Pregnancy in patients with sickle cell disease

Introduction

Women with sickle cell disease have increased pregnancy complications: pre-eclampsia, pregnancy induced hypertension, thromboembolism and caesarean rate. Fetal complications include increased rates of miscarriage, stillbirth, premature delivery and intrauterine growth retardation. Increased sickle complications also occur: acute pain crises, acute chest syndrome and infection (particularly UTI).

The high-risk nature of pregnancies in these women necessitates multidisciplinary team management. These women should be jointly managed by the Haemoglobinopathy clinic and the High Risk Obstetric (or Maternal Medicine) service which should include Obstetrician/Obstetric physician, Midwife and Anaesthetist, as soon as pregnancy is confirmed.

This Guideline has been updated to include new information covered in the most recent BSH Guideline on the management of sickle cell disease in pregnancy.

Patient Group

This protocol applies to patients with HbSS, HbSC, HbSβ thalassemia, HbSE, HbSDPunjab, HbSOArab and HbS/Lepore genotypes. Patients who are sickle cell carriers (or have sickle cell trait) are managed as patients with a normal HbAA genotype.

Summary of Practice Points

- Pre-conception screening for sickle related end organ damage should be carried out including discussion and referral for pre-implantation genetic testing if available/appropriate
- Comprehensive pre-conception drug review
- Clear documentation of roles and responsibilities for all members of the multidisciplinary team.
- Recommended schedule of clinical review – 4 weekly until 28/40, then fortnightly until 38/40, then weekly until birth.
- Recommended schedule of growth scans and uterine artery dopplers
- Management of specific sickle complications in pregnancy
- Hospital birth is recommended with adequate hydration, oxygenation, warmth, pain relief, regular (hourly) observations and fluid balance; with MDT review daily.
- Postnatally, women are encouraged to breast feed. Low molecular weight heparin (LMWH) is given for 6 weeks and a plan for contraception discussed.

1. Pre-Conception Care

Pregnancy and conception planning should form part of the annual review consultation from young adulthood. This should include discussions about reproductive options including options for fetal diagnosis – invasive/non-invasive, PGT, partner screening and optimisation of health pre- pregnancy. Preconception clinics should be available and accessible.

1.1 Genetic Screening

- Partner screening should be encouraged prior to conception

- High risk couples should be counselled before pregnancy about their risk of having an affected child and reproductive options for early fetal diagnosis. This could be non-intervention, prenatal diagnosis or pre-implantation genetic testing (PGT)

1.2 Review of Complications

- Outcome of most recent annual review consultation should be assessed for any woman planning pregnancy. Full history including ongoing complications should be documented in notes and management optimised.
- Specialist review may be required for certain conditions prior to pregnancy.
- **Renal dysfunction**
  - Monitor blood pressure prior to pregnancy and consider antihypertensives if BP is persistently raised > 130/80mmHg
  - Monitor serum creatinine and urinary protein (albumin:creatinine or protein:creatinine ratio). Investigate for non-sickle causes if urine protein is raised > 50mg/mmol, prior to pregnancy
- **Cardiac complications**
  - Pulmonary hypertension, ventricular diastolic dysfunction and early cardiac death are increased in sickle cell disease and can be evaluated for by measuring the tricuspid regurgitant jet velocity. A high TRV is associated with increase risk of pulmonary hypertension and death.
  - Women planning pregnancy should have an Echocardiogram if not performed within the last year.
  - Women should have an Echocardiogram performed if they have any symptoms suggestive of pulmonary hypertension, irrespective of the previous Echo
  - Abnormalities should be discussed/reviewed with a Cardiologist
- **Chronic lung disease**
  - Record oxygen saturations on all women
  - If indicated, sleep studies and pulmonary function tests should be requested
- **Avascular necrosis**
  - Hip problems can progress and become worse in pregnancy and should be reviewed prior to pregnancy
- **Stroke**
  - Consider regular transfusions during pregnancy if there is a history of previous stroke and currently not on regular transfusions
- **Chronic pain**
  - Refer any woman on long term opioids to a chronic pain specialist for assessment prior to pregnancy and ongoing management during pregnancy, delivery and breastfeeding
- **Retinal screening**
- **Red cell antibody screening** (see section on Transfusion)
- **Iron overload**
  - MRI heart/liver should be performed prior to pregnancy if any concerns
  - iron chelation is advised pre-conception for women who are significantly iron overloaded

