University Hospitals of Derby and Burton NHS Foundation Trust

Obstetric and Neonatal management of carriers of Haemophilia A and B – Full Clinical Guideline

Reference No.: Obst/07:23/H2

Contents

Section		Page
1	Introduction	1
2	Purpose and Outcomes	2
3	Abbreviations	2
4	Key Responsibilities / Duties	2
5	Pre-pregnancy care	2
6	Pregnancy Management	3
6.1	Prenatal diagnosis and fetal sexing	3
6.2	Antenatal management of mother	3
6.3	Labour / delivery care	4
6.4	Postpartum management	5
6.4.1	Mother	5
6.4.2	Baby	5
7	Monitoring Compliance and Effectiveness	6
8	References	6
	Documentation Control	7

1. Introduction

Haemophilia A (Factor VIII deficiency) and Haemophilia B (Factor IX deficiency) are the most severe congenital bleeding disorders. They are inherited as X-linked recessive conditions. Females in families with a history of haemophilia may be obligate or potential carriers.

A woman is considered an obligate carrier if: her father has haemophilia; she has a family history of haemophilia and one affected son; she has two sons affected with haemophilia.

A woman is considered a potential carrier if she has a maternal relative with the disorder.

The fetus of a maternal haemophilia carrier and an unaffected father will have a 50% chance of having haemophilia (if male) or of being a carrier (if female).
The fetus of a father with haemophilia will be unaffected if male and an obligate carrier if female.

Maternal carriers of haemophilia may have reduced levels of Factor VIII or IX (approx 50% of normal) and consequently may have a mild bleeding disorder. Most have levels that are unlikely to cause spontaneous bleeding and most will normalise in pregnancy. A few carriers may have clotting factor levels in the haemophilia range and may be symptomatic commensurate with their degree of clotting factor deficiency, particularly during surgery.

In women who are known carriers of haemophilia the opportunity exists to manage pregnancy, labour and delivery and the early neonatal period in order to minimize the increased risk of bleeding in both the mother and the affected fetus/neonate. Successful management of both mother and baby depends on a multidisciplinary approach (obstetric, haematological, neonatal and midwifery)

2. Purpose and Outcomes

To promote a multidisciplinary approach to management of pregnancy and the neonatal period in haemophilia carriers, in keeping with national guidance, in order to optimise outcome for both mother and baby.

3. Abbreviations

APTT	-	Activated Partial Thromboplastin Time
CCG	-	Clinical Commissioning Group
C/S	-	Caesarean Section
COCP	-	Combined Oral Contraceptive Pill
CVS	-	Chorionic Villus Sampling
DDAVP	-	Desmopressin Acetate
DNA	-	DeoxyriboNucleic Acid
ECH	-	Extra Cranial Haemorrhage
ECV	-	External Cephalic Version
EL LSCS	-	Elective Lower Segment Caesarean Section
FBC	-	Full Blood Count
FSE	-	Fetal Scalp Electrode
FVIII	-	Factor 8
FVIX	-	Factor 9
GA	-	General Anaesthetic
G&S	-	Group and Save
ICH	-	Intra Cranial Haemorrhage
IM	-	Intramuscular
IVF	-	In Vitro Fertilisation
LSCS	-	Lower Segment Caesarean Section
MRI	-	Magnetic Resonance Imaging
MROP	-	Manual Removal of Placenta
NSAID	-	Non-Steroidal Anti-Inflammatory Drugs
PCA	-	Patient Controlled Analgesia
PIGD	-	Pre Implantation Genetic Diagnosis
PPH	-	Post Partum Haemorrhage
PT	-	Prothrombin Time
PTT	-	Partial Thromboplastin Time
TXA	-	Tranexamic Acid

4. Key Responsibilities / Duties

Midwifery and medical staff are responsible for the early identification and appropriate referral of women who may be or are known to be haemophilia carriers.
The combined obstetric/haematology service is responsible for co-ordinating the development of individualised multidisciplinary care plans.

5. Pre-pregnancy care

Females with a family history of haemophilia, known carriers or those with partners with haemophilia should be offered referral to the combined obstetric haematology service for pre-pregnancy counselling and referral for genetic counselling and screening for carrier status where appropriate. The identification of a molecular marker in the family is necessary if prenatal diagnosis is to be considered in pregnancy.

