Fetal macrosomia

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Abstract

Clinical palpation, ultrasound biometry and maternal perception all can lead to the suspicion of a large-for-gestational-age fetus and fetal macrosomia. Although maternal diabetes and rare genetic syndromes may be the cause of large fetal size, most of these pregnancies will in fact be normal. Nevertheless, maternal and perinatal risks do increase with increasing fetal size. Antenatal prediction is, however, imprecise, and the evidence to date does not support intervention in non-diabetic pregnancies where there is a suspicion of fetal macrosomia.

Keywords fetal macrosomia; gestational diabetes; diabetes; Beckwith–Wiedemann syndrome; shoulder dystocia; Erb's palsy

Introduction

Fetal macrosomia is a cause of concern for both pregnant women and their clinicians owing to the associated risks of maternal and neonatal morbidity. Diagnosis can be problematic, and there is currently a lack of high-quality evidence to guide the management of women with suspected fetal macrosomia.

Definition

The most common definition of fetal macrosomia is a birth weight exceeding 4 kg, although thresholds of 3.8, 4.5 and 5 kg have been used. A birth weight of 4 kg represents the 90th centile at 40 weeks on standard growth charts. This is consistent with the definition of 'large for gestational age', namely a fetus growing above the 90th centile. As the diagnosis of fetal macrosomia is retrospective, the use of the definition of large for gestational age is more relevant antenatally when determining the need for further investigation. Macrosomia based on birth weight is more useful when considering outcomes of pregnancy. Both, however, are arbitrary thresholds, with the problems of increased fetal size relating to a continuum rather than birth weights above a single value.

Based on this definition, the incidence of fetal macrosomia in the UK is approximately 9%. This incidence is likely to increase with time as there is a change in maternal characteristics, in particular maternal body mass index. Future reference to 'fetal macrosomia' in this article is based on a birth weight of over 4 kg.

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Risk factors and triggers for growth

The triggers for fetal growth are both genetic and environmental. The initial drive is genetic, with male genotype and Caucasian ethnicity being risk factors for increased fetal size. Environmental risk factors include gestation greater than 40 weeks, a negative smoking history and the presence of maternal diabetes (both pre-pregnancy and gestational). Other risks factors are likely to have both a genetic and an environmental component and include increased age, increased parity, maternal pre-pregnancy weight and height and maternal weight gain in pregnancy. The strongest risk factors are the previous delivery of a macrosomic baby and the presence of diabetes.

The Pedersen hypothesis explains how maternal diabetes stimulates fetal growth. Maternal hyperglycaemia leads to elevated glucose levels in the fetus, causing overstimulation of the fetal pancreas and fetal hyperinsulinaemia. Insulin has many growth-promoting properties, and fetal hyperinsulinaemia therefore stimulates increased fetal growth, particularly in the third trimester. There is a well-recognised association between poor diabetic control (with significant periods of maternal hyperglycaemia) and increased rates of fetal macrosomia.

Diagnosis

The diagnosis of suspected fetal macrosomia can be clinical, ultrasonographic or maternal. Clinical assessment of symphysial-fundal height can be confounded by polyhydramnios and maternal obesity. Despite this, a number of studies have demonstrated that a clinical diagnosis of fetal macrosomia is as sensitive as the use of ultrasound. For example, a prospective study of 181 diabetic pregnancies in 1996 assessed the ability of clinical palpation and ultrasound to predict a birth weight greater than the 95th centile. This concluded that clinical examination was as predictive as ultrasound measurements, with the positive predictive value of clinical assessment being 56–80%, compared with 55–66% for ultrasound. Combining the two modalities improved prediction, but only to a small extent.

The most useful single ultrasound determinant of fetal size in the third trimester is abdominal circumference. The ability of this to predict estimated fetal weight has been improved by the use of multivariate formulae. More than 60 formulae exist to determine estimated fetal weight from ultrasound parameters. The most commonly used formulae are those from Hadlock and Shephard. However, no single formula stands out as being the most accurate and in both diabetic and non-diabetic pregnancies; the sensitivity of detecting fetal macrosomia is 50–60%, with an 8–10% margin of error in estimated fetal weight. Accuracy increases with serial measurements but decreases with increasing fetal size.

