IUGR & IUFD

429 OB/GYN Team

Sources: Lecture ppt., Hacker & Moore 4ed, BRS Ob/Gyn by Sakala 2ed

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INTRAUTERINE GROWTH RESTRICTION

Definition: birth weight of a newborn infant below the 10th percentile for a given gestational age

- LBW is defined as birth weight < 2.5 kg, so does not correct for gestation
- Small for gestational age (SGA) is not synonymous with IUGR.
- It indicates that a fetus/neonate is below a defined reference range of weight for a gestational age.
- IUGR refers to fetuses or neonates whose growth potential has been limited by pathologic processes in utero, with resultant increased perinatal morbidity and mortality

Growth-restricted fetuses are prone to problems such as meconium aspiration, asphyxia, polycythemia, hypoglycemia, and mental retardation

ETIOLOGY:

I. MATERNAL

1. Poor nutritional intake (restricts growth in 3rd trimester)
2. Cigarette smoking, drug abuse, and alcoholism
3. Cyanotic heart disease and pulmonary insufficiency
4. Antiphospholipid syndrome (autoantibody production)
5. Hereditary thrombophilias

* Antiphospholipid syndrome: Contributes to the formation of vascular lesions in both uterine & placental vasculature that may result in impaired fetal growth and demise.
* Identification of thrombophilias & Rx with heparin & low-dose aspirin has been shown to ↓ risk of IUGR.

II. PLACENTAL

Any condition in which there is placental insufficiency:

1. Essential hypertension or DM (with vascular disease)
2. Chronic renal disease
3. Pre-eclampsia & gestational HTN (if it occurs late in pregnancy & is not accompanied by chronic vascular/renal disease, significant IUGR is unlikely)
4. Placental or cord abnormalities (e.g. velamentous cord insertion)

III. FETAL

1. Intrauterine infection; malaria MAJOR CAUSE, listeriosis and TORCH (toxoplasmosis, other infections, rubella, cytomegalovirus, herpes simplex agents & syphilis)
2. Congenital anomalies: CNS, CVS, GIT, GUT or MSK structural anomalies
3. Chromosomal: abnormal fetal karyotype can be responsible for up to 20% of growth restricted fetus
    a. Early pregnancy: **triploidy** (58%)
    b. **Trisomy** (46%)
    c. Second trimester: **trisomy 21 and Turner's**
4. Inadequate nutrietion (lack of substrates: Oxygen, glucose, amino acids and lactate) e.g. babies born at higher altitudes are smaller

CLINICAL MANIFESTATIONS:

SYMMETRIC GROWTH RESTRICTION

- Ususally occurs **EARLY** (<32 weeks gestation)
- Growth of both the head and the body is inadequate
- The head-to-abdominal circumference ratio is normal, but the absolute growth rate is decreased
- Differential diagnosis:
    - Chromosomal abnormality/congenital anomalies. Findings:
        1. **Normal** uterine artery Doppler findings
        2. **Normal** liquor volume
        3. Presence of a **structural abnormality**
    - Intrauterine infection (especially CMV)
    - Uteroplacental insufficiency. It is a diagnosis of exclusion. Findings:
        1. A **history** of growth restriction in a previous pregnancy
        2. **Reduced** liquor volume
        3. **Abnormal** uterine umbilical artery waveforms on Doppler

Intrauterine CMV infection:
1) Mother may have complained of flu-like illness
2) Fetus has sonographic findings compatible with CMV (e.g. microcephaly and cerebral calcification)