Baseline Factor VIII/ IX levels should be checked to identify carriers with low levels. Immunity to Hepatitis A and B should be checked and vaccinations given as appropriate.

Discussions about options for prenatal diagnosis and management of pregnancy will depend on the parent's attitude to termination of pregnancy and haemophilia.

Pre-implantation genetic diagnosis (PIGD) by IVF can be utilized in haemophilia and may be considered by some couples in preference to prenatal diagnosis. Couples wishing to consider this option would need referral to a local fertility specialist and would require discussion with the Clinical Commissioning Group (CCG) regarding funding.

6. Pregnancy Management

Refer for early booking under combined obstetric haematology service +/- to Fetal Medicine Consultant if wish to consider first trimester prenatal diagnosis by CVS. The latter is only available to women in whom a molecular marker has been identified.

6.1 Prenatal diagnosis and fetal sexing

- CVS is the method of choice for prenatal diagnosis and can be offered at 11- 13 wks, prior to fetal sexing. Initial sex determination is undertaken and where male fetus identified proceed to gene testing. Parents should understand miscarriage risk 1 in 75, unnecessary risk to female fetus and possibility of mosaicism. Also increased bleeding potential in affected fetus
- Fetal gender can be determined by testing circulating cell free fetal DNA from maternal blood for Y chromosome specific sequences after 7 weeks gestation. This may help parents to decide whether they wish to have CVS.
- Amniocentesis can be done after 15 weeks gestation, at which stage it may be possible to determine fetal gender by ultrasound prior to the procedure, so avoiding unnecessary risk to a female fetus.
- Those women who do not wish to take the risk of an invasive procedure should be encouraged to consider fetal sex determination by ultrasound at 18-20 wks even if they wish to remain unaware of result, as this will guide pregnancy management. This should be offered in fetal medicine department. If the fetus is male it should be managed as an affected fetus (50% risk) and the option of later amniocentesis discussed
- Women who wish to avoid the miscarriage risk associated with first or second trimester prenatal diagnosis but who do wish information that would influence their intrapartum management have the option of later third trimester amniocentesis at 35-36 weeks. They need to be aware of the 1% risk of preterm labour.

Maternal Factor Levels will need checking before any invasive procedure as they will need correcting with recombinant coagulation factor concentrate before the procedure if level < 50%.

6.2 Antenatal management of mother

Check Factor VIII/IX levels at booking, 28 weeks and 34 weeks or before invasive procedures as above (one citrate blue top bottle).

Most women will be expected to normalise their FVIII levels during pregnancy but in the event of early pregnancy complications eg. Miscarriage, ectopic, TOP or if amniocentesis/ CVS required it may be too early for these changes to have occurred. FIX levels tend to remain constant. Levels <50% will need correcting before any of the above procedures- discuss with Consultant Haematologist.

If maternal factor levels remain low at 34- 36 weeks treatment to correct will be required prior to delivery (note maternal treatment will not normalize fetal factor levels).This is more likely to be required in Haemophilia B carriers.
A level of 40% is sufficient to avoid haemorrhage in early pregnancy and for vaginal delivery but a level of >50% is required for epidural, diagnostic procedures or caesarean section.

If treatment is required recombinant products should be regarded as the products of choice. Plasma derived products have the potential to transmit Hepatitis A and Parvovirus. DDAVP should be avoided in the antenatal period due to concerns about the risks of placental insufficiency due to its vaso constrictive effects, preterm labour due to its oxytocic effects and maternal risks of hyponatraemia. It can however be used during labour or postpartum.

A plan for Labour/delivery should be discussed antenatally between the Consultant Obstetrician and the mother, taking into account obstetric issues, maternal factor levels and the known or potential haemophilia status of the fetus.

The women should be referred antenatally to the obstetric anaesthetic clinic to discuss pain relief options and anaesthesia.

Any plan of care to be documented in the maternal records.

