# Intra-uterine Growth Retardation

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# Introduction

- Anderson & Hay defined IUGR as a rate of foetal growth that is less than normal for the population and the growth potential of a specific baby.
- IUGR denotes growth deviation from normal with small for gestational age babies.
- Foetus may be small – Preterm or true small for date.
- SFD are also called growth restricted babies.

# Statistics and Terminology

- LBW babies according to WHO < 2500gms.
- 6-7% of all babies born in the UK <2500gms.
- 2/3 of LBW babies are premature, 1/3 SFD.
- 70% of SFD weigh between 2000-2500gms.
- LBW can be divided depending on weight into –LBW1500- < 2500gms, VLBW 1000- < 1500gms, extremely LBW < 1000gms.
- Preterm <37 completed weeks, weight assesses foetal growth while gestational age assesses foetal maturity

# Statistics and Terminology-1

- Relationship between GA and weight is of great importance in obstetrics.
- Relationship can be represented on the Centile chart, which will denote:

✓ Appropriate growth, preterm, term baby.

✓ Excessive growth LGA, macrosomic baby.

✓ Diminished growth (SFD), preterm, post-term baby.

# Relationship between IUGR and SGA

- Two terms are not synonymous.
- IUGR is failure of normal foetal growth caused by multiple adverse effects on the foetus.
- SGA describes a baby whose weight is lower than population norms. SGA are defined as having a birth weight below the 10th centile for gestational age or 2 SD below the mean (50th centile) for the gestational age.

# Relationship Between IUGR and SGA-1

- All IUGR babies may not be SGA, all SGA may not be small as a result of growth restriction.
- Roberton reported that 50% of SGA babies in Britain have no known aetiology. They are proportionally small (weight,height, head circumference). Generally may be constitutional.

# Types of Intra-uterine Growth Retardation

- Symmetrical growth retardation (chronic): Genetically pre-determined or assault resulting from congenital infection or chromosomal abnormality occurring early in gestational life.
- It may be intrinsic factors (genetic defects), congenital infections.
- Extrinsic factors, smoking, poor dietary intake (famine), or a conbination of the two.
- Weight, height, head circumference are proportionately reduced for gestational age.

# Types of Intra-uterine Growth Retardation-1

- Asymmetrical growth retardation (Acute): Foetal weight is reduced out proportion to length and head circumference.
- Usually caused by extrinsic factors.
- Occurs in the later part of pregnancy >28weeks.
- Usually brain growth is spared, head larger than body but normal for gestational age.

# Aetiology

- Causes or risk factors can be grouped into 4:
- Genetic disorders, they are either dorminant or recessive. Dorminant gene, produces its effect even when present on only one chromosome of a pair. Risk of an affected foetus 1:2 for every pregnancy.
- Autosomal dorminant trait can be traced through several generations e.g Achondroplasia, osteogenesis imperfecta, adult polycystic kidney disease, Huntington´s chorea.
- Recessive genes need to be present in both chromosomes to manifest e,g cystic fibrosis, sickle cell. Risk of transmission 1:4 for every pregnancy

# Aetiology-1

- Some congenital abnormalities are a consequence of single gene defect.
- In an X-linked recessive inheritance the condition affects almost exclusively males, female may be carriers: haemophilia A, B and Duchenne muscular dystrophy.
- Spontaneous mutations commonly arise in X-linked recessive disorders.
- X-linked disorder in a carrier woman, 50% chance for each male to be affected, 50% carrier state for the girls.

# Aetiology-2

- Teratogenic Causes: Teratogen is any agent that raises the incidence of congenital abnormalities. It includes:
- Drugs: anticoagulants, anticonvulsivants, high dose vitamin A drugs, heroine, alcohol, nicotine, antimitotics.
- Environmental factors: Radiation, chemicals (dioxine pesticides).
- Infectious agents(Rubella, CMV, Toxoplasmosis).
- Metabolic diseases (diabetes)

# Aetiology-3

N.B Several factors may influence the effect produced by teratogen e.g embryo++, foetus+, length of exposure, toxicity of teratogen. Direct cause-effect relationship is sometimes difficult to establish.

- Multifactorial causes: Due to a genetic defect plus one or several teratogenic factors.
- Idiopathic: About 80% of abnormalities have no known cause.

# Causes of Intra-uterine Growth Retardation

- **Maternal Factors:**

✓ Pregnancy-induced hypertension /pre-eclampsia, eclampsia.

✓ Chronic hypertension.

✓ Diabetes mellitus.

