electrophoresis.[13]

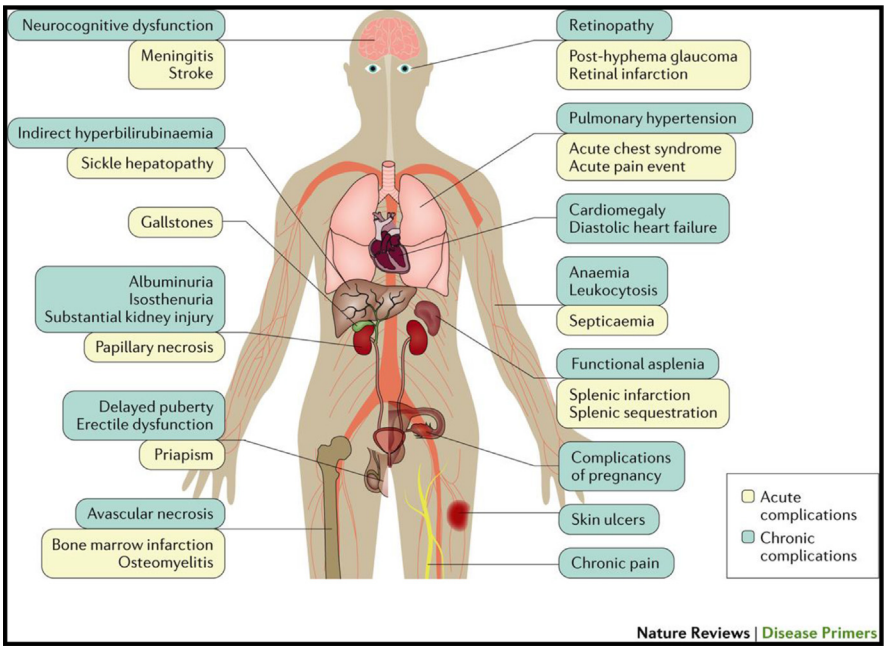
What are the manifestations of sickle cell disease?

Vaso-occlusion and chronic hemolysis occur at baseline resulting in anemia, endothelial dysfunction, and inflammation. Repeated episodes of vaso-occlusion, hemolysis, and anemia can cause chronic organ complications for individuals with SCD (Figure). When vaso-occlusion results in tissue ischemia, this is commonly called a "vaso-occlusive crisis (VOC)" or "acute painful episode." VOCs are acute painful complications of SCD and the most commonly reported reason individuals with SCD present to emergency departments.[14] Vaso-occlusive episodes cost the US healthcare system more than $800 million in 2016.[15] Patients typically present with severe back, chest, or extremity pain. In general, triggers may include infection, extreme temperatures, dehydration, acidosis, and hypoxia; however, the specific triggers for a VOC are often unknown.[16] Isolated vaso-occlusive events characterized by pain without evidence of organ dysfunction are referred to as uncomplicated VOC. In contrast, a complicated VOC refers to pain in addition to an acute organ-based complication of SCD, such as acute chest syndrome (ACS), stroke, hepatic or splenic sequestration, or osteomyelitis. Other acute complications of SCD are presented in Table 1.

What is the life expectancy of a person with sickle cell disease?

Chronic organ complications, such as renal and cardiopulmonary disease, along with ACS, are the leading causes of death for adults with SCD.[20] Advances in management have drastically increased the life span of persons with SCD.[21] With the introduction of universal newborn screening, penicillin prophylaxis for children with SCD, and hydroxyurea, among other interventions, persons in the United States with SCD have a median life expectancy of 58 years.[22] Since 1980, the life expectancy of persons with SCD has more than doubled, significantly increasing the

FIGURE
SCD clinical complications



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SCD, sickle cell disease.

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prevalence of reproductive-aged women and pregnancy in this special population.[21]

What adverse maternal and perinatal outcomes are associated with sickle cell disease in pregnancy?

Pregnancies in patients with SCD are associated with adverse maternal and perinatal outcomes.[23] Mortality is significantly increased in pregnant patients with SCD compared with pregnant patients without SCD. Worldwide maternal mortality for those with SCD has increased 10- to 18-fold compared with those without SCD, with risk attenuated to a 3- to 4-fold increase in high-income countries.[24,25] ACS and pneumonia occur in 6.5% of pregnant women with SCD, with pulmonary causes contributing to 88% of maternal deaths in patients with SCD.[26] Severe morbidities are associated with SCD in pregnancy, including bacterial infections (odds ratio [OR], 2.48),[25] pulmonary thromboembolism (relative risk [RR], 7.74),[26] and pulmonary hypertension (OR, 6.3).[26] In addition, obstetrical complications are increased in pregnant patients with SCD, including preeclampsia (RR, 2.06),[24] eclampsia (OR, 3.02),[25] cesarean delivery (OR, 1.54),[25] abruption (OR, 1.6),[27] and preterm labor (OR, 1.4).[27]

Perinatal risks are similarly increased in pregnancies complicated by SCD, including fetal growth restriction (OR, 2.79),[25] low birthweight (OR, 2.00),[25] small-for-gestational-age neonate (RR, 3.72),[24] and preterm birth (RR, 2.21).[24] Moreover, risks of stillbirth (OR, 4.05) and neonatal death (OR, 2.71) are increased.[25]

In addition, individuals with SCD may be burdened by conditions, such as fatigue, depression, and anxiety, that negatively affect their quality of life and emotional well-being.[28] These conditions may potentially be exacerbated during pregnancy and the postpartum period.

Which patients with sickle cell disease face the highest risk of mortality associated with pregnancy?

Pregnant patients with SCD have an increased risk of maternal and perinatal complications, including death. Given the unequivocal increased risk of maternal morbidity and mortality, reproductive options (including abortion) should be discussed with all pregnant patients with SCD.[24-26] Patients with SCD should be supported in making an informed decision regarding their reproductive options in a shared decision-making process in consultation with maternal-fetal medicine (MFM) subspecialists and hematologists with expertise in SCD, as appropriate. Most pregnant patients will have a successful outcome; however, there are certain patients with SCD in whom pregnancy significantly increases the risk of maternal death. Specifically, pulmonary hypertension and significant

TABLE 1
Clinical manifestations of sickle cell disease by organ system

Organ system	Complication	Clinical pearl
Neurologic	Moyamoya disease, stroke	Maintain high index of suspicion in the setting of excruciating headaches, seizures, weakness, visual disturbance, or altered mental status.
Ophthalmologic	Visual changes, vitreous hemorrhage, retinal artery stroke or occlusion	Urgently refer to ophthalmology in the setting of visual changes.[a]
Pulmonary	Pneumonia, pulmonary embolus, pulmonary hypertension, acute chest syndrome	O2 saturation, CXR, and/or CT pulmonary angiogram recommended for new pulmonary complaints.
Cardiac	Cardiomegaly, cardiomyopathy, heart failure	Low threshold to obtain echocardiogram for otherwise unexplained cardiopulmonary complaints.
Hematologic	Vaso-occlusive crises	Hydration, O2 to keep O2 saturation $\geq$95%, investigate and treat potential causes, treat pain per ASH guidelines (Table 4).[18]
Vascular	Deep venous thrombosis	Evaluate complaints of calf pain or lower extremity size discordance with venous Doppler ultrasound.
Skeletal	Avascular necrosis, especially of the femoral head	New pain with weight-bearing should be evaluated with a radiograph; MRI without contrast may be considered if radiograph normal.
Hepatic	Hepatitis, cholecystitis, infarction, venous thrombosis	Right upper quadrant pain and/or jaundice should be evaluated with a comprehensive laboratory evaluation (complete blood count with differential and either [1] comprehensive metabolic panel or [2] basic metabolic panel and liver function tests) and imaging, starting with a right upper quadrant ultrasound with Doppler.
Abdominal	Splenomegaly, splenic sequestration, splenic infarcts, thrombosis, pancreatitis	Abdominal pain can be evaluated with an abdominal examination and laboratory evaluation, including a complete blood count, amylase or lipase, and liver and renal panel. Imaging starting with abdominal ultrasound is reasonable.
Genitourinary	Hematuria, pyelonephritis	Genitourinary symptoms should initially be evaluated with a urinalysis and urine culture.
Skin	Ulcerations	Wound care should be provided to patients with ulcerations; ulcers should be monitored for signs of cellulitis with low threshold to prescribe antibiotics.
Obstetrical	Preeclampsia, preterm labor, abruption	Maintain high index of suspicion for obstetrical complications. Use low-dose aspirin for preeclampsia risk reduction.[19]

ASH, American Society of Hematology; *CT*, computed tomography; *CXR*, chest x-ray; *MRI*, magnetic resonance imaging.

[a] If visual changes are attributed to preeclampsia, and if symptoms resolve after delivery, urgent ophthalmology referral can be deferred.

