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Previous fetal death

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INTRODUCTION

Fetal death is a tragedy that causes severe distress to parents and caregivers. Parents want to know why their baby died and the chance of recurrence in future pregnancies. In the immediate postnatal period, they need extra emotional support in addition to appropriate information about the sequence of pregnancy events. Of great importance, they want all their questions answered in a timely fashion.

The obstetrician and his/her fellow health-care providers must make every attempt to identify the cause(s) of fetal death, as providing this information will improve the parents' understanding of events and may aid in grief resolution. At the first follow-up visit, the health-care provider (preferably an obstetrician or physician) should review the pregnancy events and have all relevant documents available for discussion and review. Postnatal test results and future reproductive options including contraception and lifestyle changes should be discussed as appropriate. If it might be of general or specific use, or if the parents request it, genetic counseling should be offered and the management plan for the next pregnancy should be discussed.

This chapter discusses investigations required to establish the causes of a fetal death after 20 weeks' gestation and outlines strategies to improve the chances for a successful subsequent pregnancy.

DEFINITION AND INCIDENCE

There is no standard definition for fetal death. Many countries define fetal death according to gestational age for legislation and statistical purposes[1]. As a result of such differences in definition, it is not possible to directly compare international fetal death rates.

In the United States, for example, intrauterine fetal death refers to fetal death after 20 weeks' gestation[2]. In England and Wales, on the other hand, intrauterine fetal death or stillbirth refers to fetal death after 24 weeks' gestation. Thus, the fetal death rate after 20 weeks' gestation in the United States was reported as 6.23 per 1000 total births for the year 2003[2]. In England and Wales in 2007 the stillbirth rate after 24 weeks was 5.2 per 1000[3,4]. In clinical practice, however, the evaluation of causes of fetal death is the same irrespective of the definition.

EVALUATION OF FETAL DEATH

The causes of fetal death can be subdivided into maternal, fetal, placental/cord and external factors. In some cases, fetal death may be the result of a combination of causes. In a significant number of cases, the cause(s) of death will remain unexplained in spite of extensive investigations[5–7].

Common causes of fetal death

- Maternal conditions: sepsis, diabetes and pre-eclampsia

- Fetal conditions: malformations, chromosomal and genetic disorders, infection, growth restriction and hydrops
- Placental and cord complications: abruption, infarction, tight knot in the cord and abnormal umbilical cord coiling[8]
- Fetomaternal conditions: fetomaternal hemorrhage
- Contributory (and in some instances external) factors: maternal obesity, drug misuse, advanced maternal age >40 years, social deprivation, trauma, uncontrolled medical problems including thyroid disease, cholestasis, antiphospholipid syndrome and inherited thrombophilia[3,5,9–11].

Checklist of potential procedures to be initiated after diagnosis of fetal death

- Parents should be given the opportunity to see and hold their baby and keep items of remembrance if they wish, as this may help with grief resolution[12]
- The nature of all postnatal tests should be fully explained to the parents
- Written information should be provided and the parents should be given ample time to arrive at a decision(s) if required
- Parents should be informed that their baby will be treated with care and respect during the postmortem examination. If they wish, the body will be returned in a suitable condition for viewing and further disposition after the examination
- In some countries, the UK being a prime example, parental consent must be obtained for placental histology, postmortem examination and photographs of the fetus[13]
- Parents should be encouraged to choose the funeral arrangement appropriate to their needs
- All relevant health-care professionals involved in the pregnancy care should be notified and future clinic appointments should be canceled.

History and review of medical records

In most cases of fetal death, the exact cause will not be apparent on clinical presentation. A targeted history should therefore be taken to determine the cause of death.

The pregnancy dating must be verified to exclude fetal growth restriction. In addition, enquiries should be made about specific pregnancy complications such as fever, rash, hypertension, diabetes (pre-existing and gestational), vaginal bleeding, genital tract infections and prelabor rupture of membranes. The timing and duration of exposure to any medications, including drug and alcohol misuse during pregnancy should be recorded. A family history of genetic, chromosomal and congenital malformations in both parents and any sibling should be elicited. All relevant medical records regarding any pre-existing illness should be obtained whenever possible. All antenatal test results including any abnormal findings should be noted.

