Bleeding disorders in pregnancy (GL1045)

Approval

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<th>Approval Group</th>
<th>Job Title, Chair of Committee</th>
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<tr>
<td>Maternity &amp; Children’s Services Clinical Governance Committee</td>
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Change History

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<th>Version</th>
<th>Date</th>
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<tr>
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<td>Surabhi Bisht (Consultant Obstetrician), Baljinder Chohan (ST6 Registrar)</td>
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1. Carriers of Haemophilia

Overview: Haemophilia refers to an inherited bleeding disorders caused by deficiency of coagulation factor VIII (haemophilia A), factor IX (haemophilia B), or factor XI (haemophilia C). Haemophilia A and B are X-linked recessive diseases that present in male children of carrier females. The distinction between haemophilia A and B is crucial for appropriate management. Haemophilia A is more common and likely to be more severe than haemophilia B.

1.1 Pre-pregnancy

- Pre-pregnancy counseling should be offered to discuss options for prenatal diagnosis and other aspects of pregnancy management.
- Women who may require blood product therapy should be immunised against hepatitis B.
- When there is any doubt about a woman’s carrier status, referral to the Haemophilia Centre in Oxford with Dr. Nicola Curry, is required for consideration of genetic testing.

1.2 Prenatal Diagnosis (PND)

- A multidisciplinary approach to prenatal diagnosis involving experts in the field of fetal medicine, genetic counseling, haemophilia care and molecular genetics should be adopted. This is provided in the Haemophilia clinic at John Radcliffe Hospital, Oxford. Referral and queries should be sent to: Haemophilia.reception@ouh.nhs.uk.
  - Fetal DNA testing at eight to nine weeks may be offered to patients. Fetal DNA blood sampling is generally taken only if CVS is being considered. Gestation must be confirmed by USS prior to blood sampling, as below seven weeks gestation the test is more likely to fail.
  - Chorionic villus sampling (CVS) remains the optimal method for PND of haemophilia. Women should be referred to the Fetal Medicine Unit (to Mark Sellinger/Suruchi Arora/Surabhi Bisht) at booking to discuss this option.
  - Knowledge of fetal sex is helpful in the management of labour. When the fetus is male, the risk of fetal cranial bleeding can be minimized by avoiding invasive monitoring techniques and instrumental deliveries.
  - For couples who do not wish to have invasive PND, fetal gender determination is strongly recommended by ultrasound when the anomaly scan is performed. The importance of this should be emphasized to the couple. If they do not wish to know the sex of the baby, this information should be available to the obstetrician in...
1.3 Antenatal management

- All pregnant haemophilia carriers’ women and women with other inherited bleeding disorders should be booked under care of Miss Bisht (Consultant obstetrician with special interest in haematological disorders).

- The pregnancy should be managed in close liaison with the Haematologists at the RBH and with the Haemophilia Centre at Oxford. Women are seen at least twice during their pregnancy at the RBH antenatal clinic with Miss Bisht and at the Haemophilia Center in Oxford (soon after booking and at 34 weeks gestation).

- Women with moderate and severe inherited bleeding disorders including VWD and haemophilia carrier’s women with affected male fetuses are referred to Oxford for delivery because of requirement of close monitoring of clotting factors levels for both mother and baby. The clotting factors analysis needs to be done immediately, which is readily available in Oxford (Oxford Haemophilia & Thrombosis Centre).

1.4 Monitoring and managing clotting factors during pregnancy

Factor VIII levels have been shown to increase in carriers of haemophilia A during pregnancy. The majority of patients will develop levels within the normal range, but the rise is variable and a small proportion may still have low levels at term. In contrast in carriers of Haemophilia B, factor IX levels rise only minimally, if at all in pregnancy.

- Carriers of haemophilia should have their clotting factors level (factor VIII or IX) checked at booking and at 28 and 34 weeks of gestation to allow appropriate management of labour and delivery, and to assess the need for prophylactic treatment. This is especially important in women with low pre-pregnancy levels (<50iu/dl).

