Whittington Health NHS

Sickle Cell Disease in Pregnancy

Subject:	Sickle Cell Disease in Pregnancy
Ratified By:	Maternity Clinical Guidelines and Audit Group
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Policy Executive Owner:	Clinical Director, WH ICSU
Designation of Author:	Miss A Kyei-Mensah, Dr B Davis, Dr S Makinde, Dr M Osmond
Name of Assurance Committee:	Maternity Clinical Guidelines and Audit Group
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Key Words:	Pregnancy, Sickle Cell Disease, Painful crisis

This guideline should be used in conjunction with the following guideline:

1. Sickle cell disease in adults

Version Control Sheet

Version	Date	Author	Status	Comment
1	2004	Miss Kyei - Mensah	Consultant Obstetrician	New guideline
2	2009		Consultant Obstetrician	Reviewed – No change
3	2012	Miss A Kyei-Mensah, Dr B Davis, Dr S Makinde Dr M Osmond	Consultant Obstetrician. Consultant Haematologist. Consultant Anaesthetist. SpR	New RCOG guidance
4	2015	Miss A Kyei-Mensah, Dr B Davis, Dr S Makinde,	Consultant Obstetrician. Consultant Haematologist. Consultant Anaesthetist.	Reviewed after RCOG Dec 2014 review – No change
5	2016	Miss A Kyei-Mensah, Dr B Davis	Consultant Obstetrician. Consultant Haematologist	Reviewed after UKOSS Sickle Cell outcome data published

➢ Criteria for use

All pregnant women with all genotypes of sickle cell disease, including HbSS, HbSC, HbSβ^{o} thalassaemia, HbSβ^{+} thalassaemia, HbSD^{Punjab}, HbSO^{Arab} , and other genotypes.

Pregnancies in women with sickle cell disease are high-risk; it is therefore essential that such women are managed with reference to this guideline.

➢ Background/ introduction

Aims:

1. To provide optimal care of women with sickle cell disease throughout pregnancy, during delivery and postnatally.

2. To ensure that women with sickle cell disease are aware of the genetic aspects and the availability of antenatal diagnosis as and where appropriate.

Pregnancy in women with sickle cell disease (SCD) is associated with:

Maternal complications:

<u>Sickle-related</u>

Severe anaemia
Increased frequency of sickle cell painful crisis
Increased frequency of acute chest syndrome (ACS)

<u>Pregnancy-related</u>

Pre-eclampsia (PET) and pregnancy-induced hypertension (PIH)
Venous thromboembolism
Antepartum haemorrhage
Infections: urinary tract (UTI), pyelonephritis, endometritis

- **Maternal mortality rate of 1 – 2 %**
- **6-fold increased risk of maternal mortality compared to non-sickle population**
- **ITU admission is required in 30% of HbSS and 11% of HbSC women**
- **Doubling of risk for the occurrence of PET**

Fetal complications:

Miscarriage
Fetal growth restriction (FGR)
Small for gestational age (SGA)
Prematurity
Stillbirth

- **Doubling of risk for prematurity**
- **4-fold increased risk of stillbirth in HbSS, 2-fold increased risk in Hb SC women**

- **Increased rates of:**

Meconium stained liquor
Fetal distress in labour
Emergency Caesarean section (CS)

➢ Clinical management

Ideally all sickle cell women should have received pre-pregnancy counselling. If this has not occurred, the patient must be referred urgently to the haemoglobinopathy counsellor as early in pregnancy as possible.

Medications should be reviewed preconceptually:

- Hydroxycarbamide should be stopped at least 3 months before conception
- ACE inhibitors and angiotensin receptor blockers should also be stopped before conception
- If a woman becomes pregnant whilst on any of these medications, they should be stopped as soon as possible and safer alternatives prescribed
- A detailed anomaly scan should be performed by a Fetal Medicine specialist if exposed to any of the above in pregnancy

These are high-risk pregnancies and all patients should be referred to the Obstetric Medicine Clinic as soon as possible. A viability scan should be performed at 7 - 9 weeks gestation for early dating. Routine scan and Down's screening should still be done at 11 - 13 weeks gestation.

