

Diagnosis and management of fetal growth restriction

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Introduction

Fetal growth restriction (FGR)

- Fetus that has not reached its growth potential because of genetic or environmental factors.

Origin may be

- Fetal
- Placental
- Maternal
- Significant overlap



Importance

Increased risk of adverse perinatal outcome mainly due to reduced energy reserves:

- Premature delivery
- Perinatal asphyxia, which may be accompanied by meconium aspiration or persistent pulmonary hypertension
- Impaired thermoregulation
- Hypoglycemia
- Polycythemia and hyperviscosity
- Impaired immune function
- Mortality (5-20 times higher)

Antecedent to some cases of hypertension, hyperlipidemia, coronary heart disease, and diabetes mellitus in the adult (Barker hypothesis)

Definition

Weight below the 10th percentile for gestational age

Other definitions <5th percentile, <3rd percentile

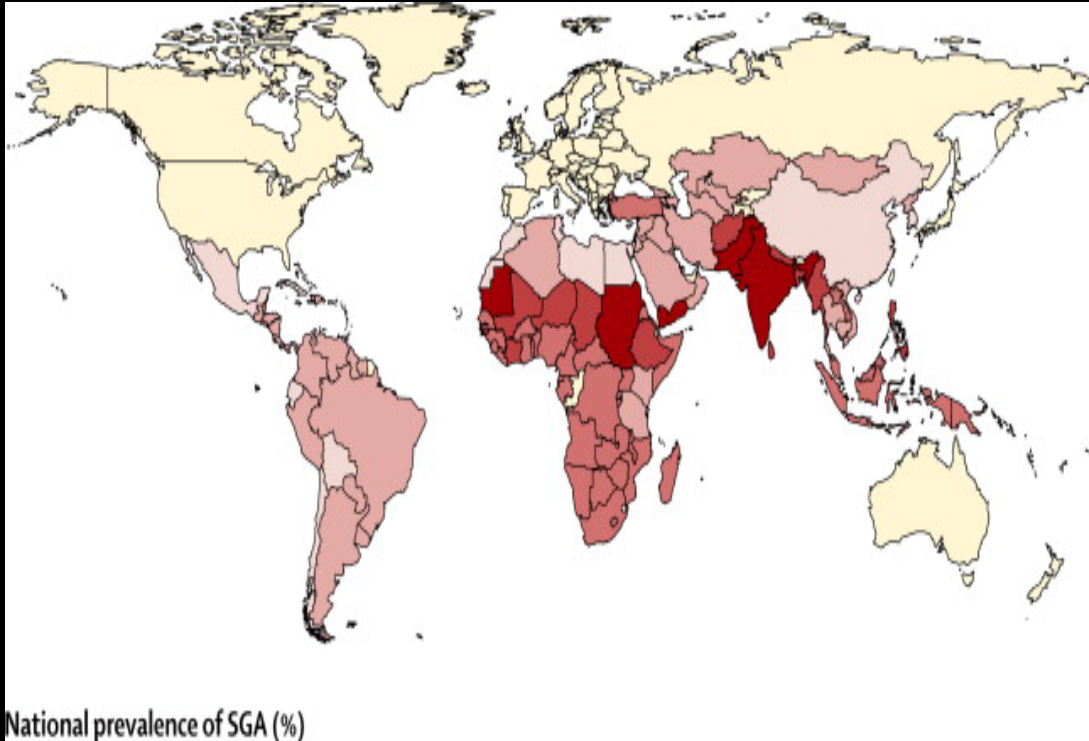
Does not differentiate between

- Constitutionally small
- Small because a pathologic process has kept them from achieving their genetic growth potential
- Not small but a pathologic process has kept them from achieving their genetic growth potential.

Requires an appropriate reference standard.