All events surrounding the fetal death must be recorded clearly and accurately in chronological order. This will ensure that parents are given consistent information and will be useful in the management of subsequent pregnancies.

Investigations

The optimum tests for the evaluation of fetal death remain controversial and a direct cause of death will be found in only in 50–75% of cases[5,6,14–16].

External examination of the stillborn fetus

A detailed external examination of the stillborn should be performed with a description of all normal features and any obvious abnormality. Photographs of the fetus and close up views of any specific abnormalities should be obtained[17], as they will provide useful information at follow-up appointments.

The fetal body weight should be obtained in addition to other body measurements, including the foot length (which may be useful in confirming gestational age before 23 weeks' gestation), and head, chest and abdominal circumferences which may help exclude fetal growth restriction[18].

Postmortem examination of the fetus and placenta

Parents should be informed that a postmortem examination is the most informative test, as postmortem examinations reveal the cause and timing of fetal death in 40–50% of cases[14,19–26]. Some common postmortem findings include fetal abnormalities, fetal infection, fetal hypoxic injury, umbilical cord complications, placental dysfunction, infection, tumors and infarction.

Of great importance, in 20–40% of cases the postmortem, combined with other tests, will provide information regarding recurrence risk and management of the next pregnancy[19,23,25,26].

Even if no specific cause is identified, a negative postmortem result is still helpful in counseling parents about the list of fetal and placental conditions that have been excluded[27].

A full postmortem examination should include fetal chromosome culture with or without DNA analysis, X-ray (if indicated), magnetic resonance imaging (MRI) (if fetal examination is declined), and, finally, gross, microbiological and histological examination of the fetus and placenta[18].

Mandatory maternal tests

Full blood count

This is an important baseline test that helps dictate further management in the acute phase, especially in the presence of vaginal bleeding, placental abruption, pre-eclampsia, ruptured membranes or chorioamnionitis.

Glycosylated hemoglobin

This test can exclude poor glycemic control as a cause of fetal death in women with unrecognized gestational and pre-existing diabetes[28,29].

Kleihauer

This test determines the presence of significant fetomaternal hemorrhage, a silent but not uncommon cause of fetal death. In rhesus (D) negative women, this test also can determine whether sufficient anti-D has been given[30,31].

Anti-red cell antibody serology

This test excludes immune hemolytic disease. In cases of fetal hydrops, it should be repeated in the postnatal period even if the previous antenatal screen was negative, as some women develop atypical red cell antibodies late in pregnancy[32–34].

Maternal serology for viral and parasitic infection

Serological testing for cytomegalovirus (CMV), toxoplasmosis, herpes simplex and parvovirus B19 should be performed to exclude congenital viral infection associated fetal death[35–38]. Rubella serology should be repeated in non-immune women[39]. Serological testing for

syphilis should be repeated if the test was not performed in pregnancy or in women with history of sexually transmitted infection and those who live in endemic areas[40].

Bacteriology

Appropriate culture samples including vaginal and cervical swabs, placental swabs and fetal swabs should be obtained to exclude congenital bacterial infection. If the mother is unwell, then blood cultures to exclude listeriosis and urine cultures should also be obtained[37,41]. The bacterial organisms commonly found on culture in association with fetal death include group B streptococcus, *Escherichia coli*, *Chlamydia* and *Ureaplasma urealyticum*, *Haemophilus influenza*, *Klebsiella* spp, coagulase negative staphylococcus and *Enterococcus faecalis*, among others[42–44].

Selective tests

Parental chromosome and DNA analyses

These examinations should be considered if there is evidence of fetal chromosome rearrangement abnormalities or a suspicion of a fetal genetic disorder[18,45,46].