- Review other significant medical history may need specialist review prior to pregnancy

1.3 Medication Review

- All women should start (or continue if already taking) Folic acid 5mg od prior to conception and continue during pregnancy and breastfeeding
- Prescribe Vitamin D for all women, following national guidelines for supplementation. Monitor levels to ensure adequate supplementation
- Penicillin V prophylaxis or alternative, should be prescribed for all women due to the increased risk of infection
- Analgesia management should be discussed with all women.
    - 1st line agents: Paracetamol and Codeine-containing agents
    - NSAIDs: use with caution before 12/40; avoid after 31/40
    - Refer to pain team if opioids are needed
- Vaccinations should be updated according to national guidance. This should include annual influenza vaccination and Pneumococcal vaccination (if not given within 5years). Defer live attenuated vaccines till after pregnancy.
- Review and discontinue potentially teratogenic drugs
    - Hydroxycarbamide should be discontinued 3 months prior to conception or immediately if conception occurs on the drug. For women with severe disease and in whom transfusion is not an option, continuation of hydroxycarbamide is an option followingdiscussion between the patient and multidisciplinary team regarding risks and benefits including plans for detailed anomaly scanning.
    - ACE inhibitors/ Angiotensin II receptor blockers (ARBs). There should be a discontinuation plan for women with chronic kidney disease prior to pregnancy. Renal team should be involved in decision making
    - Iron chelators should be stopped when attempting to conceive
    - Voxelotor, Crizanlizumab and L-Glutamine should be stopped prior to conception

1.4 Preconception counselling

Patients should be advised of the risks of pregnancy to both mother and child. Specifically, patients should be advised of:

- Risk of fetal complications including growth restriction, premature delivery and stillbirth
- Risk of maternal complications including increased rate of Caesarean section, pre-eclampsia, thromboembolic events, worsening anaemia requiring transfusion
- The increased rate of sickle crises during pregnancy (e.g. precipitated by nausea / vomiting/ dehydration)
- The need to notify the haematology service as soon as pregnancy is confirmed

2. Antenatal Care

See Table 1 for recommended Antenatal care appointment schedule (page 8)

2.1 Antenatal Haemoglobinopathy screening

- Partner testing should be offered as soon as possible, if not done prior to conception
- Counselling should be offered in the first trimester regarding the risk of having an affected child if partner is a carrier. Prenatal diagnosis should be offered as early as possible to ensure early access to termination of an affected pregnancy if requested.

2.2 Initial management

- Women should be encouraged to book with a midwife by 10/40
- Full assessment as for pre-conception (listed above) should be repeated as early as possible
- Multidisciplinary approach to management including an obstetrician and midwife with experience of high-risk antenatal care and a haematologist with links to a Specialist Haemoglobinopathy Team
- Advise women to seek medical advice if vomiting persistently
- Offer Folic acid 5mg od and prophylactic antibiotics, if not already taking
- Iron supplementation if confirmed by laboratory investigation
- Consider Aspirin 75 – 150mg from 12/40 to reduce risk of pre-eclampsia

Recommended clinical review schedule See table 1

2.3 Ultrasound scanning schedule

- All the standard ultrasound scanning according to NICE guidance should be performed
  - Viability scan 7-9 weeks
  - Dating scan 10 – 14 weeks
  - Anomaly scan – 20 weeks
- Growth scans should be performed every 4 weeks from 24/40 (i.e. 24, 28, 32 and 36 weeks), for early detection of fetal growth restriction. This aids decisions regarding appropriate time of delivery to reduce perinatal morbidity and mortality.
- If pregnancy- associated plasma protein A (PAPP-A) is low in the first trimester, consider more frequent scans from 20/40

