Sickle Cell and Pregnancy Protocol (1)

Preconception Visit

General Considerions

- **ALL** women should be screened for hemoglobinopathies regardless of race or ethnicity
- **Acute Complications:** Vasocclusion from deformed RBCs in microcirculation > Pain Crisis and Acute Chest Syndrome
- **Chronic Complications:** Long term effects from intravascular hemolysis and vascular dysfunction > pulmonary hypertension, renal disease, and leg ulceration
- 50% of pregnancies associated with SCD affected by vaso-occlusive syndromes

Future Pregnancy:

- Recommend reviewing the risks of pregnancy affected by SCD (see table)
- Establish reproductive life plan
- Discontinue hydroxyurea, ACE-I, or ARBs at least 3 months prior to pregnancy
- Iron chelating therapy should be discontinued prior to pregnancy
- **Initiate 5mg folic acid daily**
- Establish carrier status of partner; **up to a 50% risk of having an affected child if father carries SCT**
- ECHO, pulmonary sx screen, baseline Cr and urine protein screen at least 1 year from desired pregnancy

Contraceptive Counseling:
WHO classification

- Category 1 for progestin-only contraceptive methods
- Category 2 for combined hormonal contraceptive methods

Table 1. Complications of pregnancy among women with SCD

Diagnosis	OR*	95% CI	*P*
Thrombotic complications			
Deep vein thrombosis	2.5	1.5-4.1	< .001
Pulmonary embolus	1.7	0.9-3.1	.08
Cerebral vein thrombosis	4.9	2.2-10.9	< .001
Stroke	2.0	0.6-6.9	.25
Infectious complications			
Asymptomatic bacteria	6.8	3.1-14.9	< .001
Genitourinary tract infection	2.3	1.9-2.7	< .001
Pyelonephritis	1.3	1.0-1.8	.05
Pneumonia	9.8	8.0-12.0	< .001
Systemic inflammatory response syndrome	12.6	2.1-13.6	.01
Sepsis	6.8	4.4-10.5	< .001
Postpartum infection	1.4	1.1-1.7	< .001
Fetal complications			
Intrauterine growth restriction	2.2	1.8-2.6	< .001
Intrauterine fetal death	1.1	0.8-1.7	.62
Preterm labor	1.4	1.3-1.6	< .001
Obstetric complications			
Gestational hypertension and preeclampsia	1.2	1.1-1.3	.01
Eclampsia	3.2	1.8-6.0	< .001
Gestational diabetes mellitus	1.0	0.8-1.2	.74
Antepartum bleeding	1.7	1.2-2.2	< .001
Postpartum hemorrhage	0.5	0.3-0.6	< .001
Abruption	1.6	1.2-2.1	< .001

Adapted from Villers et al.[12]
CI indicates confidence interval.
*ORs are listed for women with SCD compared with women without SCD.

Sickle Cell and Pregnancy Protocol (2)

Initial Prenatal Visit

- Confirm diagnosis of SCD
- **Assess partner carrier status**
- Assess pain crisis history, night time symptoms
- Medication review - discontinue hydroxyurea and assess pain management needs, if any
- Baseline blood pressure
- Screen for sickle nephropathy
- Screen for nighttime hypoxia*
- Initiate Folic acid 5mg daily
- Initiate ASA 81mg at 12 weeks
- Assess vaccination status for encapsulated organisms: penumoccocal, meningococcal, haemophilus influenzae

VTE Prophylaxis:

- Consider for women without prior VTE
- 6 weeks VTE ppx after cesarean delivery

Labs & Studies

CBC
Type and screen
***Red cell phenotype if outside system**
Hemoglobin electrophoresis
Quantification of Hgb A2 levels
Ferritin level
Reticulocyte count
LDH
HELLP labs/or CMP
Urinalysis and Urine Culture
Urine protein screen
Hepatitis B and C screening
ECHO (within one year of pregnancy > increased R tricuspid jet velocity should be referred to cardiology/pulmonaology for possible R heart catherterization)
Retinal evaluation

Referral to Hematology
Referral to Maternal-Fetal Medicine and Genetics

Special Considerations: Transfusion

- Hgb goal >6 to prevent abnormal fetal oxygenation and IUFD
- Transfusion goals at a higher threshold may be required for ACS or obstetric indications
- Co-management with Hematology to establish simple and exchange transfusion criteria

