Frimley Health
NHS Foundation Trust

Sickle Cell Disease in Pregnancy (SCD)

Key Points

- This document is the protocol for the care and management of women with Sickle Cell Disease in Pregnancy for Frimley Health NHS Foundation Trust
- Sickle cell disease (SCD) is a group of inherited - autosomal recessive disorders caused by the 'sickle' gene, which affects haemoglobin structure
- All women with Sickle cell disease are seen in joint Obstetric Haematology clinic as well as for urgent review by the MDT on acute admissions
- At each antenatal appointment, healthcare professionals should offer consistent information and clear explanations, providing women with the opportunity to discuss issues and ask questions in order to facilitate informed choice and decisions.

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Abbreviations

ABG	Arterial Blood Gas
ACS	Acute Chest Syndrome
CS	Caesarean Section
CXR	Chest X-ray
HVS	High Vaginal Swab
IVF	In Vitro Fertilization
LMWH	Low Molecular Weight Heparin
LVS	Low Vaginal Swab
MC&S	Microscopy, Culture and Sensitivities
MDT	Multidisciplinary Team
MSU	Mid-Stream Urine
PE	Pulmonary Embolism
SCD	Sickle Cell Disease
TEDS	Thrombo-Embolus Deterrent Stockings
VBAC	Vaginal Birth after Caesarean Section
VTE	Venous Thromboembolism

Inclusivity Note

Within this document we use terms such as woman and women's health. However, it is important to acknowledge that it is not only people who identify as women for whom it is necessary to access women's health and reproductive services in order to maintain their gynaecological health and reproductive wellbeing. Gynaecological and obstetric services and delivery of care must therefore be appropriate, inclusive, and sensitive to the needs of those individuals whose gender identity does not align with the sex they were assigned at birth.

At Frimley Health we encourage our patients to tell us their preferred pronouns and we would be happy to use these at all patient encounters. We like to use a gender-additive approach meaning we use gender-neutral language alongside the language of womanhood, in order to ensure that everyone is represented and included, e.g., breastfeeding and chest feeding. If there are terms our patients would like to use, please encourage them to tell us so we can make them feel comfortable and confident in our care.

Contents

1.0 Purpose

This document is the protocol for the care and management of women with Sickle Cell Disease in Pregnancy for Frimley Health NHS Foundation Trust. It replaces any previous protocol and procedure documents. This protocol should be read in conjunction with the NICE Antenatal Care guideline and the British Society of Haematology: Management of sickle cell disease in pregnancy guideline - 2021 which has replaced RCOG Green top guideline No. 61.

2.0 Introduction

Sickle cell disease (SCD) is a group of inherited autosomal recessive disorders caused by the 'sickle' gene, which affects haemoglobin structure. The consequence of polymerisation of the abnormal sickle haemoglobin in low oxygen conditions leads to the formation of rigid and fragile sickle-shaped red cells. These cells are prone to increased breakdown, which causes haemolytic anaemia and the sickle-shaped red cells which do not flow through blood vessels easily, causing blockage (vaso-occlusion) in small vessels, leading to most of the clinical features, including acute painful crises.

The term SCD includes sickle cell anaemia (HbSS) and the heterozygous conditions of haemoglobin S and other clinically abnormal haemoglobins. These include combination with haemoglobin C (giving HbSC), combination with beta thalassaemia (giving HbSB thalassaemia) and combination with haemoglobin D, E or O-Arab. All of these genotypes will give a similar clinical phenotype of varying severity and as such should have the same level of vigilance and care as for those with HbSS.

Haemoglobin S combined with normal haemoglobin A, known as sickle trait HbAS, is asymptomatic, except for a possible increased risk of urinary tract infections and microscopic haematuria, and therefore is not considered further in this guideline as these patients are treated as per low-risk antenatal patients. These women still require screening and to assess if the father of the child also has a haemoglobinopathy gene, in order to consider the risk of the baby having a major haemoglobinopathy condition, and to potentially offer foetal pre-natal diagnostic tests.