- Prophylactic treatment is necessary for women with low factor levels (<50 iu/dl) undergoing any invasive prenatal diagnostic procedure, spontaneous miscarriage, termination of pregnancy or during labour. This should be arranged in advance with the Oxford Haemophilia Centre for elective procedures (01865-225316 during working hours, out of hours call the John Radcliffe switchboard and ask to speak with the on call Haematology Registrar at RBH).

- If treatment is required in carriers of either haemophilia A or B, recombinant factors products are the products of choice. Plasma-derived clotting factors concentrates have the potential to transmit hepatitis A and parvovirus B19, which may result in hydrops fetalis and fetal death, not like the mild infection in non-immunocompromised adults.
• It is recommended for women with very low factor levels or carrying an affected fetus to deliver at a unit where the necessary expertise in the management of this disorder and resources for laboratory testing and clotting factor treatments are readily available, such as the Oxford Haemophilia & Thrombosis Centre. In women with threatened preterm labour or requiring delivery with gestational age less than 34 weeks, discuss with Miss Bisht and the on call Paediatric Consultant.

• Women should be referred to the joint anaesthetic clinic held monthly in the RBH, to discuss options for analgesia and anesthesia (see below).

1.5 Management of labour

• FBC, coagulation screen should be checked on admission. Maternal factor VIII/IX activity should also be checked when 3rd trimester factor level is <50 iu/dl or when prophylactic treatment is given. Ideally haemophilia patients should deliver at JRH. If patients prefer to deliver at RBH or present in labour, the on call obstetric team should liaise with both Haematology at RBH and the Haemophilia Centre at JRH.

• Provided the coagulation screen is normal or has been normalised by prophylactic treatment and the factor level is above 50 iu/dl, there is no contra indication to epidural analgesia. Please refer all carriers of haemophilia to the joint Obstetric Anesthesia clinic (held at JRH/RBH) during the 3rd trimester. Factor level must also be confirmed to be above 50 iu/dl for removal of an epidural catheter after delivery.

• The risk of postpartum haemorrhage (PPH) is high. The risk of primary PPH is 22% and secondary PPH is 11%. This can be reduced by
  o Active management of 3rd stage of labour. In addition, give 600mcg of misoprostol PR after the delivery of the placenta.
  o Minimising maternal genital and perineal trauma
  o Prophylactic treatment to maintain maternal factor levels above 50 iu/dl for 3-4 days after normal vaginal deliveries and 5-7 days after operative deliveries.

• The fetus (if affected) is at risk of cranial bleeding during labour and delivery. When the fetus is an affected male or a male and haemophilia status is unknown or when fetal sex is unknown, avoid:
  o The use of fetal scalp electrodes and fetal blood sampling
  o The use of ventouse/ vacuum extraction
  o The use of difficult forceps delivery, however, low forceps delivery may be less traumatic than LSCS when the head is deeply engaged in the pelvis and delivery can be achieved by easy outlet forceps. In such circumstances, please discuss with the consultant on call for labour ward.
• Prolonged 2nd stage of labour. Any failure to progress, especially in the second stage of labour, discuss with the consultant on call. Decision for induction or augmentation of labour should always be discussed with the consultant.

• Any operative procedure when indicated should be performed by an experienced obstetrician. Please discuss with the Haemophilia team.

• In the event of a PPH, contact the Haematology team at RBH and the Haemophilia team at OUH immediately. Obstetric causes for excessive bleeding should not be overlooked. Consideration should be given to tranexamic acid to reduce bleeding in cases of heavy lochia.

1.6 Postnatal management

• Cord blood sample should be collected in a citrated tube (preferably 2 Paediatric blue top bottles, failing that one standard blue top bottles). Please do not overfill the bottles and only fill up to the line. All blood samples should be labeled appropriately including clinical details and sent to RBH Haematology lab with instructions for it to be sent to the Oxford Haemophilia Centre. During the weekend, contact the on call Haematology team at RBH and JRH via the switchboard.

