Second Trimester Pregnancy Loss at 13 – 19 Weeks of Pregnancy
Full Clinical Guideline

Reference No.: UHDB/Gynae/12:21/M7

Contents

1. Introduction and Background

Spontaneous miscarriage is the commonest complication of pregnancy and occurs in about one fifth of clinical pregnancies (1). The majority of miscarriages occur in the first 12 weeks of pregnancy. The miscarriage rate is reduced to approximately 1% if a live fetus has been identified by ultrasonography at 10 weeks gestation in a normal population (2). In low risk women the risk of miscarriage in the second trimester is approximately 0.5% (3).

2. Purpose and Scope

The purpose of this guideline is to improve the management of women with miscarriage between 13^{+0} to 19^{+6} weeks of pregnancy. This guidance should not be implemented until a robust diagnosis of miscarriage has been made.

Please refer to obstetric guidelines when pregnancy loss is diagnosed at 20^{+0} weeks gestation and over. Click here to go to the clinical guideline

In case of silent miscarriage ≥13 weeks with fetal size suggesting demise prior to 13 weeks, consider management as per early pregnancy loss guidelines. Click here to go to the clinical guideline

3. Abbreviations

GAU	-	Gynaecology Assessment Unit
IV	-	Intravenous
PM	-	Post Mortem
PV	-	Per Vaginum
PoC	-	Products of Conception
RPoC	-	Retained Products of Conception

4. Causes of miscarriage between 13+0 and 19+6 weeks of pregnancy

Pregnancy loss between 13^{+0} and 19^{+6} weeks of pregnancy may be caused by fetal structural abnormalities, maternal uterine abnormalities and cervical weakness (4). Many studies have shown associations between second trimester pregnancy loss and Factor V Leiden mutation, protein S deficiency and the prothrombin G20210A mutation (5). Antiphospholipid antibodies can cause placental thrombosis resulting in an increased risk of second trimester pregnancy loss (6). Chromosomal abnormalities also cause pregnancy loss in the second trimester.

Infection has been implicated in 10-25% of second trimester pregnancy losses (7). Many infectious agents have been suggested, including bacteria, spirochetes, protozoa, viruses and fungi (8). Bacterial vaginosis has been associated with second trimester pregnancy loss and treating it may reduce risk of late miscarriage in women with a history of preterm delivery (9).

Establishing a cause and effect relationship may sometimes be difficult. Causation is well established for chromosomal and fetal structural problems. However, depending on how extensively the woman is investigated, the cause of second trimester loss may remain unexplained.

5. Clinical Assessment

A common presentation is vaginal bleeding and/or abdominal pain. There may be a history of passage of amniotic fluid or products of conception. Attention should be paid to a history of a vaginal discharge and whether it is offensive or not. However, the presenting symptoms can be subtle and may sometimes reflect an underlying associated medical disorder or complication such as infection. A past history of previous pregnancy loss and/or cervical surgery, should be recorded. In some circumstances, the woman may be asymptomatic and the diagnosis is made unexpectedly at the time of a routine ultrasound examination.

Examination should include the woman's vital signs and abdominal examination looking for any tenderness. A speculum examination should be performed - pooling of amniotic fluid may be evident in the posterior vaginal fornix. In the absence of ruptured membranes a gentle vaginal examination should be performed to assess the cervix and the extent of any vaginal bleeding. A high vaginal swab should be sent for microbiological culture and sensitivity.

6. Investigations

Ultrasound should include checking the fetal heart activity, liquor volume and placental site. A repeat ultrasound scan by an appropriately trained ultrasonographer may be required, for example, to confirm fetal demise or a fetal structural abnormality.

Laboratory tests

- Check FBC, clotting screen, Group and Save.

- Infection screen (HVS, endocervical swabs, MSU, CRP, blood cultures) should be performed if maternal infection is suspected, particularly in the presence of pyrexia, flu-like symptoms, abnormal liquor or prolonged rupture of membranes.