SCD is one of the most commonly inherited conditions worldwide with 300,000 born with the condition each year. 75% of these births occur in the continent of Africa, however, there is an increasing prevalence of SCD in Europe and the United States. The UK has the largest population of patients with SCD compared to the rest of Europe with approx. 15,000 affected individuals and 300 babies born with the condition each year. The highest prevalence is amongst Black Caribbean, Black African and Black British women.

There are approximately 110–200 pregnancies in women with SCD per year in the UK. Pregnancy in women with SCD is associated with higher risk of mortality and morbidity.

Labour increases the risk of triggering a sickle cell crisis in women with sickle cell disease.

The purpose of this guideline is to describe the management of pregnant women with sickle cell disease. It includes antenatal, intrapartum and postnatal management.

3.0 Genetic Testing

Screening and Prenatal Diagnosis for Sickle Cell Disease and its variants is not in the remit of this guideline and can be viewed in detail in the 'Antenatal Sickle Cell & Thalassaemia Screening Programme protocol guideline' -March 2021.

4.0 Factors affecting pregnancy, labour and the puerperium

Maternal

Increased risk of

- Infection – UTI, pneumonia, endometritis
- Acute chest syndrome – fever, tachypnoea, pleuritic chest pain
- Thromboembolism – (1.5-5x higher risk of VTE in SCD)
- Pre-term labour,
- Pre-eclampsia and Pregnancy Induced Hypertension
- Maternal death
- Exacerbation of anaemia
- Acute Painful crises
- Admission to ITU/High Dependency Care
- Blood transfusion

Fetal

Increased risk of

- miscarriage
- intra-uterine growth restriction and low birth weight
- prematurity
- fetal distress
- stillbirth/neonatal death
- meconium-stained liquor
- fetal distress in labour and Emergency Caesarean section (CS)

5.0 Preconception Care

A comprehensive annual review under haematology is part of recommended routine care for all those with SCD. This should be established when the patient is under paediatric care and therefore before pregnancy. A discussion of reproduction, pregnancy and contraceptive options as well a review of chronic complications should be part of this annual review, however, preconception clinics with a specialist Obstetricians or Haematologist should be available and accessible. Formal annual reviews are offered to all known patients with sickle cell anaemia via the Haemoglobinopathy Co-ordinating Centres.

The following table shows the conditions which should be reviewed and what investigations should be done:

Chronic complication	Action to be taken
Renal disease and hypertension	Blood pressure, protein/creatinine ratio (PCR) >30 mg should be investigated to exclude non-sickle causes. Anti-hypertensive should be started for persistent blood pressure over 130/80 mm Hg
Pulmonary hypertension	Echocardiography if not performed within 1 year or if symptomatic. Abnormalities should be discussed with a cardiologist
Chronic lung disease	Oxygen saturations on all women. Sleep studies and pulmonary function tests if indicated
Avascular necrosis	Review hip complications which may worsen during pregnancy
Stroke	If history of previous stroke, consider role of transfusion during pregnancy if not already receiving this. Any sickle patient with a previous history of stroke would be likely to be already established on a regular red cell exchange programme.
Chronic pain	Women on long-term opioids should be referred to a chronic pain clinic for assessment and managed by pain specialist during pregnancy

Ideally, they should have preconception care with a haematologist and contraception by their GP before planning for pregnancy

6.0 Antenatal management

Mainstay of management is the monitoring and prevention of general and SCD specific complications.

