INTRAUTERINE GROWTH RESTRICTION (IUGR)

Osama M Warda MD

Prof. OBS/GYN

Mansoura University

Definition

- Failure of the fetus to reach growth potential associated with increased morbidity and mortality
- *Ponderal index (PI) :* less than 10^{th} centile.

(used to identify infants whose soft tissue mass is bellow normal for the stage of skeletal development)

$$PI = BWX100/(CHL)^3$$

BW=birth weight

cHL= crown-heel length

Epidemiology of IUGR

- IUGR associated with 3-10 % of all pregnancies
- IUGR Facts
- Perinatal mortality rate is 5-20 times higher for growth retarded fetuses .
- 2nd leading contributor to the Perinatal mortality rate
- 20% of all stillbirths are IUGR
- Incidence of intrapartum asphyxia in cases of IUGR has been reported to be 50%.
- Early and proper identification and management lowers this perinatal mortality and morbidity

Incidence of LBW

- The incidence of LBW, defined as the proportion of newborns weighing less than 2,500 grams, is monitored through both health system surveillance and household surveys. In 2013, nearly 22 million newborns—an estimated 16% of all babies born globally that year—had LBW. Accurate monitoring is challenging, however, since nearly half of the world's infants are not weighed at birth.(UNECEF, 2017)

Normal Fetal Growth

- Normal fetal growth is characterized by *cellular* hyperplasia followed by hyperplasia and hypertrophy and lastly by hypertrophy alone.

Normal intrauterine growth

STAGE 1	STAGE 2	STAGE 3
HYPERPLASIA	HYPERPLASIA/HYPERTROPHY	HYPERTROPHY
4-20 weeks	20-28 weeks	28-40 weeks
Rapid mitosis	Declining mitosis	Rapid hypertrophy
Increasing DNA content	Increasing cell size	Rapid increasing cell size
		Rapid accumulation of fat , muscle, connective tissue
SYMMETRIC	MIXED-ASYMMETRIC	ASYMMETRIC

Fetal growth indices

Weight gain:

- Fetal growth accelerates from about 5g /day

at 14 -15 wks of gestation to 10g/ day at 20 wks.

- Peaks at 30 -35g / day at 32-34wks
- After which growth rate decreases.

Fetal growth indices

- Symphysio-fundal height increases by about 1cm per wk between 14 and 32 wks.

- *Abdominal girth* increases by 1 inch per wk after 30 wks. It is about 30 inches at 30wks in an average built woman.

Classification of IUGR

1- Symmetrical IUGR

- Head circumference, length, and weight are all proportionally reduced for gestational age (below 10th percentile).

- It is due to either *decreased growth potential* of the fetus or *extrinsic conditions* active early in pregnancy .

2- Asymmetrical IUGR:

-Fetal weight is reduced *out of proportion to length and head circumference .*

-The usual causes are *utero-placental insufficiency*, maternal malnutrition, or extrinsic conditions appearing late in pregnancy.

Etiology

- IUGR is a manifestation of fetal, maternal and placental disorders that affect fetal growth.

A. Fetal Causes

1. Chromosomal Disorders; usually result in early onset IUGR.

- Trisomies 13, 18, 21 contribute to 5% of IUGR cases
- Sex chromosome disorders are frequently lethal, fetuses that survive may have growth restriction (Turner Syndrome)

Etiology

Fetal causes:

2. Congenital Infections:

- The growth potential of fetus may be severely impaired by intrauterine infections.
- The timing of infection is crucial as the resultant effects depends on the phase of organogenesis.
- **Viruses**- rubella, CMV, varicella and HIV

- rubella is the most embryotoxic virus, it cause capillary endothelial damage during organogenesis and impairs fetal growth.

- CMV causes cytolysis and localized necrosis in fetus.

- Protozoa- like malaria, toxoplasma, trypanosoma have also been associated with growth restriction.

Etiology

Fetal causes;

3. Structural Anomalies: All major structural defects involving CNS,CVS,GIT, Genitourinary and musculoskeletal system are associated with increased risk of fetal growth restriction.

- If growth restriction is associated with polyhydramnios, the incidence of structural anomaly is substantially increased.

Etiology

Fetal causes:

4. Genetic causes-Maternal genes have greater influence on fetal growth.

- Inborn errors of metabolism like agenesis of pancreas, congenital lipodystrophy, galactosemia, phenylketonuria also result in growth restriction of fetus.

Etiology

B. Placental causes

Placenta is the sole channel for nutrition and oxygen supply to the fetus.