ASYMMETRIC GROWTH RESTRICTION

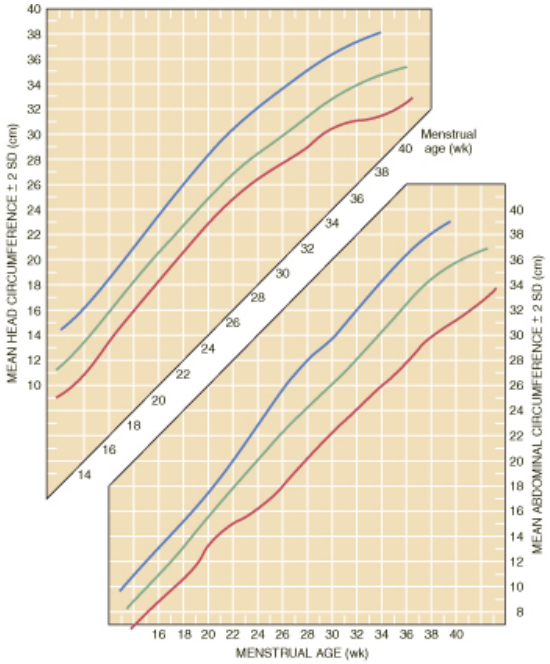
- Usually occurs late (>32 weeks)
- The head size is proportionally larger than the abdominal size
    - The brain is preferentially spared at the expense of "nonvital" viscera
- Most likely cause is utero-placental insufficiency, often associated with the development of **PRE-ECLAMPSIA**

DIAGNOSIS

It is important to establish the **correct gestational age of the fetus**, identify high-**risk factors** from the obstetric history, and serially assesses fetal growth by fundal height or ultrasonography

Factors to be evaluated in dating a pregnancy:
1. Accuracy of the date of the last normal menstrual period
2. Evaluation of uterine size on pelvic examination in 1st trimester
3. Evaluation of uterine size in relation to gestational age during subsequent antenatal visits (concordance or size-for-dates)
4. Gestational age when fetal heart tones were first heard using a Doppler ultrasonic device (usually at 12-14 wk)
5. Date of quickening (usually 18-20 wk in a primigravida and 16-18 wk in a multigravida)
6. Sonographic measurement of fetal length (crown-rump) in 1st trimester is most accurate

- Serial uterine **fundal height measurements** should serve as the **primary** screening tool for IUGR.
- A more thorough **sonographic** assessment should be undertaken when
  - The **fundal height** is > 3 cm behind a well-established gestational age
  - The **mother has high-risk conditions** such as preexisting hypertension; chronic renal disease; advanced diabetes with vascular involvement; preeclampsia; viral disease; addiction to nicotine, alcohol, or hard drugs; or the presence of serum lupus anticoagulant/antiphospholipid antibodies
- Serial U/S can identify 50-90% of cases
- Sonographic parameters used to diagnose IUGR:
  - Biparietal diameter (BPD)
    - Normal in **asymmetric**
  - Head circumference
  - **Abdominal circumference**: single **most effective** parameter for predicting fetal weight, because it is reduced in both symmetric and asymmetric IUGR



  - Head-to-abdominal circumference ratio (normal in **symmetric** IUGR)
    - Before 34 weeks: **head** circumference > **abdominal** circumference
    - At 34 weeks: head circumference ≃ abdominal circumference
    - After 34 weeks: **abdominal** circumference > **head** circumference
  - Femoral length
  - Femoral-length-to-abdominal-circumference ratio
  - Amniotic fluid volume (**reduced** in **asymmetric**)
    - The sum of the 4 deepest vertical pools in the 4 abdominal quadrants. Normal is 5-25 cm. Oligohydramnios is <4 cm.

Decreased fetal renal perfusion → ↓ urine output → oligohydramnios

  - Calculated fetal weight (**reduced** in **symmetric** IUGR)
  - Umbilical and uterine artery Doppler
    - In normal pregnancies, end diastolic flow is usually present in ther umbilical arteries by the early 2nd trimester and increases until term
    - Growth restricted fetuses often have absent or reversed end-diastolic flow in the umbilical artery – this suggests increased resistance in the feto-placental circulation
- It is helpful to plot out each serial measurement on a standard growth curve

MONITORING:

Serial fetal measurement (every 2 weeks)

1. Abdominal circumference
2. Amniotic fluid index
3. Cardiotocography
4. Doppler ultrasound
    a. Fetuses with absent end-diastolic flow are hypoxaemic, these changes may appear up to **5 weeks before demise**
    b. Reversed end-diastolic flow is suggestive of preterminal compromise; the fetus may die **within 1-2 days** if not delivered

BIOPHYSICAL PROFILE

1. Breathing
    a. Requires about **40 mins** observation of fetal breathing movements
2. Tone
3. Movement
4. Amniotic fluid volume
5. Cardiotocography

> *A persistently abnormal biophysical score is associated with absence of end-diastolic flow.*

MANAGEMENT

PREPREGNANCY

Prevention: anticipate risks that can be modified before a woman becomes pregnant.