- Antenatal care should be undertaken at a specialist Sickle Cell disease centre/tertiary centre. Many women however choose to deliver at Frimley Health. Each woman is then discussed at the regional Haemoglobinopathy service. If there are specific obstetric concerns then we may advise transfer to the Tertiary Centre.
- If not booked locally, it is possible that a woman with SCD may present in an emergency therefore this guideline explains the minimum care to be provided.
- The care of women with SCD should be done in conjunction with NICE antenatal care guidance. https://www.nice.org.uk/guidance/ng201/chapter/Recommendations
- All women with Sickle cell disease are seen in joint Obstetric Haematology clinic. Multidisciplinary team approach is vital, including a consultant obstetrician and an experienced haematologist to give individualised care tailored to the woman's history and disease severity
- The woman should book for antenatal care as early as possible and should be seen in antenatal clinic before the end of the 1st trimester
- At the first visit:
    - Full Medical History should be sought including:
        - Frequency, nature and pattern of sickle cell crises, ITU admissions, and their usual analgesic requirements
        - Infections and Routine sickle cell crisis management
        - Transfusion history
        - Acute/chronic complications
        - History of atypical red cell antibodies
        - Where is their care usually obtained and under which Haematologist
    - Ask about difficulties in cannulation
    - Full clinical examination – e.g., BP to screen for hypertension
    - Refer for full ophthalmological examination if not checked in the last year.
- A woman with sickle cell disease must be seen at a minimum
    - Every 4 weeks until 28 weeks then
    - Every 2 weeks until delivery
    - FBC, BP, saturations and urinalysis/MSU should be undertaken at each visit
- Target BP should be 130/80 and medication started if consistently over this
- SCD can increase incidence of chronic kidney disease. If evident, woman needs monthly U&Es
- Arrange an appointment at the anaesthetic clinic
- If anaemic, give iron supplementation only if Ferritin >50ug/L and after discussion with the Haematology Consultant
- Red cell antibodies should be checked at booking, 28 weeks, 34 weeks, or before each transfusion if necessary
- Maternal echocardiogram to exclude pulmonary hypertension and check cardiac function, particularly in those with iron overload.
- CTG from 26/40 weeks
- Antihistamine, laxatives and antiemetics as required
- Information and education should be given to patient at all opportunities. This should include crisis prevention measures such as rest, warmth and avoidance of dehydration and infections.

6.1 – Medication Review

- Folic acid 5mg daily is mandated for patients with SCD in view of their haemolytic anaemia that puts them at increased risk of folate deficiency.
- Vitamin D 25mcg/1000 units daily is recommended as deficiency is common in patients with SCD.
- Penicillin prophylaxis is recommended throughout the pregnancy. Patients with SCD are at risk of infection in particular from encapsulated bacteria. There is minimal evidence to support the use of prophylactic antibiotics in pregnancy but in view of hyposplenism and increased of pneumonia antibiotic coverage is recommended
    - Phenoxymethylpenicillin (Pen V) 500 mg OD and maximum 500 mg BD (OD could be an option to improve patient compliance).
    - Erythromycin 500mg BD if penicillin allergic
- Vaccinations should be kept updated as per national recommendations for SCD (Meningitis C, Hepatitis B and Haemophilus influenza) and should include annual flu vaccination and the Pneumococcal vaccine within the last 5 years
- Covid vaccination is strongly advised due to their high-risk status
- Due to increased risk of PET and PIH, aspirin 150mg OD should be given from 12/40 to 36/40
- Stop hydroxycarbamide, Iron chelators and ACE-Inhibitors/ARBs preferably 3 months prior to conception
    - If a woman becomes pregnant whilst on any of these medications, they should be stopped as soon as possible and safer alternatives prescribed if available.
    - Decision about management of such cases should be with haematologists.
    - A detailed anomaly scan should be performed by a Fetal Medicine specialist if exposed to any of the above in pregnancy and also review by MDT with haematologist for further management
- Paracetamol and dihydrocodeine first line for pain relief. NSAIDs used with caution <12/40 and avoided post 31/40. Referral to Pain clinic and haematologist may be necessary for appropriate choice of pain management.
- If iron deficiency is suspected, confirm by iron studies before prescribing iron medication
- General practitioner / haematologist and Obstetrician prescribe folic acid 5mg and Vitamin D throughout pregnancy and preconception except if known to haematologists.
- Same is for penicillin prophylaxis in view of ongoing care of sickle cell disease

6.2 Ultrasound

- Viability scan between 7-9 weeks
- Ultrasound growth scans should be performed every 2-4 weeks from 24 weeks
- Consider uterine artery Dopplers at 24 weeks