- Based on birth weights across gestation (most baby delivered preterm will be growth restricted)
- Ultrasound estimated fetal weights across gestation (limited by the inaccuracy and imprecision)
- customized

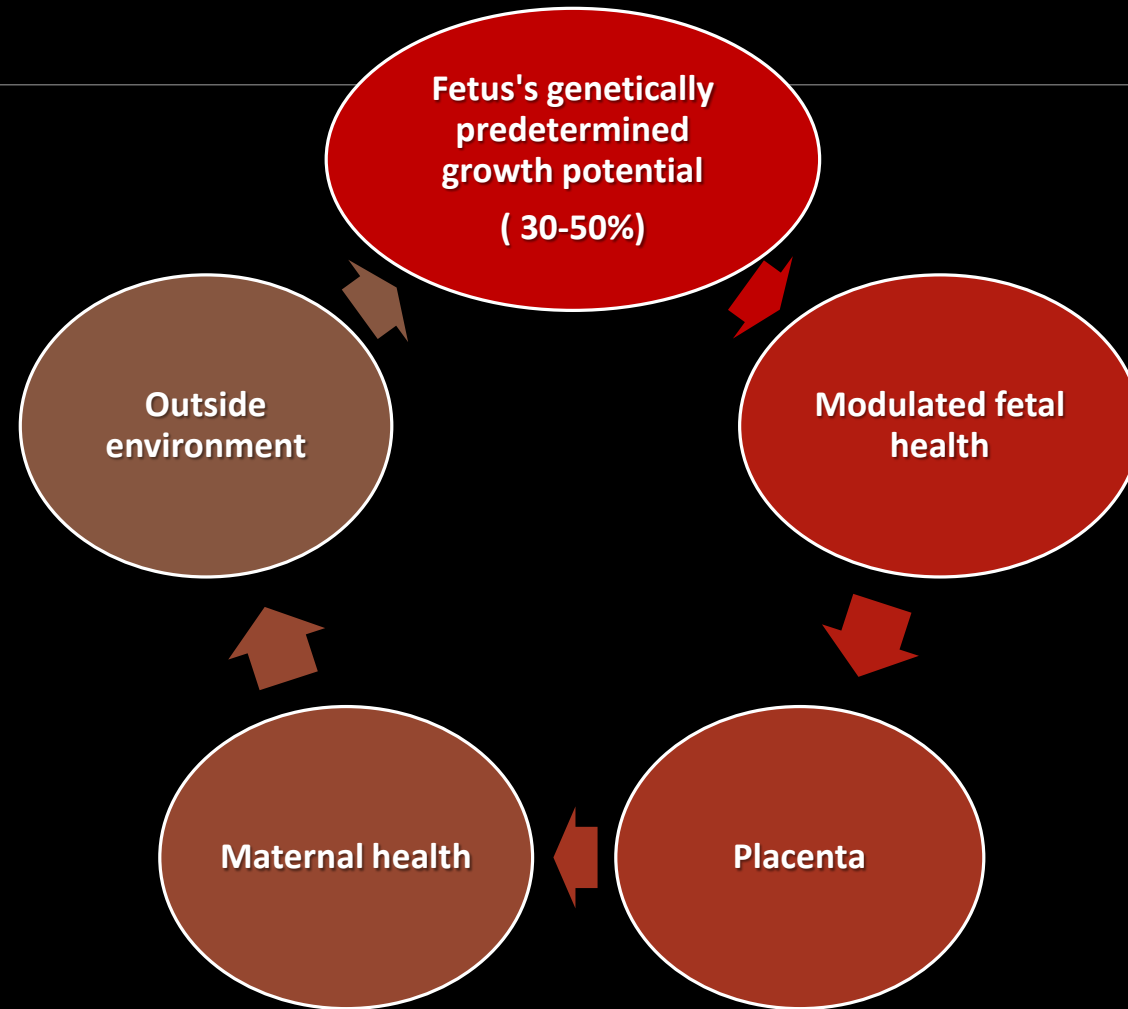
Epidemiology



3-10% in developed countries

20-50% in developing countries

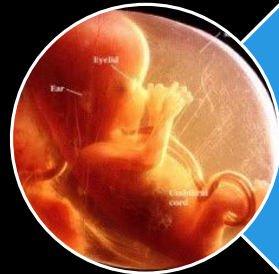
NORMAL FETAL GROWTH



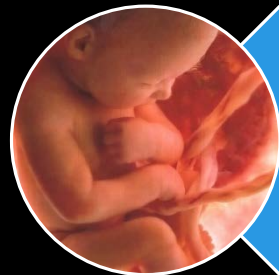
Fetal growth



The first phase
-Cellular hyperplasia
Symmetric



The second phase
-Hyperplasia and hypertrophy
Mixed- asymmetric

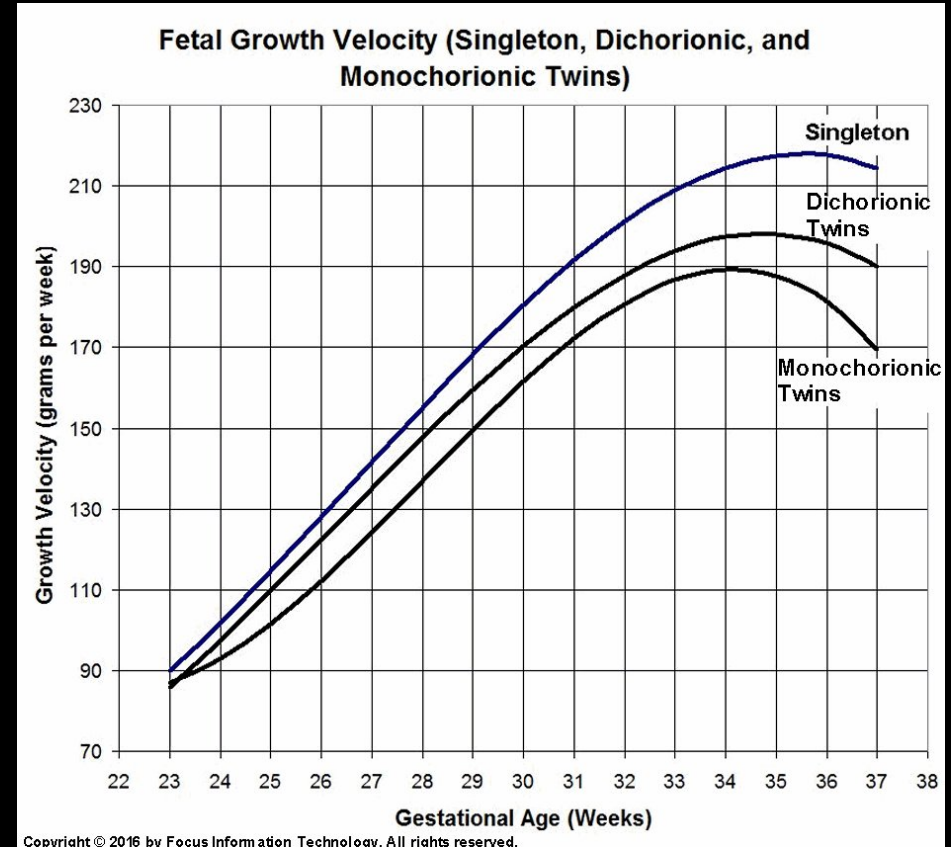


The third
-Hypertrophy (rapid accumulation of fat, muscle,
connective tissue)
Asymmetric

Quantitative growth

Singleton fetal growth

- 5 g/day at 14 to 15 weeks
- 10 g/day at 20 weeks
- 30 to 35 g/day at 32 to 34 weeks



Symmetric and asymmetric growth restriction

Symmetric FGR

- 20-30%
- Small sized organs due to global impairment of early fetal cellular hyperplasia

Asymmetric FGR

- 70-80%
- Greater decrease in abdominal size (eg, liver volume and subcutaneous fat tissue)
- Result from the capacity of the fetus to adapt to a hostile environment by redistributing blood flow