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cardiomyopathies classified as modified World Health Organization class IV diseases are contraindications to pregnancy.[29] In addition, the inability to receive blood products because of severe alloimmunization and lack of available matched blood and other rare and severe complications of SCD that confer additional risks of morbidity and mortality (e.g., moyamoya syndrome) should be identified and incorporated into individualized counseling with a high degree of caution against attempting or continuing a pregnancy.

What is the prepregnancy and pregnancy management for a patient with sickle cell disease?

There are 4 general categories of evaluation and counseling for the patient with SCD who is pregnant or contemplating pregnancy: prepregnancy counseling, baseline maternal assessment, medication assessment, and genetic counseling. **We recommend that patients with SCD be managed by a multidisciplinary team that includes maternal-fetal medicine, hematology (ideally a hematologist specializing in SCD), genetics,**

pain management, and social work or behavioral health (as appropriate) starting in early pregnancy (Best Practice).[30-32]

What prepregnancy and early pregnancy care specific to sickle cell disease should be provided?

Prepregnancy counseling

Prepregnancy counseling allows a patient with SCD the opportunity to make an informed decision regarding pregnancy after consideration of the maternal and fetal risks and the potential risks to the offspring. Reproductive planning options that reduce fetal risks include preimplantation genetics and using donor egg or sperm (screened for hemoglobinopathies). However, in vitro fertilization and donor egg or sperm are associated with a myriad of maternal risks, including preeclampsia and neonatal risks, including prematurity.[33-35] Reproductive planning options that mitigate maternal risk for individuals with SCD include surrogacy and adoption. Referrals to MFM, genetics, and reproductive endocrinology specialists, as appropriate, should be made in the prepregnancy period depending on individualized reproductive planning needs and desires. In addition, this is an opportunity to educate patients about disease management and prenatal genetic counseling and testing options, which may improve informed decision-making, healthcare utilization, and rates of depression associated with SCD.[36] Prepregnancy counseling for patients with SCD should include baseline maternal assessment, medication assessment, and genetic counseling, as described in detail below.[32]

Baseline maternal assessment

A thorough history should be obtained, including an assessment of previous SCD complications and current medications. Laboratory evaluation includes assessing for anemia, evaluating iron stores, obtaining a type and screen to assess for alloimmunization, and assessing thoroughly end-organ function, as outlined in Table 2. Understanding a patient's current health status aids in counseling regarding the likelihood of pregnancy complications. For example, a patient without end-organ damage and previous uncomplicated term deliveries incurs a different level of risk in pregnancy compared with a patient with severe anemia on hydroxyurea with a history of ACS. Patients with SCD should be optimized and comanaged by a hematologist who is up to date on health maintenance screening according to the National Heart, Lung, and Blood Institute (NHLBI)[37] and American Society of Hematology (ASH)[38,39,18,40,41] guidelines. Ideally, health maintenance should be optimized before pregnancy. For patients with a lapse in care, pregnancy represents a unique window for heightened adherence and, for some, access to healthcare that they did not have before. Therefore, referrals for SCD management should be expedited during pregnancy. A transition from pediatric specialty care to adult specialty care may be needed, particularly for young patients with SCD previously managed by pediatric hematologists.

Baseline medication assessment

Many individuals with SCD are on several medications for disease treatment and pain management. Many medications may be safely continued during pregnancy, whereas others should be switched to a safer alternative or discontinued. Table 3 outlines common medications used in SCD management and principles of management for the pregnant patient. Recommendations regarding medication continuation must account for the patient's disease severity and desires after discussing risks, benefits, and alternatives. New evidence emerges regularly; referencing perinatal medication databases such as Reprotox®[49,50] may provide current information on specific drug risks for individualized counseling.

Genetic counseling

All patients with SCD should be offered genetic counseling, ideally before pregnancy, to be informed of their risk of having offspring who are carriers or affected with SCD. Key components of genetic counseling include disease characterization (i.e., HbSS, HBSC, and HbSβ+) for both patient and partner. Individuals who are at risk of having a child with SCD and present for prepregnancy counseling should be informed about alternative reproductive options. Patients with SCD who present during pregnancy should also be offered genetic counseling and informed of the risk of having a child born with SCD, along with screening and testing options (including newborn screening) for the current pregnancy. Antenatal diagnostic options, including chorionic villus sampling and amniocentesis should be offered.

Newer noninvasive (cell-free DNA) screening tests that report the fetal risk of SCD are commercially available,[78,79] but not currently recommended in pregnancy.[80] If, despite this, a patient undergoes screening with positive cell-free DNA screening results for SCD, confirmatory diagnosis should be offered. If not performed antenatally, the diagnosis can be confirmed postnatally.

What vaccinations should patients with sickle cell disease receive in pregnancy?

Pregnant patients with SCD should receive all routinely recommended antenatal vaccinations.[81-84] Patients can be reassured that the COVID-19 vaccines currently available in the United States do not appear to increase the rates of VOC.[85] Additional vaccines, which should be administered (if due) during pregnancy for patients with SCD, include meningococcal vaccination (MenACWY) every 5 years[86] and pneumococcal vaccination (PPSV23) $\geq$5 years after the first dose.[87] It is important to remember that many pregnant patients have significant barriers to care, and pregnancy may represent a unique window whereby patients have access to lifesaving immunizations. **We recommend that**

TABLE 2
Baseline maternal assessment for the prepregnancy or pregnant patient with sickle cell disease

Baseline assessment	Assessment and management principles
BP	Baseline assessment of BP to permit BP assessment throughout gestation relative to patient's baseline, acknowledging that BP in patients with SCD is often lower than individuals without SCD.
Iron stores	Baseline assessment of iron and iron stores (serum iron, transferrin, total iron-binding capacity, transferrin saturation, ferritin). Prenatal vitamins without iron should be the default. Iron administration is strictly reserved for patients with iron deficiency.
Anemia	Complete blood count to assess baseline hematocrit level and platelet count. Type and screen to assess for alloimmunization.
Leukocytes	Patients with SCD often have elevated leukocytes. Noting the WBC count at baseline may assist later in pregnancy if a leukocyte abnormality is noted; some data suggest a higher WBC is associated with poorer SCD outcomes.[42,43]
Neurologic	Obtain thorough neurologic history, including history of headaches and strokes. Obtain past records where indicated. Understanding patient's headache history may assist later in pregnancy to differentiate between patient's baseline headaches and a severe feature of preeclampsia.
Ophthalmologic	Baseline assessment of previous visual complications. Eye examinations are recommended every 1–2 y.[37] If patient is not up to date, expedited referral should occur during pregnancy.
Dental	Patients with SCD have an increased risk of dental complications that can adversely affect the mother's health and pregnancy outcomes. Routine dental care during pregnancy is strongly recommended. Dental referral for routine maintenance should be expedited during pregnancy if patient does not have a provider and/or if dental maintenance is not current.[44,45]
Cardiac	In accordance with ASH guidelines, providers should have a low threshold to obtain a screening echocardiogram for patients with SCD with comorbidities (chronic hypertension, lupus, etc.) and/or cardiopulmonary symptoms given the risks of pulmonary hypertension and cardiomyopathy. Specific cardiopulmonary symptoms[38] that should trigger screening with echocardiography include: • Dyspnea at rest or with exertion that is out of proportion to known condition, increased compared with baseline or unexplained • Hypoxemia at rest or with exertion that is out of proportion to known condition, increased compared with baseline or unexplained • Chest pain at rest or with exertion that is out of proportion to known condition, increased compared with baseline or unexplained • Increase in exercise limitation compared with baseline that is unexplained by other factors • History of recurrent hypoxemia at rest or with exertion • Evidence for sleep-disordered breathing with or without hypoxemia • History of syncope or presyncope • Evidence for loud P2 component of second heart sound or unexpected or new murmur on examination • Signs of heart failure and/or fluid overload on examination • History of pulmonary embolism
Vascular	Baseline assessment of previous thromboembolic events and anticoagulation, if indicated, per national guidelines.[46,47]
Pulmonary	Baseline assessment of O2 saturation. If <95%, obtain CXR and echocardiogram. Consider pulmonary function tests if symptoms persist.
Hepatic	Baseline assessment of liver function panel. Note that most patients with SCD have unconjugated hyperbilirubinemia at baseline.[48]
Renal	Baseline assessment of renal function and assessment of proteinuria.
Urine	Baseline urine culture at the initial prenatal visit and a urine assessment (dipstick, urinalysis, or other) at each prenatal visit.
Vitamin D	Baseline assessment of vitamin D.

ASH, American Society of Hematology; *BP*, blood pressure; *CXR*, chest x-ray; *SCD*, sickle cell disease; *WBC*, white blood count.
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pregnant patients with SCD receive all routinely recommended antenatal vaccinations in addition to meningococcal and pneumococcal vaccination if due (GRADE 1A).[32]

In addition to routine prenatal care, what additional items should be considered for the pregnant patient with sickle cell disease?