- Single umbilical artery
- abnormal placental implantation
- velamentous umbilical cord insertion
- bi-lobed placenta
- placental hemangioma have all been associated with fetal growth restriction

Etiology

C- Maternal causes:

1. Maternal Characteristics: those contributing to IUGR are;

- Extremes of maternal age
- Grand multiparity
- History of IUGR in previous pregnancy
- Low maternal weight gain in pregnancy

Etiology

C- Maternal causes:

2. Maternal diseases: Uteroplacental insufficiency resulting from medical complications like:

- Hypertension
- Renal disease
- Autoimmune disease
- Hyperthyroidism
- Long term insulin dependent diabetes

Etiology

Maternal causes contd..

- **Smoking**- active or passive, especially during third trimester is important cause of IUGR. Nicotine has vasoconstrictive effect on the maternal circulation and leads to formation of toxic metabolites in fetus.
- **Alchohol and Drugs**- Alcohol crosses the placenta freely. It acts as a cellular poison reducing fetal growth potential.Cocaine and opiates are potent vasoconstrictors .Warfarin, anticonvulsants and antineoplastic agents are also implicated in growth restriction

Etiology

Maternal causes contd..

- **Thrombophilias-** antiphospholipid antibody syndrome and other thrombophilias leading to placental thrombosis and impaired trophoblastic function.
- **Nutritional Deficiency**- leads to deficient substrate supply to the fetus

Diagnosis of IUGR

Identifying mothers at risk:

- Poor maternal nutrition
- Poor BMI at conception Pre-eclampsia
- Renal disorders
- Diseases causes vascular insufficiency
- Infections (TORCH)
- Poor maternal wt. gain during pregnancy

Diagnosis of IUGR

- *Determination of gestational age is of utmost importance*-

  – Can be calculated from the date of LMP-

---> If LMP is not reliable

– Ultrasound dating before 21 wks of pregnancy provides more accurate estimate.

Diagnosis of IUGR

Clinically –Serial measurement of fundal height and abdominal girth . S-F height normally increases by 1cm per wk between14 and 32 wks.

- A lag in fundal ht. of 4wks is suggestive of moderate IUGR.

- A lag of >6 wks is suggestive of severe IUGR.

Diagnosis of IUGR

- **Ultrasound:**

Fetal biometry:

1- BPD : - When growth rate of BPD is below 5th percentile, 82% of births are below 10th percentile

2- AC and EFW are most accurate ultrasound parameters for diagnosis of IUGR. *AC < 5mm/wk reduction is suggestive of IUGR.*

Diagnosis of IUGR

- **Ultrasound:**

Fetal biometry:

3. Measurement ratios- there are some age independent ratios to detect IUGR

- HC/AC: Persistence of a head to abdomen ratio <1 late in gestation is predictive of asymmetric IUGR.
- FL : serial measurements of femur length are effective for detecting symmetric IUGR

Diagnosis of IUGR

- **Ultrasound:**

- Placental Morphology: Acceleration of placental maturation may occur with IUGR .
- Placental volume: helpful in predicting subsequent fetal growth.
- Amniotic fluid volume: Amniotic fluid index(AFI) between 8 and 25 is normal.

Diagnosis of IUGR

Doppler Ultrasonography

Doppler flow studies are important adjuncts to fetal biometry in identifying the IUGR fetuses at risk of adverse outcome.

- *Uterine artery flow abnormalities*: predict IUGR as early as 12-14 wks of gestation

- *Umblical Artery doppler*:- In IUGR there is increased umbilical artery resistance (RI)

Diagnosis of IUGR

Doppler Ultrasonography

Middle cerebral artery doppler: in a normal fetus has relatively little flow during diastole. Increased resistance to blood flow in placenta results in redistribution of cardiac output to favor cardiac and cerebral circulations leading to increased flow in the diastolic phase

Diagnosis of IUGR

Doppler Ultrasonography

Ductus venosus doppler:

- In the normal fetus, flow in the ductus venosus is forwards , moving towards the heart during entire cardiac cycle.
- When circulatory compensation of the fetus fails, the ductus venosus waveform shows absent or reverse blood flow during atrial contraction-→ Perinatal mortality being 63-100%.

Sequential changes of doppler studies in decompensating fetal growth restriction

Initial changes	**Decreased amniotic fluid index** **Increased uterine artery resistance with EDV**
Early changes **(in 50% 2-3 wks before nonreactive FHR)**	**Decreased MCA resistance (brain sparing)** **Absent uterine artery EDV**
Late changes **~ 6 days before nonreactive FHR**	**Increased resistance in DV-reversed EDV in uterine artery**
Very late changes **(in 70%, 24 hrs before changes in BPP)**	**Reversed flow in DV and pulsatile flow in umbilical vein**

(BPP- biophysical profile , DV- ductus venosus, EDV – end diastolic velocity, FHR- fetal heart rate , MCA – mmiddle cerebral artery)

Diagnosis of IUGR

Placental magnetic resonance imaging :

Assess severity of fetal IUGR on the basis of decreased placental volume and thickness.