Coagulation profile

Coagulation profile testing is indicated if there is vaginal bleeding, the dead fetus is retained in the uterus for more than 2–3 days or the patient opts for expectant management. A slow decline in the plasma fibrinogen level is expected after the dead fetus has been retained in the uterus for more than 4 weeks, although abrupt changes in the coagulation system have also been reported a few days after fetal death[47,48].

Renal, thyroid and liver function tests and bile salts

These tests are indicated if there is a clinical suspicion of pre-eclampsia, sepsis, cholestasis and thyroid problems[49,50].

Urine toxicology

Urine toxicology is indicated if substance abuse is suspected[51].

Blood film for malaria parasites

This is indicated in endemic regions or for those with a history of travel to these areas[52].

Maternal thrombophilia screen

The link between maternal thrombophilia and fetal death is controversial. If, however, evidence of placental vascular thrombosis and infarction is present, then antiphospholipid screen (lupus anticoagulant and anticardiolipin antibodies) and inherited thrombophilia screen (factor V Leiden mutation, prothrombin gene mutation antithrombin III, protein C, protein S deficiency and hyperhomocysteinemia) are indicated[53–56].

Maternal autoantibody screen

If fetal hydrops or endomyocardial fibroelastosis is found at postmortem, maternal blood should be tested for the presence of anti Ro and anti La antibodies to exclude pre-existing autoimmune disease[57].

Maternal alloimmune antiplatelet antibodies

Analysis for maternal alloimmune antiplatelet antibodies is indicated in the presence of fetal hemorrhage at postmortem[58].

Figure 1 provides an example of a simple, structured fetal death outcome form for collating test results. It can be used to provide parents and clinicians with relevant clinical information at the follow-up visits and will be relevant in future pregnancies.

Date of delivery: Gestational age at delivery: Birth weight: Gender:

MOTHER

Blood tests
HbA1C (glycosylated):
FBC: Hemoglobin: Platelet:
Clotting profile: PT and APTT: Fibrinogen:
Blood group: Rhesus: Atypical red cell antibody:
Kleihauer:

Biochemistry
Renal, thyroid, liver function tests, bile salts:

Serology
Toxoplasmosis
Rubella
Cytomegalovirus
Parvovirus B19
Syphilis

Antiphospholipid screen
Anticardiolipin antibody
Lupus anticoagulant

Bacteriology
High vaginal swab
Chlamydia swab
Listeria
Urine culture
Blood culture
Urine toxicology

Inherited thrombophilia screen
Protein C Protein S
Anti thrombin III Factor V
Prothrombin Homocysteine
Autoantibody screen
Anti-Ro Anti-La
Alloimmune antiplatelet antibody
Anti-HPA 1a antibody

PLACENTAL

Gross examination:
Cultures:
Maternal side:
Fetal side:
Histology:

FETAL

Gross external examination (specify abnormality):

Photographs:

Postmortem:

Chromosomes/DNA studies:

X-ray/MRI findings:

Ear, nose and throat swabs culture:

GENETICS

Parent chromosomes/DNA studies: Mother

Partner:

Summary:

Mother's age: Pregnancy complications:

Mode of delivery:

Cause of death (and mechanism if known):

Contributing factors:

Co-morbidity/pre-existing illnesses

Figure 1 Fetal death outcome form. HbA1C, glycosylated hemoglobin; FBC, full blood count; PT, prothrombin time; APTT, activated partial thromboplastin time; MRI, magnetic resonance imaging

EMOTIONAL SUPPORT

Pregnancy loss is an exceedingly stressful life event and may have short- and long-term adverse effects on the mental health of parents and existing children. Continuing emotional support and/or pastoral care should be provided to help families cope with and recover from the fetal loss. They also should be offered bereavement counseling and provided with written information regarding family support groups[59–61].