<u>At the first visit</u>:

- Full medical history:
  -
  - pattern/frequency of crises, history of ACS, ITU admissions, usual analgesic requirements
  - transfusion history – some may have been previously managed on a transfusion programme, which can lead to iron overload and may affect the heart and liver
  - history of atypical antibodies to blood, which may make cross-matching difficult
  - The Haematologist looking after them will usually know these facts if the woman herself does not, or is unsure
- Ask about difficulties in cannulation
- Immunisation status – i.e. Pneumovax should be given every 5 years and flu vaccine given annually
- Full clinical examination – e.g. BP to screen for hypertension
- Haemoglobinopathy screen for patient and partner - if not already done
- Liver function tests (LFT's), urea & electrolytes (U&E's), serum creatinine and urate
- Hepatitis B & C screen if not already known
- Blood group/antibody screen – full red cell phenotype should be requested on form
- Rubella immunity
- Syphilis serology
- Mid-stream urine (MSU) to check for proteinuria and UTI – **MSU is required at every visit**
- Fasting blood sugar

Refer for full ophthalmological examination if not checked in the last year.

All sickle patients require antibiotic prophylaxis due to their functional hyposplenism and should be prescribed **penicillin V 250mg bd,** or **clarithromycin 250mg bd** if allergic to penicillin. This continues throughout pregnancy and post-delivery.

Red cell turnover is increased so prescribe **folic acid 5mg daily** – preconception if possible and continue throughout pregnancy.

➢ Antenatal Care Arrangements

Close co-operation between the Haematology and Obstetric Consultants is essential.

Patients should be referred to the Obstetric Medicine Clinic.

Refer patients to the Obstetric Anaesthetic Clinic to discuss analgesic requirements in labour.

Midwifery-led care is **not** appropriate. Women should be seen in the hospital antenatal clinic at a minimum of fortnightly intervals from 24 weeks gestation.

A clear management plan must be documented by the Obstetrician at review in the Obstetric Medical Clinic.

Monitoring investigations:

- Full blood count (FBC) for haemoglobin (Hb); urinalysis for protein and MSU for culture at each visit
- Serum ferritin – ***only prescribe iron if serum ferritin is low*** after discussion with the Haematology consultant.

  High serum ferritin concentrations may indicate iron overload from previous transfusions.
- Red cell antibodies at booking, 28 weeks, 34 weeks, or before each transfusion if necessary
- Uterine artery Doppler at 24 weeks (PET screening test)
- Serial growth scans every 2 - 4 weeks from 24 weeks gestation
- Maternal echocardiogram – to exclude pulmonary hypertension and check cardiac function, particularly in those with iron overload (these will be women who have previously been managed on a transfusion programme).

Antenatal care:

- Women with SCD should avoid conditions which can trigger crises – e.g. cold, dehydration, stress and exhaustion

- Hyperemesis should be treated promptly to avoid dehydration and sickle crises
- Low dose aspirin 75 mg daily should be prescribed from 8 weeks gestation to reduce the risk of developing PET

➢ Complications of Sickle Cell Disease

Management of Painful Crises

Acute sickle pain is the commonest complication, affecting 77% of HbSS and 27% of Hb SC women. There must be a multidisciplinary discussion to decide the best place to manage the woman using the standard protocol for painful crises. Currently the optimal area is Mary Seacole South Ward in the monitored area opposite the nurses' station. The antenatal or Labour Ward may be indicated depending on the gestation and presence of additional obstetric factors.

Inform the Sickle Cell Clinical Nurse Specialist (normal working hours only) and the on-call Haematology Registrar or Haematology Consultant (available on call 24 hours a day, 7 days a week).

Severe sickle pain is usually treated with Morphine, Diamorphine, or Oxycodone and most patients will have individualised protocols for management, which can be accessed electronically in the "SICKLE CELL PROTOCOLS" folder on the I drive [I:\Doctors' Shared Folder\Junior Doctors Shared Folder\A&E\SICKLE CELL PROTOCOLS].