Haemophilia carrier status in itself is not a contra-indication to vaginal birth, but there will be a number of constraints on intrapartum management of women known to be carrying a potentially affected or affected male child. Even female fetuses may have an increased risk of bleeding with traumatic delivery (due to a combination of lyonization and immaturity of the fetal liver) although this risk is likely to be less. The option of elective Caesarean Section to reduce the risk of neonatal ICH may be considered on an individual basis.

The optimal mode of delivery for the fetus at risk of haemophilia remains the subject of debate due to continuing uncertainty about the risk of intra-cranial (ICH) and extra-cranial bleeding (ECH) in fetuses with underlying haemorrhagic disorders. The overall risk of ICH appears to be low (0.05% following spontaneous delivery and 0.035% following planned Caesarean section) and increased following delivery by Ventouse or forceps (0.11 – 0.15%) and Caesarean section during labour (0.05%). Additionally the risk of subdural bleeding appears to be highest following forceps or Ventouse delivery. Whilst avoiding instrumentation during labour may well reduce the risk of ICH it does not prevent it, equally whilst ICH is less commonly reported after EL LSCS, this mode of delivery may carry increased morbidity for the mother. All of these factors need to be taken into account in order to individualise care plans

A neonatal alert should be completed if the mother is carrying an affected or potentially affected male child.

6.3 Labour / delivery care

On admission check FBC, Clotting, G&S and Factor VIII/IX if < 50% at last check or if greater than 2 weeks since last.

Aim for vaginal delivery unless obstetric contraindication to this or antenatally determined plan recommends Caesarean Section. Spontaneous labour is preferable to induced labour as the latter is likely to be longer and have an increased risk of need for operative delivery.

Avoid maternal IM analgesia if level< 40%. Pethidine may be administered subcutaneously if necessary, at the same dosage. The onset time may be slightly longer than for IM administration.

Regional anaesthesia:
Is considered safe if coagulation screen is normal and factor levels >50 iU/dL.
If levels <50 iU/dL, consider Remifentanil PCA / GA and inform consultant anaesthetist on call.
If time does not allow for assessment of the factor levels, if levels were >50iU/dL in third trimester and the platelet count, partial thromboplastin time (PTT) and prothrombin time (PT) are within normal range it is reasonable to proceed with a regional technique.

If the decision is made to proceed with neuraxial anaesthesia or analgesia, then it should be performed by the most experienced anaesthetist available on Labour Ward at the time, in discussion with the Consultant Anaesthetist on call.

For epidurals, high concentration top-ups should be avoided, unless for LSCS. If motor block occurs then it should be monitored closely and if prolonged (>4hr postpartum) and not showing progressive resolution urgent MRI should be considered and sought.

It is important remove the epidural catheter as soon as possible after the delivery as the pregnancy-induced rise in factor levels may **quickly** reverse after birth and bleeding in the spinal canal may then arise. If there is a significant delay in removing the epidural catheter (>4hr) then it would be advisable to **check factor levels prior to the removal** of epidural catheter.

If anaesthesia is required postpartum eg tears / MROP then it would be wise to consider GA especially if later than 4hr postpartum, unless there are significant risks with a GA.

Intramuscular analgesia and non-steroidal anti-inflammatory drugs (NSAID) should be avoided if factor levels are below normal, consideration should be given to IV PCA analgesia in these circumstances.

Intrapartum management decisions should be made in conjunction with a Consultant Obstetrician or other suitably experienced Obstetrician to minimise the risk of traumatic bleeding for both mother and baby. If the fetus is confirmed unaffected after prenatal diagnosis or is female, normal intrapartum care should be offered. If the fetus is a potentially affected male or of unknown sex the labour/delivery should be managed as if affected fetus and procedures that carry an increased risk of cranial bleeding should be avoided where possible.

- Principles of management are to achieve the least traumatic delivery possible utilising senior midwifery and medical staff
- Avoid FSE/ Fetal blood sampling
- Normal vaginal delivery should be conducted by an experienced midwife to reduce the risk of perineal trauma
- Ventouse, rotational and mid cavity forceps carry a significant increase in the risk of cranial bleeding and should be avoided unless delivery by C/S considered more traumatic.
- Low cavity forceps likely to be less traumatic than a full dilatation C/S but should only be undertaken by a senior obstetrician.
- Early recourse to Caesarean Section if significant delay in labour
- Active management of the third stage should be practised, physiological management is contraindicated
- Prompt repair of perineal trauma by suitably experienced operator
- There is little data to inform management of breech presentation but there would be concerns about the risk of ICH with both ECV and vaginal breech birth

6.4 Postpartum management

See section on postpartum spinals and removal of epidural catheters above.

