Sickle Cell Anemia in Pregnancy

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August 2025 edit includes a change to the title from Sickle Cell Disease to Sickle Cell Anemia to ensure that there is no confusion between sickle cell anemia and sickle cell trait.

Background

Sickle cell anemia (SCA),), is an abnormality of red blood cells (RBCs) that may result in circulatory impairment, tissue infarction, marked anemia, infection, fetal growth restriction, preterm delivery, preeclampsia, and stillbirth. **Acute complications of SCA** include vaso-occlusive pain crises, tissue ischemia, tissue infarction and osteomyelitis, acute chest syndrome, increased cardiac output with subsequent cardiomegaly, stroke, splenic sequestration, acute renal failure, ocular complications (conjunctival vessel changes, vitreous hemorrhage), venous thromboembolism (VTE), and cholecystitis. **Chronic complications include** chronic pain, narcotic dependence, cholelithiasis, renal dysfunction, cardiomegaly, hypertension, pulmonary hypertension, pulmonary fibrosis, iron overload, folate deficiency, and red cell alloimmunization. Neonatal complications include preterm birth, fetal growth restriction, anemia (especially if there is maternal alloimmunization), hyperbilirubinemia, and neonatal withdrawal syndrome.

Recommended Vaccines

Annual
- Influenza
- COVID
- RSV

If not done previously or non-immune
- Pneumococcal: PCV 20
- Haemophilus influenzae type B
- Meningitis vaccines
  - Men ACWY (due every 5 years)
  - Men B* (due every 2-3 years)
- Hepatitis A (two doses 4 weeks apart)
- Hepatitis B (three doses, at 0, 1 and 6 months)

*Men B has not been extensively studied in pregnancy. Therefore, recommend vaccination when benefits outweigh the risks of unknown complications

Antepartum Management

Prenatal Care

Patients with (SCA) should be managed by a multidisciplinary team including a Maternal-Fetal Medicine specialist, Hematologist, and Pain Management specialist if available.

Table 1 lists the initial evaluation that should be started at the onset of prenatal care if not done previously.[1] Patients should be asked about their pain management pln, and Texas PMP

Aware should be reviewed in early pregnancy. **Important for patients cared for by BCM practice**: Narcotic flowsheet (in EPIC) for outpatient medications/current dosages.

Please see Society for Maternal-Fetal Medicine Consult Series #68: Sickle cell disease in pregnancy for further clinical guidance on management of sickle cell disease during pregnancy.[1]

Table 1. *Baseline maternal assessment for patients with SCA*[1]

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.

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

Sickle Cell Crisis[1-4]

The following checklist is recommended for the initial work up and management of patients who present with symptoms concerning for a sickle cell crisis. Crises can be triggered by many situations, including infections, environmental changes (i.e. weather), dehydration, labor. However, a heightened level of suspicion is necessary in patients with SCD as crises can lead to organ injury, acute chest syndrome (ACS), stroke, and/or heart failure, among other potentially life-threatening conditions.

Initial Evaluation

The goal of the initial evaluation is to determine if this is a **simple isolated vaso-occlusive crisis (VOC)** or a **complicated VOC** that is associated with end-organ dysfunction and injury. See Figure 1 for summary.

- ☐ Common vital sign changes (MEWS should be activated for all usual triggers)
  - Blood Pressure: Hypertension
  - Heart Rate: Tachycardia
  - Respiratory Rate: Tachypnea
  - Oxygen Saturation (SpO2): Hypoxemia
  - Temperature: Mild to moderate fever of 37.8C or greater (can be due to tissue ischemia but must have a heightened suspicion for infection)
- ☐ Patient History
  - Review of systems
    - Respiratory symptoms concerning for possible pneumonia vs. acute chest syndrome
    - Other symptoms that point to an infectious cause (i.e. UTI, pyelonephritis, pneumonia, osteomyelitis)
  - Increased need for pain medication
  - Recent environmental changes, stress, dehydration
  - **Evaluate home pain regimen to determine potential patient pain management needs**