Daily folic acid supplementation is recommended for pregnant patients with SCD. RBC turnover occurs more frequently in patients with SCD (and other hemolytic anemias), and folic acid supplementation repletes folate stores needed for hematopoiesis.[88] Similar to all pregnant patients, prenatal vitamins are recommended for pregnant patients with SCD. However, iron-free prenatal vitamins should be the default for patients with SCD unless iron deficiency is documented.[89] **We recommend prenatal vitamins without iron unless iron deficiency is confirmed and initiation of 4 mg of folic acid for pregnant patients with SCD (GRADE 1B).[32,90-92]**

TABLE 3
Common medications used in SCD management—management principles for the prepregnant or pregnant patient with SCD

Medication	Management principles
Anticoagulation	For patients requiring lifelong anticoagulation or who have an indication for antepartum anticoagulation, unfractionated or low-molecular-weight heparins are preferred as they do not cross the placenta. It may be preferable to initiate or transition to heparin-based anticoagulation with early confirmation of an intrauterine pregnancy.
ACE-i or ARBs	ACE-i or ARBs are associated with increased risk of fetal anomalies, fetal renal failure, and perinatal death.[51-53]
Penicillin	Patients entering pregnancy on daily prophylactic penicillin may safely continue this during pregnancy. Pregnancy itself is not an indication to initiate penicillin prophylaxis.
Hydroxyurea	Hydroxyurea induces production of hemoglobin F and reduces red cell sickling, pain crises, hospitalization, and transfusion. As animal studies demonstrate an increased rate of fetal anomalies, it is generally discontinued in pregnancy.[54-56] Certain high-risk situations may warrant the use of hydroxyurea in pregnancy after organogenesis. Shared decision-making should guide the use of hydroxyurea.
Iron chelators (deferoxamine, deferiprone, deferasirox)	Iron chelators are commonly used in patients with sickle cell anemia to reduce iron overload as a result of repeated blood transfusion. Data regarding the use of deferoxamine in pregnancy is reassuring and may be considered.[57-59]
Crizanlizumab	Crizanlizumab is a monoclonal antibody that reduces VOC.[60] It has the potential to cause fetal harm and shared decision-making should guide potential continuation.
L-glutamine oral powder	L-glutamine oral powder (marketed as Endari) is an amino acid that reduces acute complications of SCD. The use of Endari in pregnancy has not been reported. In the absence of data, shared decision-making should guide use of Endari.
Voxelotor	Prevents deoxygenated SS hemoglobin from polymerizing by increasing affinity for oxygen.[61] No data in human pregnancy. Shared decision-making should guide use of voxelotor.
Opioids	Many patients with SCD are prescribed daily opioid therapy to manage painful effects of the disease. Pregnancy should not prompt discontinuation of opioid therapy. Pregnancy increases the risk of pain and VOC. Patients with SCD should be managed by a multidisciplinary team and a single pain provider when feasible.
NSAIDs	NSAID use in the first trimester of pregnancy may be associated with fetal loss[62] or congenital anomalies.[63-65] Third-trimester use may be associated with premature closure of the ductus arteriosus and pulmonary hypertension.[66,67] Short courses of NSAIDs may be considered after shared decision-making for acute pain or tocolysis before 32 wk of gestation.
Nonopioid or non-NSAID pain medications	In addition to opioids and NSAIDs, many patients with SCD rely on other medications to treat pain, including cyclobenzaprine, gabapentin, and pregabalin. Of these medications, cyclobenzaprine (Flexeril) has the most favorable safety profile.[68] Offspring of animals exposed to gabapentin had an increased risk of fetal growth restriction and congenital anomalies,[69,70] although this has not been replicated in observational human studies.[71,72] Congenital anomalies have been identified in patients taking pregabalin,[73] although a definitive association has not been established. In summary, cyclobenzaprine seems to be safe throughout gestation. Gabapentin and pregabalin may be considered via shared decision-making after thorough counseling regarding risks and benefits with the patient.
Antidepressants	Patients with SCD and depression who enter pregnancy on antidepressants should have a thorough review of their psychiatric history, as is recommended for all pregnant people. Mental health conditions are associated with maternal morbidity,[74] and psychiatric medications should not be withheld from pregnant patients.
Antiemetics	Regular use of anti-emetics is common for the patient with SCD. Pregnancy poses additional challenges, including an increased risk of nausea, vomiting, and dehydration. Patients with SCD and dehydration have an increased risk VOC. Although the addition of doxylamine and vitamin B6 may provide a modicum of improvement, additional antiemetics will likely be needed for patients who need them at baseline. Some reports suggest ondansetron increases the risk of clefting and congenital heart disease,[75] although more rigorous studies refute this.[76] Promethazine is not thought to increase the risk of adverse perinatal outcomes.[77] Shared decision-making should guide the use of antiemetics.

ACE-I, angiotensin-converting enzyme inhibitor; *ARB*, angiotensin-receptor blocker; *NSAID*, nonsteroidal anti-inflammatory medication; *SCD*, sickle cell disease; *VOC*, vaso-occlusive crisis.
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Patients with SCD have an increased risk of urinary tract infections.[93-95] In addition to a baseline urine culture at the entry to prenatal care, many providers obtain urine cultures each trimester because of the increased risk of asymptomatic bacteriuria. Evidence to support this is lacking. However, a baseline urine culture at the initial prenatal visit

and some form of urine assessment, such as dipstick or urinalysis, at each prenatal visit are suggested.

Patients with SCD have an increased risk of vitamin D deficiency; therefore, checking a baseline vitamin D level is suggested.[96] Repletion of vitamin D at 1000 to 2000 international units daily seems safe in pregnancy.[97]

What fetal surveillance is indicated for the pregnant patient with sickle cell disease?

Pregnant patients with SCD should undergo an ultrasound when they present for prenatal care to confirm the presence of a viable intrauterine pregnancy and to reliably date the pregnancy. Early confirmation of an intrauterine pregnancy is important as this may affect medication management concerning teratogen exposure. A detailed anatomic survey should be performed ≥18 weeks of gestation to screen for congenital anomalies, particularly among patients taking potential teratogens immediately before or during the first trimester of pregnancy.

Fetal growth surveillance by ultrasound is indicated given the increased risk of fetal growth restriction in patients with SCD.[25,32,98] Severe forms of SCD, including HbSS and HbSβ^0 disease, confer the greatest risk.[99] **We recommend fetal growth surveillance every 4 weeks beginning in the 28th week of gestation (GRADE 1C).**[100]

Antenatal fetal surveillance is indicated for pregnant patients with an increased risk of stillbirth. A 2016 meta-analysis, including data from 9 countries, found that patients with SCD have a significantly increased risk of stillbirth with an OR of 4.05.[25] In contrast, a contemporary statewide retrospective cohort study found no significant increase in stillbirth among women with SCD.[23] The authors hypothesized that this finding reflected improved antenatal surveillance and management. It is unknown if third-trimester antenatal fetal surveillance reduces stillbirth risk in pregnancies complicated by SCD with normally grown fetuses; however, it is reasonable to consider antenatal fetal surveillance for all patients with SCD given the above RR for stillbirth and the unknown degree to which fetal growth restriction is responsible for the increase in risk. Patients with SCD and a growth-restricted fetus should be assigned to antenatal fetal surveillance according to guidelines for fetal growth restriction.[100,101] **For patients with uncomplicated SCD and a normally-grown fetus, we suggest weekly or twice weekly antenatal testing beginning at 32 to 34 weeks of gestation. For patients with complicated SCD (i.e., maternal hypertension, VOC, fetal growth restriction, or other coexisting complication), we suggest initiating individualized antenatal testing at diagnosis or at a gestational age when delivery would be considered if results are abnormal (GRADE 2B).**[102]

Other forms of SCD (e.g., hemoglobin SC disease) have less clear effects on the risk of perinatal death.[103,104] Therefore, in the absence of other complications, antenatal fetal surveillance for patients with hemoglobinopathies other than HbSS or HbSβ^0 disease should be individualized and should take into account factors, such as fetal growth and disease severity.[102]

Management and treatment

What is the general management of vaso-occlusive crises?

Individuals presenting with uncomplicated VOC (i.e., pain without evidence of organ dysfunction) are typically managed with oral or intravenous (IV) fluids and analgesic medications. Pain caused by an uncomplicated VOC may last up to 2 weeks. RBC transfusion is not recommended for uncomplicated VOC.[41,18] Providers should observe for acute complications of SCD in patients presenting with VOC and alter the management plan accordingly. Complicated VOC should be treated in collaboration with a hematologist and may require additional assessment, diagnostic evaluation, and RBC transfusion in addition to pain management.

ACS deserves particular attention in the evaluation of VOC as it is the leading cause of death among patients with SCD.[105] ACS is diagnosed by imaging findings consistent with a new pulmonary infiltrate and one additional item, which may include oxygen desaturation, cough, temperature of ≥101.3°F, tachypnea, or wheezing.[106,107] ACS should be kept on the differential diagnosis, and a hematologist, pulmonologist, or other SCD specialist should be consulted for prompt evaluation and treatment. The management of ACS includes pain control (at a dose that provides adequate pain control but avoids sedation), IV fluids, broad-spectrum antibiotics, supplemental oxygen, and blood transfusions to decrease HbS to <30%.[107,108] Incentive spirometry should be performed every 2 hours while the patient is awake.[107,108]

How should a vaso-occlusive crisis be treated in pregnant patients?