7. Management options

The diagnosis of miscarriage should be discussed sympathetically in private with the woman and her partner. The management options should be outlined and a plan documented in the clinical notes. It should also be explained that it might be necessary to modify the planned management depending on how the clinical circumstances evolve.

The management may involve awaiting spontaneous miscarriage (i.e. expectant) or medication management of miscarriage. Where there is evidence of maternal compromise (e.g. sepsis, heavy bleeding), immediate steps towards delivery may be required. However, a more expectant approach can be discussed if the woman's condition is stable.

In the case of silent miscarriage diagnosed ≥ 13 weeks but fetal size consistent with demise prior to 13 weeks, surgical evacuation may be appropriate. Click here to go to the clinical guideline for early pregnancy loss.

If the mother chooses expectant management then arrangements for review should be made. If delivery is delayed >48 hours, repeat FBC and clotting screen weekly. Also advise that if expectant management is performed the appearance of the baby may deteriorate. All mothers should be given a 24 hour contact number if they are managed as an outpatient for any time between diagnosis and delivery. Advice should be given to return to hospital should the mother experience symptoms such as abdominal pain, vaginal bleeding, feeling unwell or have any concerns about her well-being.

Infection is more likely to occur when the cervix is dilated, if the membranes are ruptured or if the uterine contents have protruded through the cervix.

Antibiotic administration should be considered on an individual basis.

Extremely rarely a hysterotomy may need to be considered due to failed attempts at induction of miscarriage or deteriorating maternal condition. The decision regarding mode of delivery in such complex cases should be made by a consultant.

8. Admission

Continuity of care is important and an individual nurse/midwife should be assigned to the woman, if possible. Appropriate support services should be contacted in relation to the woman's admission including members of the hospital bereavement team.

The woman should be closely supervised for changes in her clinical circumstances or for evidence of deterioration in her vital signs and modified early warning score.

9. Analgesia

Analgesia is important for women having medication management of miscarriage including paracetamol, codeine, Entonox, oral morphine, subcutaneous morphine or pethidine.

10. Medication Management of Miscarriage

A combination of mifepristone and misoprostol is recommended as the first-line pharmacological intervention for management of miscarriage up to 19^{+6} weeks.

Sensitivity to misoprostol increases with gestation and is further increased by both fetal demise and administration of mifepristone 36 to 48 hours prior to misoprostol (there is no evidence against earlier induction of labour following mifepristone – induction can occur anytime from 6 hours to 48 hours after administration).

Increasing dosage of misoprostol increases the likelihood of successful delivery but also increases the incidence of side effects, which include fever, chills, abdominal pain, nausea, vomiting and diarrhoea. Although fever is a side effect of misoprostol the woman should still be closely monitored clinically for any signs of infection.

10.1 Stage 1: Mifepristone 200mg orally

This drug must only be administered in hospital and patients should be observed when taking this medication. Contraindications include:

- uncontrolled or severe asthma
- chronic adrenal failure
- acute porphyria

Cautions:

- asthma
- risk factors for cardiovascular disease; prosthetic heart valves or endocarditis
- haemorrhagic disorders.

A single dose of mifepristone 200 milligrams oral is given. The mother should be allowed home after one hour wherever possible.

Prior to going home, staff should ensure that the woman has contact numbers for the unit which will enable her to obtain appropriate advice at any time over the next 48 hours.

A delay is required to optimise the effect of Mifepristone. This is ideally 36 to 48 hours. During this time the woman may be at home, but should be advised to attend if any bleeding or pain. The woman needs to be given information on where to attend and how to contact this department.

10.2 Stage 2: Misoprostol

After 36-48 hours, Misoprostol 200mcg is given every 4 hours (PV, Sublingual or Buccal); maximum of 6 doses.

Note oral administration (swallowing) of misoprostol has lower efficacy and so oral administration should not be used with pregnancy ≥ 7 weeks gestation unless vaginal, sublingual or buccal routes of administration of misoprostol are unacceptable to the woman.