One study examined the predictive skills of women themselves. A total of 106 parous women at term were asked to estimate fetal weight, and this was compared with clinical and ultrasound judgements. Maternal estimates were within 10% of the actual weight in 69.8% of women. Maternal assessment in this study was more accurate than either clinical or ultrasound

assessment. The ability of primigravid women to predict fetal size is likely to be far less impressive.

As no current method of assessing suspected fetal macrosomia is reliable, other methods are being investigated. Although both 3D ultrasonography and magnetic resonance imaging are promising, these are currently unlikely to be used outside the research setting. The use of customised growth charts may also be helpful as these may more usefully predict which babies may be unduly large with respect to their mothers, although the advantage of these has yet to be substantiated.

Action on diagnosis

The diagnosis of large for gestational age may be made either at the time of anomaly scanning (if accurate dating by early scanning has been performed) or in the third trimester based on clinical or ultrasound findings. Even allowing for the inaccuracy of diagnosis, additional tests need to be considered to assess for underlying maternal disease and the normality of the infant. Diabetes needs to be diagnosed or excluded, although the decision to perform a formal glucose tolerance test will depend on the clinical situation.

A number of uncommon fetal syndromes are associated with large fetal size (Table 1), and these should be borne in mind with the very large fetus when diabetes has been excluded. The details of these conditions are beyond the scope of this article, but certain features are shared between the separate diagnoses, including:

- a prenatal onset of growth acceleration;
- an increased risk of exomphalos, umbilical hernia or congenital diaphragmatic hernia;
- some degree of developmental delay (although IQ can be normal);
- an increased risk of neonatal hypoglycaemia;
- an increased risk of childhood tumours (e.g. Wilms' tumour);
- advanced skeletal maturation.

Other features are, however, more specific and can help to pinpoint the actual diagnosis. Simpson–Golabi Behmel syndrome, for example, is also associated with postaxial polydactyly and syndactyly.

There is no agreed threshold at which testing for maternal diabetes or repeated anomaly scanning is indicated, and individualising management is the most appropriate option. A fetus on the 90th centile at 20 weeks is likely to be constitutional for a tall Caucasian couple, and reassurance may be most appropriate. The same scan findings in a smaller Asian couple with previous 2.5 kg babies at term should, however, prompt further investigation.

Once fetal macrosomia is suspected, the need for further fetal monitoring, if any, must be considered. In diabetic pregnancies, the role of ultrasound is well established as the trajectory of serial ultrasound measurements can detect growth acceleration, and this is associated with worse pregnancy outcomes. In non-diabetic pregnancies, where growth acceleration is unlikely, the role of serial ultrasound measurements remains unclear. Serial scanning may lead to an over-reliance on an imprecise estimate of fetal weight and cause undue anxiety to the pregnant woman in a situation in which management will not be altered anyway. Reassurance at the time of initial diagnosis may be more appropriate. Unexplained antepartum stillbirth, for example, is significantly less likely to occur in fetuses over 4 kg than those between 2.5 and 3.9 kg.

Planning birth with suspected fetal macrosomia

The main concerns of both pregnant women and clinicians relate to the impact that the size of the baby will have on vaginal birth. There are known maternal and fetal morbidities associated with fetal macrosomia. A macrosomic fetus significantly increases the risks of longer first and second stages of labour, instrumental vaginal delivery (odds ratio of 1.76 compared with infants 2.5–4 kg in one large retrospective study), emergency caesarean

Syndromic causes of fetal macrosomia

Syndrome	Genetics
Beckwith–Wiedemann syndrome	Usually sporadic Autosomal dominant inheritance has been noted Mutations within chromosome 11p15 (a highly imprinted area of the genome that includes the gene for insulin-like growth factor 2) A molecular genetic cause can be found in 70% of cases
Sotos syndrome	Usually sporadic (new mutations) but autosomal dominant inheritance is seen Mutations within *NSD1* (nuclear receptor SET domain-containing protein)
Weaver syndrome	Autosomal dominant inheritance Most cases sporadic Uncertain genetic cause
Marshall–Smith syndrome	Sporadic Unknown aetiology
Simpson–Golabi–Behmel syndrome	X-linked recessive inheritance Mutations within *GPC3* (glypican-3 gene) Female carriers may have a mild phenotype

Table 1