IUGR

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A fetus that is less than the 10th centile for GA is described as being small for gestational age (SGA).

An SGA fetus may be

- constitutionally small; in other words their growth potential was reached, and they were destined to be that small.

- Many fetuses that are SGA, however, have failed to reach their full growth potential, a condition called fetal growth restriction (FGR) or IUGR.

IUGR is associated with a significant increased risk of perinatal morbidity and mortality.
IUGR

Growth-restricted fetuses are more likely to suffer

- Intrauterine hypoxia/asphyxia
- Stillbirth
- Demonstrate signs and symptoms of hypoxic-ischaemic encephalopathy (HIE), including seizures
- Multiorgan damage or failure in the neonatal period.
- Neonatal hypothermia, hypoglycaemia, infection and necrotizing enterocolitis.
reduced fetal growth is strongly associated with a number of chronic conditions later in life.

This increased susceptibility results from adaptations made by the fetus in an environment limited in its supply of nutrients.

These chronic conditions include:
- coronary heart disease
- stroke
- diabetes
- hypertension.
Fetal size can be assessed antenatally in two ways:
- externally by using a tape measure to assess the uterine size (symphysis-fundal height [SFH] measurement)
- using ultrasound

The fetal size is described in terms of its size for gestational age and is presented on centile charts. Centile charts can be designed for a population.
Interventions to deliver the growth-restricted fetuses early from the intrauterine environment may improve outcome.

It is important to note, however, that not all growth-restricted fetuses are SGA, in that while their birthweight is within the normal range for gestation (above the 10th centile) they still may have failed to reach their full growth potential.
Determinants of fetal growth and birthweight

Determinants of fetal growth and birthweight are multifactorial.

- The ultimate birthweight is therefore the result of the interaction between the fetus and the maternal uterine environment.

- Fetal growth is dependent on adequate delivery to, and transfer of nutrients and oxygen across, the placenta, which relies on appropriate maternal nutrition and placental perfusion.
Causes of fetal growth restriction

- **Reduced fetal growth potential**
  - Aneuploidies, e.g. trisomy 18,21,13
  - Single gene defects (e.g. Seckel’s syndrome)
  - Structural abnormalities (e.g. renal agenesis)
  - Intrauterine infections (e.g. cytomegalovirus, toxoplasmosis)

- **Maternal factors**
  - Undernutrition (e.g. poverty, eating disorders)
  - Maternal hypoxia (e.g. living at altitude, cyanotic heart disease)
  - Drugs (e.g. alcohol, cigarettes, cocaine)

- **Placental factors**
  - Reduced uteroplacental perfusion (e.g. inadequate trophoblast invasion, sickle cell disease, multiple gestation)
  - Reduced fetoplacental perfusion (e.g. single umbilical artery, twin-to-twin transfusion syndrome)
Fetal influences

- **Genetic**
  - Fetal genome plays a significant role in determining fetal size.
  - Obvious and sometimes severe IUGR is seen in fetuses with chromosomal defects such as the trisomies, particularly of chromosomes 13 (Patau’s syndrome) and 18 (Edward’s syndrome).
  - Less severe IUGR is common in trisomy 21 (Down’s syndrome).
  - Structural abnormalities (e.g. renal agenesis)
  - The other genetic influence is fetal sex, with slightly greater birthweights in males.

- **Infection**
  - Rubella, cytomegalovirus, *Toxoplasma* and syphilis, it is common to test the maternal blood for antibodies to these infections.
Maternal influences

Physiological influences

- Include maternal height, pre pregnancy weight, age and ethnic group.
- Heavier and taller mothers tend to have bigger babies
- certain ethnic groups lighter babies (e.g. South Asian and Afro-Caribbean).
- Parity is also an influence with increasing parity being associated with increased birthweight.
- Age influences relate to the association with age and parity (i.e. older mothers are more likely to be parous).
- In older women, however, the increased risk of chromosomal abnormalities and maternal disease, for example hypertension, lead to lower birthweights.
- Teenage pregnancy is also associated with IUGR.

Behavioural
Chronic disease

- Chronic maternal disease may restrict fetal growth.
- Such diseases are largely those that affect placental function or result in maternal hypoxia.