Clinical assessment

Reasonable screening tool in low risk pregnancies

No high quality evidence that alternative approaches improve outcome

Base on assessment of past present risk factors

Physical examination

Ultrasound studies

Accurate assessment of gestational age

Knowledge of LMP

Early ultrasound

Serial ultrasound

Symphysis fundal height measurement

simple, inexpensive, and widespread

Discordance >2cm

Controversial accuracy

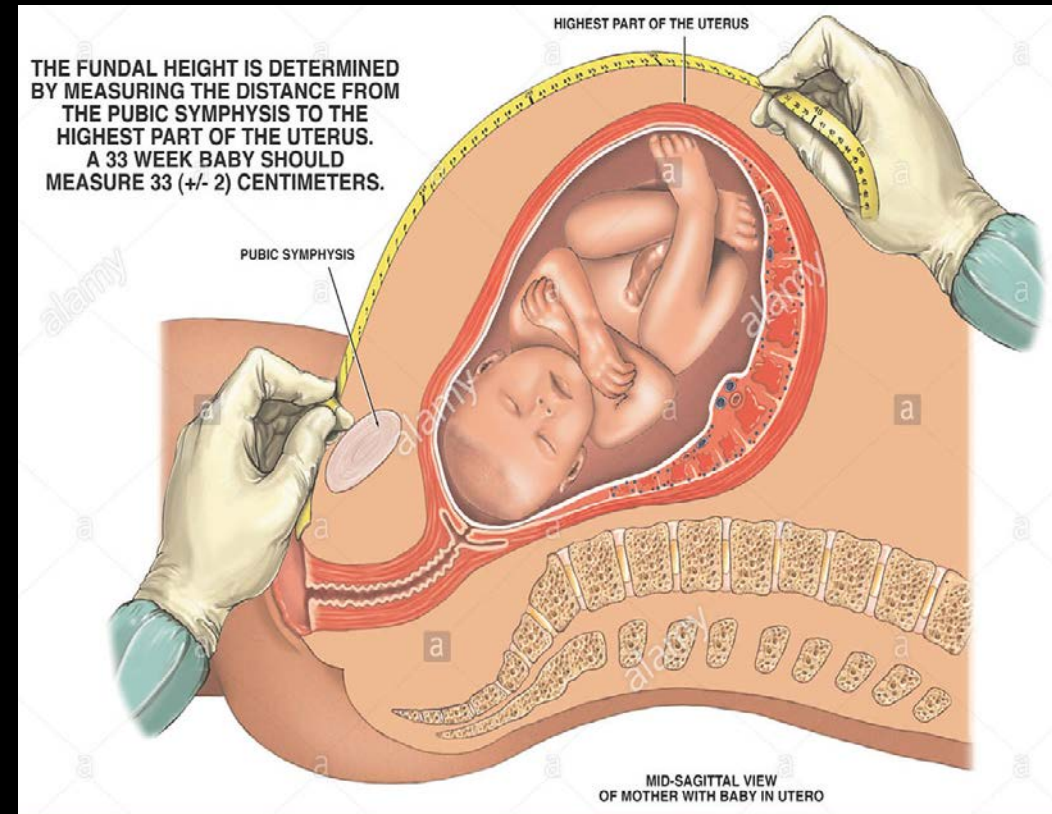
- Wide range of sensitivities: 13-86% detection

Affected by

- BMI
- Bladder volume
- Ethnic group

Best if done

- Same clinician
- Unmarked tape
- Plotted to reflect individual patient



SONOGRAPHIC DIAGNOSIS

Estimated fetal weight (EFW)

- Most common method
- Sensitivity, specificity, positive and negative predictive values of EFW for FGR <10 percentile are approximately 90, 85, 80, and 90 percent, respectively, when performed proximate to delivery
- Sensitivity is higher in severe FGR

SONOGRAPHIC DIAGNOSIS

Abdominal circumference (AC)