Monthly Labs & Studies

CBC
CMP
Urinalysis and Urine Culture
Quantification of Hgb A2 levels

ECHO as indicated per Cardiology and symptoms

Sickle Cell and Pregnancy Protocol (3)

Second Trimester

- Targeted anatomy US at 18-20 weeks
- Anticipatory guidance counseling regarding NAS if patient has high opioid needs in pregnancy

Third Trimester

- Most pain episodes occur in the third trimester
- Growth US q4weeks starting at 28 weeks
- Antenatal testing at 32-34 weeks
- Anesthesia Consult; avoid GETA

Monthly Labs & Studies

CBC
CMP
Urinalysis and Urine Culture
Quantification of Hgb A2 levels

Repeat ECHO as indicated per Cardiology and symptoms

***Continued co-management of lab indices with established Hematology specialist is preferred. UNC Hematology recommends monthly follow up with their team.**

Delivery Considerations

- Delivery at a tertiary care center with adequate blood bank
- Vaginal delivery favored with cesarean for routine obstetrical indications
- Avoid prolonged second stage of labor
- Transfusion goal Hgb 10-11 prior to cesarean delivery if possible**
- Avoid cell saver
- Delivery at 39 weeks encouraged in the absence of other comorbidities

VTE Prophylaxis:

- 6 weeks VTE ppx after cesarean delivery

Sickle Cell and Pregnancy Protocol (4)

Special Considerations: Vaso-occulsive Crisis

- Develops in 7-10% of pregnancies complicated by SCD
- Manage at a hospital with ability to provide ICU level care with Hematology available for co-management

Initial evaluation should include the following

- Detailed history and physical to determine precipitating cause
- CXR to assess for infiltrate if pulmonary symptoms or hypoxia
- Low threshold for head CT imaging if neurologic sequelae
- IVF support
- Supplemental oxygen
- NAIDs (GA dependent), narcotics for pain management
- Maintain normal body temperature
- Evaluate for need for simple or exchange transfusion

Postpartum

Lactation:

- Breastfeeding encouraged
- Encourage aggressive pulmonary toilet
- Hydroxyurea excreted in breastmilk; joint decision making with patient on breastfeeding goals and need to restart hydroxyurea
- Opioids can be continued during breastfeeding but risks should be discussed
- Painful crisis occur in the postpartum period for 7-25% of women

Contraceptive Counseling: WHO classification

- Category 1 (no restrictions) for progestin-only contraceptive methods
- Category 2 (generally use, but follow up may be needed) for combinded hormonal contraceptive methods

Notes:

*Importance of focus and clarity with instructions
*Screening for nighttime hypoxia by pulse oximetry can be arranged with home O2 services

References

1.Asare EV, Olayemi E, Boafor T, et al. Third trimester and early postpartum period of pregnancy have the greatest risk for ACS in women with SCD.*Am J Hematol.*2019;94(12):E328-E331.
2.Asma S, Kozanoglu I, Tarim E, et al. Prophylactic red blood cell exchange may be beneficial in the management of sickle cell disease in pregnancy.*Transfusion.*2015;55(1):36-44.
3.Boafor TK, Olayemi E, Galadanci N, et al. Pregnancy outcomes in women with sickle-cell disease in low and high income countries: a systematic review and meta-analysis.*BJOG.*2016;123(5):691-698.
4.Boga C, Ozdogu H. Pregnancy and sickle cell disease: A review of the current literature.*Crit Rev Oncol Hematol.*2016;98:364-374.
5.Naik RP, Lanzkron S. Baby on board: what you need to know about pregnancy in the hemoglobinopathies.*Hematology Am Soc Hematol Educ Program.*2012;2012:208-214.
6.Patil V, Ratnayake G, Fastovets G. Clinical 'pearls' of maternal critical care Part 2: sickle-cell disease in pregnancy.*Curr Opin Anaesthesiol.*2017;30(3):326-334.
7.Shirel T, Hubler CP, Shah R, et al. Maternal opioid dose is associated with neonatal abstinence syndrome in children born to women with sickle cell disease.*Am J Hematol.*2016;91(4):416-419.
8.Zia S, Rafique M. Comparison of pregnancy outcomes in women with sickle cell disease and trait.*J Pak Med Assoc.*2013;63(6):743-746.
9.Sheth S, Licursi M, Bhatia M. Sickle cell disease: time for a closer look at treatment options?*Br J Haematol.*2013;162(4):455-464.