Intrauterine fetal death

Farah Siddiqui

Lucy Kean

Abstract

Sadly, the death of a fetus may occur at any stage of a pregnancy, including during the labour process. A pregnancy loss will be devastating for the expectant parents. Obstetricians should be familiar with the management of intrauterine fetal death as prompt and appropriate counselling will aid the couple's grief process. Understandably, couples wish to know the cause and chances of recurrence; thus, the full investigation of possible aetiological factors using a pragmatic approach will help in the postnatal counselling and management of future pregnancies. This review also explores the legal and ethical aspects of postmortem consent.

Keywords bereavement; intrauterine fetal death; stillbirth; postmortem; viral infections are often

Introduction

Many definitions exist for intrauterine fetal death (IUFD); older definitions use a gestational age of 28 weeks, and the WHO classification includes a birthweight of greater than 500 g. The legal definition which is used by the Confidential Enquiry into Maternal and Child Death (CEMACH) is 'a child that has issued forth from its mother after the 24th week of pregnancy and which did not at any time after being completely expelled from its mother breathe or show any other signs of life' [Section 41 of the Births and Deaths Registration Act (1953), as amended by the Stillbirth Definition Act (1992)]. CEMACH reported the incidence of IUFD in England and Wales to be 5.3 per 1000 births in 2006.

Mortality in singleton pregnancies has declined from 51.5 per 10 000 births in 1982–1990 to 42.0 in 1991–2000 (RR 0.82, 95% CI 0.76–0.87). During these periods there was a greater decline in mortalities from multiple pregnancies, from 197.9 to 128.0 per 10 000 (RR 0.65, 95% CI 0.51–0.83). In singletons, the largest reductions occurred in intrapartum-related deaths and deaths due to congenital anomalies, antepartum haemorrhage and pre-eclampsia. There was little change in the rate of unexplained antepartum death occurring at term (RR 0.97, 95% CI 0.84–1.11) or preterm (RR 0.94, 95% CI 0.82–1.07); these account for about half of all late fetal deaths.

Farah Siddiqui *MB ChB DM MRCOG is a Sub Specialty specialist Registrar at the Fetal and Maternal Medicine, Nottingham NHS trust, City campus, Nottingham, UK.*

Lucy Kean *BM BCh DM FRCOG is a Consultant at the Fetal and Maternal Medicine, Nottingham NHS trust, City campus, Nottingham, UK.*

Aetiology

Chromosomal abnormalities

These account for 30 – 60% of early fetal demise. The incidence increases with maternal age. Approximately 7% of fetuses with chromosomal abnormalities will survive to term. The commonest chromosomal abnormality is autosomal trisomy.

Genetic anomalies affect the development of the fetus and the placenta. One recent study found an increase in apoptosis and a decrease in cell proliferation in chromosomally abnormal placentae compared to chromosomally normal placentae, implying that genetic abnormalities can lead to changes that affect trophoblast development and proliferation.

Karyotype analysis often fails from the placenta, fetal blood (via an intracardiac sample) and fetal skin post delivery. Where there are specific concerns, the genetics laboratory may be able to help with specific diagnoses by utilizing other techniques such as fluorescent in-situ hybridization. Fetal chondrocytes have the most prolonged cell viability, and a small sample from the iliac crest can sometimes provide a diagnosis. Performing a fetal karyotype by transabdominal chorionic villus sampling before delivery avoids the problems associated with delay and infection of the placenta during delivery, although this is often not acceptable to the woman.

Fetal structural anomalies

These account for 35% of fetal deaths, and commonly include cardiac anomalies and renal abnormalities.

Infection

This is a significant risk for the fetus. The infection is often an ascending bacterial infection, such as *Escherichia coli* or Group B streptococcus, which triggers a cytokine cascade leading to fetal damage, preterm labour and intrauterine fetal death.

Viral infections are often asymptomatic in adults but can be devastating to the fetus. For example, transplacental transmission of parvovirus B19 can result in fetal anaemia, hydrops and fetal death. Parasitic infections such as malaria and toxoplasmosis are also associated with fetal death.

Typically infections are classed as a non recurring cause of fetal death.

Maternal diabetes

Prior to the introduction of insulin, the life-expectancy of a diabetic was short; women who reached childbearing age were faced with infertility, recurrent miscarriages, congenital malformations and a stillbirth rate of almost 100%. The introduction of insulin has increased life-expectancy. However, despite insulin treatment and apparent good glycaemic control, a diabetic pregnancy is still associated with increased risks to the fetus and newborn compared to the non-diabetic pregnancy. Spontaneous miscarriages may be as high as 17%; congenital malformation rates are 4 – 10 times greater than in the non-diabetic population; stillbirth and perinatal mortality rates are five times greater; neonatal and infant mortality rates are 15 and 3 times greater, respectively.

Gestational diabetes is associated with an increased risk of fetal death. However, maternal glucose metabolism returns to normal almost as soon as the fetus dies. Blood sugar estimation is generally unhelpful. Also, as the derangement is generally

mild, HbA1c measurements are usually normal. Women with unexplained stillbirth have a four-fold increase in glucose abnormalities in subsequent pregnancies. Therefore, if this diagnosis is suspected, formal glucose testing should be undertaken in the next pregnancy.