. Opiates can be given orally (PO), intramuscularly (IM), or intravenously (IV) – patients should be monitored with hourly observations if given IV.

N.B. - avoid Entonox outside labour
- Pethidine is **NOT** to be used for sickle pain due to risk of seizures

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. A chest x-ray should be done if there is chest pain or shortness of breath. Initial investigations include FBC, U&E's and LFT's.

Other treatments:

- Oral or IV fluids (Hartmann's) of at least 60 ml/kg/24 hours
- Facial or nasal oxygen if oxygen saturation is < 95%

- Anti-emetics, antihistamines, or laxatives for side-effects of opiates
- Blood cultures and broad-spectrum antibiotics if signs or suspicion of infection

Acute Chest Syndrome (ACS)

ACS complicates up to 10% of HbSS and 4.5% of HbSC pregnancies.

In 50% of cases, there has been a painful crisis in the preceding fortnight.

It may mimic bacterial pneumonia; in practice it is not necessary to differentiate between the two. All patients with suspected acute chest syndrome should be treated promptly with antibiotics.

- **Symptoms** – shortness of breath, chest pain, cough
- **Signs** – increased respiratory rate, fever, chest signs (signs of consolidation, usually bilateral and generally 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 (PE), fluid overload, opiate toxicity, hypoventilation due to pain.
- If PE is suspected – use TEDS and prescribe **therapeutic** doses of tinzaparin until this is excluded, according to the protocol for acute management of venous thromboembolism in pregnancy (see below)

	Please see Whittington Health Guideline: **'Venous Thromboembolism in Pregnancy and the Puerperium – Acute Management'**

ACS may require treatment with top-up transfusion if Hb is less than 60 g/l, or exchange transfusion if there is severe hypoxia**.** The type of transfusion (top-up or exchange will be decided by the Haematology team.

Acute Stroke

Stroke can be due to infarction or haemorrhage.

- Acute neurological symptoms require urgent brain imaging
- Consult Haematologist to consider urgent exchange transfusion, which may reduce long-term sequelae

Acute Anaemia

Acute anaemia may be due to erythrovirus (human parvovirus B19), which can cause an aplastic crisis.

- Full blood count (FBC) will show a low reticulocyte count
- Treatment is with blood transfusion and the woman must be isolated
- Vertical transmission can cause hydrops fetalis, so refer to a Fetal Medicine specialist for scan.

➢ Thrombotic Risk

There is an increased risk of thrombosis. Patients should be included in the high-risk group for thromboprophylaxis after CS (see Labour and Delivery section) and if they have had a previous thrombotic episode should be treated according to the protocol for thromboprophylaxis in pregnancy (see below).

Women with SCD should receive TEDS and prophylactic low molecular weight heparin LMWH (Tinzaparin dose according to weight) during antenatal admissions.

➢ Please see Whittington Hospital NHS Trust Guideline:
'Thromboembolism Prophylaxis During and After Pregnancy'

➢ Transfusion

Blood transfusions will be considered on an individual basis. Any decisions to transfuse are to be taken only after discussion with the Consultant Haematologist.

Indications for transfusion include:

- Women with previous serious medical, obstetric or fetal complications. This includes previous sickle-related problems in pregnancy

- Women who are on a transfusion regimen before pregnancy for primary or secondary stroke prevention or for the prevention of severe disease complications
- Women on hydroxycarbamide for severe disease prior to pregnancy
- Acute chest syndrome or acute stroke
- Multiple pregnancies
- Acute anaemia
- Severe anaemia with evidence of fetal growth restriction (FGR) or small for gestational age fetus (SGA)

Where transfusion is required it is essential that the patient's full red cell phenotype is known and blood must be matched for Rh and Kell blood groups. If there are clinically significant red cell antibodies (current or historical) then the red cells selected should be negative for the corresponding antigens. Only CMV negative blood should be used.