Symptoms of Sickle Crises

Vaso-occlusive pain crisis: Musculoskeletal pain (back, chest, extremity) that commonly follows a pattern from prior crises

Acute Chest Syndrome: imaging findings consistent with a new pulmonary infiltrate and one additional item, which may include oxygen desaturation, cough, temperature of 38.5C, tachypnea, or wheezing

Hepatic Crisis: Vaso-occlusion of hepatic microvasculature simulates acute cholecystitis with fever, RUQ pain, leukocytosis and elevations in ALT/AST & bilirubin

- ☐ Laboratory Assessment and Common Findings
  - CBC with differential
    - WBC: Leukocytosis (due to tissue ischemia and/or infection)
    - Hgb: Anemia
    - Plt: variable
    - LDH: Elevated > 600 indicating hemolysis
  - Hemoglobin electrophoresis: High HbS (can be used for treatment monitoring but should not be relied on for initial management)
  - Reticulocyte count
  - Peripheral smear
  - CMP
  - LDH
  - Type and screen
  - Urine culture
  - Other cultures based on patient symptoms (sputum, vaginal, blood)
- ☐ Imaging (should be based on symptoms)
  - Chest X-Ray with pulmonary symptoms
  - Fetal imaging as needed
- ☐ Fetal assessment (CEFM + Toco until stable)
  - May see non-reassuring fetal heart tones that often improve with maternal stabilization
  - Significantly increased risk of IUFD in patients with SCA

Initial Management prior to admission

- ☐ See Figure 1 for recommended management
- ☐ Pain medication (Table 2)

- First line is a trial of **Ketorolac** 15-30mg in the second trimester (and with no other contraindications such as peptic ulcer disease or chronic kidney disease)
- Acetaminophen 650 mg q6H PO or 1g IV (contraindicated if AST/ALT significantly increased)
- **Opioids** should not be withheld
  - Chronic opioid regimen (if applicable) should be continued, and additional opioids may still be necessary

☐ Acute Chest Syndrome
- Consult Critical Care and admit to CCU
- Consult Hematology
- Initiate broad spectrum antibiotics (community-acquired pneumonia coverage if no other source of infection identified)
- Consider simple blood transfusion (pending discussion with Hematology)
- Oxygen administration may be given for patients with dyspnea or respiratory distress and saturations above 95%.