- Sensitivity, specificity, positive and negative predictive values of 61, 95, 86, and 83 percent, respectively
- More sensitive in asymmetric FGR
- More sensitive later in gestation
- More sensitive when the interval between measurements is more than two weeks

Small AC also correlates with parameters of morbidity associated with FGR

Biochemical markers of hypoxia and acidemia are more common when the AC is below the 5th percentile for GA



Management

Confirming the diagnosis

Cause and severity of FGR

Counseling

Monitoring fetal growth and wellbeing

Optimal time for and route of delivery

Confirm the diagnosis

<10 percentile weight for gestational age

- constitutionally small VS. fetus with growth potential is restricted

Constitutionally small fetus

- Modest smallness
- Normal growth velocity across gestation
- Normal physiology (ie, normal amniotic fluid volume and umbilical artery Doppler)
- Abdominal circumference growth velocity above the lowest decile
- Appropriate size in terms of maternal characteristics (height, weight, race/ethnicity).

Determine the cause

Complete history

Physical examination

Obstetrical imaging and laboratory evaluations

Fetal survey

Detailed fetal anatomic survey

- 10 % of FGR have congenital anomalies
- 20-60% of fetuses with congenital anomalies are FGR
 - (Detection of trisomy 18 is as high as 100% at 18-22 weeks)

Fetal genetic studies

Trisomies 13, 18, 21 contribute to 5-10% of IUGR cases

karyotype/microarray is indicated:

- Early (<24 weeks), severe (<5%le), symmetrical FGR
- Major fetal structural abnormalities
- Ultrasound markers associated with aneuploidy, (ie, increased nuchal fold, abnormal hand positioning)

Usually not performed after 24 weeks with normal anatomy yield is low

Confined placental mosaicism is detected after delivery in approximately 10% of placentas associated with otherwise idiopathic FGR

Workup for infection

Maternal history, physical examination or fetal ultrasound findings

- Cytomegalovirus
- Toxoplasmosis
- Rubella
- Varicella
- Malaria

Timing of infection is crucial

Amniotic fluid DNA testing can also be performed for specific infections

PREGNANCY MANAGEMENT

FGR associated with congenital or chromosomal anomalies depends on the specific abnormality and management focuses on that specific anomaly

PREGNANCY MANAGEMENT

Optimal management of FGR related to uteroplacental insufficiency has not been established

Limited evidence from randomized trials

key elements of fetal assessment and guide pregnancy management decisions:

- Serial ultrasound evaluation of fetal growth
- Fetal behavior (biophysical profile [BPP])
- Impedance to blood flow in fetal arterial and venous vessels (Doppler velocimetry)

The purpose is to identify those fetuses that are at highest risk of in utero demise and neonatal morbidity and thus may benefit from preterm delivery

Doppler velocimetry

Doppler velocimetry of the umbilical artery is a good tool for fetal assessment in FGR when the etiology is placental dysfunction related to progressive obliteration of the villus vasculature.

Placental vascular changes lead to fetal hemodynamic changes that can be evaluated by umbilical artery Doppler.

General sequence of Doppler and biophysical

- Reduction in umbilical venous flow is the initial hemodynamic change.
- Venous flow is redistributed away from the fetal liver and towards the heart.

- Umbilical artery Doppler index increases (diminished end diastolic flow) due to increased resistance in the placental vasculature.

- Middle cerebral artery Doppler index decreases (increased end diastolic flow), resulting in preferential perfusion of the brain (brain sparing effect).

- Increasing placental vascular resistance results in absent and then reversed end diastolic flow in the umbilical artery.

- Middle cerebral artery Doppler index normalizes or abnormally increases as diastolic flow falls due to loss of brainsparing hemodynamic changes.

- As cardiac performance deteriorates due to chronic hypoxia and nutritional deprivation, absent or reversed end diastolic flow in the ductus venosus and pulsatile umbilical venous flow may develop. These can be preterminal events.