VOC in pregnant patients is initially treated with hydration and aggressive pain management. Oxygen need not be initiated unless O2 saturation levels are <95%, in which case additional pulmonary assessment is needed. The threshold for oxygen supplementation in the pregnant patient is lower than in the nonpregnant patient with SCD to maintain an effective gradient for fetal gas exchange.[109] In addition, hydration should be administered, although the rate and volume of fluid administration must be balanced with risks of volume overload and pulmonary edema. Isotonic IV and oral fluids are preferred; hypertonic fluids are not recommended. In the patient with dehydration, fluids may be continued until clinical improvement.

An evaluation for infectious etiology or trigger for VOC should be performed and treatment initiated as indicated and treated. The initial workup in pregnancy includes a CBC with differential, lactate dehydrogenase, comprehensive metabolic panel, urinalysis, and urine culture. Routine radiography is not needed. A chest radiograph should be obtained if the patient has respiratory symptoms, hypoxia, or a significant decrease in hemoglobin level. Patients should be

treated with IV opioids for acute VOC according to their individualized pain plan (if present) or according to the ASH guideline on management of pain (Table 4).[18]

Anemia assessment is crucial for patients who present with a drop in hemoglobin level compared with their baseline.[41] Although transfusion may be considered for those whose hemoglobin level is significantly lower than baseline depending on the clinical context, it is important to exclude causes of anemia other than splenic sequestration that might require different management strategies, such as hemolysis, acute bleeding, or ACS. Exchange transfusions are indicated in the acute setting for patients presenting with symptoms of acute ischemic stroke, severe ACS (or any cause of hypoxic respiratory failure), or multisystem organ failure.[117] A hemoglobin electrophoresis may be obtained to determine the percentage of hemoglobin S but is not needed in the acute setting and can be estimated on the basis of the patient's previous transfusion history. In general, the goal of an exchange transfusion is to decrease the abnormal hemoglobin level (HbS or HbS+C) to <30%.[118]

What principles of pain management should be utilized in managing a patient with sickle cell disease?

Outside of pregnancy, individuals with SCD are ideally managed using principles of pain management outlined in the 2020 ASH guideline for SCD on the management of acute and chronic pain.[18] With few exceptions, as outlined in Table 4, **we recommend following evidence-based guidelines for the management of chronic and acute pain during pregnancy (Best Practice)**.[119] Table 4 summarizes key ASH recommendations and good practice statements for the management of acute and chronic pain (left column) and presents Society for Maternal-Fetal Medicine pregnancy-specific modifications where applicable (right column). Shared decision-making should guide pain management in pregnant patients with SCD, and all patients should have an individualized pain management plan.

Pregnant patients presenting with acute SCD pain should receive rapid assessment and administration of analgesia according to standard protocols and order sets to reduce the risk of undertreating pain.[119] Opioid dosing for acute pain should be tailored to the patient with consideration of their baseline opioid therapy and previous effective therapy. The dose of opioids needed to manage acute pain will vary according to the patient and may be higher than standard doses prescribed for postoperative pain.

Opioid therapy for chronic pain can be considered for pregnant patients with SCD after shared decision-making. Harm reduction strategies for chronic opioid therapy include co-prescribing naloxone and prescribing the lowest effective opioid dose. Morphine milligram equivalents (MME) should be documented.[120] Many online MME calculators exist, one of which is the Centers for Disease Control and Prevention (CDC) Opioid Guideline Mobile App.[121] The usefulness of "pain contracts" is not known, but a well-written patient agreement can help establish informed consent, improve adherence, and mitigate risk when initiating opioid therapy.[122] Referral to a pain specialist should be considered for pregnant patients with chronic SCD pain.[123] Attention should be paid to the risk of bias when assessing the opioid needs of an individual with chronic pain conditions, and an addiction medicine consultation should be considered if there is a concern for the need to differentiate opioid use disorder from chronic pain needs.[124]

How should pregnant patients with sickle cell disease on opioid therapy be counseled regarding the risk of neonatal opioid withdrawal syndrome?

Available evidence suggests that approximately 1 in 4 infants born to a mother with SCD will have neonatal opioid withdrawal syndrome (NOWS). In one series, 4 of 15 infants (27%) born to mothers with hemoglobin SS disease were diagnosed with NOWS. The risk factors included antepartum admission, VOC, and exchange transfusion.[125] In another series, 5 of 23 mothers (22%) with SCD who received opioids and 4 of 15 mothers (27%) with SCD who received daily opioids had an infant with NOWS.[126] Another review demonstrated that the risk of NOWS was associated with mean daily opioid dose; median maternal oral morphine doses were 416, 139, and 4 mg for infants with severe, mild, and no NOWS, respectively.[127] Patients with SCD using opioids during pregnancy should be counseled about the risk of NOWS and should participate in shared decision-making about an opioid dosing strategy to balance neonatal risks with the adequacy of pain management to maintain their well-being. Infants exposed to opioids in utero should be monitored for signs and symptoms of NOWS.[128] Prenatal consultation with pediatrics is encouraged to develop a monitoring and treatment plan. The Eat, Sleep, Console treatment model prioritizes infant comfort and family involvement in care and is associated with reduced length of hospital stay, exposure to pharmacologic agents, and overall cost of treatment.[128–130] Patients can be reassured that breastfeeding is beneficial for infants with NOWS.[131,132]

What is the role of transfusion in pregnant patients with sickle cell disease?

Of note, 3 types of transfusions are used in the care of patients with SCD: simple transfusions consisting of red cell transfusion only, manual exchanges consisting of manual phlebotomy before transfusion of 1 to 2 units of packed RBCs, and automated exchange transfusions, which consist of the simultaneous removal of the patient's full blood volume with an infusion of blood products. Transfusions are indicated during pregnancy for acute complications of SCD, such as stroke and ACS. In a 1988 randomized controlled trial, prophylactic transfusions during pregnancy reduced the number of pain crises compared with transfusions only when medically indicated but did not

TABLE 4
ASH SCD guideline for the management of acute and chronic pain and SMFM pain management principles for the pregnant patient

Select ASH recommendation[18]	SMFM principles for the pregnant patient
Acute pain	
For adults and children with SCD presenting to an acute care setting with acute pain related to SCD, the ASH guideline panel recommends rapid (within 1 h of ED arrival) assessment and administration of analgesia with frequent reassessments (every 30—60 min) to optimize pain control.	Obstetrical triage units should develop protocols and/or EMR order sets to facilitate timely assessment and administration of analgesia to optimize pain control.
For adults and children with SCD presenting to an acute care setting with acute pain related to SCD for whom opioid therapy is indicated, the ASH guideline panel suggests tailored opioid dosing based on consideration of baseline opioid therapy and previous effective therapy.	A tailored opioid dosing plan and controlled substance agreement should be outlined in the medical record to facilitate optimal pain management in the obstetrical triage unit.
For adults and children with acute pain related to SCD, the ASH guideline panel suggests a short course (5—7 d) of NSAIDs in addition to opioids for acute pain management.	NSAID use in the first trimester of pregnancy may be associated with miscarriage[62] or congenital anomalies, specifically cardiac malformations[63,64] and gastroschisis.[65] Third-trimester use may be associated with premature closure of the ductus arteriosus and pulmonary hypertension.[66,67] Short courses of NSAIDs may be considered after shared decision-making for acute pain during the second trimester of pregnancy.
For adults and children presenting for acute pain related to SCD, the ASH guideline panel suggests against corticosteroids for acute pain management.	Antenatal corticosteroids should be used for fetal lung maturity when a preterm birth is suspected according to national guidelines,[110] but should not be used for pain management.
For adults and children presenting with acute pain related to SCD who are hospitalized, the ASH guideline panel suggests a subanesthetic (analgesic) ketamine infusion as adjunctive treatment of pain that is refractory or not effectively treated with opioids alone.	Ketamine is not routinely used in obstetrics given adverse neurologic effects in animal offspring.[111,112] Alternatives are preferred if available.
For adults and children presenting with acute pain related to SCD, the ASH guideline panel suggests regional anesthesia treatment approaches for localized pain that is refractory or not effectively treated with opioids alone.	The use of regional anesthesia rarely applies to the pregnant patient outside of the intrapartum setting. If SCD pain requires regional anesthesia treatment, multidisciplinary planning with MFM, obstetrical anesthesia and/or pain management should occur.
For adults and children who seek treatment of acute pain, the ASH guideline panel suggests massage, yoga, TENS, VR, and guided AV relaxation in addition to standard pharmacologic management.	These nonpharmacologic modalities are generally safe in pregnancy. Care should be taken in yoga or massage to avoid lying flat to prevent compression of the great vessels impeding venous return.
For adults and children who develop acute pain episodes requiring hospital care, the ASH guideline panel suggests using SCD-specific hospital-based acute care facilities (i.e., day hospitals and infusion centers, all with appropriate expertise to evaluate, diagnose, and treat pain and other SCD complications) vs typical ED-based care.	Depending on gestational age, pregnant patients may need to undergo assessment of well-being before transitioning to a specialized SCD-specific care facility.
Chronic pain	
For adults with SCD who have chronic (as opposed to episodic) pain from the SCD-related identifiable cause of avascular necrosis of the bone, the ASH guideline panel suggests use of duloxetine (and other SNRI medications, because there is evidence of a class effect) as an option for management, in the context of a comprehensive disease and pain management plan.	Duloxetine is not known to cause congenital anomalies but, as with other SNRIs, has been associated with other perinatal complications. Risks and benefits should be discussed, and this medication should not be withheld from pregnant patients.
For adults with SCD who have chronic (as opposed to episodic) pain from the SCD-related identifiable cause of avascular necrosis of bone, the ASH guideline panel suggests the use of NSAIDs as an option for management, in the context of a comprehensive disease and pain management plan.	Shared decision-making should guide the use of NSAIDs. NSAIDs should be avoided in the first and third trimesters of pregnancy; short courses (i.e., 48—72 h) may be used in the second trimester of pregnancy.