6.4.1 Mother

Most bleeding problems in haemophilia carriers occur postpartum as Factor levels may fall rapidly. The risk of primary PPH is 22% and secondary PPH 11%. If postpartum bleeding occurs, employ usual obstetric haemostatic measures but check Factor levels urgently and correct if levels low < 50%.
Monitor FVIII/IX daily and maintain levels above 50% for 3/7 following vaginal delivery and 5 days after Caesarean Section.

Early postpartum haemorrhage should be managed with the usual obstetric haemostatic measures and correction of maternal hypovolaemia. If problematic and associated with low factor levels can be treated with factor replacement or DDAVP (if Haemophilia A, DDAVP non effective in Haemophilia B) after discussion with the Consultant Haematologist. If DDAVP is required postpartum it can be used in breastfeeding mothers as it does not cross into breast milk.

Later PPH / heavy lochia may be best managed with TXA, COCP or Mirena Coil.

6.4.2 Baby

If male infant, a cord sample should be taken in a citrate tube for coagulation screening and Factor VIII/IX assays after discussion with Haematology Consultant.
Where severe haemophilia A or B is suspected the diagnosis should be confirmed by factor assay within the first few hours after delivery.
If there is any uncertainty about contamination of the cord sample with maternal blood a venous sample should be obtained from the baby.

Avoid IM injections or heel stab until clotting factor results known. Give Vitamin K orally if any significant delay anticipated in obtaining result.

Approximately 1/3 of cases of haemophilia are due to new mutations so haemophilia may present with unexpected intra-cerebral haemorrhage following birth. In these cases haemophilia may not be suspected and mild prolongation of the APTT may be interpreted as normal for the newborn. Specific Factor VIII assays will be required

7. Monitoring Compliance and Effectiveness

Audit compliance through Combined Obstetric Haematology Service

8. References

Chalmers E, Williams M, Brennand J, Liesner R, Collins P, Richards M on behalf of Paediatric Working Party of the United Kingdom Haemophilia Doctors Organization; Guideline on the management of haemophilia in the fetus and the neonate; BJH Guideline approved by the British Committee for Standards in Haematology; British Journal of Haematology:154; 208-215, 2011

Clark P & Greer A: Bleeding Disorders in pregnancy; Chapter 4 pp 66-76. In Practical Obstetric Haematology; Taylor and Francis Group; 2006

Guidelines for Management of Pregnancy and Delivery in Women who are either carriers or patients with bleeding disorders: Australian Haemophilia Centre Directors Organisation; June 2007

Srivastava A et al. Guidelines for the management of haemophilia: Haemophilia(2012), 1-47

Lee CA et a. The obstetric and gynaecological management of women with inherited bleeding disorders

Documentation Control

Reference Number: OBST/07:23/H2	**Version:** **UHDB Version 2**		**Status: FINAL**	
Version / Amendment	Version	Date	Author	Reason
	1	Jan 2013	Miss R Hamilton Consultant Obstetrician	New Guideline
	2	Oct 2017	Miss R Hamilton Consultant Obstetrician	Review
UHDB	1	June 2020	Miss R Hamilton Consultant Obstetrician	Review
	2	June 2023	Miss R Hamilton Consultant Obstetrician	Review
Intended Recipients:				
Training and Dissemination: Cascaded through lead midwives/doctors; Published on Intranet, NHS mail circulation list. Articles in Business Unit newsletter				
Consultation with:	Dr McKernan / Obstetric Anaesthetists / Neonatologists			
Business Unit Sign off:	02/05/2023: Maternity Guidelines Group: Miss S Rajendran - Chair 19/06/2023: Maternity Governance Group - Mr R Deveraj			
Notification Overview sent to TIER 3 Divisional Quality Governance Operations & Performance: 20/06/2023				
Implementation date:	05/07/2023			
Review Date:	July 2026			
Key Contact:	Joanna Harrison- Engwell			