6.3 – Thromboembolism

- A risk assessment should occur at the first appointment, any admission, labour and repeated early in postnatal period.
- As per ‘Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium Green-top Guideline’ No. 37a LMWH should be considered from 28/40 until 6/52 postnatal.
- If any of the following are present, LMWH should be started from the beginning of pregnancy
    - Personal or family history of unprovoked VTE
    - Age >35yrs
    - Obesity BMI >30

  - Parity >3
  - Smoker
  - Varicose Veins
  - Multiple Pregnancies
  - IVF
- LMWH should be prescribed and given on any admission to hospital.
- Regarding VTE, see VTE guidelines

6.4 Timing of Birth

Women with SCD should be offered elective birth between 38-40 weeks due to the increased risk of perinatal morbidity in the later stages of pregnancy.

6.5 Mode of Delivery

Vaginal delivery is encouraged. Caesarean Section should only be offered for Obstetrics reasons.

6.6 Blood Transfusion

Transfusion is required for severe anaemia (below baseline Hb) and to reduce sickle related complications. Blood needs to be extended cross matched, including CMV negative, also Kell and Rh matched, also needs to be HbS negative and ideally less than 7 days old . Blood Bank should be made aware specifically that the patient has sickle cell anaemia. They will ensure an extended red cell phenotype is kept on file and will issue the closest possible matched blood available. Transfusion should be weighed up against alloimmunisation and risk vs. benefit discussed with the patient. Transfusion is NOT given just for chronic anaemia.

7.0 Management of Acute Pain crisis

Acute pain is the most common complication of SCD in pregnancy affecting up to 57% of women. A pain plan should be made in advance during the first MDT ANC appointment.

- Management under MDT. INFORM senior obstetrician, anaesthetist and haematologist of admission
- Prompt recognition of crisis is important. Symptoms include bone pain (usually arm or leg), joint pain (single or multiple joints), chest pain and abdominal pain
- Reverse likely cause, e.g., dehydration due to vomiting, infection, VTE
- Monitor saturations regularly – 2 hourly
- If Sats <95% then medical/haematological review required. THINK Acute Chest Syndrome or PE
  - Facial or nasal oxygen if Sats <95%
- LMWH during admission
- Admission is warranted if:
  - Pain not settled with simple analgesia
  - Fever
  - Atypical pain
  - Short of Breath
  - Chest Pain
- Mild Pain – Hydration, Warmth, Paracetamol and Codeine
- Moderate to Severe Pain –
  - Analgesia should be administered within 30 mins of arrival and controlled within 60 mins.
  - Morphine /Diamorphine/oxycodone may be required.
  - Avoid Pethidine due to risk of seizures
  - MEOWS and pain score every 1-2 hours
  - Monitor fluid balance and hydrate with IVI as needed. Review 12 hourly
  - Give Entonox as appropriate
- Rule out infection – CXR, MSU, full septic screen

- The woman's urine must be checked daily for evidence of proteinuria. Urine and/or blood cultures should be sent if there are signs of infection.
- Low threshold for antibiotics. Give if fever or high suspicion of infection
- Oral or IV fluids to ensure Euvolemia

8.0 Management of Acute Chest Syndrome (ACS)

If HbSS and unwell = Rule out sickle crisis first. Affects 10% of SCD women in Pregnancy. It is characterised by pain, fever and/or respiratory symptoms and a new pulmonary infiltrate on chest X-ray.

- Symptoms – shortness of breath, chest pain, cough
- Signs – increased respiratory rate, fever, signs of consolidation usually bilateral and basal, infiltrates on chest x-ray.
- N.B. chest may be clear on examination and chest x-ray features may be delayed by several hours)
- Differential diagnosis – pneumonia, pulmonary embolus, fluid overload, opiate toxicity, hypoventilation due to pain.