Society for Maternal-Fetal Medicine. Sickle cell disease in pregnancy. Am J Obstet Gynecol 2024. *(continued)*

TABLE 4
ASH SCD guideline for the management of acute and chronic pain and SMFM pain management principles for the pregnant patient *(continued)*

Select ASH recommendation[18]	SMFM principles for the pregnant patient
Given the prevalence of psychological comorbidities that are present in the context of pain, it is good practice to routinely screen for depression and anxiety and to perform targeted screening for other psychological comorbidities.	Similar to all pregnant people, patients with SCD and chronic pain should undergo screening for depression and anxiety in the first trimester of pregnancy, third trimester of pregnancy, and after delivery. Those with an identified mental health condition should be screened monthly.[113]
For adults who have SCD-related chronic pain with no identifiable cause beyond SCD, the ASH guideline panel suggests SNRIs (e.g., duloxetine and milnacipran) as options for pain management.	As above, duloxetine is not known to cause congenital anomalies in pregnancy, but care should be individualized.
For adults who have SCD-related chronic pain with no identifiable cause beyond SCD, the ASH guideline panel suggests TCAs (e.g., amitriptyline) as an option for pain management.	It is recommended to avoid amitriptyline in the first trimester of pregnancy because of anomalies detected in animal models receiving high doses;[114,115] second- and third-trimester use can be considered after shared decision-making.
For adults who have SCD-related chronic pain with no identifiable cause beyond SCD, the ASH guideline panel suggests gabapentinoids (e.g., pregabalin) as options for pain management.	It is not recommended to use pregabalin in the first trimester of pregnancy;[73] second- and third-trimester use can be considered after shared decision-making.
For adults and children with SCD who have chronic pain related to SCD, the ASH guideline panel suggests cognitive and behavioral pain management strategies in the context of a comprehensive disease and pain management plan.	This recommendation requires no modification for pregnancy.
For adults with SCD who have chronic pain related to SCD, the ASH guideline panel suggests other provider-delivered integrative approaches (e.g., massage therapy and acupuncture) as available, as tolerated, and conditional upon individual patient preference and response. These approaches should be delivered in the context of a comprehensive disease and pain management plan.	Massage therapy, with slight position modifications avoiding the supine position, and acupuncture are safe in pregnancy.
For adults and children with SCD and emerging and/or recently developed chronic pain, the ASH guideline panel suggests against the initiation of COT unless pain is refractory to multiple other treatment modalities.	After shared decision-making, initiation of COT during pregnancy may be considered for refractory pain. A clear plan should be made regarding postpartum COT transition.
For adults and children with chronic pain from SCD who are receiving COT, are functioning well, and have perceived benefit, the ASH guideline panel suggests shared decision-making for continuation of COT.	Shared decision-making regarding continuation of COT in pregnancy is recommended.
Other considerations	
For adults and children with chronic pain from SCD who are receiving COT, are functioning poorly, or are at high risk of aberrant opioid use or toxicity, the ASH guideline panel suggests against continuation of COT.	SCD-related pain should be adequately treated, but patients at risk of aberrant opioid use or toxicity may be more appropriately managed by a single pain or addiction provider.
It is good practice to implement harm reduction strategies for patients on COT, including strongly considering co-prescribing naloxone, avoiding co-prescribing opioids and benzodiazepines, and prescribing the lowest effective opioid dose.	Patients receiving COT should receive the lowest effective dose along with a prescription of naloxone.[116] In addition, benzodiazepines should be avoided in a patient receiving opioids.
It is good practice to consider collaboration with pain medicine specialists for the management of individuals living with SCD who have chronic pain.	A multidisciplinary approach, including pain medicine specialists, is recommended for the management of the pregnant patient with SCD. Involving pain medicine specialists who can provide continuity care after delivery is preferred.
In cases in which the clinician has valid and substantial evidence of aberrant opioid use, it is good practice to consider consulting an addiction medicine physician.	Pregnant patients with SCD and substantiated aberrant opioid use should be referred to an addiction specialist for treatment.

Society for Maternal-Fetal Medicine. Sickle cell disease in pregnancy. Am J Obstet Gynecol 2024. *(continued)*

TABLE 4
ASH SCD guideline for the management of acute and chronic pain and SMFM pain management principles for the pregnant patient *(continued)*

Select ASH recommendation[18]	SMFM principles for the pregnant patient
For adults and children with SCD and recurrent acute pain, the ASH guideline panel suggests against chronic monthly transfusion therapy as a first-line strategy to prevent or reduce recurrent acute pain episodes.	Red blood cell transfusion is not recommended for the pregnant patient with acute pain in the absence of another indication.

Shading indicates American Society of Hematology (ASH) recommendations that require significant modifications during pregnancy. ASH recommendations for which there are no major modifications in pregnancy are unshaded.

ASH, American Society of Hematology; *AV*, audiovisual; *COT*, chronic opioid therapy; *EMR*, electronic medical record; *ED*, emergency department; *MFM*, maternal-fetal medicine; *NSAID*, nonsteroidal anti-inflammatory medication; *SCD*, sickle cell disease; *SMFM*, Society for Maternal-Fetal Medicine; *SNRI*, serotonin and norepinephrine reuptake inhibitor; *TAC*, tricyclic antidepressant; *TENS*, transcutaneous electrical nerve stimulation; *VR*, virtual reality.

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change other key maternal and perinatal outcomes. Concerns were raised by the authors regarding risks of alloimmunization, iron overload, hospital admissions, and excess healthcare costs.[133] A 2015 systematic review and meta-analysis of studies of prophylactic transfusion in pregnancy identified 12 studies with 1291 participants found a moderate to high risk of bias among included studies and found an association between prophylactic transfusion and reduction in maternal mortality, VOC, pulmonary complications, venous thromboembolism (VTE), pyelonephritis, perinatal mortality, neonatal death, and preterm birth.[134] Subsequently, a 2016 Cochrane Review (which included only the 1988 randomized controlled trial [RCT]) concluded that "prophylactic blood transfusion to pregnant women with sickle cell anemia confers no clear clinical benefit compared with selective transfusion."[135] In response to the available evidence, the ASH recommends the following regarding transfusion in pregnant patients with SCD:

- There is insufficient evidence to recommend a strategy of prophylactic transfusion rather than standard care.
- Prophylactic transfusion at regular intervals at the onset of pregnancy should be considered for women with the following:
  - A history of severe SCD-related complications before current pregnancy (including during previous pregnancies) to reduce recurrent pain episodes, incidence of ACS, or other (SCD-related) comorbidities
  - Additional features of high-risk pregnancy (e.g., additional comorbidities: other medical conditions or nephropathy)
- Women who develop SCD-related complications during the current pregnancy would benefit from initiating regular transfusions.[41]

Practically speaking, there is insufficient evidence to recommend routine chronic transfusion therapy (CTT) for most pregnant patients with SCD; individualized consideration should be given to patients with more severe historical features, such as those receiving chronic transfusion before pregnancy and those with a history of stroke.[32,41] **We suggest the use of prophylactic transfusions be individualized for high-risk patients with SCD in accordance with ASH guidelines and directed by a hematologist and maternal-fetal medicine subspecialist in shared decision-making with the patient (GRADE 2B).**

What are the risks and benefits of blood transfusion in pregnancy?