Diagnosis of IUGR

Neonatal Assessment

- Reduced birth weight for gestational age
- Physical appearance: thin loose, peeling skin, scaphoid abdomen, dis-propotionately large head
- Appropriate growth charts should be used
- Ponderal index
- Ballard score

MANAGEMENT

- **Principles**:

1. Identify the cause of growth restriction.
2. Treat the cause if found.
3. General management

MANAGEMENT

First step is to identify the etiology of IUGR:-

- Maternal history pertaining to the risk factors of IUGR.
- Clinical examination- maternal habitus, height, weight, BP etc.

MANAGEMENT

Laboratory investigations:

- Hb, HCT to detect polycythemia Blood sugar
- Renal function tests,
- Serology for TORCH

MANAGEMENT

FETAL EVALUATION:

- Ultrasound for growth restriction, amniotic fluid, congenital anomalies and
- Doppler evaluation

MANAGEMENT

Treatment of underlying cause

- Hypertension,
- Cessation of smoking,
- Protein energy supplementation in poorly nourished and underweight women.

MANAGEMENT

GENERAL MANAGEMENT:

- Bed rest in left lateral position to increase utero-placental blood flow
- Maternal nutritional supplementation with high caloric and protein diets, antioxidents, hematinics and omega 3 fatty acids, arginine .
- Maternal oxygen therapy: Adminetration of 55% oxygen at a rate of 8L/min round the clock has shown decreased perinatal mortality rate.

MANAGEMENT

Pharmacological therapy

Aspirin in low doses(1-2 mg/kg body wt.) have been tried but all have failed to show any significant difference in incidence of IUGR.

Thus there is no form of therapy currently available which can reverse IUGR, the only intervention possible in most cases is delivery.

- DELIVERY:

Since IUGR fetus is at increased risk of intrauterine hypoxia and intrauterine demise, the decision needs to delicately balance the risk to the fetus in utero with continuation of pregnancy and that of prematurity if delivered before term.

The optimum timing of delivery is determined by

- Gestational age,
- Underlying etiology,
- Possibility of extrauterine survival and
- Fetal condition.
- Strict fetal surveillance is needed to monitor fetal well being and to detect signs of fetal compromise

MANAGEMENT

ROLE OF STEROIDS:

Antenatal glucocorticoid administration reduces the incidence of respiratory distress syndrome, intra-ventricular hemorrhage and death in IUGR fetuses weighing less than 1500gm.

MANAGEMENT

MODE OF DELIVERY:

Fetuses with significant IUGR should be preferably delivered in well equiped centres which can provide intrapartum continuous fetal heart monitoring , fetal blood sampling and expert neonatal care.

MANAGEMENT

VAGINAL DELIVERY:

- can be allowed as long as there is no obstetric indication for cesarian section and fetal heart rate is normal.
- Fetuses with major anomaly incompatible with life should also be delivered vaginally.

- NEWBORN MANAGEMENT :
- Delivery
- Resuscitation
- Prevention of heat loss
- Hypoglycemia
- Hematologic disorders
- Congenital infections
- Genetic anomalies

COMPLICATIONS OF IUGR

Perinatal mortality and morbidity of IUGR infants is 3-20 times greater than normal infants.

- *Antepartum period*-: increased incidence of still births & oligohydramnios
- IUGR is found in 20% of unexplained stillbirths.
- *During labor-* higher incidence of meconium aspiration , fetal distress , intra-partum fetal death

COMPLICATIONS

Neonatal period:

- increased incidence of
  - Hypoxic ischemic encephalopathy
  - Persistent fetal circulation insufficiency
- They have difficulty in temperature regulation because of absent brown fat and small body mass relative to surface area.
- Lack of glycogen stores may predispose to hypoglycemia
- Chronic intrauterine hypoxia may lead to polycythemia, necrotizing enterocolitis, other metabolic abnormalities.

COMPLICATIONS

- Childhood-

  - increases mortality from- -infectious diseases & congenital anomalies .

  - Incidence of cerebral palsy are 4-6 times higher.

  - Subtle impairment of cognitive performance and educational underachievement.

- Long term complications- increased risk of coronary heart disease, hypertension, type II diabetes mellitus, dys-lipidemia and stroke.

PROGNOSIS

- Mortality increases with prematurity.
- Neurodevelopmental morbidities are seen

5- 10 times more often in IUGR infants.