

Prematurity and Intrauterine Growth Retardation

2.0 Contact Hours

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Prematurity and Intrauterine Growth Retardation

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Prematurity and intrauterine growth retardation are associated with increased neonatal mortality rate. There are multiple factors which result in either prematurity or intrauterine growth retardation. The gestational age is assessed by a modified Ballard Score. Depending on the gestational age, the newborn is classified as preterm, term or post-term. Based on the weight for gestational age, intrauterine growth retardation is diagnosed.

Both prematurity and intrauterine growth retardation are associated with various complications. If not properly identified and treated, they may result in various long term disabilities. This course consists of two parts. The first one deals with risk factors, complications and management of prematurity and the second one with intrauterine growth retardation.

Upon completion of this course, the learner will be able to:

1. Discuss how gestational age is calculated
2. Discuss the classification of newborns based on gestational age
3. Discuss the classification of newborns based on birth weight
4. Discuss the risk factors and complications seen in preterm infants and how to manage them
5. Discuss the risk factors and complications seen in intrauterine growth retardation infants and how to manage them

Infant classification by gestational age

Newborns are classified according to both birth weights and gestational age. The classification is as follows:

- Preterm – Liveborn infants delivered before 37 weeks from the first day of the last menstrual period are termed premature or preterm infants.
- Term – Liveborn infants delivered between 37 weeks and 41 weeks and 6 days from the first day of the last menstrual period are termed term infants.
- Post-term- Liveborn infants delivered after 42 weeks from the first day of the last menstrual period are termed post-term infants.

These infants can be small for gestational age, appropriate for gestational age or large for gestational age which is based on the birth weight. The birth weight classification is –

- Macrosomia – Infants born with a birth weight of 4000 grams or more
- Normal birth weight – Infants born with birth weight between 2500 and 3999 grams
- Low birth weight – Infants born with birth weight less than 2500 grams. These babies are again classified according to gestational age as follows -
 - Preterm AGA – Premature but appropriate size for gestational age
 - Preterm SGA- Premature but with weight small for gestational age
 - Term SGA – Term but small for gestational age
- Very low birth weight – Infants born with birth weight less than 1500 grams

Calculating gestational age

Gestational age is calculated using Modified Ballard Score. There are two groups of parameters that are to be assessed in this scoring system. They are physical maturity and neuromuscular maturity. The various parameters that are to be assessed under each of these are:

Physical maturity

- Lanugo
- Plantar surface
- Breast
- Eye/ear
- Genitals

A score of '-1 to '5' is given to each of these parameters based on the findings on physical examination and the level of maturity.

Neuromuscular maturity

- Square window
- Arm recoil
- Popliteal angle
- Scarf sign
- Heel to ear

A score of '-1 to '5' is given to each of these parameters based on the findings on physical examination and the level of maturity.

The scores from both of these categories are added and the gestational age is calculated from that. A score of '-10' indicates a gestational age of 20 weeks and a score of 50 indicates 44 weeks. The score increases by 5 and the gestational age correspondingly increases by 2 weeks. The modified Ballard score is accurate to ± 2 weeks.

Prematurity

About 9% of all births are premature births. In most of the cases the cause is unknown. The various risk factors of prematurity include:

- Low socioeconomic status – This is based on family income, educational level, residency, social class or occupation.
- African-American women – These women experience more than twice the rate of premature delivery than do white women, delivering almost a third of all premature infants.
- Maternal activity – Any activity requiring long standing or physical stress can cause prematurity. This is not significant in mothers from higher socioeconomic groups who have better medical care.
- Women under age 16 or over 35 – These women are more likely to deliver low birth weight infants. Age is more significant in whites than in blacks.

- Acute or chronic maternal illness – The following illnesses in the mother can cause prematurity:
 - Diabetes mellitus
 - Thyroid disease
 - Renal disease
 - Urinary tract disease
 - Heart disease
 - Lung disease
 - Anemia
 - Rh isoimmunization
 - Platelet isoimmunization
 - Thrombocytopenia
- Multiple gestations – About 50% of multiple gestations end up in prematurity.
- Prior poor birth outcome – This is the single strongest predictor of poor birth outcome. A premature first birth is the best predictor of a preterm second birth.
- Obstetric factors – These include uterine malformations, uterine trauma, placenta previa, abrupio placentae, incompetent cervix, premature rupture of membranes and amnionitis.
- Fetal conditions – These include erythroblastosis fetalis, fetal distress and intrauterine growth retardation. These conditions may require preterm delivery.
- Inadvertent early delivery – Because of incorrect estimation of gestational age, the fetus may be delivered early.

Complications

Prematurity can be associated with various complications, some of which may be fatal. The complications may involve any of the organ systems due to immaturity. The complications include:

Respiratory problems

Respiratory complications are very common among premature infants. The various respiratory complications that may be encountered in preterm infants are:

- Birth asphyxia – Birth asphyxia is an insult to the fetus or newborn due to lack of oxygen and lack of perfusion to various organs
- Respiratory distress syndrome – It is also called hyaline membrane disease. This occurs due to surfactant deficiency. It occurs in 60-80% of infants less than 28 weeks or gestational age and in 15-30% of those between 32-36 weeks. When there is surfactant deficiency, the alveoli in the lungs collapse. This results in respiratory distress.
- Apnea of prematurity - This is a disorder of respiratory control and may be obstructive, central or mixed. The frequency of apnea is inversely proportional to the gestational age. In preterm infants, the apnea is rare on the first day of life. Apnea immediately after birth signifies another illness. The onset of apnea of prematurity occurs on 2nd – 7th day of life.
- Bronchopulmonary dysplasia – It is also called chronic lung disease. It occurs as a result of lung injury in infants requiring mechanical ventilation and oxygen supplementation.
- Wilson Mikity Syndrome- It is usually seen in infants less than 32 weeks of gestational age. It is characterized by insidious onset of dyspnea, tachypnea, chest retractions and cyanosis during the first month of life.