The patient should be made aware that administration by sublingual (sl) or buccal route is associated with higher likelihood of headache. Misoprostol tablets administered buccally or sublingually may take approximately 20 minutes to dissolve, may not dissolve fully and are associated with an unpleasant taste in the mouth. If this is unacceptable, the tablet may be dispersed in 10ml of water. The tablet should disperse in less than 2 minutes, and should be administered immediately after dispersal.

Side effects include fever, nausea, vomiting, abdominal cramping and diarrhoea.

Warning for all staff regarding handling the broken Misoprostol tablets:
Staff who are or may become pregnant should not handle the broken or crushed tablets. If handling the broken tablets is necessary, gloves should be worn, and care should be taken to avoid inhalation of any powder.

Offer loperamide to ladies having diarrhoea as a side effect.
Two tablets (4 mg) initially, followed by one tablet (2 mg) after every loose stool. The usual dosage is 3-4 tablets (6 mg-8 mg) per day. The maximum daily dose should not exceed 8 tablets (16 mg).

In those cases where delivery has not occurred 24 hours after commencing misoprostol, a further identical course of misoprostol may be administered on the instructions of the consultant gynaecologist on call.

11. Special Circumstances

Women with ruptured membranes
A recent randomised prospective trial has shown that oxytocin is as efficient as misoprostol in inducing delivery of second trimester miscarriage but has a longer mean time to delivery (26).

Women with uterine scar
The incidence of uterine rupture is low (0.2%) with medication management of miscarriage but is increased in the presence of a uterine scar (e.g. following previous caesarean section) to around 4%. There is no good study evidence to identify any one best method of induction in this situation. The misoprostol doses above should be used with caution. All staff should be vigilant to clinical features that may suggest uterine scar dehiscence or rupture, i.e. maternal tachycardia, atypical pain, vaginal bleeding, haematuria and maternal collapse.

12. Consent

Valid written consent must be obtained before starting medication management of miscarriage.

13. Delivery of the Placenta

There is a higher incidence of retained products of conception (RPoC) compared to first trimester miscarriage. A low threshold for evacuation of retained products of conception (ERPoC) should therefore be adopted if the placenta or membranes appear incomplete or if the woman experiences excessive bleeding.

If there is a delay in delivery of the placenta of more than one hour, the bladder should be emptied and surgical evacuation considered. Commence an IV infusion of 40 units of oxytocin in 500 mL of normal saline at 125 mL/hr over 4 hours and/or ergometrine 0.5 mg IV if bleeding.

14. Examination of Fetus and Placenta

The registrar on call should examine the fetus and placenta and record the observation findings in the hospital notes.

15. Caring for Parents Post Delivery

Commence appropriate checklists available.

Staff should gently explain to the couple what their baby might look like after birth and they should be offered the opportunity to see or hold their baby. Staff should also make the couple aware that the gender of the infant may not be easily identified at this gestation. Hence, in cases of uncertainty, the fetal gender should not be assigned and confirmation of gender may be available through cytogenetics or post-mortem examination.

16. Mementos and Photographs

Mementos include hand and foot prints (may not be possible at earlier gestations), cord clamp, identity band. Most parents welcome these tokens and they can be presented in memory boxes.

Photographs of the baby are valuable and can be taken with the parents' own camera.

If mementos and/or photographs are not taken home by parents these can be stored in the hospital records (with the mother's verbal consent) should the parents wish to access them at a later date.

17. Psychological Support

At 16 weeks gestation and over, parents should be offered support from the Bereavement Support Midwife. Such support is available at earlier gestations if felt to be of benefit – please liaise with the Bereavement Support Midwife on a case by case basis.

Information about support organisations and groups should be offered. If the woman has ongoing psychological concerns or a known psychiatric disease the General Practitioner should be made aware of this.

18. Investigation of Miscarriage

The aim of investigation is to determine the cause of miscarriage. There should be clarity as to who is responsible for reviewing and acting upon the results of tests ordered. Establishing a cause and effect relationship may be difficult.