If there are atypical antibodies present – inform Haematologists when planning elective delivery in order to avoid delays in blood cross-matching.

➢ Admission

<u>If admitted to A & E:</u>

The A&E and medical consultants should be notified immediately of her presence. They should communicate promptly with the on-call Obstetrics, Haematology and Anaesthetics consultants particularly if she is in the 3rd trimester.

If the woman requires supportive management, institute IV fluids, oxygen and analgesia as appropriate BEFORE transfer to the appropriate medical ward or Labour Ward to avoid delays in treatment.

Have a low threshold to institute the sepsis bundle because sickle patients are more susceptible to infection.

Please see Whittington Hospital NHS Trust Guideline:

➢ **Sickle cell disease in adults**

➢ Labour and Delivery

On admission to Maternity Triage or Labour Ward, immediately inform the on-call Obstetrics, Haematology and Anaesthetics consultants, and the Neonatal Registrar.

Aim for a normal vaginal delivery unless there are clear obstetric reasons for a CS.

If there is a history of cannulation difficulties, ask the Labour Ward Anaesthetist to cannulate the woman.

Discuss suitable positions for delivery in women with joint problems.

Women with SCD should avoid conditions that trigger crises – i.e. cold, dehydration, stress and exhaustion:

- Ensure the woman is kept warm
- All women should have an IV infusion of Hartmann's 1 litre 8 hourly, with close monitoring of fluid balance throughout the labour
- Prolonged labour can cause a crisis – if progress is slow, expedite delivery as appropriate

There should be continuous electronic fetal monitoring (EFM).
Vital signs should be recorded at least half hourly on a MEOWS chart.

- Monitor oxygen saturations – if < 95%, check arterial blood gases (ABG) and commence oxygen therapy
- Any temperature above 37.5°C should be investigated and broad-spectrum antibiotics considered. Have a low threshold for instituting the sepsis bundle.

Cord blood is to be sent for haemoglobin electrophoresis.

Analgesia in labour

Refer to the Obstetric Anaesthetist's management plan written after antenatal review.

Usually these women will have the normal range of analgesia for women in labour – e.g. Entonox, Diamorphine, or an epidural.

- Pethidine is **not** to be used (risk of seizures)

Some may have tolerance to opioids (this is more likely if they have required high doses of opioids for sickle crises prior to, or during their pregnancy). If this is the case, the 'usual' doses (5 - 7.5 mg of Diamorphine IM) may be ineffective.

If a woman is not getting adequate relief from the usual doses of Diamorphine please ask the Anaesthetist to review her.

The Anaesthetist may prescribe larger doses of Diamorphine or an alternative such as Remifentanil, or Morphine via a patient controlled analgesia (PCA) device.

Inform Paediatricians early if larger doses of Diamorphine or a Morphine PCA are used so that they can attend the delivery, as there is increased risk of respiratory depression in the neonate.

Anaesthesia for Caesarean Section

This may best be provided by use of a Combined Spinal Epidural (CSE), or if she has an epidural during labour it can be 'topped up'.

The epidural component can be used to provide post-operative analgesia.

In addition to 3 mg of Diamorphine being given via the epidural catheter at the end of the CS, it can also be given at intervals over the next 24 hours, as required, as the woman will be on the labour ward observation unit during this time. Therefore, **do not remove the epidural at the end of the CS**.

Notes to Anaesthetists:

- ***Spinal anaesthesia*** *– if used, add 350 micrograms of Diamorphine to* the Bupivacaine to provide post-operative analgesia
- **General anaesthesia** – if given in the absence of regional anaesthesia, be aware that larger than usual IV Morphine doses may be required to ensure that the woman is comfortable on emergence
- Please note – in the early post-operative phase some of these women will require higher, more frequent doses of opioids than are usually given. Larger doses do mean slightly more transmission to breast milk, but this is not usually a problem
- Find out what the woman usually takes for a sickle crisis and ensure this is prescribed
- Prescribe Paracetamol and Ibuprofen unless contra-indicated

Post-operatively

- 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
- Monitor the respiratory rate for 12 hours after administration of spinal Diamorphine, and 2 hours after the administration of each dose of epidural Diamorphine
- This will include 2 - 4 litres/min of oxygen via nasal cannulae and continuous monitoring of the oxygen saturation to maintain > 94%
- The Anaesthetist and Obstetrician should liaise closely regarding the removal of the epidural catheter and timing of heparin prophylaxis.