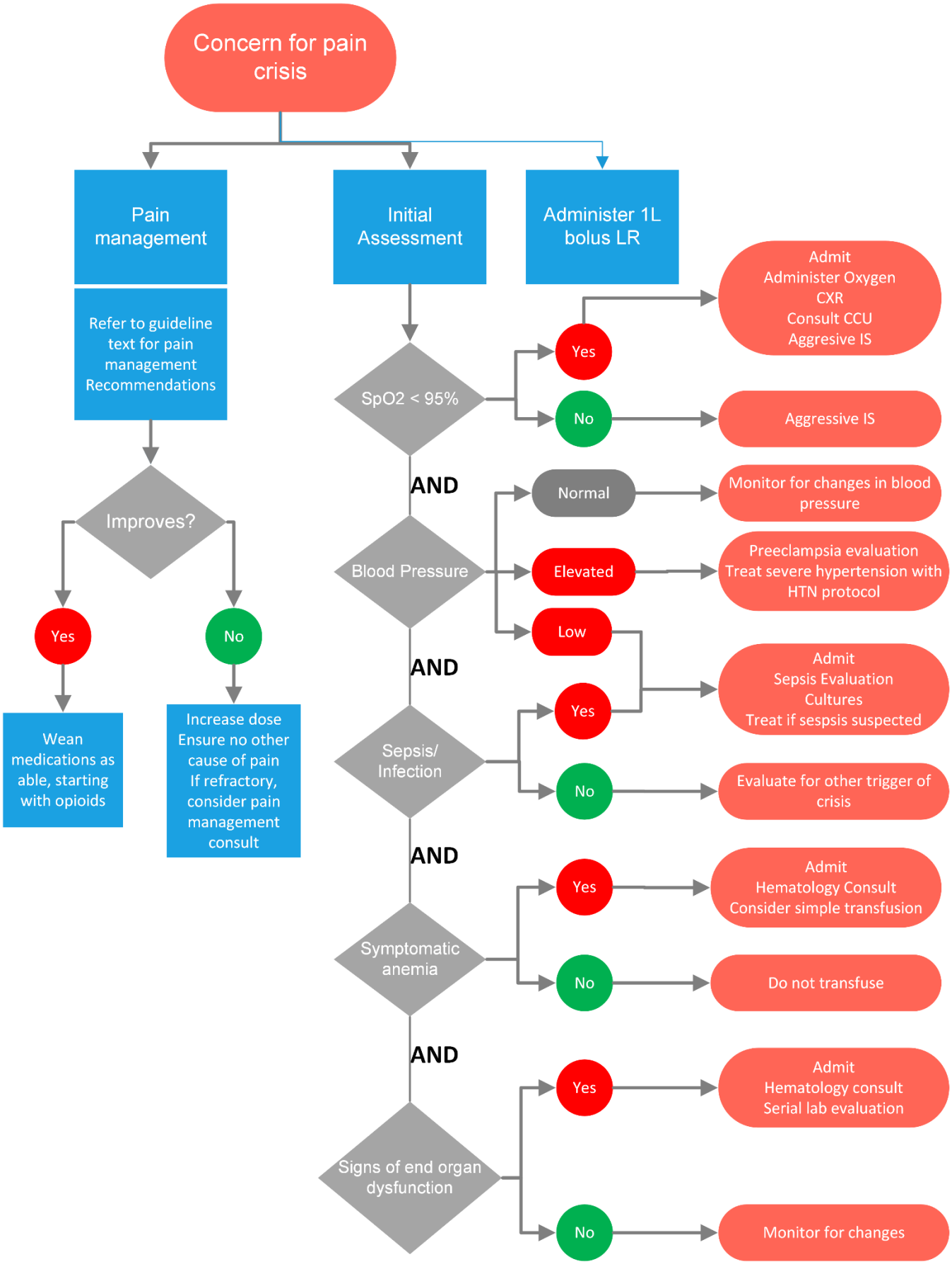
☐ Have a **low** threshold for hospital admission for patients with persistent VOC requiring additional pain medication, frequent crises, and/or signs of end-organ dysfunction

Table 2. *Pain management for sickle crisis in pregnancy*[2]

Medication	Oral	Parenteral	Side effects	Teratogenicity
Morphine	10–30 mg every 3–4 h	5–10 mg every 2–4 h	Sedation, constipation, pruritus, and respiratory depression	No human reports of birth defects. NAS
Hydromorphone	7.5 mg every 3–4 h	1.5 mg every 3–4 h	Sedation, constipation, pruritus, and respiratory depression	No human reports of birth defects. NAS
Codeine	15–60 mg every 3–6 h	NA	Sedation, constipation, pruritus, and respiratory depression	Reports in human pregnancies inconsistent. NAS
Ibuprofen[b]	600–800 mg every 6–8 h	NA	Dyspepsia, GI bleeding, nausea, and tinnitus	Inconsistent reports suggest increased risk for miscarriage. Concerns for premature ductal closure.
Ketorolac[b]	10 mg every 4–6 h	30 mg every 6–8 h	Headache, nausea, abdominal pain, dyspepsia, and GI bleeding	Concerns for premature ductal closure
Acetaminophen	300–1000 mg every 4–6 h	NA	Nausea, rash, headache, and hepatotoxicity	Considered safe although some inconsistent reports of association with childhood asthma or cryptorchidism

NAS: neonatal abstinence syndrome.
[a] Data on cost obtained from drugstore.com and does not necessarily reflect inpatient costs.
[b] Can consider occasional use in the second trimester as an adjuvant to opiate treatment (not first line).