- Admit under joint care of obstetrics and haematology in ITU or high dependency ward and not labour ward. INFORM Haematology Consultant. Needs urgent haematology review.
- Keep woman warm
- Perform ABG. Main differential of ACS is PE
    - If PE is suspected – use TEDS and prescribe therapeutic doses of LMWH until this is excluded
- Fluid balance chart and increase hydration either orally or intravenously
- Basic management will include prompt pain relief, incentive spirometry and treatment of bacterial or viral infection.
- Perform full infection screen (MSU, HVS, LVS, Blood cultures, CXR and sputum MC&S) and prescribe antibiotics as required.
    - It may mimic bacterial pneumonia; in practice it is not necessary to differentiate between the two as all patients with suspected acute chest syndrome should be treated promptly with antibiotics.
- Ideally blood transfusion and exchange transfusion should be performed in tertiary centre, however in emergency situation this can be performed on site with recommendation and approval by tertiary team.
- Crisis is not an indication for delivery. Any delivery decision should be made purely on obstetric grounds. If at all possible, **delivery should be postponed** until after the crisis has resolved.

9.0 Acute Stroke Management

- Acute Stroke can be either haemorrhagic or ischaemic in SCD. Acute neurological impairment will require urgent exchange transfusion and a medical review as an emergency. The appropriate imaging for prompt diagnosis should be promptly requested as for non-pregnant women, i.e., (CT brain, MRI brain etc). Urgent haematology review will be required including consideration for exchange .

Care of acute chest syndrome and stroke patients should be led by regional maternal medicine network team and should be known to local haematologist and maternal medicine team.

Mode and timing and place of delivery is to be informed by MDT which should include maternal medicine, anaesthetics, and haematology team.

10.0 Management of labour and birth

Avoid long labour due to increased risk of intrapartum crisis. Inform MDT team and on-call haematology doctor on arrival of patient into hospital with labour

- Labour and delivery should occur on Labour Ward after discussion with tertiary centre
- FBC, Group and Save, U+Es, LFT, clotting studies, HbS%(requested as a Haemoglobinopathy screen) , and reticulocytes. This can be requested as ‘acute sickle admission panel ‘ on Epic following discussion with haematologist.
- X-match 2 units red cell blood
- Lower threshold for performing septic screen > 37.5^{o}C. Prophylactic antibiotics not indicated
- MSU, HVS
- Oxygen saturation. Avoid hypoxia – monitor O_2 saturations and give O_2 by mask with reservoir bag if saturations < 95%
- Keep patient warm
- Avoid dehydration and monitor urine output
- Augment immediately in case of PPROM due to increased complications with infection if > 34/40
- Prolonged labour can cause a crisis – if progress is slow, expedite delivery as appropriate
- Continuous electronic fetal monitoring – high incidence of IUGR and fetal hypoxia
- All women should have an IV infusion of 1 litre 8 hourly with close monitoring of fluid balance throughout the labour
- Any temperature above 37.5 ^{o}C should be investigated and broad-spectrum antibiotics considered.
- Advise active management of the third stage

10.1 Analgesia

- All forms of labour analgesia may be used
- AVOID pethidine due to risk of seizures
- Avoid general Anaesthetic if possible

11.0 Postnatal management

Crisis in the postnatal period remains increased with 21-25% of women with SCD having crisis at this time with common postoperative complications including UTI, endometritis, sickle cell crisis. Those who have had a general anaesthetic have an increased risk of crisis postnatally.

- Patients must remain on the Labour Ward Recovery Ward for at least 24 hours and receive high dependency care
- There should be a daily review by the Haematology team during this time
- Discharge from the Labour Ward Recovery Unit or the postnatal ward must be sanctioned by a consultant.
- Record vital signs and oxygen saturations every 4 hours until the woman is mobile. Observe for signs of sickling, infection, thromboembolism, pulmonary oedema.
- Encourage early mobilisation
- Ensure the woman is kept warm

- Maintain good hydration and oxygenation for at least 24 hours. Give intravenous fluid as required
- If oxygen saturations fall <92%, a haematologist and anaesthetist must be informed as ventilation continuous positive airway pressure (CPAP) may be necessary.
- Prompt investigation of fevers and early treatment with antibiotics is essential.
- Reassessment of VTE risk should happen early in the postnatal period. As per Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium Green-top Guideline No. 37a LMWH should be given for 6 weeks postpartum independent of any further risks unless there is active excessive bleeding.
- Anti-embolism stockings should be worn throughout the admission.
- Breastfeeding should be encouraged
- Adopt good management of pain. NSAIDs are routinely administered in the postpartum period and can be used during breastfeeding. Avoid precipitants of pain. Routine consultation with Infant Feeding Team to ensure good position, latch and to rule out any problems eg tongue tie which may cause nipple pain/trauma
- Have a low threshold for involvement of the critical care outreach team or ITU consultant if there are signs of physiological compromise.
- Care to be undertaken in labour ward until deemed fit for postnatal ward or discharge home.