Conditions include:
  - Hypertension (essential or secondary to renal disease)
  - Lung or cardiac conditions (cystic fibrosis, cyanotic heart disease).
  - Hypertension can lead to placental infarction that impairs its function.
  - Maternal thrombophilia can also result in placental thrombosis and in
Placental influences

To ensure that the fetus receives adequate oxygen and nutrients from the mother.

Placental insufficiency occurs when there is inadequate transfer of nutrients and oxygen across the placenta to the fetus.

- abruption.
- Recurrent (antepartum haemorrhage)
- Hypertensive disorders of pregnancy
- (e.g. inadequate trophoblast invasion, sickle cell disease, multiple gestation) Reduced fetoplacental perfusion (e.g. single umbilical artery, twin-to-twin transfusion syndrome)
Determination of gestational age and assessment of fetal size and growth

Up to approximately 20 weeks gestation, the range of values around the mean for measurements of fetal length, head size and long bone length is narrow and hence assessment of gestation which is based on these measures is accurate.

- The crown–rump length (CRL) is used up to 13 weeks + 6 days,
- Head circumference (HC) from 14 to 20 weeks’ gestation.
- Biparietal diameter (BPD) and femur length (FL) can also be used to determine gestational age.
Essentially, the earlier the measurement is made, the more accurate the prediction, and measurements made from an early CRL (accuracy of prediction 6 ± 5 days) will be preferred to a BPD at 20 weeks (accuracy of prediction 6 ± 7 days).

In the latter part of pregnancy, measuring fetal abdominal circumference (AC) and HC will allow assessment of the size and growth of the fetus and will assist in the diagnosis and management of fetal growth restriction (IUGR).

In addition to AC and HC, BPD and FL, when combined in an equation, provide a more accurate estimate of fetal weight (EFW) than any of the parameters taken singly.
In pregnancies at high risk of IUGR, serial measurements are plotted on the normal reference range.

Growth patterns are helpful in distinguishing between different types of growth restriction (symmetrical and asymmetrical).

Asymmetry between head measures (BPD, HC) and AC can be identified in IUGR, where a brain-sparing effect will result in a relatively large HC compared with the AC.

The opposite would occur in a diabetic pregnancy, where the abdomen is disproportionately large due to the effects of insulin on the fetal liver and fat stores. Cessation of growth is an ominous sign of placental failure.
Symmetrically small fetuses are normally associated with factors that directly impair fetal growth such as chromosomal disorders and fetal infections.

Asymmetrical growth restriction is classically associated with uteroplacental insufficiency that leads to reduced oxygen transfer to the fetus and impaired excretion of carbon dioxide by the placenta.

A fall in $pO_2$ and a rise in $pCO_2$ in the fetal blood induces a chemoreceptor response in the fetal carotid bodies, with resulting vasodilatation in the fetal brain, myocardium and adrenal glands, and vasoconstriction in the kidneys, splanchnic vessels, limbs and subcutaneous tissues.
When there is fetal hypoxia, more of the well-oxygenated blood from the umbilical vein is diverted through the ductus venosus, which means that the liver receives less.

The result of all these circulatory changes is an asymmetrical fetus with relative brain sparing and reduced abdominal girth and skin thickness.

The fetal hypoxaemia also leads to severe metabolic changes in the fetus reflecting intrauterine starvation.
Pregnancies at risk of IUGR

- Multiple pregnancies
- History of IUGR in previous pregnancy.
- Current heavy smokers.
- Current drug users.
- Women with underlying medical disorders: hypertension; diabetes; cyanotic heart disease
- Antiphospholipid syndrome.
- Pregnancies where the symphysis–fundal height is less than expected
Assessment of fetal wellbeing. In brief, the detection of an IUGA infant contains two elements:

- first the accurate assessment of gestational age
- second, the recognition of fetal smallness.

Early measurement of the fetal crown–rump length before 13 weeks plus 6 days gestation head circumference between 13 weeks plus 6 days and 20 weeks’ gestation remains the method of choice for confirming gestational age.

Thereafter the most precise way of assessing fetal growth is by ultrasound biometry (biparietal diameter, head circumference, abdominal circumference and femur length) serially at set time intervals (usually of 4 weeks and no less than 2 weeks).