2.4 VTE risk assessment and thromboprophylaxis

- RCOG greentop guideline: https://www.rcog.org.uk/globalassets/documents/guidelines/gtg-37a.pdf
- VTE risk assessment should be performed in early pregnancy, if admitted to hospital, intrapartum and early postpartum period
- Consider VTE prophylaxis from 28/40 until 6 weeks postpartum. May need to start earlier if there are additional risk factors
- VTE prophylaxis should be given throughout any hospital admission unless contraindicated

2.5 Blood transfusion in pregnancy

- Transfusion is not routinely indicated in pregnancy but should be considered in:
  - Previous or current medical, obstetric or fetal problems related to SCD
  - Women previously on hydroxycarbamide due to severe disease

- Multiple pregnancy
- Women receiving long term transfusions for stroke prevention or amelioration of severe sickle complications
- Consider in worsening anaemia or acute SCD complications (acute chest syndrome, stroke)

- Criteria for red cell selection for transfusion: ABO-compatible, extended Rh- and Kell-matched, CMV-negative units. If there are clinically significant red cell antibodies (current or historical) then the red cells selected should be negative for the corresponding antigens.
- The risks and benefits of prophylactic transfusion during pregnancy should be discussed with the patients as part of the haematology/obstetric consultation.
- Full transfusion history should be obtained
- Antibody screen should be performed according to usual antenatal guidance.
- Ensure Red cell genotype/phenotype is performed prior to transfusion

2.6 Management of Specific Sickle Cell Disease Related Complications

*2.6.1 **Acute Painful Episodes*** – http://nssg.oxford-haematology.org.uk/red-cell/documents/acute-management-sickle-cell-disease/S8-painful-crises-in-scd.pdf

- Pregnancy is associated with an increased risk of painful crisis
- Patients can be managed according to the Regional Guidelines for painful crisis.
- There should be multidisciplinary management during any admission with a painful crisis irrespective of which ward the patient is admitted to
- There should be local guidelines regarding appropriate ward location depending on gestational age and need for continuous fetal monitoring
- Use NSAIDs with caution before 12 weeks, and avoid after 31 weeks
- Monitor fluid balance and oxygen saturations regularly. Consider imaging for PE if saturations < 95%
- Assess for possible infection and treat with antibiotics according to local guidance
- Ensure full history and examination to exclude potential non-sickle causes for pain
- Ensure VTE prophylaxis is prescribed unless contraindicated

*2.6.2 **Acute Chest Syndrome (ACS)*** – http://nssg.oxford-haematology.org.uk/red-cell/documents/acute-management-sickle-cell-disease/S10-acute-chest-syndrome-in-scd.pdf

- Increased incidence of ACS in pregnancy
- Follow regional guideline for management
- Patient can present with ACS or may develop following painful crisis, therefore vigilance should be maintained during a hospital admission
- All hospitals should have a treatment pathway for ACS which should include referral to HDU or ICU

*2.6.3 **Other Acute Complications***

- Acute stroke

  Should be considered in women presenting with acute neurological impairment and requires urgent consideration of exchange transfusion.

http://nssg.oxford-haematology.org.uk/red-cell/documents/acute-management-sickle-cell-disease/S13-acute-neurological-complications-in-scd.pdf

- Acute erythrovirus infection
  - Should be considered in women presenting with acute anaemia http://nssg.oxford-haematology.org.uk/red-cell/documents/acute-management-sickle-cell-disease/S12-acute-anaemia-in-scd.pdf