Under-investigation hinders efforts at gaining an accurate diagnosis. On the other hand, unfocussed investigation could yield results that were not contributory to the loss. Thus clinicians should consider the clinico-pathological correlation between abnormal investigation results and the clinical condition.

The following investigations should be offered to ALL parents experiencing a miscarriage at 13+0 – 19+6 weeks gestation:

1) Screen for fetal infections:
a. Placental swabs from both maternal and fetal aspects
b. Maternal serology for TORCH screen and Parvovirus B19

2) Thrombophilia screen –
i.e. at delivery:
- Lupus anticoagulant
- Anticardiolipin antibodies

and at least 8 weeks postnatal:
- Factor V Leiden
- Protein C
- Protein S
- Antithrombin III
- Prothrombin gene variants

If anticardiolipin antibodies or lupus anticoagulant were positive at delivery they should be repeated 12 weeks after delivery. Protein S is usually low at delivery so may also need repeating to ensure it has normalised.

3) If there is no obvious cause:
- Thyroid function tests
- HbA1C

4) Placental pathology
This is recommended in all cases. Even if nothing specific is identified on placental histology the negative finding is always useful. The placenta may, however, show an unexpected positive finding that may have implications especially in cases such as recurrent pregnancy loss as part of an undiagnosed autoimmune spectrum. Swabs and cord samples (if appropriate) should be taken prior to placing the placenta in formalin. The appropriate placental pathology request form should be completed and sent with the placenta.

19. Selective Investigation - only perform if there is a clinical indication

1) If the mother has fever, flu-like symptoms, purulent or offensive amniotic fluid then maternal infection screening should be performed including:
- Listeria monocytogenes
- High vaginal swab
- Endocervical swabs for Chlamydia and bacteriology

- Maternal blood cultures
- MSU

2) If fetal anomaly diagnosed or chromosomal abnormality suspected:
Offer fetal chromosome analysis (with the exception of an isolated neural tube defect). Place 2-3 cm of umbilical cord in sterile saline (not formalin) in a leak-proof, sterile, plastic container. The container should be carefully labelled, wrapped with absorbent material and placed in a sealable polythene sample bag.

If there is no identifiable or obtainable umbilical cord, take a 2 cm^3 sample of placenta and send in saline to cytogenetics lab as soon as practically possible.

Please note:
Parental chromosomes are not routinely required. They should be obtained only if:
- Fetal chromosomal analysis shows an unbalanced translocation
- Fetal karyotype fails with a fetal abnormality on ultrasound or post mortem

3) If history suggests maternal substance abuse
Maternal urine for cocaine metabolites (maternal consent required)

4) If hydrops fetalis is present
- Red cell antibody screen
- Maternal anti-Ro and anti-LA antibodies (also test if PM shows endomyocardial fibroelastosis or AV node calcification)

5) Request for Post Mortem
Post mortem examination should be offered if there were signs of fetal abnormality on obstetric ultrasound scan or on external examination of the baby after delivery. Offer the parents the opportunity to discuss their options. If a post mortem is accepted, informed written consent should be taken by a registrar or consultant.

6) If fetal intracranial haemorrhage on post mortem examination
Maternal alloimmune anti-platelet antibodies. Blood samples required from mother and father.

20. Rhesus Anti-D Prophylaxis

Non-sensitised Rhesus (Rh) negative women should receive prophylactic anti-D Immunoglobulin.

21. Thromboprophylaxis

All women should be risk assessed for venous thromboembolism and thromboprophylaxis prescribed if appropriate.

22. Discharge

Before discharge a doctor should review the woman. Parents should be provided with contact information for follow-up.

23. Lactation Suppression

Following pregnancy loss after 14 weeks gestation, many women may commence lactation. This may be a distressing experience so the option of lactation suppression must be discussed. A single oral dose of cabergoline 1 mg post-delivery is the optimal treatment, with fewer side effects and less rebound lactation.

