Mid-Trimester Pregnancy Loss

Kelly M. McNamee, MBChB[a,*], Feroza Dawood, MBChB, MRCOG, MD[a], Roy G. Farquharson, MD, FRCOG[b]

KEYWORDS

- Mid-trimester loss • Late pregnancy loss • Recurrent miscarriage
- Miscarriage investigations • Antiphospholipid syndrome • Bacterial vaginosis
- Cerclage

KEY POINTS

- Women with mid-trimester pregnancy loss (MTL) represent a heterogeneous group, with widely varying presentations and origins.
- An implemented protocol with standardized investigations is essential to identify any potential cause for an MTL.
- Consideration for transabdominal cerclage requires appropriate patient selection.
- An MTL may have more than one cause; the presence of dual or even triple pathology increases the risk of a further MTL or preterm delivery dramatically.
- Well-designed trials to study MTL are required to establish robust evidence-based practice and improve the treatment and care clinicians can provide.

INTRODUCTION

Mid-trimester loss (MTL) is defined as a pregnancy loss between 12 and 24 weeks' gestation.[1] The true incidence of this complication is difficult to ascertain, because no accurate data collection has been published.[2] It is estimated to affect 2% to 3% of recognized pregnancies.[3] MTL has often been classified together with first trimester losses or omitted altogether. An overlap also exists among MTL, preterm delivery (PTD), and preterm prelabor rupture of membranes (PPROM), and these conditions may often be a continuum of associated factors. The distinction between MTL and PTD is defined as the gestation of fetal viability (currently 24 weeks' gestation); both complications are known to have a similar origin.[4]

A dearth of knowledge exists regarding the optimal treatment and investigations for a distinct MTL cohort. Women who have an MTL represent a heterogeneous group, displaying widely varying presentations and origins.[2] Causative factors include

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[a] Department of Obstetrics, Liverpool Women's Hospital, Crown Street, Liverpool L8 7SS, UK;
[b] Department of Gynaecology, Liverpool Women's Hospital, Crown Street, Liverpool L8 7SS, UK
* Corresponding author.
E-mail address: kellymcnamee@doctors.org.uk

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antiphospholipid syndrome (APS), cervical weakness, infection, placental insufficiency, and congenital uterine anomalies (CUAs). Despite this, the cause remains unknown in 50% to 60% of women.[1–3,5] An important consideration is that an MTL may have more than one cause. The presence of dual or even triple pathology dramatically increases the risk of a further MTL or PTD.

An implemented protocol with standardized investigations is essential to identify any potential cause for an MTL. Classifying pathology is important for determining future pregnancy management, especially in the presence of repeated MTL.

SCREENING PROTOCOL

When investigating a woman with a history of an MTL, a thorough objective approach is required. An accurate clinical event history can often expose a potential cause (**Table 1**). A detailed family history can identify hereditary factors, such as thrombophilia or chromosomal translocation, thus guiding appropriate evaluation. Complex maternal illnesses, such as poorly controlled diabetes, uncontrolled hypertension, and thrombophilia, have been known to cause MTL. Poorly controlled thyroid disease is also associated with MTL and PTD; however, if the maternal disease has contributed to a pregnancy complication, confirmation should be sought as evidence (ie, placental pathology).[5] A sudden asymptomatic intrauterine death can be associated with APS, whereas cervical weakness classically presents as silent cervical dilatation with evidence of fetal heart activity. Infection can present as spontaneous rupture of membranes with a closed cervix.[2]

A clinical event picture can be mixed and difficult to interpret. Occasionally, women with more than one MTL can describe very different histories emphasizing the possibility of dual/triple pathology. Differing causal factors can predominate at different gestations in different pregnancies within the same individual.[2] Although a local investigative audit showed the distribution of pathology, it may not be truly representative of all MTLs because of referral bias (**Fig. 1**).

After a detailed history, a series of investigations should be performed (**Fig. 2**). Diagnosis of APS can be complex and is usually a combination of clinical manifestation and presence of lupus anticoagulant and/or anticardiolipin antibodies.[6] With a history of MTL, a high vaginal swab (HVS) can diagnose/exclude possible infection. A repeated HVS is recommended in the first trimester of a subsequent pregnancy to exclude bacterial vaginosis (BV), the presence of which may fluctuate over time. The Nugent criteria are used because they include an intermediate-flora classification characterized by abnormal genital-tract colonization that may be a transition stage on the way to full-fledged BV.[7] The cervix may be evaluated with a transvaginal ultrasound to measure cervical length and with hysteroscopy, but assessment also requires a convincing history. CUAs can also be diagnosed through ultrasound (3-dimensional if facilities allow) and/or hysteroscopy.

Table 1
Clinical history sequence

Event vs Factor	Cervix	Liquor Present on Vaginal Speculum Examination	Fetal Heart Activity
Cervical weakness	Open	Absent until expulsion of sac	Present
Thrombophilia/APS	Closed	Absent	Absent
Bacterial vaginosis	Closed	Present	?Present until sac expulsion