Heparin prophylaxis after CS – please refer to:

	Whittington Health Guideline: **'Thromboembolism Prophylaxis During and After Pregnancy'**

➢ Postnatal Care

Common postoperative complications - UTI, endometritis, sickle cell crisis

Ensure adequate hydration with fluid balance chart and keep oxygen saturation above 94%.

High dependency care should be continued **for at least 24 hours** regardless of mode of delivery, as acute crisis and other complications of SCD can occur in up to 25% of women during the puerperium.

Prompt investigation of fevers and early treatment with antibiotics is essential.

Have a low threshold for involvement of the critical care outreach team (CCOT) or ITU consultant if there are signs of physiological compromise.

All women should receive prophylactic LMWH (Tinzaparin) whilst in hospital.

- After vaginal delivery – Tinzaparin is continued for **10 days post-discharge**
- After CS – Tinzaparin is continued for **6 weeks**

- All women should continue to wear TEDS during the puerperium (6 weeks)

Early contraceptive advice should be given:

- Barrier methods and progesterone-only contraceptives are safe and effective – e.g. progesterone only pill (POP), Mirena IUS
- Oestrogen-containing contraceptives – no evidence of greater VTE risk in SCD women, but use as second line

Discharge from the Labour Ward Recovery Unit or the postnatal ward must be sanctioned by a Consultant.

Women should be seen in the Obstetric Medicine clinic for their 6 week postnatal check.

➢ Contacts (inside and outside the Trust including out-of-hours contacts)

Dr Bernard Davis, Consultant Haematologist via hospital switchboard.
Miss Amma Kyei-Mensah, Consultant Obstetrician via hospital switchboard.
Mr Ashokkumar, Consultant Obstetrician via hospital switchboard.

Out of hours, contact on-call Consultants via switchboard.

➢ References (evidence upon which the guideline is based)

1. Pregnancy outcome in patients with sickle cell disease in the UK – a national cohort study comparing sickle cell anaemia (HbSS) with HbSC disease. British Journal of Haematology 2015;169: 129-137.

2. Management of acute painful crises in sickle cell disease. British Journal of Haematology 2003;120(5):744-752.

3. Howard RJ. Management of Sickling Conditions in Pregnancy. British Journal of Hospital Medicine 1996;56:7-10.

4. Royal College of Obstetricians and Gynaecologists. Management of Sickle Cell Disease in Pregnancy. Green Top Guideline No. 8. London:RCOG;2011. Review 2014 – no change.

5. Adverse maternal and perinatal outcomes in pregnant women with sickle cell disease: systematic review and meta-analysis. Blood 2015; 125 (21): 3316-3325.

- **Compliance with this guideline (how and when the guideline will be monitored e.g. audit and which committee the results will be reported to) Please use the tool provided at the end of this template**

To be completed and attached to any procedural document when submitted to the appropriate committee for consideration and approval

		Yes/No	Comments
1.	**Does the procedural document affect one group less or more favourably than another on the basis of:**		
	• Race	No	
	• Ethnic origins (including gypsies and travellers)	No	
	• Nationality	No	
	• Gender	No	
	• Culture	No	
	• Religion or belief	No	
	• Sexual orientation including lesbian, gay and bisexual people	No	
	• Age	No	
	• Disability - learning disabilities, physical disability, sensory impairment and mental health problems	No	
2.	**Is there any evidence that some groups are affected differently?**	No	
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	No	
4.	**Is the impact of the procedural document likely to be negative?**	No	

		Yes/No	Comments
5.	**If so can the impact be avoided?**	N/A	
6.	**What alternatives are there to achieving the procedural document without the impact?**	N/A	
7.	**Can we reduce the impact by taking different action?**	N/A	

If you have identified a potential discriminatory impact of this procedural document, please refer it to the Director of Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact the Director of Human Resources.