Umbilical artery Doppler (UAD)

Numerous randomized trials that UAD significantly reduce perinatal death, as well as unnecessary induction of labor in the preterm growth restricted fetus

A 2013 systematic review of 18 trials

- Doppler vs. no Doppler
- 29% reduction in perinatal deaths
- Significantly fewer labor inductions and cesarean deliveries

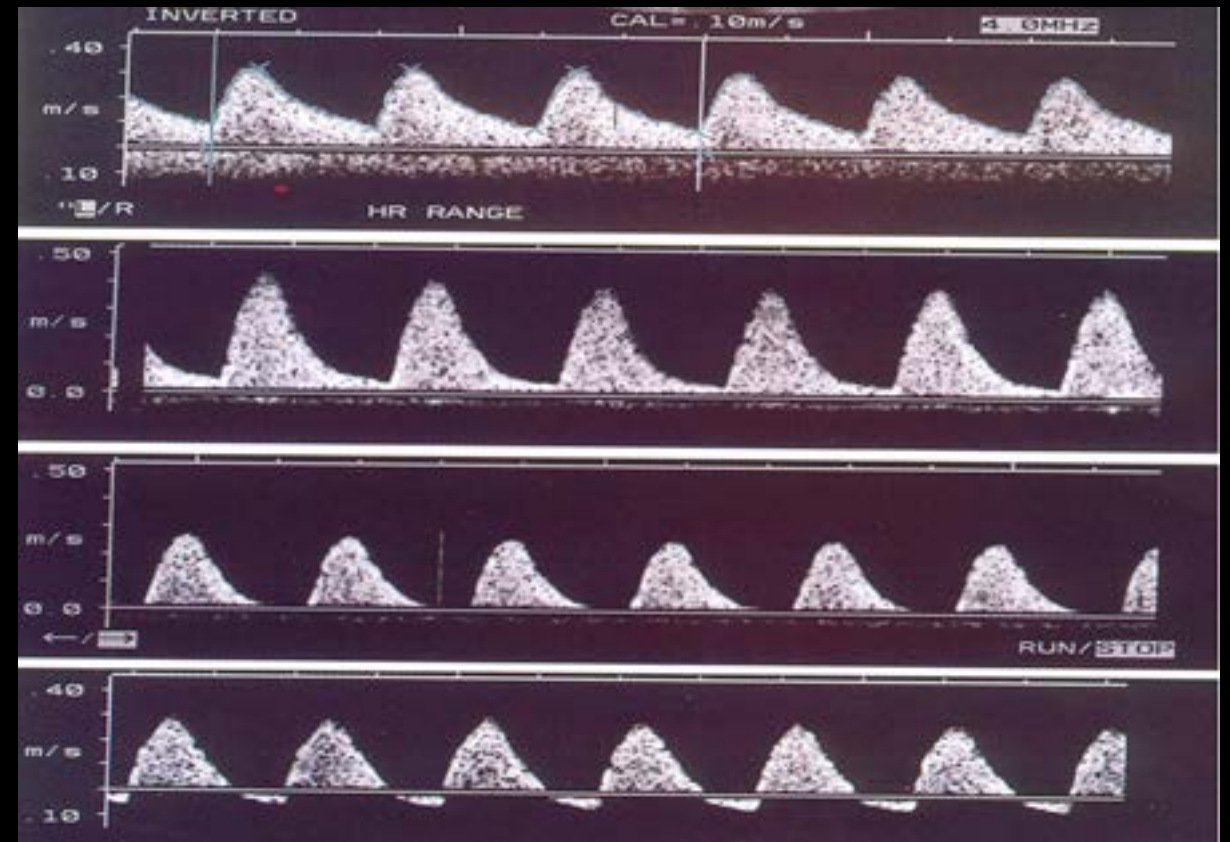
UAD

Normal diastolic flow (lowest rate of perinatal morbidity or mortality)

Decreased end diastolic flow (30% villous vasculature ceases to function)

Absent end diastolic flow (60-70% villous vasculature is obliterated)

Reversed diastolic flow is associated with poorer neonatal outcomes than absent diastolic flow