✓ Undernutrition.

✓ Smoking, alcohol misuse.

✓ Drugs –therapeutic (anticancer, narcotic or addictive drugs).

# Causes of Intra-uterine Growth Retardation-1

- ✓ Renal disease, collagen disorders, anaemia.
- ✓ Irradiation.
- ✓ Young and elderly mothers.
- ✓ Poor obstetric history. Underweight mother /small stature.
- ❑ **Foetal Factors:**
- ✓ Multiple gestation.
- ✓ Chromosomal/genetic abnormality (particularly trisomy, inborn errors of metabolism, dwarf syndromes).
- ✓ Intra-uterine infections: Toxoplasmosis, Rubella, CMV, herpes simplex, syphilis.

# Causes of Intra-uterine Growth Retardation-2

- **Placenta Factors:**

✓ Abruptio placenta.

✓ Placenta praevia.

✓ Chorioamnionitis.

✓ Abnormal cord insertion (Battledore).

✓ Single umbilical artery syndrome.

N.B Placental insufficiency is usually the underlying pathology (decreased nourishment for the foetus, glycogen store reduced). Consequence hypoglycaemia, hypothermia, premature delivery.

# Diagnostic Techniques

- Ultrasonography: Assess foetal growth.
- High risk women, serial US at 28, 32, 36 weeks.
- Doppler US, assesses placental blood flow.
- Biophysical profile (Manning et al, 1980)
- Evaluate signs of foetal hypoxia, compromised placenta function.
- Score is calculated using five criteria:
- ✓ Foetal breathing movements (3rd trimester). 1 movement/30 minutes lasting at least 30 seconds.
- ✓ 3-4 foetal movements/30 minutes.
- ✓ Foetal tone, 1 motion of extension to rapid flexion.

# Diagnostic Techniques-1

- ✓ Foetal reactivity: 2 or more foetal heart acceleration of >15 beats/ minute, in 40 minutes.
- ✓ Duration 15 seconds and associated with foetal movements.
- ❑ Qualitative amniotic fluid volume:
- ✓ Pocket of AF measuring >100mm, in two perpendicular planes.
- ❑ Screening for foetal abnormalities in maternal serum:
- ➢ Neural tube defect, alpha fetoprotein in the serum and AF as from 6 weeks gestation. Detection rate of 98% from maternal serum between 15-18 weeks of gestation.

# Diagnostic Techniques-2

- 2% of women have raised alphafetoprotein levels of unknown origin. US more specific for NTD.
- Other causes of raised alpha fetoprotein, multiple pregnancy, threatened abortion, error of dates.
- Down syndrome:
- Alpha fetoprotein, reduced in most pregnancies.
- HCG usually raised.
- Unconjugated estriol assay.
- Assay of HCG, alpha fetoproteins. Blood sampling between 15-18 weeks.

# Diagnostic Techniques-3

- Invasive diagnostic test: Indicated when increased risk for chromosomal/genetic disorders exist.
- Chorionic villi sampling (CVS), >10weeks of gestation, foetal karyotype, DNA analysis. Specimen obtained by transcervical or abdominal route. Complication 0.5-2% miscarriage, infection, bleeding, early CVS limb reduction abnormalities.
- Amniocentesis: 15-18 weeks, cytogenetics (karyotyping), DNA. Biochemical analysis. Loss rate higher than CVS, miscarriage 1%, amniotic fluid leakage 2-3%.

# Diagnostic Techniques-4

- Foetal blood sampling: Decline in usage in recent years, because of improved molecular and cytogenetic techniques. Useful for intrauterine transfusion in Rhesus isoimmunisation.
- MRI

- Similar results to US
- Better results for brain abnormalities.
- May be used for post-mortem analysis.
- Analysis of foetal cells in maternal circulation.

# Foetal Therapy

- Therapeutic amniocentesis, excess AF, as in monochorionic twins with twin-twin transfusion syndrome, discordant placental circulation, discordant growth/ AF volume (foetus papyraceus or compressus).
- Intra-uterine transfusion or exchange trans fusion (Rhesus isoimmunisation, anaemia).

# Management

Some infections acquired before or during pregnancy that may cause IUGR are:

- **Toxoplasmosis,** Agent-Toxoplasma gondii.
  - Found in uncooked meat, faeces of dogs and cats.
  - Risk factors: Eating uncooked meat, housing domestic pets (dogs, cats), poor hand hygiene, contact with soil, consumption raw vegetable.

