

Clinical Guidance

Haemoglobinopathies in Pregnancy

Summary

Haemoglobinopathy is the leading single gene defect in the UK. 12% of mothers who book at St Thomas' are carriers of haemoglobin gene variant. 30 - 40% of our mothers are at risk of this gene variant. For those mothers who have the disease the morbidity mortality ratio in pregnancy is high. This guideline alludes to the management of haemoglobinopathy in pregnancy as well as antenatal screening for haemoglobinopathy.

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Haemoglobinopathies in Pregnancy

Screening

Haemoglobinopathies are a group of genetic disorders affecting haemoglobin structure or synthesis.

Aim of screening: To minimize delays in antenatal investigation for women at risk of having an affected infant and to improve co-ordination, communication and liaison between healthcare professionals.

Criteria

Antenatal screening for haemoglobinopathies is offered to all pregnant women at Guy's and St Thomas' NHS Foundation Trust' (National screening Programme, 2005).

It is vital that haemoglobinopathy results for women at risk and their partners are obtained as early in pregnancy as possible (B). This enables counselling, the possibility of prenatal diagnosis and prompt consequent management.

The woman should understand why the blood test is being taken before venepuncture. She should be alerted to the possibility of advising testing of father of the child. If the partner is not available counselling should still be offered.

(Class C Recommendation)

Before testing - Ensuring the Haemoglobinopathies Screening Programme (HCP) is met through standardized questioning of the patient and partner.

- Document woman's family origin in the notes and on the Family Origin Questionnaire (FOQ) form
- Document partner's family origin (also on the FOQ form)
- Discuss the issues and rationale for test
- Provide information leaflet
- Discuss our policy, which is to inform the woman of the result, place a copy in her hand held notes.
- Prepare her to expect contact from the South East London Sickle/Thalassaemia Centre if the result is positive.

The blood test of woman and/or partner can be ordered electronically or by using the special paper request form which incorporates the FOQ. When ordering electronically an electronic version of the FOQ must be completed, this is printed and sent to the laboratory with the specimens. The woman's full name, date of birth and hospital number must be included in the form along with the number of weeks gestation at time of sampling. FOQ, weeks gestation at sampling and coverage are key performance indicators against which the department is assessed nationally. **Ensure that you highlight that it is booking bloods.**

Follow up and Results

Through arrangements with the laboratory, for the samples designated antenatal booking bloods, the South East London Sickle Cell/Thalassaemia Centre receives all results for which counselling and follow-up is required. Results are sent daily and the target turn around time is 3 working days. Counsellors will arrange appropriate follow-up and referrals. Women with a positive result will be sent a letter by the haemoglobinopathy counsellors. This letter includes

the appropriate leaflet and the date for a genetic counselling appointment. Attendance can be with or without her partner. The woman's partner will be offered screening if not already tested.

Further information/leaflets will be given by the Specialist Nurse Counsellor. The counselling session is usually held at the hospital of confinement or at the South East London Sickle/Thalassaemia Centre. (Address below)

Results

Results will fall into the following groups:

- a) **Normal**
 No abnormality has been detected. These results will be posted with an accompanying letter, which the woman should file in her notes.
- b) **Inconclusive**
 Further management advice will be given.
- c) **Traits or Carrier**
 For women with haemoglobinopathy trait e.g. AS, AC, the partner should be advised to attend for testing.
- d) **Haemoglobinopathy disease:**
 e.g. HbSS, HbSC, β thalassaemia major: **For guidelines see page 4**

For further advice or clarification, contact:

**Service Co-ordinator/Specialist Nurse Counsellors
 South East London Sickle Cell/Thalassaemia Centre
 Wooden Spoon House
 5, Dugard Way, Off Renfrew Road
 Kennington
 London
 SE11 4TH
 Tel. 020 7414 1363 Fax 020 7414 1357**

Prenatal Counselling and diagnosis

Aim

To identify couples at risk of having a child with sickle cell disease and, β -Thalassaemia major in time, allowing fetal diagnosis, and the exploration of termination of the pregnancy, where appropriate. In doing so, we should bear in mind that in most African-Caribbean cultures, termination will not be considered once quickening starts (i.e. from 16 weeks onwards (Class B recommendation).

Women should be offered prenatal diagnosis when

1. She and her partner are both traits (1 in 4 chance of the fetus being affected).
2. She has a trait but no result from partner who is from high risk group³ (Uncertain risk)

Prenatal Diagnosis

Prenatal diagnosis can be performed by chorionic villous sampling, amniocentesis or fetal blood sampling. This is performed in the Fetal Medicine Unit (FMU). Appointments must be

made in advance by either the Sickle Cell counsellor or Guys' Clinical Genetics Department, as co-ordination with laboratories is vital.