Checklist for the Review and Approval of Procedural Document

To be completed and attached to any procedural document when submitted to the relevant committee for consideration and approval.

	Title of document being reviewed:	Yes/No	Comments
1.	**Title Sickle Cell Disease in Pregnancy.**		
	Is the title clear and unambiguous?	Yes	
	Is it clear whether the document is a guideline, policy, protocol or standard?	Yes	
2.	**Rationale**		
	Are reasons for development of the document stated?	Yes	
3.	**Development Process**		
	Is it clear that the relevant people/groups have been involved in the development of the document?	Yes	
	Are people involved in the development?	Yes	
	Is there evidence of consultation with stakeholders and users?	Yes	
4.	**Content**		
	Is the objective of the document clear?	Yes	
	Is the target population clear and	Yes	

	Title of document being reviewed:	Yes/No	Comments
	unambiguous?		
	Are the intended outcomes described?	Yes	
5.	**Evidence Base**		
	Are key references cited in full?	N/A	
	Are supporting documents referenced?	N/A	
6.	**Approval**		
	Does the document identify which committee/ group will approve it?	Yes	
7.	**Dissemination and Implementation**		
	Is there an outline/plan to identify how this will be done?	Yes	
8.	**Document Control**		
	Does the document identify where it will be held?	Yes	
9.	**Process to Monitor Compliance and Effectiveness**		
	Are there measurable standards or KPIs to support the monitoring of compliance with and effectiveness of the document?	Yes	
	Is there a plan to review or audit compliance with the document?	Yes	
10.	**Review Date**		
	Is the review date identified?	Yes	
	Is the frequency of review identified? If so is it acceptable?	Yes	
11.	**Overall Responsibility for the Document**		
	Is it clear who will be responsible for co-ordinating the dissemination, implementation and review of the document?	Yes	

Executive Sponsor Approval			
If you approve the document, please sign and date it and forward to the author. Procedural documents will not be forwarded for ratification without Executive Sponsor Approval			
Name		Date	
Signature			

Relevant Committee Approval			
The Director of Nursing and Patient Experience's signature below confirms that this procedural document was ratified by the appropriate Governance Committee.			
Name		Date	
Signature			
Responsible Committee Approval – only applies to reviewed procedural documents with minor changes			
The Committee Chair's signature below confirms that this procedural document was ratified by the responsible Committee			
Name		Date	
Name of Committee		Name & role of Committee Chair	
Signature			

Tool to Develop Monitoring Arrangements for Policies and guidelines

What key element(s) need(s) monitoring as per local approved policy or guidance?	**Who will lead on this aspect of monitoring?** **Name the lead and what is the role of the multidisciplinary team or others if any.**	**What tool will be used to monitor/check/observe/Assess/inspect/ authenticate that everything is working according to this key element from the approved policy?**	**How often is the need to monitor each element?** **How often is the need complete a report ?** **How often is the need to share the report?**	**What committee will the completed report go to?**
Standard of care in the management of pregnancy in women with Sickle Cell	Miss A Kyei-Mensah, Maternal Medicine Dr B Davies, Consultant Haematologist	Audit every 3 – 5 years	This is subject to a 3 – 5 yearly audit, findings to be presented in the form of a report which will be presented initially 3 – 5 yearly and more often thereafter if necessary	These reports will be reviewed by the Maternity Clinical Guidelines and Audit Group. It is their responsibility to monitor the findings from each report. Evidence to support this will be found in the form minutes. Key factors to be noted are: -Audit findings -Deficiencies -Whether this is improvement from previous audit findings -Action planning with a named person who is responsible -Next date where an update will be given and by whom