Incidence:

- More common in pregnancy than rubella/salmonella.

# Management-1

- UK 640 babies infected each year.
- Eastern England, infection rate 3-16/10.000 women.
- France, 4900 cases of primary infection during pregnancy annually.
- Brazil has the highest prevalence.

❖ **Congenital toxoplasmosis:** Primary infection, transmission rate 19%.

➢ Foetal complications: IUD, SFD, hepato-splenomegaly, jaundice, anaemia, hydrocephalus, chorioretinitis.

# Management-2

- Diagnosis, PCR of T. gondii, mouse inoculation of AF (during pregnancy)
- At birth T. gondii IgA 64% in cord blood, 66% neonatal blood, IgM 41% cord blood, 42% neonatal blood.
- Treatment: Pyrimethamine/sulfadiazine, Rovamycine.
- N.B Antenatal treatment and reduction of congenital toxoplasmosis not proven.
- Prevention, Education ( 60% reduction of primary infection), serologic screening during pregnancy.

# Management-3

- **Varicella zoster (VZV),** highly contagious virus, herpes family.
- Transmission: Respiratory droplets, contact with vesicles.
- Incubation: 10-20 days. After primary infection virus remains dormant in sensory nerve root ganglia, recurrent infection, herpes zoster (shingles).
- Effect on pregnancy: Infection< 20 weeks gestation, foetal risk 2%. 20-36 weeks milder disease. >36 weeks, foetal infection rate 50%.

# Management-4

- Foetal varicella syndrome: skin lesion, chorioretinitis, cataract, skeletal abnormalities, microcephaly.
- Diagnosis: PCR, VZV DNA in amniotic fluid.
- Treatment: At risk women (contact), varicella zoster immune globulin (VZIG) within 72 hours.
- Prevention: Education, vaccination before or after pregnancy.

# Management-5

- **Rubella:** Viral infection, spread by droplet infection.
- Vaccination coverage: 92% industralised countries, 36% within transition economies, 28% developing countries.
- Effect on pregnancy: Primary infection <12 weeks of gestation, infection rate 85%. >16 weeks infection risk is rare.
- Congenital infection: spontaneous abortion, cataracts, congenital heart defects, sensori-neural deafness, microcephaly, meningoencephalitis, thrombocytopenia, significant developmental delay.

# Management-6

- Diagnosis: History of rash or contact, assay IgG/IgM Abs, cordocentesis-rubella IgM Abs cord blood, detection viral RNA by CVS, amniocentesis, foetal blood. In neonates- US, isolation of rubella virus, throat, urine and cerebrospinal fluid.
- Prevention: Education, strategies that target all children, school girls, women before marriage (MMR vaccine).
- **Disseminated candidiasis**, cause LBW/SFD, with risk of systemic infection. Risk factor: prolonged use of 3rd generation cephalosporins.

# Management-7

- **Foetal Alcohol syndrome:** Causes IUGR, with microcephaly, flat facies, close set eyes, small up-turned nose, thin upper lips, low set ears, small stature and mental retardation.

# Conclusion

- The management of women with IUGR, guided by the foetal weight, gestational age, presence or absence of major malformation incompatible with extra-uterine life, foetal response to stress of uterine contractions and the infra-structure and neonatal care available in the said institution.
- Delivery can be conducted by the vaginal route (preferred), or by C/S.

# Physical Findings of the Babies

- **Asymmetrical (Acute).**
  - Head larger than body, normal for gestational age.
  - Bones within gestational norms for length and density.
  - Anterior fontanelle may be larger than expected, decreased membraneous bone formation.
  - Abdomen scaphoid or sunken, shrinkage of liver and spleen, depletion of glycogen store and RBC mass respectively.

# Physical Findings of the Babies-1

- Hypoglycaemia
- Decreased subcutaneous fat, loss skin turgor.
- Old appearance.
- Vernix caseosa is reduced or absent.
- Desquamation of skin, continuous exposure to liquor, dry, pale and coarse skin.
- Babies appear hyperactive, hungry with a lusty cry, severely affected. .

# Physical Findings of the Babies-2

- **Symmetrical (Chronic).**
- Diminutive in size.
- Do not appear wasted.
- Have subcutaneous fat appropriate for gestational age.
- Skin is taut.
- Vigorous, less likely to develop hypoglycaemia or polycythaemia.
- Increased risk of congenital malformation.
- Risk of infection to carriers, transplacental infection.
- Genetically small (symmetrical growth)

N.B Normal babies, be treated in accordance to their gestational age.