3. Intrapartum Care

3.1 Timing and Mode of Delivery

- Birth plan should be agreed by the MDT and documented in patient records accessible to all healthcare professionals involved in the woman's care
- Pregnant women with a normal growing baby should be delivered between 38 – 40 weeks because of the increased risk of late pregnancy placental complications
- Aim for hospital delivery
- Women can be offered vaginal delivery even after previous caesarean if there are no contraindications
- Caesarean section may be needed for obstetric reasons
- Women who either have avascular necrosis or have had previous hip replacement should have a discussion regarding suitable delivery positions prior to delivery
- For women receiving red cell exchange transfusions in pregnancy, it may be necessary to plan induction of labour to ensure transfusion within 7 days of delivery.

3.2 Analgesia and anaesthetic in Labour and Delivery

- All women should be offered an anaesthetic review by 32 weeks. This should include an analgesia and anaesthetic plan for labour
- Epidural analgesia should be encouraged early in labour
- Regional anaesthetic should be used for caesarean section; avoid general anaesthetic if possible
- Opiates can be used in labour; avoid Pethidine as this increases the risk of seizures in SCD
- Nitrous oxide (Entonox) may be used for short periods for pain relief without precipitating a crisis

3.3 Monitoring in Labour

- Women should be advised to deliver in hospital that are able to manage both complications of SCD and high-risk pregnancies
- Relevant MDT should be informed as soon as labour is confirmed. This should include senior midwife in charge, Obstetric Consultant, Obstetric Anesthetist and Haematologist
- Liaise with blood bank and to ensure availability of blood especially if there are red cell antibodies
- During labour, women should be kept warm and well hydrated. Intravenous fluid may be required. Avoid fluid overload using strict fluid balance chart
- Hourly observations should be carried out including oxygen saturations. Oxygen supplementation if oxygen saturations fall below 97%
- Continuous fetal monitoring is recommended due to increased risk of fetal distress and stillbirth

- Avoid prolonged labour >12 hours
- Ensure active management of third stage of labour to reduce risk of postpartum haemorrhage

4. Postpartum Care

4.1 General postpartum care

- There is an increased risk of painful crises in the immediate postnatal period and women should be advised of this
- Hydration and oxygenation should be maintained
- Encourage early mobilisation
- Encourage breastfeeding
- Manage painful crises as per non-pregnant women: http://nssg.oxford-haematology.org.uk/red-cell/documents/acute-management-sickle-cell-disease/S8-painful-crises-in-scd.pdf
- Haematology and obstetric teams should review daily

4.2 Analgesia in the postpartum period

- NSAIDs are safe whilst breastfeeding and can be used
- Codeine should not be given during breastfeeding. Dihydrocodeine and tramadol and other opioids can be used with caution

4.3 VTE prophylaxis

- Routine care should be provided as per the NICE guideline on postnatal care
- Antithrombotic stockings are recommended
- Prophylactic low molecular weight heparin should be commenced as soon as bleeding is satisfactory and should continue for 6 weeks postpartum

4.4 Contraception

- Contraceptive advice should be given to the woman before leaving hospital and communicated to her primary care team on discharge
- Progesterone only preparations may have some clinical benefit
- Long-acting reversible form of contraception e.g. Levornorgestrel IUS or intramuscular depo-medroxyprogesterone acetate are preferred options
- Concerns with potential increased risk of blood loss with Copper IUD
- Barrier methods are safe but less effective than other forms of contraception

Table 1 – Antenatal Care for Women with SCD

Appointment	Care for women with SCD during pregnancy
First appointment (primary care or hospital appointment)	Offer general health information, advice and support Offer partner testing if not already done