24. Contraception

Contraception should be discussed before discharge home.

25. Further Management of Baby including Transfer to Mortuary and Funeral Arrangements

Allow parents the time they wish to spend with their baby before transferring the baby to the mortuary. Prior to transfer, ensure two name bands are completed stating 'baby of (mother's name), mother's hospital number, date and time of delivery as well as hospital delivered at'. Attach one name band to the baby. At earlier gestations place the name band around baby's abdomen. If any personal items, such as a teddy bear, or blanket are to accompany the baby, then these should be labelled with baby's identification bands.

Occasionally the family may wish to take their baby home. This is not always ideal as the baby may deteriorate rapidly and parents should be informed of this. The parents' wishes should be supported. There is no legal reason why they cannot take their baby home or directly to the funeral directors of choice. The baby must be taken home in an appropriate casket or Moses basket. The transport home must be appropriate, i.e. private not public transport. The mortuary must be informed if the parents are taking their baby home.

Whilst there is no legal requirement to bury or cremate babies who are miscarried <20 weeks gestation, many families will wish to. Parents should be given details of the options available, e.g. hospital cremation, private burial or private cremation.

Complete a certificate for burial or cremation (sensitive disposal) and send to the mortuary. If the family are arranging their own funeral the certificate of disposal should be sent with the family who should be advised to give it to their funeral director.

26. Other Considerations

All outstanding appointments with midwifery, ultrasound or medical staff should be cancelled to avoid potential upset. A letter should be sent electronically to the mother's GP to explain that she has had a pregnancy loss.

27. Follow up

An e-discharge summary will be completed for the GP on discharge from hospital.

Discuss with the mother, when and where the postnatal follow up should take place. An appointment with the appropriate consultant should be offered to discuss the results of investigations, maintaining continuity where possible. Explain to the parents that it may take 8 weeks or more to receive investigation results.

If the woman is booked under a consultant obstetrician, a follow up appointment should be arranged with that consultant. Otherwise, a follow up appointment should be arranged with the consultant gynaecologist on call when the diagnosis of miscarriage was made. In individual cases the consultant gynaecologist may liaise with a consultant obstetrician to see the patient for follow up.

Follow up of parents after a pregnancy loss is a key element of care, with an opportunity to assess maternal recovery both physically and psychologically as well as to convey information about investigations performed and put in place a management plan for future pregnancies if that may be considered in the future.

At the follow up consultation, discuss the following:

- Results of investigations
- Cause of miscarriage, if known
- Pre-pregnancy plan for next pregnancy
- Smoking status
- Folic acid advice
- BMI optimisation
- Any psychological issues
- Other medical issues
    - Medications
    - Pre-pregnancy other medical conditions
- Pregnancy plan for next pregnancy
    - Book under Consultant Obstetrician

    - Consider whether aspirin or LMWH are indicated
    - Consider cervical length scans depending on likely cause of miscarriage
    - Offer extra ultrasound scans for reassurance
- Consider extra precautions for post natal depression

28. Monitoring Compliance and Effectiveness

As per agreed Business Unit audit forward programme

29. References

Clinical practice guideline: the management of second trimester miscarriage. Institute of Obstetricians and Gynaecologists, Royal College of Physicians of Ireland and Directorate of Strategy and Clinical Programmes,
Health Service Executive Ireland, July 2014.

The North West Second Trimester Pregnancy Loss Guideline: Ensuring optimal management for families who experience a second trimester pregnancy loss. Greater Manchester and Eastern Cheshire Strategic Clinical Network, March 2017.

RDH operational

The woman can be admitted to Ward 209 for management up to 19^{+6} weeks gestation. There may be special circumstances where Labour Ward is the most appropriate place for care at earlier gestations, and the consultant gynaecologist should decide this with the consultant obstetrician.

QHB operational

The woman can be admitted to ward 30 up to 15^{+6} weeks gestation. Anyone at 16 weeks and over are cared for on labour ward / Snowdrop Suite.

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