Serial ultrasound biometry is usually performed in ‘at risk’ pregnancies
Surveillance of the IUGR fetus

In the IUGR fetus tests of fetal wellbeing include:

- Umbilical artery Doppler wave form analysis: absence or reversed flow of blood in the umbilical artery during fetal diastole requires delivery in the near future
- Serial biometry and amniotic fluid volume measurement performed at no less than 2-weekly intervals.
- Fetal cardiotocography
Antenatal corticosteroids

- Ideally, a course of antenatal corticosteroids is given in the week before preterm delivery is anticipated.

- Timing is estimated based on multiple factors, including the severity of IUGR, Doppler findings, comorbid conditions, and rate of deterioration in fetal status.

- Administration of antenatal corticosteroids, including the minimum and maximum gestational age at administration and dosing, is to be considered.
Timing delivery

There is little consensus about the optimum time to deliver the growth-restricted fetus.
PROGNOSIS

Perinatal

- Stillbirth, neonatal death, neonatal morbidity, and abnormal neurodevelopmental outcome are more common in growth-restricted fetuses than in those with normal growth.
- The prognosis worsens with early onset and increasing severity of growth restriction.
- Severe bronchopulmonary dysplasia, severe necrotizing enterocolitis, severe retinopathy of prematurity requiring treatment, grade III or IV intraventricular hemorrhage.
An association has been observed between poor fetal growth, early accelerated postnatal growth, and later development of obesity, metabolic dysfunction, insulin sensitivity, type 2 diabetes, and cardiovascular and renal diseases (e.g., coronary heart disease, hypertension, chronic kidney disease).

The combination of prematurity and severe IUGR increases the risk of long-term neurodevelopmental abnormalities and decreased cognitive performance.
RECURRENT RISK

- There is a tendency to repeat small for gestational age (SGA) deliveries in successive pregnancies.

- Growth restriction, preterm delivery, preeclampsia, abruption, and stillbirth can all be sequelae of impaired placental function.

- The highest risk of stillbirth was in women who delivered a preterm SGA infant.
Prevention in subsequent pregnancies

- In subsequent pregnancies, we address any potentially treatable causes of IUGR.

- Low-dose aspirin may be effective when IUGR is secondary to preeclampsia since aspirin appears to reduce the risk of developing preeclampsia in women at moderate to high risk of developing the disorder.

- Anticoagulation with unfractionated heparin or low-molecular weight heparin.

- The combination of low dose aspirin and LMWH.
A birth defect is any structural anomaly present at birth.

These defects can be caused by genetic abnormalities and/or environmental exposures, although the underlying etiology is often unknown.

Birth defects can be isolated or present in a characteristic combination or pattern that may affect one or more organ systems.

Major congenital malformations are abnormalities that have medical, surgical, or cosmetic significance.

They occur in approximately 2 to 4 percent of livebirths and are more common in stillborn spontaneous miscarriages.
Malformations

Malformations are defects of organs or body parts due to an intrinsically abnormal developmental process. In this process, a structure is not formed, is partially formed, or is formed in an abnormal fashion.

- Malformations often result from a defect in embryonic development. Thus, most occur prior to the eighth week after conception.
- However, malformations can also occur in body structures that develop or continue to develop after this time, such as the central nervous system (CNS), external and internal genitalia, and teeth.
- Malformations can result from genetic or teratogenic environmental factors.
Malformations can be classified as major and minor.

Major malformations are those that have medical and/or social implications. These often require surgical repair or are life threatening.

The neural tube defects, such as meningomyelocele or orofacial clefting (cleft lip and palate), are examples of common major malformations.
Minor

- Minor malformations have mostly cosmetic significance.
- They rarely are medically significant or require surgical intervention.
- They represent part of the normal variation in the general population.
- Examples of minor anomalies include ear tags, clinodactyly (incurving of the fifth finger) and single transverse palmar creases.
- Minor anomalies are common,
- Infants with three or more minor anomalies are at increased risk of having a major defect or syndrome.
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<th>Term</th>
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<td>Malformation</td>
<td>Defects of organs or body parts due to an intrinsically abnormal developmental process</td>
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<tr>
<td>Deformation</td>
<td>Abnormalities of the shape and position of body parts due to extrinsic intrauterine mechanical forces that modify a normally formed structure</td>
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<tr>
<td>Disruption</td>
<td>Defects of organs or body parts that result from destruction of or interference with normal vascular development</td>
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<tr>
<td>Dysplasia</td>
<td>Anomalies that result from the abnormal organization of cells into tissues</td>
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