• Results of clotting factors should be conveyed to the parents by the Obstetric and Paediatric teams at RBH. An early appointment to see the Paediatric Haemophilia team should be made at the JRH.

• Intramuscular injections and venepunctures should be avoided in neonates affected with haemophilia or whose coagulation status is unknown. Vitamin K should be given orally and routine immunisations should be given subcutaneously. Circumcision should be delayed until the coagulation status of the neonate is known and appropriate management can be arranged by the haematologist.

• Cranial ultrasound/computed tomography (CT) scans should be arranged for all neonates with haemophilia if labour has been premature, traumatic, e.g. following forceps delivery or prolonged labour, or if there are any clinical signs suggestive of intracranial bleeding.

• If there is a clinical suspicion of intracranial bleeding, please discuss immediately with the haemophilia team in Oxford and treat the baby with the agreed dose of recombinant clotting factor (as advised by Oxford); commonly to raise the plasma clotting factor to 100 IU/dL. Further treatment will be required if a bleed is confirmed by radiological imaging. Please liaise with the Haemophilia Centre.

• Parents will be given follow-up counseling by the haemophilia team in Oxford and babies with haemophilia and other inherited bleeding disorders will be registered at Oxford Haemophilia & Thrombosis Centre.
• Community midwives should be informed of affected babies and together with the mothers should be made aware of the early signs of intracranial haemorrhage (e.g. lethargy, vomiting, seizures and poor feeding).

2. Factor XI deficiency

The principles for management of pregnancy in women with FXI deficiency are similar to those of carriers of haemophilia. Summary of recommendations include:

• Pregnancy in women with FXI deficiency requires specialised and individualised care provided collaboratively by an obstetrician, haematologist and anaesthetist.

• Due to the unpredictability of the condition, attempts should be made to identify the individual's clinical bleeding tendency and the coexistence of confounding factors.

• Prenatal diagnosis should be discussed and offered to patients where there is a risk of severe factor XI deficiency.

• Factor XI levels should be checked at booking, 28 and 34 weeks and prior to invasive procedures. Many patients can be managed expectantly but patients with severely low levels or a positive bleeding history should be given prophylaxis to cover invasive procedures.

• Delivery plan should be made in advance. It is recommended for women with FXI deficiency to deliver at a unit where the necessary expertise in the management of this disorder and resources for laboratory testing and clotting factor treatments are readily available.

• Women with severe deficiency and/or a bleeding history, should receive prophylaxis at the onset of labour or prior to planned induction or caesarean section. Where prophylaxis has been given, it should be extended to 3 days post-partum or 5 days following caesarean section.

• Oral Tranexamic acid 1000 mg qds should be offered to all women with factor XI deficiency during labour and post-partum.

• Active management of third stage should be practiced in women with FXI deficiency.

• Care should be taken to avoid unnecessary trauma to the baby at delivery and an umbilical cord sample for FXI level should be obtained.
3. Von Willebrand disease (VWD)

The principles for management of pregnancy in women with VWD are similar to those of carriers of haemophilia. Summary of recommendations include:

- Pregnancy in women with VWD should be managed by a multidisciplinary team including an obstetrician, haematologist and anesthetist.

- Factor levels including VWF:Ag, VWF:AC and FVIII:C should be checked at booking, 28 and 34 weeks and prior to invasive procedures. Platelet count must also be checked in patients with type 2B VWD. Prophylactic treatment should be given when factor levels are <50 IU/dl to cover invasive procedures and delivery.

- DDAVP can be used in pregnancy, but repeated administration or use in pregnancies complicated with pre-eclampsia must be avoided. Close monitoring for water retention and Hypernatraemia must accompany its use. Fluid restriction to 1 liter per 24 hours following DDAVP administration is recommended. Dose calculation and authorization for the use DDAVP should only be done by the haemophilia team.

- Women with type I VWD generally do not require prophylactic treatment for delivery, as their VWD levels will have risen sufficiently during pregnancy. In type 2 VWD, treatment may be required, depending on blood levels. Women with type 3 VWD will require treatment for all types of delivery.