Blood transfusions in high-resource countries are considered safe and have low rates of adverse outcomes. The benefits of CTT, as described in a randomized trial, included reduced frequency of pain crises.[133] In addition, observational data consisting of a systematic review and meta-analysis found that CTT reduced maternal mortality, pulmonary complications, pulmonary embolism, pyelonephritis, perinatal mortality, and preterm birth.[134] Risks of blood transfusion during pregnancy include those inherent to blood transfusions in all patients, plus added risks to the pregnant patient and the developing fetus. Specifically, transfused blood should be cytomegalovirus (CMV) negative to avoid fetal CMV infection.[136] Additional risks of blood transfusion include iron overload and alloimmunization. Liver iron concentration monitoring and chelation therapy are indicated to prevent the adverse consequences of iron overload, which include fibrosis and cirrhosis.[137,138] For patients with alloimmunization, early communication with the local blood bank is important to ensure matched blood can be obtained if needed. Furthermore, the pregnant patient with antibodies associated with hemolytic disease of the fetus and newborn should be managed according to national guidelines.[139,140]

In addition, delayed hemolytic transfusion reactions (DHTRs) should remain on the differential diagnosis for a pregnant person with SCD who presents with pain and dark urine after a previous blood transfusion. The duration from red cell transfusion to DHTR can range from days to weeks and is typically, but not always, diagnosed by the identification of new antibodies on their antibody screen.[141] Supportive care, steroids, and intravenous immunoglobulin are likely the best approaches to treat a pregnant person with

SCD and DHTR. Avoiding blood transfusions is ideal, although this can be challenging in a person with a low hemoglobin level approaching delivery. Multidisciplinary planning is crucial in these challenging cases. MFM specialists should be vigilant to keep DHTR on the differential diagnosis as they manage patients with SCD in conjunction with a hematologist, preferably one who specializes in SCD.

What is the role of disease-modifying therapy, including hydroxyurea, in the management of sickle cell disease?

All individuals with SCD should be offered disease-modifying therapy at baseline. For individuals with a history of recurrent VOC, ACS, stroke, or other chronic organ complications, additional emphasis on disease-modifying therapy is needed. Hydroxyurea is the best-studied disease-modifying therapy in SCD, attenuating the number of VOC episodes and slowing the progression of end-organ disease.[142] Chronic red cell transfusion is the only disease-modifying therapy proven to decrease the risk of ischemic stroke in patients with CNS vasculopathy. Newer therapies (L-glutamine, voxelotor, and crizanlizumab) remain inconclusive in their potential for long-term efficacy and lack data on use during pregnancy.[142] Of these therapies, only CTT is considered safe in pregnancy.[134] About these newer therapies, shared decision-making should help guide whether certain agents should be continued during pregnancy.

Hydroxyurea has historically not been recommended in pregnancy primarily because of teratogenic effects found in animal models.[54-56] Although available data are limited, a thorough search did not locate any reported cases of individuals taking hydroxyurea for SCD who had an infant with a birth defect,[143,144] and a systematic review is ongoing.[145] A 2022 retrospective study of 1788 pregnancies, among which 241 (16%) were conceived while on hydroxyurea, did not demonstrate independent associations between use during conception and adverse pregnancy outcomes.[146] However, among patients with SCD using hydroxyurea during conception and continuing use during pregnancy, there were increased risks of miscarriage or stillbirth (OR, 2.21; 95% confidence interval [CI], 1.09−7.38) and increased risk of low birthweight (OR, 2.98; 95% CI, 1.09−7.38) among term infants, after adjustment for markers of disease severity.

Of note, one strategy for individuals of childbearing potential is to recommend discontinuation of hydroxyurea if planning to conceive within 3 months or to discontinue hydroxyurea in the event of an unexpected pregnancy.[32] However, this recommendation should be individualized and risk stratified by trimester in collaboration with an expert in SCD. Because of the limited available low-quality data balanced with maternal and perinatal risks, we recommend that principles of informed consent and shared decision-making be applied to the use of hydroxyurea in pregnancy. Counseling should include animal model data, timing when teratogenicity is most likely (i.e., periconception to first trimester of pregnancy), availability of cross-matched blood, likelihood of developing severe morbidity if hydroxyurea is discontinued (based on patient-level disease characteristics), and that beneficial effects from hydroxyurea may take 6 months to observe from initiation of treatment. Although hydroxyurea is not indicated for most pregnant individuals with SCD, **we recommend shared decision-making occur regarding the use of hydroxyurea in pregnancy, in conjunction with a SCD specialist and maternal-fetal medicine subspecialist, accounting for the timing of use and individual disease severity (GRADE 1C).**

What blood pressure and preeclampsia management principles should be observed for the pregnant patient with sickle cell disease?

Pregnant patients with SCD, especially those with HbSS or HbSβ^0 disease, often have lower baseline blood pressure (BP) than pregnant patients without SCD.[147−150] This may be due to lower body mass index, anemia, nitric oxide deficiency, or other causes. Obstetrical providers should note the patient's baseline (prepregnancy) BP and first-trimester BPs so the relative change compared with the patient's baseline can be noted throughout gestation. Patients with SCD have an increased risk of preeclampsia.[95] In addition, individuals with SCD are at increased risk of microalbuminuria and chronic kidney disease, separate from pregnancy.[151] Therefore, baseline preeclampsia laboratory test results (which are included within the baseline assessment of end-organ damage shown in Table 2) should be obtained. The administration of low-dose aspirin should be initiated at 12 weeks of gestation to reduce the risk of preeclampsia.[7,152] Preeclampsia in patients with SCD should be managed according to existing guidelines.[19]

Pregnant patients with SCD should be counseled about an increased risk of preeclampsia. Providers should remain aware that new-onset hypertension in patients with SCD, even if mild, may represent a significant increase in mean arterial pressure from the patient's baseline. Providers should recognize that a systolic BP of 30 mm Hg or a diastolic BP of 15 mm Hg above baseline, even if it does not reach "mild hypertension," represents a significant physiological change and warrants assessment of maternal end-organ damage and continued close surveillance.[153,154] Furthermore, the development of severe hypertension should be considered relatively more ominous in the pregnant patient with SCD and low baseline BP and should be evaluated and treated accordingly to reduce the risk of stroke.

At what gestational age should the patient with sickle cell disease be delivered?

For patients with uncomplicated SCD, normal BP, and a normally grown fetus, delivery is recommended between 39 0/7 and 39 6/7 weeks of gestation, consistent with existing guidelines for timing of delivery in patients with

comorbidities associated with an increase in maternal and perinatal risk.[155] Patients with SCD and preeclampsia and/or fetal growth restriction should undergo delivery according to specified guidelines.[19,101] For patients with SCD complicated by multiple VOC, significant alloimmunization, or other SCD-specific complications, ideal delivery timing is unclear. Because of the lack of clear data in this area, the timing of delivery for patients with complicated SCD should be individualized, weighing the maternal and perinatal risks with risks of prematurity.

What peripartum considerations are recommended for patients with sickle cell disease?

Preparation of patients with SCD for a safe delivery with adequate pain management should include multispecialty collaboration. A consultation with an obstetrical anesthesia specialist is advised to discuss methods of analgesia and anesthesia, particularly for patients who experience chronic pain. Patients with a history of transfusion should undergo an antibody screen at least 2 days before anticipated delivery if feasible, and obstetrical teams should determine blood preparation needs based on systems-level and patient-level factors, including availability of products, current hemoglobin level, and degree of sensitization, if any. The mode of delivery for patients with SCD is based on usual obstetrical indications; vaginal delivery is the preferred mode of delivery when possible. Avascular necrosis of the femoral head does not preclude vaginal delivery.[156]

Should patients with sickle cell disease undergo prophylactic transfusion prior to a planned cesarean?

"The TAPS (The Transfusion Alternatives Preoperatively in Sickle Cell Disease) Study" was an RCT that investigated the effect of preoperative transfusions to reach a hemoglobin level of 10 g/dL and/or hemoglobin S level of $<60\%$ on perioperative complications in patients with SCD scheduled to undergo low- or medium-risk surgeries.[157] Postoperative ACS was significantly less likely in the transfused group. This led the authors to recommend preoperative transfusions for eligible patients undergoing surgery. Based on this trial, and others,[158,159] the ASH SCD guideline on transfusion support "suggests preoperative transfusion over no preoperative transfusion in patients with SCD undergoing surgeries requiring general anesthesia and lasting more than 1 hour" and remarks that "clinicians should aim for total hemoglobin levels of more than 9 g/dL before surgery."[41] Robust data for pregnancy and cesarean deliveries routinely performed under general anesthesia are not available, limiting the applicability of the TAPS findings and ASH guidelines for use in helping patients with SCD prepare for delivery. Therefore, in the absence of data, the decision of whether or not to transfuse before a cesarean delivery should be individualized. For example, a patient with a history of ACS with a hemoglobin level of 7 g/dL and 3 previous cesarean deliveries would likely benefit from a planned RBC transfusion before cesarean delivery, whereas a patient with a hemoglobin level of 9 g/dL undergoing a primary cesarean delivery for breech presentation likely would not need a transfusion before a cesarean delivery. As is recommended for all pregnant patients with SCD admitted to the hospital, the blood bank should be alerted so that matched blood can be available as needed.

What are recommended components of postpartum care for sickle cell disease patients?