POSTNATAL FOLLOW-UP

A postnatal appointment should be organized when all test results are available. This appointment usually needs to take place 6–12 weeks after the sentinel event. At this visit, the pregnancy events and all circumstances surrounding the fetal death should be reviewed. An interval medical history should be obtained. In addition, specific enquiries should be made about contraception use, anxiety and depression symptoms and medication[61].

When discussing postnatal test results with the parents, it is important to explain the differences between specific cause(s) of death, contributory factors and any coincidental finding as this will affect the recurrence risk estimate and subsequent pregnancy care.

The couple must also be given ample opportunity to ask questions[12,59].

PRE-PREGNANCY EVALUATION AND PREGNANCY PLANNING

Specific measures

If a specific cause of death is identified, it may then be possible to estimate recurrence risks and identify interventions that could improve the chances of a successful subsequent pregnancy.

- If there is evidence of fetal chromosomal abnormalities, fetal structural malformations or suspicion of a genetic disorder, it may be necessary to check the parent's chromosomes with or without DNA analysis to exclude an inherited chromosomal or genetic abnormality[18]. In addition, parents should be referred to a clinical geneticist to discuss the likely recurrence risk of specific defects as well as future reproductive options, including prenatal diagnosis and management of subsequent pregnancy.
- Women with active chronic medical problems such as hypertension, diabetes, thyroid and autoimmune disorders have an increased recurrence risk of fetal death and other pregnancy complications. Ideally, chronic medical problems should be addressed, controlled and medications optimized prior to the next pregnancy[5,50]. Details of such plans are discussed in other chapters of this book.
- A history of fetal death and ischemic placental disease is associated with an increased recurrence risk of placental complications. In subsequent pregnancies, fetal growth should be monitored by serial third trimester ultrasound examinations[62,63]. The predictive value of uterine artery Doppler screening in the context of a previous fetal death is not known[64].

General measures

- Women should be advised to take supplemental folic acid to reduce the risk of neural tube defects (see Chapter 22)
- Women who have not had and thus are susceptible to rubella, hepatitis B and varicella should be vaccinated
- Women who smoke should be advised that smoking cessation before and/or during

pregnancy leads to improved pregnancy outcomes[65]

- Women with alcohol and drug addiction should be referred to the appropriate agencies for intensive help directed to cessation or, in the worst case, moderation
- Maternal obesity is associated with increased pregnancy complication rates for both the mother and the fetus[66,67]. Obese women should be advised that weight loss would improve outcomes as well as enhance fetal monitoring in subsequent pregnancies
- Women with unresolved or complicated grief and signs of depression require additional support from appropriately trained health-care professionals. A psychiatric referral for counseling and treatment may be warranted[68,69].

Interpregnancy interval

- The optimum interpregnancy interval after fetal death remains unknown; however, normal bereavement generally resolves within 6–12 months in most instances[70,71]
- Couples should be advised to delay the next pregnancy until they feel emotionally capable of undertaking it[72].

Management of subsequent pregnancy

A history of previous unexplained fetal death confers a 2–10-fold increased risk of a repeat fetal death and a 4-fold increased risk of gestational diabetes in a second pregnancy when compared with women with previous uncomplicated pregnancies[64,73,74]. Such 'high-risk' women will therefore need specialist antenatal care, testing to exclude gestational diabetes and close supervision in subsequent pregnancies[63,64,73–77].

Fetal monitoring

There is no evidence that intensive fetal monitoring reduces the risk of fetal death in future pregnancies. Serial third trimester ultrasound examinations are commonly used to identify poor fetal growth which may precede fetal death[9,64]. In addition, serial ultrasound examinations may help reassure parents with heightened anxiety levels that fetal growth is satisfactory[64,78,79].

Timing of delivery

Elective induction at term in subsequent pregnancies does not increase live birth rates. Depending on the timing of previous fetal death, however, many obstetricians offer elective delivery after 37 weeks to allay parental anxiety and avoid the risk of sudden fetal death[75,79]. Additionally, elective delivery at term gives parents some element of control over their pregnancy outcome.

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