- Delivery plan should be made in advance and for women with severe VWD, delivery should be planned at a unit where the necessary expertise in the management of this disorder and resources for laboratory testing and clotting factor treatments are readily available.

- Epidural anaesthesia can be offered for use in majority of women with type 1 VWD whose von Willebrand factor activity is >50IU/dl (or raised to >50IU/dl by prophylactic treatment). It should be carried out by an experienced anesthetist. It is not recommended for use in type 2 or 3 VWD.

- Women with von Willebrand factor activity <50IU/dl should receive prophylactic treatment at the onset of established labour or prior to planned caesarean section.

- Active management of third stage should be practiced in women with VWD.

- Factor levels should be monitored post-delivery and prophylaxis given to maintain von Willebrand factor activity and factor VIII levels >50IU/dl for at least 3 days, or 5 days following caesarean section.

- Oral Tranexamic acid 1000 mg qds or combined oral contraceptive pill should be given to all women with VWD to control prolonged and/or intermittent secondary postpartum haemorrhage, and is often recommended to be taken until the lochia runs clear after hospital discharge.
• Invasive monitoring techniques, vacuum extraction and rotational/mid-cavity forceps should be avoided and a cord blood sample should be sent for assessment.

• Intramuscular injections and venepunctures should be avoided in neonates whose coagulation status is unknown. Vitamin K should be given orally and routine immunisations should be given subcutaneously. Circumcision should be delayed until the coagulation status of the neonate is known and appropriate management can be arranged by the haematologist.
Appendix 1 - PATHWAY FOR PREGNANT WOMEN WITH/CARRIERS OF INHERITED BLEEDING DISORDERS:

PLEASE CONTACT HAEMOPHILIA TEAM FOR ALL PREGNANT PATIENTS WITH BLEEDING DISORDERS, INCLUDING THOSE WHO ARE CARRIERS FOR BLEEDING DISORDERS

GENERAL ADVICE THROUGHOUT PREGNANCY:

- Refer all patients to the Haemophilia and Thrombosis Centre (OHTC)
  - Pre-natal diagnosis may be required, refer as early as possible
  - Blood tests to check at time of referral:
    - Haemophilia A carrier: FVIII level
    - Haemophilia B carrier: FIX level
    - Patients with VWD: FVIII, VWF Ag, VWF CBA, VWFcP1bM, FBC
    - Rare bleeding disorders: discuss with Haemophilia team
  - Referrals and queries to: Haemophilia.reception@ouh.nhs.uk or contacts below
  - Fetal DNA blood sampling is generally taken only if CVS is being considered
- Please discuss any unexpected bleeding with the haemophilia team
- Haemostatic therapy may be required for any intervention or procedure: please discuss with the haemophilia team

Pre-delivery:
- The patient will be reviewed by a multi-disciplinary team, in 1st and 3rd trimesters and a decision will be made about the most suitable hospital for delivery
- Depending on blood results and type of inherited bleeding disorder, a haemostasis treatment plan will have been made which will include:
  - Management for mother:
    - Need for clotting factor concentrate/haemostatic drugs at delivery
    - Blood sampling frequency
    - Guidance about neuraxial anaesthesia
  - Management for baby:
    - Need to avoid instrumental delivery, fetal scalp electrodes
    - Use of IM/ oral vitamin K
    - Blood sample requirements from the cord

Post-delivery:
- Haemostasis treatment (where required) will be guided by clotting sample results
- The team will provide advice on duration of haemostasis treatment, as well as thromboprophylaxis

Local Haematology Contacts:

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<tr>
<th>Contact</th>
<th>Phone Number</th>
<th>Bleep</th>
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<tr>
<td>Haematology registrar on call</td>
<td>01865 225316</td>
<td>5529</td>
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<tr>
<td>Haemophilia Nurses</td>
<td>Bleep 5064</td>
<td></td>
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<td>Haemophilia reception</td>
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Oxford Haemophilia &Thrombosis Centre Contacts for adults:

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4. References