In addition to routine postpartum care, patients with SCD require additional postpartum considerations. Patients with SCD have an increased risk of VTE. Intrapartum and postpartum, when patients with SCD are not ambulatory, sequential compression devices should be applied, and early postpartum ambulation should be encouraged. Postoperative prophylactic anticoagulation should be considered after cesarean delivery before hospital discharge, given the increased VTE risk.[160–162]

Patients with SCD have an increased risk of postoperative ACS.[157] It is best practice to keep an incentive spirometer at the bedside of hospitalized patients with SCD to reduce the risk of pulmonary complications.[163,164]

A pain management plan for patients with SCD is important. Patients with SCD who undergo cesarean delivery have surgical pain that should be adequately treated and may require higher doses of opioids because of opioid tolerance. Opioid prescriptions for pain after cesarean delivery should be prescribed according to guidelines for the management of pain in patients with SCD and the patient's individualized pain plan. Adjuncts to opioids for postoperative pain include nonsteroidal anti-inflammatory medications, gabapentin, and regional blocks from anesthesiologists or pain management specialists.[165,166]

Finally, it is crucial to ensure a smooth transition from obstetrician-gynecologist or MFM subspecialist care to primary care, including a referral to a hematologist or SCD specialist if the patient is not already established.[167] If feasible, patients should have a follow-up appointment with an SCD specialist scheduled upon discharge from the delivery-associated hospitalization. This may enhance access to life-saving disease-modifying therapy early in the postpartum period.[168] In addition, postdelivery counseling with an MFM specialist to review the course and outcome of the pregnancy and to set the stage for prepregnancy counseling before future pregnancies is advised.

Should pregnant patients with sickle cell disease receive anticoagulation?

Patients with SCD have an increased risk of venous thromboembolic events.[26,160,161] Patients should be counseled to present to their clinician with new-onset chest pain, cardiopulmonary complaints, or calf pain. Prophylactic anticoagulation to reduce the risk of VTE should be considered for pregnant patients with SCD who are admitted to the hospital if decreased mobility is anticipated

Summary of recommendations

Number	Recommendation	GRADE
1	We recommend that patients with SCD be managed by a multidisciplinary team that includes MFM, hematology (ideally a hematologist specializing in SCD), genetics, pain management, and social work or behavioral health (as appropriate) starting in early pregnancy.	Best practice
2	We recommend that pregnant patients with SCD receive all routinely recommended antenatal vaccinations in addition to meningococcal and pneumococcal vaccinations if due.	1A
3	We recommend prenatal vitamins without iron unless iron deficiency is confirmed and initiation of 4 mg of folic acid for patients with SCD.	1B
4	We recommend fetal growth surveillance every 4 wk beginning in the 28th week of gestation.	1C
5	For patients with uncomplicated SCD and a normally grown fetus, we suggest weekly or twice-weekly antenatal testing beginning at 32–34 wk of gestation. For patients with complicated SCD (i.e., maternal hypertension, VOC, fetal growth restriction, or other coexisting complication), we suggest initiating individualized antenatal testing at diagnosis or at a gestational age when delivery would be considered if results are abnormal.	2B
6	We recommend following evidence-based guidelines for the management of chronic and acute pain during pregnancy.	Best practice
7	We suggest the use of prophylactic transfusions be individualized for high-risk patients with SCD in accordance with ASH guidelines and directed by a hematologist and MFM subspecialist in shared decision-making with the patient.	2B
8	We recommend shared decision-making occur regarding the use of hydroxyurea in pregnancy, in conjunction with an SCD specialist and an MFM subspecialist, accounting for the timing of use and individual disease severity.	1C
9	We recommend that reliable contraception be offered to patients with SCD to decrease the risk of an unintended pregnancy and associated maternal and perinatal risks.	1B

MFM, maternal-fetal medicine; *SCD*, sickle cell disease; *VOC*, vaso-occlusive crisis.

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or if other risk factors develop. Patients with a previous or current VTE should be managed according to national guidelines.[47,169] The risk of thrombosis increases as pregnancy progresses with the highest risk in the postpartum period (2.1%; 95% CI, 1.5–3.1) comparable with the per pregnancy VTE risk encountered in pregnant patients with factor V heterozygote (0.5%–3.1%) and prothrombin gene heterozygote (0.4%–2.6%) status.[46,161,170] Therefore, provided there is no contraindication concerning one's individual bleeding risk, postpartum prophylactic anticoagulation may be considered for the postpartum patient with SCD to reduce the risk of VTE.

What contraceptive choices should be offered to patients with sickle cell disease?

Recent studies of patients with SCD found that 56% of patients were not using any form of contraception[171] and that 58% had an unintended pregnancy at least once.[172] Patients with SCD have an increased risk of maternal morbidity or death as a result of pregnancy.[171] Reliable contraception should be offered to decrease the risk of unintended pregnancy and associated maternal and perinatal risk. According to the CDC Medical Eligibility Criteria for Contraceptive Use, various forms of contraception are appropriate for people with SCD.[173] Combined hormonal contraception (CHC) is associated with an increased risk of VTE, and the presence of SCD increases the risk of thrombotic events in the setting of CHC use.[174] In addition, some individuals with SCD have significant comorbidities that preclude the use of estrogen, including past or present thromboembolism, previous stroke, or hypertension. For these reasons, progestin-only methods, including long-acting reversible contraception (LARC), are favored for patients with SCD.[175] Offering LARC immediately after delivery may increase access to reliable contraception and is also recommended.[176] In addition to contraceptive benefits, depot medroxyprogesterone acetate may reduce the risk of sickle pain crises and is another option for these patients.[177] **We recommend that reliable contraception be offered to patients with SCD to decrease the risk of an unintended pregnancy and associated maternal and perinatal risks (GRADE 1B).** All conversations regarding contraception should be individualized and employ principles of shared decision-making and be sensitive to historical contraceptive coercion in this patient population.[178]

What lactation guidance should be provided to pregnant and postpartum patients with sickle cell disease?

Similar to all patients, pregnant patients with SCD should be provided education regarding maternal and neonatal benefits of breastfeeding and adequate support to optimize the chance for breastfeeding success. Patients who discontinued medications used for the management of SCD with knowledge of pregnancy should be provided counseling in the second and/or third trimester of pregnancy regarding the compatibility of their prepregnancy

Society for Maternal-Fetal Medicine Grading System: Grading of Recommendations Assessment, Development, and Evaluation (GRADE) recommendations[226]

GRADE of recommendation	Clarity of risk and benefit	Quality of supporting evidence	Implications
1A. Strong recommendation, high-quality evidence	Benefits clearly outweigh risks and burdens or vice versa.	Consistent evidence from well-performed, RCTs or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of benefit and risk.	Strong recommendation that can apply to most patients in most circumstances without reservation. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
1B. Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risks and burdens or vice versa.	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence of some other research design. Further research (if performed) is likely to have an effect on confidence in the estimate of benefit and risk and may change the estimate.	Strong recommendation that applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
1C. Strong recommendation, low-quality evidence	Benefits seem to outweigh risks and burdens or vice versa.	Evidence from observational studies, unsystematic clinical experience, or RCTs with serious flaws. Any estimate of effect is uncertain.	Strong recommendation that applies to most patients. Some of the evidence base supporting the recommendation is, however, of low quality.
2A. Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens.	Consistent evidence from well-performed RCTs or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of benefit and risk.	Weak recommendation; best action may differ depending on circumstances or patients or societal values.
2B. Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burdens; some uncertainty in the estimates of benefits, risks, and burdens.	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence of some other research design. Further research (if performed) is likely to influence confidence in the estimate of benefit and risk and may change the estimate.	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances.
2C. Weak recommendation, low-quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens.	Evidence from observational studies, unsystematic clinical experience, or RCTs with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation, other alternatives may be equally reasonable.
Best practice	Recommendation in which either (1) there is an enormous amount of indirect evidence that clearly justifies a strong recommendation, direct evidence would be challenging and an inefficient use of time and resources, to bring together and carefully summarize, or (2) a recommendation to the contrary would be unethical.		

Adapted from Guyatt et al.[227]

GRADE, Grading of Recommendations Assessment, Development, and Evaluation; *RCT*, randomized controlled trial.

Society for Maternal-Fetal Medicine. Sickle cell disease in pregnancy. Am J Obstet Gynecol 2024.