Near the end of this sequence, biophysical changes usually become apparent:

Nonstress test (NST) becomes nonreactive

BPP score falls

Late decelerations accompany contractions

Cardiovascular (Doppler) and behavioral (BPP) can be independent resulting discordant Doppler and BPP findings

This means if delivery needs to be planned both identities need to be taken into consideration

Ambulatory monitoring

Women FGR may maintain normal activities

No data on base indication for hospitalization

Hospitalization becomes an option when daily/ frequent monitoring is required (setting of reverse diastolic flow or decreased BPP)

- Delivery is usually imminent

Fetal weight assessment

Persistent growth deficiency in multiple examinations over many weeks strengthens the likelihood of FGR

Normal growth velocity in a small fetus suggests a constitutionally small but normal fetus

Serial ultrasounds every 2-4 weeks

- Longer interval for mild FGR
- Shorter interval for moderate to severe IUGR (ie, <5%ile, oligohydramnios, abnormal dopplers)

Nonstress test and biophysical profile

NST with amniotic fluid or BPP or combination of both tests is reasonable for monitoring fetal wellbeing

- observational studies that reported lower rates of fetal death when comparing tested population vs. historically not tested
- Same or lower rates of fetal death in tested pregnancies (primarily high risk) than in a contemporary untested general obstetrical population (primarily low risk)

Biophysical profile

BPP evaluates both acute and chronic fetal physiologic parameters

- Easy to perform
- Fetal death within one week of a normal test score is rare

Nonstress test and amniotic fluid assessment

Amniotic fluid volume assessment should also be performed weekly

Chronic placental insufficiency results in both FGR and oligohydramnios

Observational studies have reported that pregnancies complicated by FGR and oligohydramnios have a modestly increased risk of perinatal mortality

Normal amniotic fluid volume is infrequently associated with either FGR or fetal demise, unless the cause is a congenital malformation or aneuploidy

How often should you do monitor?

Weekly

More frequently (twice) when associated with other anomalies (ie, oligohydramnios, preeclampsia, decelerating fetal growth, severe growth restriction, increasing umbilical artery Doppler index)

Daily if absent or reversed end diastolic flow

Antenatal steroids

one course of antenatal corticosteroids is given between 24 and 34 weeks of gestation in the week before delivery is expected

Maternal interventions

No evidence of the benefit of any intervention

- Maternal nutritional supplementation
- Oxygen therapy
- Plasma volume expansion
- Low dose aspirin
- Bed rest
- Sildenafil

Antihypertensive therapy of hypertensive gravidas does not improve fetal growth

It's very important to monitor these patient's blood pressure, low blood pressure could jeopardize fetal blood flow

Timing delivery

Multiple trials have attempted to determine the ideal time of delivery

1. Growth Restriction Intervention Trial
 - 24 and 36 weeks
 - Immediate (n = 296) or delayed (n = 291) delivery if their obstetrician was uncertain about when to intervene
 - Fewer stillbirths (2 versus 9 with delayed delivery) but more neonatal and infant deaths (27 versus 18) specially if delivered before 31 weeks
2. Disproportionate Intrauterine Growth Intervention Trial At Term
 - over 36.0 weeks
 - Induction of labor or expectant monitoring
 - No difference between the two approaches

Ideally

Gestational age

UAD

BPP score (or nonstress test)

Presence or absence of risk factors for, or signs of, uteroplacental insufficiency

Reversed diastolic flow deliver ≥ 32 -34 weeks

Absent diastolic flow deliver ≥ 34 weeks

Decreased diastolic flow deliver at 37 -38 weeks

If other signs of placental insufficiency oligohydramnios, preeclampsia or hypertension, renal insufficiency, fetal growth arrest, estimated weight < 5 percentile deliver at 37 -38 weeks

Normal Doppler delivery at 39-40 weeks

INTRAPARTUM MANAGEMENT

Inform neonatal team:

- Passage of meconium with risk of aspiration
- Neonatal polycythemia
- Impaired thermoregulation
- Hypoglycemia and other metabolic abnormalities