Maternal age

The effect of maternal age on perinatal deaths is described by a U-shaped curve with the highest death rates in very young and older mothers. Mothers younger than 20 and those older than 40 have the highest rates of stillbirth (5.6 and 8.1 per 1000 total births, respectively). The cumulative risk of IUFD at 38 weeks of gestation in an uncomplicated patient aged 40 or over is similar to the risk of IUFD at 41 weeks in an uncomplicated patient younger than age 35. These data raise the suggestion that routine antenatal testing beginning at maternal age 40 and at 38 weeks' gestation should be considered.

Maternal body mass index

The CEMACH report of 2006 showed that among the women who had a stillbirth and a recorded body mass index (BMI), 26% (761/2924) were obese (BMI > 30). Other studies have demonstrated that nulliparous women with a BMI greater than 30 have a four-fold increase in the risk of IUFD compared with women with a BMI between 20 and 25. This may reflect a higher incidence of hypertensive disease and abnormal glycaemic control in these women.

Cord complications

A nuchal cord is found in 23% of all deliveries, both live and stillborn infants. Multiple nuchal loops are found in 3.7% of stillborns. A pathological examination is important to determine whether the finding is a postmortem event, as the demised fetus can become entangled in the cord during delivery. The incidence of true umbilical knots is 1% and is associated with a mortality rate of 2.7%. Again, the mere presence of knot does not predict fetal death; if the knot is loose, fetal circulation can be maintained.

Decreased Wharton's jelly in certain areas of the cord, most notably the fetal and placental insertions, can result in occlusion of fetal blood flow if the vessels are twisted sufficiently. It is vital not to attribute fetal death to a knot or nuchal cord without postmortem confirmation as this can deny parents knowledge of the real cause of death.

Placental complications

If the umbilical cord inserts into the placenta abnormally, this can be associated with fetal death. Marginal insertions are present in 5–7% of pregnancies and can lead to fetal death if these vessels rupture or are compressed. Velamentous insertions, where the cord inserts into the external membranes of the placenta, are more common in monochorionic twins, but also occur in 1% of singleton pregnancies. The cord vessels in this case are not surrounded by Wharton's jelly and thus are prone to torsion, rupture (vasa previa) and inflammation if they cross the cervix.

Placental abruption, the premature separation of the placenta from the uterus, has an incidence of 1% and leads to fetal death in 0.12%. Symptoms may include bleeding, abdominal pain or reduced fetal movements. The cause of the abruption is often not known; however, risk factors include smoking, cocaine use, trauma, pre-eclampsia, hypertension, thrombophilia and prolonged rupture of membranes.

Thrombophilias

Thrombophilias associated with placental abruption include factor V Leiden mutations, prothrombin gene mutations, hyperhomocysteinaemia, activated protein C resistance, antithrombin III deficiency and anticardiolipin antibodies. These thrombophilias are also associated with intrauterine growth restriction and pre-eclampsia.

Antiphospholipid syndrome can lead to IUFD. There is evidence that low-dose aspirin and low-molecular-weight heparin improve pregnancy outcome amongst those who present with recurrent miscarriage. Women with unexplained stillbirth are also more likely to be heterozygous for factor V Leiden mutation, and to be protein S or C deficient. Interestingly, these fetuses may not be growth restricted, although there may be placental features that point to an underlying thrombophilia.

Obstetric cholestasis

The development of intense pruritis with no rash after 24 weeks' gestation in association with abnormal liver function tests which improve after delivery suggests obstetric cholestasis. The condition is poorly understood although it is associated with a perinatal mortality rate (PMNR) which is improving with active management; from 13.4 in 1984 to 8.4 in 2002. The cause of the fetal death is thought to be anoxia, possibly related to the placental passage of bile salts. Fetal assessments with umbilical artery Doppler and cardiotocography (CTG) are not predictive of fetal death.

Diagnosis

Women often present with a history of reduced fetal movements. The absence of a fetal heart beat on auscultation should always be confirmed by an ultrasound scan by experienced personnel, which can be challenging, especially if the woman presents in labour.

On ultrasound examination, a four chamber view of the fetal heart should be obtained and watched for 1 minute for cardiac pulsations. Colour flow mapping can be useful in obese women. At the time of the ultrasound scan, the presence of skin oedema, hydrops, overlapping of the skull bones (Spalding sign) and the amount of liquor is useful in determining the timing of death; the femur length is useful for estimation of the gestation.

Management

Prevention of Rhesus (D) isoimmunization

Changes in the uteroplacental blood flow dynamics rapidly result in maternal transfusion of fetal blood; thus, Rhesus D-negative women should be administered anti-D; a Kleihauer test will confirm whether a further dosage is required.

Providing choice and establishing safety of the mother

Patient safety should be a prime concern:

- Ensure the maternal blood pressure is not raised and there is no proteinuria, in order to exclude significant pre-eclampsia;