Seminars in Fetal & Neonatal Medicine (2007) 12, 383–397

available at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/siny

Seminars in FETAL & NEONATAL MEDICINE

Prediction and perinatal outcomes of fetal growth restriction

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KEYWORDS
Pregnancy outcome;
Fetal growth restriction;
Doppler;
Fetal heart rate monitoring;
Fetal death;
Ductus venosus;
Developmental origins of health and disease;
Barker hypothesis

Summary Assessment of fetal growth and wellbeing is one of the major purposes of antenatal care. Some fetuses have smaller than expected growth in utero and while some of these fetuses are constitutionally small, others have failed to meet their growth potential, that is they are growth restricted. While severe growth restriction is uncommon, the consequences of it being undetected may include perinatal death or severe morbidity. It is, therefore, important to have strategies in place to detect the fetus at risk of growth restriction. These would include an assessment of 'prior risk' from maternal history and examination combined with the results of biochemical and ultrasound investigations, the most promising of which are uterine artery Doppler and biochemistry. We discuss some of the factors to consider when stratifying the obstetric population into degrees of likelihood for growth restriction, and discuss aspects of the management and outcome of pregnancies complicated by growth restriction.

Introduction

Monitoring the wellbeing and growth of the fetus is a major purpose of antenatal care.[1] Many fetuses delivered with a lower than expected birth weight are healthy, thriving infants, whereas others are small because their growth *in utero* has been impaired and they have increased perinatal morbidity and mortality.[2,3]

A distinction therefore needs to be made between the fetus that is 'constitutionally' small for gestational age (SGA) and one whose growth has been restricted *in utero*. A diagnosis of growth restriction implies that a 'fetus has not achieved its optimal growth potential';[4] a prerequisite for making this assessment is that the expected growth pattern of the fetus could have been predicted. Although ultrasound biometry in the second trimester may give some suggestion of expected growth, in practice it is only with serial measurements (either clinically or with ultrasound) that reduced growth velocity can be demonstrated. Once a clinical suspicion of poor growth has arisen, it is common practice to use ultrasound evidence of size, particularly the abdominal circumference (AC) falling below a particular centile, most commonly the 10th, 5th or 3rd, to 'diagnose' intrauterine growth restriction (IUGR). However, we know that not every fetus that is growth restricted may necessarily be small for its gestational age, or vice versa, as SGA is a statistical definition based on birth weight.

A commonly used cut-off for SGA is birth weight below the 10th centile. Tables with 10th centile birth weights are

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doi:10.1016/j.siny.2007.07.002

readily available but may not be relevant to a specific obstetric population, because factors such as ethnic mix, socioeconomic status and altitude may influence the birth weight distribution in a population. Charts from different countries, or even different cities within a country, may have little relevance to one another. A fetus that appears small may not only be meeting its own growth potential (presumably acquired from its genetic parents, or in the case of egg donation, the embryo recipient),[5] but may not even be small on charts from a different population.

The overlap between SGA and IUGR is, therefore, often unclear and differentiating between a healthy small fetus and one that is hypoxic (or even suffering from infection or indeed aneuploidy) may be difficult from a single clinical or ultrasound measurement. An AC below the 10th centile may identify the fetus at risk of IUGR, but only about 50% of these fetuses may turn out to be growth restricted postnatally.[6] The postnatal diagnosis of IUGR may be made by a form of body mass index (BMI) known as the Ponderal Index. However 40% of newborns with a birth weight of <10th centile had a normal Ponderal Index, yet 50% of newborns identified as growth restricted by Ponderal Index had a birth weight above the 10th centile.[7] Furthermore, at autopsy, an elevated brain-weight/liver-weight ratio provides evidence of IUGR, but is somewhat too late to guide management of the affected pregnancy; in itself this ratio is insufficient to demonstrate IUGR.[8]

Management of the growth restricted fetus

Optimal management of the growth restricted pregnancy requires three key events:

- Identification of the fetus at risk in the obstetric population
- Confirmation of the diagnosis of IUGR, and distinction from the healthy, small fetus
- Ongoing care of the growth restricted fetus, culminating in decisions about delivery mode and timing

Identifying the pregnancy at risk of IUGR

Is there some way of identifying women and fetuses at risk, of screening for IUGR? An obstetric population will contain individuals at high or low risk; but there are, of course, widely known predisposing factors for the likelihood of an outcome, such as IUGR. Once a population is stratified for risk, we can determine what screening methods are appropriate and whether they should be applied to a whole population or only those at high risk. As a rule, the positive predictive value (PPV) of a screening test will be lower in a low-risk than in a high-risk population, thus monitoring must be carried out to balance benefit without causing unnecessary anxiety in those screened. Wilson's criteria for a screening test (simplified in Table 1) are often cited as conditions a disease or syndrome should meet before screening is offered.

Although IUGR meets some of these criteria, there are others that it clearly does not. As alluded to earlier, making the diagnosis of 'growth restriction' can be difficult and may only become apparent with repeated observations of a fetus. Doubt still remains about the most appropriate time to intervene, in this context, with delivery.

Table 1 Wilson's criteria as applied to intrauterine growth restriction

Criteria met	Criteria not met or where there is uncertainty
The condition should be an important health problem	There should be a test for the condition that is easy to perform and interpret, acceptable, accurate, reliable, sensitive and specific
The natural history of the condition should be understood	There should be an accepted management for the disease
There should be a recognisable latent or early symptomatic stage	Treatment should be more effective if started early
	Diagnosis and treatment should be cost-effective

In identifying pregnancies at risk for IUGR, we should first consider the maternal history of the condition, obtain a history of relevant risk factors and perform an appropriate clinical examination. Further specific investigations can then modify the prior risk based on history and examination, allowing a clinician and the woman to form an impression of the likelihood of IUGR complicating the pregnancy.

Risk-assessment from history and examination

Risk factors for growth restriction and SGA are summarised in Table 2. Each factor will be considered in more detail below.

Past obstetric history

History has a habit of repeating itself. Women who have had a previous SGA or growth restricted baby have an increased risk in subsequent pregnancies. However some risk factors, such as drug use and smoking behaviour, weight and systemic disease may be modified prior to pregnancy. IUGR has multiple causes and, as such, the recurrence risk will be dependent on the previous (if identifiable) cause.

Diabetes

Although much of the focus in diabetic pregnancies is on the prevention of macrosomia, these pregnancies are also at risk of IUGR, particularly in cases where there is microvascular disease. A 20% incidence of SGA was reported in a group of diabetic women with good blood sugar control compared with roughly 10% incidence in women with less tight control (mean blood glucose 95 ±5).[9]

Hypertension

The main risk for IUGR is that of developing superimposed pre-eclampsia. The risks of IUGR in mild hypertension (>140/90 mmHg) are not greatly increased: a recent review