	Review partner results and discuss PND if appropriate Clinical history to assess SCD complications Assess retinal, renal and cardiac complications as necessary Review medications Ensure women are taking 5 mg folic acid and prophylactic antibiotics and discuss vaccinations Document baseline oxygen saturations and blood pressure Send MSU for culture
Booking appointment: see multidisciplinary team plus midwife with experience in high-risk obstetrics if possible	Information, education and advice about SCD and pregnancy Review partner results and discuss PND if appropriate Baseline full blood count, renal function test, urine protein/creatinine ratio, liver function test, ferritin and group and screen Extended red cell phenotype if not previously performed Prescribe 75–150 mg aspirin Start vitamin D prophylaxis if not already on this Risk assessment for VTE and consider thromboprophylaxis Review individual pain management plan
10–14 weeks	First-trimester ultrasound scan
16 weeks: see midwife plus multidisciplinary review	Routine as per NICE; repeat MSU Multidisciplinary review (consultant obstetrician and haematologist)
20 weeks: see midwife plus multidisciplinary review	Detailed ultrasound as per NICE antenatal guideline Repeat FBC and MSU
24 weeks: see multidisciplinary team	Ultrasound monitoring of fetal growth and amniotic fluid volume Repeat FBC and MSU
26 weeks: see midwife	Routine check including blood pressure and urinalysis
28 weeks: see multidisciplinary team	Ultrasound monitoring of fetal growth and amniotic fluid volume Repeat MSU

	Repeat FBC and group and antibody screen Review VTE risk factors and consider thromboprophylaxis
30 weeks: see midwife and offer antenatal classes	Routine check including blood pressure and urinalysis
32 weeks: see multidisciplinary team	Routine check Ultrasound monitoring of fetal growth and amniotic fluid volume Repeat MSU and FBC Offer anaesthetic assessment at 32 weeks or earlier if indicated
34 weeks: see midwife	Routine check including blood pressure and urinalysis
36 weeks: see multidisciplinary team	Routine check Repeat MSU and FBC Ultrasound monitoring of fetal growth and amniotic fluid volume Consider whether to stop aspirin prior to delivery Offer information and advice about: • Timing, mode and management of the birth • Care of baby after birth • Analgesia and anaesthesia
38 weeks: see midwife and obstetrician	Routine check Discuss timing and mode of delivery
39 weeks: see midwife	Routine check and review delivery plan
40 weeks: see obstetrician	Routine check and offer fetal monitoring if the woman declines delivery by 40 weeks of gestation

Source: Oteng-Ntim, Eugene & Pavord, Sue & Howard, Richard & Robinson, Susan & Oakley, Laura & Mackillop, Lucy & Pancham, Shivan & Howard, Jo. (2021). Management of sickle cell disease in pregnancy. A British Society for Haematology Guideline. British Journal of Haematology. 194. 10.1111/bjh.17671

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Royal College of Obstetricians and Gynaecologists Green-top guideline no 37a: Management of Venous Thromboembolism during pregnancy, and the puerperium

https://www.rcog.org.uk/globalassets/documents/guidelines/gtg-37a.pdf

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Oteng-Ntim E, Chase AR, Howard J, et al (2008) Sickle cell disease in pregnancy. Obstetrics, Gynaecology and Reproductive Medicine 18:10, 272-278

Standards for the clinical care of adults with sickle cell disease in the UK (2018), Chapter 18, Sickle Cell Society Link here

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Review

Name	Revision	Date	Version	Review date
Wale Atoyebi	Pre-peer review	Jan 2013	1.0	Jan 2015
Deborah Hay	Routine review	Aug 2015	1.2	Jan 2017
Dr Deborah Hay	Updated anticoagulation guidance	Sept 2016	1.3	Sept 2017
Dr Magbor Akanni Dr Wale Atoyebi Dr Lucy McKillop	Routine review, plus new SCD guidelines	November 2018	2.1	November 2020
Dr Magbor Akanni Sandy Hayes	Protocol re-written to reflect the new SCD guidelines.	July 2022	3.0	July 2024

Appendix

Contacts for local teams

Haematology Centre	High risk Obstetric team	Haemoglobinopathy lab	Antenatal/Prenatal diagnosis team
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