Phone numbers

FMU	Ext: 82318	
Genetics	Ext: 81364	Fax 71881369
Sickle Cell counsellors	020 7414 1363	

Patients with haemoglobinopathy

All women with sickle cell disease, or other serious haemoglobinopathy, should be booked by the Tower team midwives and be seen by Dr Oteng-Ntim on the Tuesday afternoon clinic. The patients will then be referred to the monthly, joint antenatal, sickle cell clinic with the Haematology team. This ensures that patients with haemoglobinopathies are cared for by the multidisciplinary team with expertise in this field. The team includes psychologists and women will be offered the opportunity to see them for review if they wish.

The specialist Nurse Counsellors will refer women with sickle cell disease not previously known to the service (and who have been identified through the routine antenatal screening programme) to Dr Oteng-Ntim. Copies of the referral will be sent to the Tower team midwife, the Sickle Clinical Nurse Specialist and Dr Howard (Haematology Consultant) at St Thomas'.

The Consultant ANC, 8th floor North Wing, St Thomas' Hospital, Tuesday PM weekly.

Joint Antenatal/Sickle Cell Clinic: Thursday AM once a month usually last Thursday of the month in the morning.

Patient referral may occur through:

- Sickle cell nurse counsellor
- Sickle cell nurse specialist
- Tower team midwives
- Patient's GP

Management of pregnant women who are haemoglobinopathy carriers (Hb AS, Hb A β thal, Hb A α Thal, HbAC)

Care as for any pregnant woman

Clearly mark notes to indicate haemoglobinopathy carrier

NB Possible increased risk of urinary tract infections

Ensure partner tested.

If partner is also a carrier, then neonatal testing should be performed before discharge

If partner's status unknown, ensure neonatal diagnosis arranged (this is routinely performed on the Guthrie card)

Management of women affected by haemoglobinopathies

Haemoglobinopathy disorders that matter in pregnancy are:

- Sickle Cell Disease (SCD)
- β thalassaemia major
- E/B thalassaemia
- Haemoglobin H disease.

In the local area the most common haemoglobin disorder is Sickle Cell Disease.

Sickle cell disease

Sickle cell disease includes women with Hb SS, Hb SC, Hb SB, Thalassaemia and Hb SD. Sickle haemoglobin is a variant of the β -chain haemoglobin. Sickling of red cells occurs particularly in response to hypoxia, cold, acidosis and dehydration. Intravascular sickling leads to vaso-occlusive symptoms and tissue infarction with severe pain.

Complications for women with SCD can occur during the antenatal period, labour, and the puerperium.

Complications in pregnancy:

Maternal

- Infection (UTI, Pneumonia, Puerperal sepsis)
- Acute chest syndrome (Fever, tachypnoea, pleuritic chest pain)
- Pulmonary thrombosis, thromboemboli
- Increased incidence of preterm labour, pre-eclampsia and caesarean section
- Increased risk of maternal death (approx. 1%)

Fetal

- Increased risk of miscarriage
- Increased risk of intra-uterine growth restriction
- Increased risk of prematurity
- Increased risk of fetal distress
- High risk of stillbirth/neonatal death (perinatal mortality 15% i.e.: 15x general population)

Care of women with SCD during pregnancy

Women with sickle cell disease are at risk of a sickle crisis in pregnancy, labour and the early puerperium, particularly if they become dehydrated, acidotic or infected. Their care should involve specific measures to prevent these complications.

Antenatal care

Aims

Antenatal care aims to give appropriate care to ensure healthy mother and baby.

Avoidance and early treatment of crises

Haemoglobinopathy screen of partner and offer counselling and prenatal diagnosis

Clinic

A high risk obstetric clinic takes place on Tuesday afternoon at St Thomas' where pregnant women with sickle cell disease are seen. Other high risk obstetric cases are seen in this clinic as well.

Every 4 weeks (the last Thursday of the month) there is an interdisciplinary clinic involving the consultant obstetrician with special interest in sickle cell disease and midwives with special expertise in looking after high risk mothers. This is attended by:

- Consultant Haematologist with an interest in sickle cell disease
- Sickle Clinical Nurse Specialist
- Community sickle cell nurses

Booking appointments

- **Booking:** Monday afternoons on the 8th floor North Wing, St Thomas' Hospital by Tower team.
- Booking between 6 and 10 weeks is recommended for women with Haemoglobinopathies.
- Referral and appointment for pre-natal counselling by sickle cell counsellors.
- Check partner's status. If AA, then reassure.
- First trimester diagnosis by chorionic villous sampling may be done between 11-14 weeks gestation.
- Ensure all women are taking Folic acid 5mg daily and advice regarding penicillin prophylaxis 5(B).