11.1 Contraception

Given the health risks of an unintended pregnancy, counselling about contraception is an important component in the care of women with SCD and appropriate advice should be conveyed to the woman's primary care workers.

All progesterone-only preparations, including the progesterone-only pill, injectable contraceptives and the levonorgestrel intrauterine system (LNG-IUS) can be used and indeed there is some evidence of clinical benefit in the use of progesterone in SCD. Long-acting reversible contraception is preferred. Consider insertion of IUS or implant prior to discharge on the postnatal ward.

Both the Copper Intrauterine Device (due to the potential risk of increased blood loss) and the combined oral contraceptive pill (due to increased risk of thrombosis) are UKMEC category 2. They can be used if the benefit outweighs the risk and other forms of contraception are contraindicated.

12.0 Neonatal management

- Babies with a major haemoglobinopathy will not be affected until fetal (HbF) haemoglobin concentrations are lowered at about 3 months
- Neonatal opiate withdrawal may be a problem where the mother has been prescribed strong opiates for crisis management for at least a week prior to delivery. Naloxone is contraindicated if the mother has had regular opiates

Send a routine blood spot for screening. If the parents are anxious for an early result, send an additional single blood spot on day 1.

13.0 Communication

If there are communication issues (e.g., English as a second language, learning difficulties, blindness/partial sightedness, deafness) staff will take appropriate measures to ensure the patient (and her partner, if appropriate) understand the actions and rationale behind them. Trust interpreter guidance should be considered

14.0 Incident management

Any adverse incident will be reported via the internal RL system for investigation, management and learning.

15.0 References

1 Royal College of Obstetricians and Gynaecologists Green top guideline 61 Management of sickle cell disease in pregnancy July 2011

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5 Oteng-Ntim E, Ayensah B, Knight M, Howard J. Pregnancy outcome in patients with sickle cell disease in the UK–a national cohort study comparing sickle cell anaemia (HbSS) with HbSC disease. Br J Haematol. 2015;169:129–37.

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8 Pamela Stratton, Standardizing care of those at great risk: the importance of sickle cell in pregnancy practice guidelines, British Journal of Haematology, 10.1111/bjh.17667, 194, 6, (950-953), (2021).

9 British Society for Haematology (2021) 'Management of sickle cell disease in pregnancy. A British Society for Haematology guideline', *British Journal of Haematology*, 194(6), pp. 980-995. Available at: https://doi.org/10.1111/bjh.17671

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Contributor(s):	Dr N. Philpott (Haematology Consultant)
Lead Director / Chief of Service:	B Sagoo (Chief of Service, O&G)
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This guideline has been registered with the Trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt, contact a senior colleague or expert. Caution is advised when using guidelines after the review date.
This guideline is for use in Frimley Health NHS Foundation Trust hospitals only. Any use outside this location will not be supported by the Trust and will be at the risk of the individual using it.

Version History

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1 (FPH)	2007	P Webb, A Kirkpatrick, J Frohlich	Final	
2 (FPH)	2010	R Morris	Final	
3 (FPH)	2012	D Aggarwal, C Akem-che	Final	
1.0	May 2022	A Catton, P Doncheva, O Eniola	Final	Adapted from FPH guideline for use across FHFT.
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Related Documents

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Guideline	NICE: Antenatal Care
Guideline	British Society of Haematology: Management of Sickle Cell Disease
Guideline (FH)	Antenatal Sickle Cell and Thalassaemia Screening Protocol