Guidelines

Organization	Title	Year of publication
ACIP	General best practice guidelines for immunization[81]	2023
ACIP	Meningococcal vaccination[86]	2020
ACIP	Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions[87]	2012
ACOG	ACOG Clinical Practice Guideline No. 4: screening and diagnosis of mental health conditions during pregnancy and postpartum[113]	2023
ACOG	ACOG Committee Opinion No. 495: vitamin D: screening and supplementation during pregnancy[97]	2011
ACOG	ACOG Committee Opinion No. 691: carrier screening for genetic conditions[13]	2017
ACOG	ACOG Committee Opinion No. 713: antenatal corticosteroid therapy for fetal maturation[110]	2017
ACOG	ACOG Committee Opinion No. 743: low-dose aspirin use during pregnancy[152]	2018
ACOG	ACOG Committee Opinion, No. 828: indications for outpatient antenatal fetal surveillance[102]	2021
ACOG	ACOG Practice Advisory: cell-free DNA to screen for single-gene disorders[80]	2019
ACOG	ACOG Practice Advisory: hemoglobinopathies in pregnancy[7]	2022
ACOG	ACOG Practice Bulletin No. 192: management of alloimmunization during pregnancy[139]	2018
ACOG	ACOG Practice Bulletin No. 196: thromboembolism in pregnancy[47]	2018
ACOG	ACOG Practice Bulletin No. 197: inherited thrombophilias in pregnancy[46]	2018
ACOG	ACOG Practice Bulletin No. 212 Summary: pregnancy and heart disease[29]	2019
ACOG	ACOG Practice Bulletin, No 222: gestational hypertension and preeclampsia[19]	2020
ACOG	ACOG Practice Bulletin, No 227: fetal growth restriction[100]	2021
ASH	Guidelines for sickle cell disease: cardiopulmonary and kidney disease[38]	2019
ASH	Guidelines for sickle cell disease: management of acute and chronic pain[18]	2020
ASH	Guidelines for sickle cell disease: prevention, diagnosis, and treatment of cerebrovascular disease in children and adults[39]	2020
ASH	Guidelines for sickle cell disease: stem cell transplantation[40]	2021
ASH	Guidelines for sickle cell disease: transfusion support[41]	2020
ASH	Guidelines for management of venous thromboembolism: venous thromboembolism in the context of pregnancy[169]	2018
ASRM	Combined hormonal contraception and the risk of venous thromboembolism: a guideline[174]	2017
ASRM	Provision of fertility services for women at increased risk of complications during fertility treatment or pregnancy: an ethics committee opinion[33]	2022
British Society for Haematology	Management of sickle cell disease in pregnancy[32]	2021
CDC	CDC clinical practice guideline for prescribing opioids for pain[124]	2022
CDC	U.S. medical eligibility criteria for contraceptive use[173]	2016
National Institute for Health and Care Excellence	Sickle cell disease: managing acute painful episodes in hospital[119]	2012
SMFM	SMFM Clinical Guideline #8: The fetus at risk of anemia-diagnosis and management[140]	2015
SMFM	SMFM Consult Series #48: Immediate postpartum long-acting reversible contraception for women at high risk of medical complications[175]	2019
SMFM	SMFM Consult Series #52: Diagnosis and management of fetal growth restriction[101]	2020

Society for Maternal-Fetal Medicine. Sickle cell disease in pregnancy. Am J Obstet Gynecol 2024. *(continued)*

Guidelines *(continued)*

Organization	Title	Year of publication
Society of Obstetric Medicine of Australia and New Zealand	Guidelines for the management of hypertensive disorders of pregnancy[154]	2014
US Preventative Services Task Force	Folic acid supplementation for the prevention of neural tube defects[91]	2017

The content of this document reflects the national and international guidelines related to the management of sickle cell disease in pregnancy.

ACIP, Advisory Committee on Immunization Practices; *ACOG*, American College of Obstetricians and Gynecologists; *ASH*, American Society of Hematology; *ASRM*, American Society for Reproductive Medicine; *CDC*, Centers for Disease Control and Prevention; *SMFM*, Society for Maternal-Fetal Medicine.

Society for Maternal-Fetal Medicine. Sickle cell disease in pregnancy. Am J Obstet Gynecol 2024.

medications with lactation. Resources, such as LactMed,[179] can provide contemporary, individualized information to enhance shared decision-making. Many medications, including hydroxyurea, can be used safely during lactation.[180–182] Preliminary data suggest that exclusive breastfeeding is associated with improved anthropometric indicators in children with SCD.[183]

Are there special considerations for the pregnant patient with sickle cell disease and moyamoya disease?

Moyamoya disease is a rare vascular disorder of the brain resulting in compensatory vascular growth to bypass blocked cerebral vessels that can develop in individuals with SCD.[184–187] Symptoms of moyamoya disease include headaches, seizures, visual disturbances, paralysis, weakness, paresthesia, and aphasia. If a patient with SCD presents with new-onset neurologic symptoms, consultation with neurology and appropriate imaging studies are recommended. Patients with moyamoya disease have an increased risk of hemorrhagic stroke, which may be aggravated by anticoagulation; therefore, anticoagulation is generally deferred.[187,188] The combination of SCD, moyamoya, and hypertensive disorders of pregnancy can lead to irreversible encephalopathy or death.[189] Patients with continuing pregnancies should be closely managed by a multidisciplinary team. Acknowledging a lack of data, a BP goal of $<$130/80 mm Hg is reasonable for these patients to reduce the risk of maternal stroke and death. In the setting of a previous or current thromboembolism, a multidisciplinary team should outline a plan of care acknowledging that under-anticoagulation could lead to a life-threatening embolus and that over-anticoagulation could lead to a hemorrhagic stroke. Late preterm or early-term delivery may be considered in patients with SCD and moyamoya to reduce the risk of preeclampsia, sudden labile BP spikes, and risk of hemorrhagic stroke and death. Patients with SCD and moyamoya disease who develop severe preeclampsia assume a significant risk of maternal morbidity and mortality. The combination of SCD, moyamoya, and preterm preeclampsia with severe features may be an indication for delivery before 34 weeks of gestation. In such cases, individualized care planning should be undertaken with MFM and other involved specialists. Delaying delivery until antenatal corticosteroid administration should be individualized on the basis of the degree of maternal hypertension, gestational age, and other comorbidities.

Are there any counseling or management considerations for patients with isolated sickle cell trait?

The presence of isolated SCT in pregnancy has an unclear effect on perinatal outcomes. Although some studies have demonstrated increased rates of adverse outcomes, such as stillbirth, preeclampsia, preterm delivery, and VTE among patients with isolated SCT, others have failed to demonstrate an independent association between isolated SCT and any such outcomes.[190–192] In 2020, the British Society for Haematology, noting the high worldwide prevalence of SCT, put out a call for further study.[193] In the absence of high-quality data linking isolated SCT to adverse pregnancy outcomes, prenatal care and genetic counseling regarding a potential risk to offspring should be provided if both parents are carriers of SCT or a related hemoglobinopathy. An association between SCT and urinary tract infections has been reported,[194] although the benefits of increased screening in this population are not clear.[195]

How does racism impact patients with sickle cell disease?

Any discussion of SCD must acknowledge the effects of racism.[30,31,196–198] Structural racism fuels several health disparities among populations affected by SCD, including inadequate healthcare coverage and access to care,[199–201] lack of quality care because of inadequate provider knowledge of evidence-based guidelines,[202–207] lack of sufficient

specialty care,[196] and lack of adequate research into optimal prevention and treatment of morbidity and mortality associated with SCD vs other chronic illnesses.[208] Optimization of health outcomes for patients with SCD requires reducing the impact of structural racism at the national and institutional level.[30]

In addition, interpersonal racism affects patients with SCD in the form of implicit bias and explicit discrimination. There are published reports of racial disparities in pain management[209,210] and bias against Black patients,[211,212] patients with chronic pain,[213,214] women with pain,[215–217] and, specifically, patients with SCD.[218,219] The intersection of discrimination and chronic pain faced by patients with SCD may have a compounding effect on the overall burden of SCD.[220–222] In addition, discrimination contributes to the undertreatment of pain in patients with SCD, who may be unfairly labeled "difficult" or "drug-seeking" when requesting appropriate pain management.[223–225] To minimize the effect of interpersonal racism on patients with SCD, healthcare providers must recognize and correct implicit biases, endeavoring to treat patients equitably, regardless of race.[30]

Recommendations for future research on sickle cell disease in pregnancy

With rare exceptions, management recommendations throughout this document are largely based on observational data. SCD research receives less federal and foundation funding per patient compared with other comparable diseases,[208] and rigorous data on the management of pregnant people with SCD are especially limited. We encourage funding allocations that prioritize equity and aim to reduce this disparity, such as federal support for comprehensive SCD centers. We advocate for the inclusion of pregnant patients with SCD in ongoing research studies and for additional rigorous, prospective, randomized studies to help inform care. We recognize that improving outcomes for pregnant patients with SCD and their children requires addressing the effect of racism at the institutional level through efforts, such as antiracism taskforces, reporting systems for racist behavior, implicit bias training, and open dialogue with colleagues.

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All authors and committee members have filed a disclosure of interests delineating personal, professional, business, or other relevant financial or nonfinancial interests in relation to this publication. Any substantial conflicts of interest have been addressed through a process approved by the Society for Maternal-Fetal Medicine (SMFM) Board of Directors. The SMFM has neither solicited nor accepted any commercial involvement in the specific content development of this publication.

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  https://doi.org/10.1016/j.ajog.2023.10.031