Booking procedure and bloods are the same as for routine booking.

- Check woman's blood group phenotype and request if not recorded.
- Check Hepatitis B status, immunize post-delivery if not immune.
- Assess thrombotic risk. If high risk (i.e. personal or family history of thrombosis) discuss with haematology team and consider prophylactic thromboprophylaxis with enoxaparin 40mg daily. If normal risk commence aspirin 75mg once daily, if no contra-indications.

Schedule of antenatal care

Follow-up clinic: Tuesday afternoon, 1400 to 1700 hours on 8th floor North Wing, ANC

Women will be seen:

- Every four weeks until 24 weeks gestation
- Fortnightly until 32 weeks gestation
- Weekly till delivery.
- Four weekly in the joint sickle-obstetric clinic

Give appropriate advice:

- Increased risk of crisis/IUGR/PET/fetal loss/sickling in uteroplacental circulation.
- Self treatment of crisis at home is not appropriate during pregnancy because of the need to monitor the fetus 7.
- More frequent schedule of care and timing of scans
- Prophylactic penicillin V 250mg daily recommended to prevent infection with pneumococcus
- Ensure understanding of risk factors for precipitating sickle cell crisis
- Advise attendance on Antenatal Day Unit, if they have pain or other concerns
- Haemoglobin and MSU monthly
- Only prescribe iron after discussion with Consultant obstetrician or haematologist
- Offer antenatal classes from 26 weeks gestation
- Encourage mother to meet neonatal team and visit unit for familiarisation if neonatal complications expected
- Notify neonatologist in writing if neonatal complications expected

Consider delivery by induction of labour at 38-40 weeks (discuss with Dr Oteng-Ntim).

Ultrasound: Important because of high rate of IUGR and very high perinatal mortality
 Early dating scan or nuchal translucency scan
 Anomaly scans with uterine artery Doppler at 20 weeks (Class C recommendation)
 Four weekly scans for growth and liquor volume from 24 weeks (Class B)
 Umbilical artery Doppler if growth and liquor volume abnormal
 If uterine artery notches seen at 20-24 weeks – consider increased dose of aspirin (increased to 150mg od) or prophylactic heparin.

In-patient care

On admission, Inform Dr Oteng-Ntim or the Sickle cell team via the sickle cell nurse practitioner (bleep 1843) or sickle SpR (bleep 0248)
 If out of hours, inform haematologist and obstetrician on call.

Reasons for admission include:

- Sickle cell crisis
- Pain
- Increasing anaemia
- Chest pain or dyspnoea
- Pre-eclampsia
- Induction of labour
- Infection
- Labour

Take any deterioration in maternal health seriously.

If in doubt, contact Dr Oteng-Ntim via switch board or the Haematology consultant, Dr Jo Howard (ext 82741 or mobile via switchboard)

Inform women about the extra risk of crises during pregnancy and the need to attend hospital early if crisis is suspected.

Have a low threshold for admission if women with sickle cell disease are unwell (e.g. malaise, fever, breathlessness or pain). Make a clear differential diagnosis and plan and discuss with Dr Oteng-Ntim. Women having crises will generally be admitted to HDU.

Sickle cell crisis

Precipitating factors:

- Infection
- Fever
- Pre-eclampsia
- Cold
- Acidosis
- Dehydration
- Prolonged Labour
- Operative delivery

Management:

- Keep warm
- Admit to HDU
- Hydration
 - Encourage oral fluids. If unable to maintain oral intake give i.v. fluids to reduce risk of dehydration

- 3 litres/24 hours (Hartman's 1L over 8 hours)
- Maintain strict fluid balance chart.
- Encourage normal diet (eating and drinking if not in labour)
- Hourly observations of TPR and BP and pulse oximetry whilst on HDU
 - If febrile >37.50C take blood cultures, MSU and consider appropriate antibiotics.
 - If O₂ sats <94% on air – take Arterial Blood gases and get urgent medical/haematology opinion
 - If PO₂ <9kPa on air – discuss need for urgent exchange transfusion with haematology team
- Humidified O₂ 4l/min if sats.<92%
- Pain relief
 - May be regular, prn, parenteral or PCA-Morphine- or oral Sevredol depending on the level of pain. If unsure contact the sickle team or on call haematologist
 - Avoid non-steroidal anti-inflammatory drugs (unless postnatal)
- Investigations
 - Infection screen
 - FBC
 - CRP
 - U&E's
 - LFT's
- Physiotherapy if evidence of chest complications
- Daily CTG (>26 weeks)
- Daily urinalysis