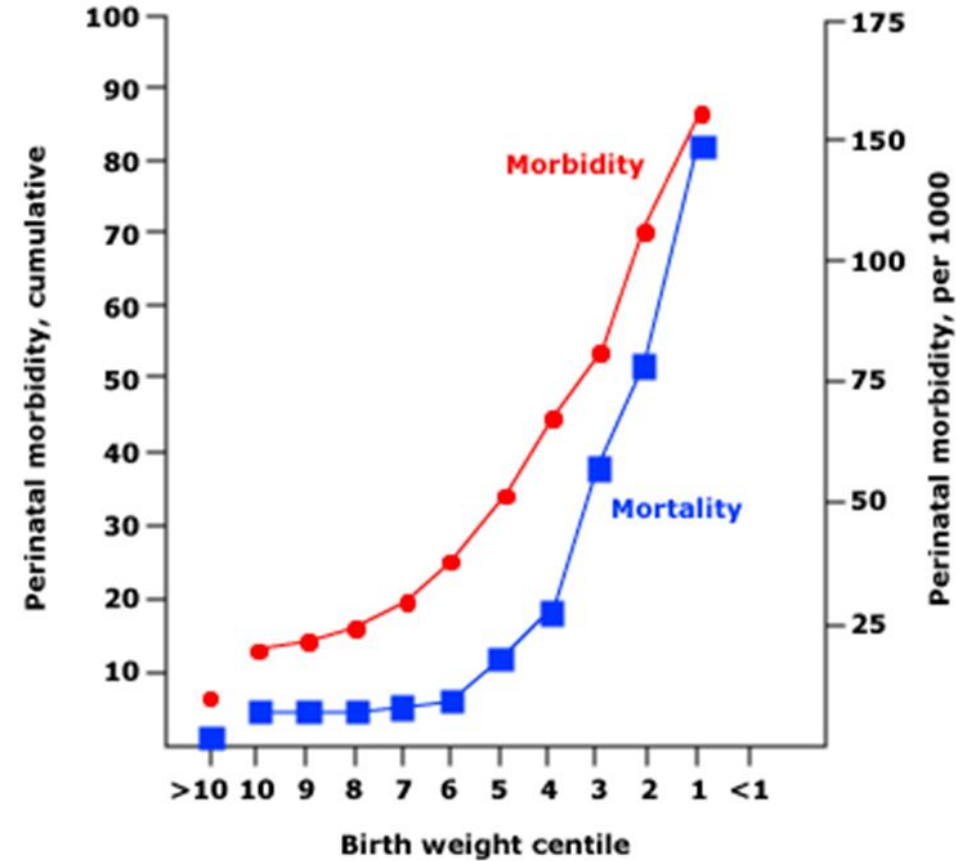
Umbilical cord blood analysis should be considered as a component of establishing baseline neonatal status

Higher frequency of cesarean delivery for nonreassuring fetal heart rate

PROGNOSIS

Perinatal

- Stillbirth, neonatal death, neonatal morbidity, and abnormal neurodevelopmental outcome
- Association with development of obesity, metabolic dysfunction, insulin sensitivity, type 2 diabetes, and cardiovascular and renal disorders



RECURRENCE RISK

Risk of a nonanomalous SGA birth (<5 percentile) in the second pregnancy of women whose first delivery was “SGA” versus “not SGA” was 23 and 3%, respectively

Take home message

An estimated fetal weight <10 percentile signifies a small for gestational age fetus

Differentiate between FGR and constitutionally small

Detailed fetal anatomic survey

Evaluation of the fetal karyotype/microarray as indicated

Assess for infection if history or ultrasounds indicates it

Serial ultrasound evaluation for fetal growth, fetal behavior and Doppler

Delivery will depend gestational age, Doppler ultrasound of the umbilical artery, biophysical profile score (or nonstress test), and the presence or absence of risk factors for, or signs of, uteroplacental insufficiency

Thank you