1. Improving nutrition
2. Smoking cessation (even second-hand)
3. Antiphospholipid syndrome associated with the delivery of a prior IUGR infant → **low-dose aspirin** in early pregnancy may reduce recurrence of recurrent IUGR.
4. Hereditary thrombophilias → **low-dose heparin** ± low-dose aspirin reduces the risk of recurrent IUGR.
5. Work fatigue → decrease physical activity/sick-leave/hospitalization

ANTEPARTUM

Goal: expedite delivery before the occurrence of fetal compromise but after fetal lung maturation.

- Regular fetal monitoring with a twice-weekly nonstress test (NST) and BPP
    - Normal results and U/S findings suggest normal growth → no intervention
    - U/S findings strongly suggest IUGR ± abnormal fetal surveillance → delivery is at gestational ages of 34 weeks or later, or at any gestational age if pulmonary maturity is documented.

  - If there is severe **oligohydramnios** → amniocentesis is not safe → **deliver** without assessing lung maturity
    - Because these fetuses are at great risk of asphyxia, and the stress associated with IUGR usually accelerates fetal pulmonary maturity
  - If U/S findings are inconclusive for IUGR → bed rest, fetal surveillance, and serial U/S measurements 3 times/week
- Alternative: Fetal movement assessment (kick count) each evening while resting
  If patient does not perceive 10 movements in 1 hour → BPP
- Uterine/umbilical artery Doppler can be used to evaluate high-risk patients

LABOR AND DELIVERY

- IUGR not an absolute contraindication to induction of labor but cesarean section should be considered because the IUGR fetus cannot tolerate asphyxia.
- During labor, patients must be **electronically monitored** to detect the earliest evidence of fetal distress
- With Absent end-diastolic flow (AEDF) or reversed EDF → caesarean section
- After birth:
  - Carefully examine the infant to rule out congenital anomalies and infections.
  - Monitor blood glucose levels, because the fetuses do not have adequate hepatic glycogen stores, and hypoglycemia is a common
  - Monitor for hypothermia
  - Respiratory distress syndrome is more common in the presence of fetal distress, because fetal acidosis reduces surfactant synthesis and release
- The prognosis is generally good if chromosomal abnormalities, autoimmune disease, congenital anomalies, and infection are excluded.

INTRAUTERINE FETAL DEATH

- IUFD is fetal death **after 20 weeks gestation but before the onset of labor**
- It includes delayed miscarriage (occuring before 28 weeks), and those occuring later that result in a macerated stillborn
- It complicates about 1% of pregnancies

Maceration is a destructive process which first manifests as blistering and peeling of the fetal skin (12-24 hours after fetal death.)
The ligaments are softened and the vertebral column is liable to sag. The skull bones overlap each other at the sutures because of the shrinkage of the brain (Spalding's sign). It usually takes > 1 week for Spalding's sign to appear.

ETIOLOGY

1. IDIOPATHIC

> 50% of cases Associated causes include hypertensive diseases of pregnancy, diabetes mellitus, erythroblastosis fetalis, umbilical cord accidents, fetal congenital anomalies, fetal or maternal infections, fetomaternal hemorrhage, antiphospholipid antibodies and hereditary thrombophilias.

2. PLACENTA OR CORD PROBLEMS

1. Abruptio placenta with fetomaternal hemorrhage
2. Placental insufficiency due to pre-eclampsia

3. MATERNAL

1. Systemic disease:
    a. Antiphospholipid syndrome
    b. Type I DM
    c. Chronic hypertension
    d. Chronic nephritis/renal disease
    e. Hyperpyrexia
2. Trauma (usually penetrating)
3. Isoimmunization: hemolysis of fetal RBCs by maternal IgG → severe anemia/hydrops