Figure 1. *Management of Pain Crisis*[2]



Inpatient care

Antepartum patients should be admitted to either Antepartum service or ICU depending on patient stability.

- ☐ Rest
- ☐ VTE Prophylaxis (Lovenox 40 mg daily)
- ☐ Strict Intake and Output monitoring (due to risk for pulmonary edema)
- ☐ Oxygen supplementation if SpO2 ≤95%
- ☐ Complete infectious work up if not done
- ☐ Pain Management
  - First line is a trial of **Ketorolac** 15-30mg q6 hr in the second trimester (and no other contraindications such as peptic ulcer disease or chronic kidney disease)
  - Acetaminophen 650 mg q6H PO or 1g IV (contraindicated if AST/ALT significantly increased)
  - **Opioids** should not be withheld
    - Chronic opioid regimen (if applicable) should be continued, and additional opioids may still be necessary
    - IV Morphine sulfate loading dose 4 mg IV plus an **antihistamine** such as Hydroxyzine 50 mg IM (favor) q6 hr PRN or Benadryl 25-50 mg IV q6 hr PRN
    - Maintenance during acute phase of Morphine sulfate 1-2 mg IV q4 hrs or low-dose PCA pump
      - Plan for 24-48 hours of basal and demand and then change to 24-48 hours of demand only
  - Sedation assessments should be performed frequently for patients receiving narcotics, especially if other sedating agents are co-administered.
  - Avoidance of agents with codeine (Tylenol 3 or 4) for postpartum people who are breastfeeding
- ☐ Prevent/Treat constipation
  - Daily stool softener, laxatives as needed
- ☐ Antibiotics if an infection is suspected
- ☐ Blood transfusion only if complicated VOC (Table 3)
- ☐ Exchange transfusion indications (Table 3)

Table 3. Indications for therapeutic blood transfusion

Consult hematology and consider a simple vs. an exchange transfusion if patient presents with any of the following
Hemodynamic instability
Acute chest syndrome
Acute stroke
High-output cardiac failure
Multi-organ failure
Symptomatic anemia (dyspnea, marked fatigue)
Severe, refractory pain crisis (>10 days)
Persistence of preeclampsia sequelae despite delivery
Reticulocytopenia (common after Parvovirus B19 infection; can occur with any infection)

Acute chest syndrome (fever, tachypnea, chest pain, hypoxia, and radiologic chest infiltrates).
High-output cardiac failure (characterized by an elevated resting cardiac index beyond the normal range of 2.5–4.0 L/min/m^2).

Criteria for hospital discharge

- ☐ Resolving crisis
- ☐ Adequate pain control on PO medication
- ☐ Treatment of infection if present
- ☐ Reassuring Fetal status

Follow up plan

a. OB visits
    i. Antepartum
    ii. Postpartum – contraception: progestin IUDs, progestin-only OCPs owing to risk of VTE with combined hormonal methods containing estrogen
b. Hematology visit
c. Pain control – transition to Hematology

References

1. Sinkey RG, Ogunsile FJ, Kanter J, Bean C, Greenberg M. Society for Maternal-Fetal Medicine Consult Series #68: Sickle cell disease in pregnancy. *Am J Obstet Gynecol*. 2024;230(2):B17-B40. doi:10.1016/j.ajog.2023.10.031
2. Parrish MR, Morrison JC. Sickle cell crisis and pregnancy. *Semin Perinatol*. Aug 2013;37(4):274-9. doi:10.1053/j.semperi.2013.04.006
3. Sosa IR, Udden MM. Sickle Cell Disease and Pregnancy. John Wiley & Sons, Ltd; 2018:791-801.
4. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of Sickle Cell Disease: Summary of the 2014 Evidence-Based Report by Expert Panel Members. *JAMA*. 2014;312(10):1033-1048. doi:10.1001/jama.2014.10517