Blood transfusion

A randomized trial comparing prophylactic transfusion versus need based transfusion showed no difference in fetal outcome. As multiple transfusion increases the risk of blood borne infections, isoimmunization and the need for hospital admissions, transfusion should be reserved for symptomatic patients who are unresponsive to conservative management⁷ (A)

Possible indications for transfusion include:

- Hb < 7g/dl
- Recurrent crisis
- Previous poor obstetric history
- Patients on hydroxycarbamide pre-conception

ALL TRANSFUSIONS MUST BE DISCUSSED WITH THE HAEMATOLOGY TEAM
All blood must have full Rhesus and Kell phenotyping

Transfusion (top up and /or partial exchange)

- Request forms for blood must be clearly marked indicating patient has SCD
- Check patient's ID against blood ID as per protocol
- Observe patient for signs of incompatibility (rash, loin pain, rigors)
- Hourly Temperature, Pulse and Oximetry during transfusion
- Strict fluid balance chart
- Medications as prescribed (e.g. Diuretics)

Infections

- 4 hourly temperature, pulse and respiratory rate
- IV access and bloods (U&E's, LFT's)
- IV Hydration and appropriate antibiotics
- Temp > 37.5°C, take blood cultures and MSU

Pre-eclampsia - As per usual management of PET

Spontaneous rupture of membranes (SRM)

Because of the infection and complication risk, early induction and avoidance of multiple VE's is recommended for women with Sickle Cell Disease.

Induction of labour - Regime as per protocol

Premature labour/Tocolysis - as per protocol

Fetal Surveillance

If a woman with sickle cell disease reports reduced fetal movements take this seriously. A CTG must be performed if more than 26 weeks. If there has not been a scan in the last week, then a scan should be performed for liquor volume, umbilical Dopplers and fetal growth (i.e. if no scan for more than 2 weeks). Only if fetal movements have returned and the CTG and growth are normal should she be advised home after discussion with SR/consultant.

Labour and delivery

Inform:

- Most senior obstetrician on call in the hospital
- On call consultant, if out of the hospital
- Consultant Anaesthetist on call
- Haematology consultant or on call SpR
- Sickle Clinical Nurse Specialist Bleep 1843 Ext 82710

Management and Investigations

- Keep warm and well oxygenated
- Hourly temp, pulse and Blood pressure
- Pulse oximetry. If saturations less than 94%, do ABGs and give O2 4l/min and get urgent medical/haematology opinion
- If evidence of chest complications, ask for physiotherapist input.
- Keep well hydrated- obtain IV access and give 11 Hartman's over 8 hours
- Strict fluid balance chart
- Bloods on admission: FBC, G&S, Ab screen,
- HbSS/HbSC level if patient has been transfused
- Prolonged labour (>12 hours) should be avoided, with early recourse to caesarean section as increased stress may trigger a crisis.
- If painful crisis occurs give morphine/diamorphine
- Continuous CTG.
- Choice of analgesia: Patient's choice, but to minimize distress, have a low threshold for epidural.

- PCA may be considered
- Advise neonatologist of delivery

Postnatal care

Post delivery, women with sickle cell disease should be admitted to HDU and at any time in pregnancy when a sickle crisis is suspected (after assessment on the hospital birth centre or day assessment unit). There should be a low threshold for admission of any woman with sickle cell disease.

Initial care

Keep warm

Continue hydration: 1 litre 8 hourly for 24 hours

Pulse oximetry: If O₂ sats < 94%, ABGS and give O₂ and urgent medical/haematological opinion

Chest X-ray if any chest pain or low saturation, because of risk of sickle chest.

If pyrexial - blood cultures and MSU

Co-amoxiclav and Clarithromycin are antibiotics of choice post delivery if required for a chest infection.

Consider metronidazole and cefadroxil for 7 days post-delivery for endometritis

IM/SC pain control:

Morphine sulphate 5-10mg im at 2-4 hourly intervals

PCA may be considered

Anticipate the need for laxatives and anti-emetics with opiate analgesia

Naloxone contraindicated if maternal opiate habituation

Give 6 weeks of prophylactic enoxaparin (refer to TED guideline) irrespective of mode of delivery.

On going care

- **Contraception:** No contraception is absolutely contra-indicated although the IUCD may be inappropriate because of the risk of infection 6(B). The Miraena coil may be highly recommended. The progestogen only pill (Cerazette) is recommended in preference to the oral contraceptive pill.
- Continue on prophylactic penicillin V and folic acid
- Outpatient appointment for the joint antenatal sickle cell disease clinic in 6 weeks
- Book into the Friday am sickle clinic in the haematology department in 3 months
- Universal neonatal screening on day 3 with Guthrie test (B). Results available in 6 weeks.

References

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