* Antiphospholipid Syndrome: Hx of stroke, venous thrombosis, or recurrent abortions + ↑ PTT + ↑ anticardiolipin antibodies, lupus anticoagulant or antiphospholipid antibodies
* Type I DM:
- IUFD occurs if there is vascular disease, poor control, polyhydraminos and macrosomia
- Probable causes are fetal hyperinsulinemia and hypoxia.
- Macrosomic fetus outgrows the placental abilities

4. FETAL

1. Chromosomal abnormalities: monosomy x (Turner's) or trisomies e.g. Down's
2. Structural anomalies e.g. cardiac defects, osteogenesis imperfecta
3. Infections: 2nd trimester infections rarely lead to death, except
    a. Parvovirus B19 → fetal erythroid progenitor cell destruction → severe anemia/hydrops
    b. Syphilis, *Listeria*, *Mycoplasma* and CMV → inflammation and edema of placental villi → fetal hypoxia
4. Non-immune hydrops e.g. alpha-thalassemia, infections, fetomaternal hemorrhage. Mortality ~ 90%

Hydrops fetalis is a condition in the fetus characterized by an accumulation of fluid, or edema, in at least two fetal compartments.

DIAGNOSIS

- Fetal death should be suspected when
  - **Absence of fetal movements**
  - The **uterus is small for dates**
  - The **fetal heart tones are not detected on Doppler**
- Fetal death is confirmed by U/S showing lack of fetal movement and absence of fetal cardiac activity (100% accurate)

Radiographic findings (not used anymore):
- Robert's sign: gas in the great vessels
- Spalding's sign: overlapping of the skull bones due to collapse of the brain
- Angulation of the spine: exaggerated curvature, due to loss of tone in paraspinal muscles

A positive pregnancy test does not exclude an IUFD, because the placenta may continue to produce hCG.

MANAGEMENT

WATCHFUL EXPECTANCY

- 80% of patients experience spontaneous onset of labor within 2 to 3 weeks of fetal demise.
- Women who fail to go into labor spontaneously are managed by induction of labor or dilation and evacuation (D&E)

INDUCTION OF LABOR

Justifications: Slight possibility of chorioamnionitis and 10% risk of DIC **when a dead fetus is retained for > 5 weeks**

1. Cervical examination:
   a. If favorable (effaced, dilated, soft) → Cytotec (prostaglandin E1) followed by oxytocin
   b. If unfavorable
      i. Vaginal suppositories of prostaglandin E2 (dinoprostone) 13-28 wks
         - 50% of patients experience nausea and vomiting or diarrhea with temperature elevations, these side effects are transient
         - Contraindicated in patients with **prior uterine incisions** (e.g., cesarean, myomectomy) because of the risk of uterine rupture and in patients with a history of **bronchial asthma** or active pulmonary disease
      ii. IV Nalador (Sulprostone; prostaglandin E2)
      iii. Misoprostol (Cytotec; prostaglandin E1)
         - Has less gastrointestinal side effects
      iv. Dilatation & evacuation if gestational age < 20 weeks

MONITORING OF COAGULOPATHY

- Weekly fibrinogen levels with a hematocrit and platelet count
- If the fibrinogen level is decreasing obtain coagulation profile
    - ↑ PT and PTT, the presence of fibrinogen-fibrin degradation products (FDPs), and ↓ platelet count → DIC
- If labs show mild DIC but no bleeding → delivery
- If labs show severe DIC or there is bleeding → resuscitation (e.g. with fresh-frozen plasma/volume expanders) then delivery

FOLLOW-UP

Determine the cause of the intrauterine death:

1. TORCH and parvovirus studies and cultures for Listeria
2. Testing for the presence of anticardiolipin antibodies
3. Testing for the hereditary thrombophilias
4. If congenital abnormalities are detected → fetal chromosomal studies, total body radiographs and a complete autopsy.
    a. The autopsy report must be discussed in detail with both parents
5. In a stillborn fetus → tissue for chromosomal analysis (fascia lata is best)
6. Fetomaternal hemorrhage can be detected by identifying fetal erythrocytes in maternal blood (Kleihauer-Betke test)

Subsequent pregnancies occurring in a woman with a history of IUFD must be managed as high-risk cases.