Neurologic problems

The neurologic complications include:

- Intracerebral hemorrhage – Intracerebral hemorrhage occurs in 20-40% of infants born prematurely. Bleeding can occur in epidural, subdural or sub arachnoid spaces. It can also occur in the parenchyma of cerebrum and cerebellum and also in to the ventricles.
- Perinatal depression – It occurs in 9% of the premature babies.

Cardiovascular problems

The cardiovascular complications include:

- Patent ductus arteriosus with or without heart failure – Patent ductus arteriosus is common in preterm babies. It presents with a harsh systolic murmur heard over

the entire precordium, but loudest at the left upper sternal border and left infraclavicular areas.

- Cardiac dysfunction due to sepsis
- Hypotension due to hypovolemia

Hematologic problems

The hematologic problems include:

- Anemia of prematurity – It is an exaggeration of the normal physiological anemia. The causes of anemia of prematurity are:
 - Decreased red blood cell mass
 - Decreased red blood cell lifespan
 - Vitamin E deficiency
- Hyperbilirubinemia – The physiological jaundice is exaggerated in premature infants. The serum bilirubin levels tends to rise and reach the peak level of 10-12 mg /dL between 4to 7 days possibly rising over 15 mg/dL without any specific abnormality of bilirubin metabolism. Levels under 2 mg/dL may not be seen until one month of age. This physiological jaundice is due to:
 - Increased red blood cells in infants
 - Increased production of abnormal red blood cells that are destroyed
 - The bilirubin that is produced keeps circulating by a process called enterohepatic circulation instead of getting excreted
 - Immature liver which could not excrete bilirubin

Nutritional problems

The nutritional requirements of preterm infants are different from that of term infants.

The various factors that influence the nutritional needs in a preterm infant include:

- Increased expenditure of energy – Preterm infants require 90-120 kcal /kg /day.
- Increased water requirement due to increased loss
- Increased protein requirement - 3-3.6 gm/kg/day

- Increased need for essential fatty acid because of poor absorption and increased requirement for brain growth
- Increased calcium requirement because of limited absorption
- Increased phosphorus and magnesium requirement
- Increased requirement of iron because of diminished stores

Gastrointestinal problems

Prematurity is the single greatest risk factor for necrotizing enterocolitis. This is a serious disease of unknown cause characterized by various degrees of mucosal or transmural necrosis of the intestine. The mean gestational age of necrotizing enterocolitis is 30-32 weeks. The overall mortality is 9-28% regardless of the surgical or medical treatment.

Metabolic problems

The metabolic problems include:

- Hypoglycemia – A blood glucose level of less than 40 mg/dL is called hypoglycemia in a newborn. The significance of hypoglycemia depends on the infant's gestational age, chronological age and other risk factors. Hypoglycemia in a premature infant is mainly due to poor stores and decreased synthesis.
- Hypocalcemia – Calcium is essential for bone integrity and for various biochemical processes. An infant is said to have hypocalcemia if the total serum calcium level goes below 7 mg/dL or an ionized calcium concentration goes below 4 mg/dL. Preterm newborns are born amid the third trimester growth spurt. They are poorly adapted to the cessation of maternal calcium flow and at birth face a calcium crisis. Birth asphyxia also contributes to hypocalcemia which is possibly related to renal insufficiency, acidosis and impaired parathormone secretion or responsiveness.

Renal problems

The renal problems include;

- Low glomerular filtration rate

- Inability to handle water, solute and acid loads
- Difficulty in managing electrolyte imbalance

Temperature regulation problems

- Hypothermia – Premature infants have poor temperature maintenance due to the following reasons:
 - Increased body surface area
 - Decreased subcutaneous fat
 - Decreased brown fat
 - Decreased caloric intake
 - Inadequate oxygen consumption

Hypothermia leads to hyperbilirubinemia, sepsis, apnea and poor growth.

Thermo neutral environment is very important.

Immunologic problems

Premature infants are at an increased risk of infection due to deficient humoral and cellular immune response.

Ophthalmologic problems

Retinopathy of prematurity – It is a multifactorial vasoproliferative retinal disorder that increases with decreasing gestational age. It is the second most common cause of blindness for children under 6 years of age according to a study conducted in Massachusetts.

Management

If preterm delivery is anticipated, then delivery should be conducted in an appropriately equipped and staffed hospital. Shifting the preterm infant to another center may unduly delay the initiation of treatment leading to many complications. Even in the well equipped hospital, the trained personnel should be ready with the necessary equipment. Anticipating problems and being well prepared to treat them is better than

reacting to problems already present. The two most important things that should always be ready are facilities for adequate oxygen delivery and maintenance of thermoneutral environment.

Management during neonatal period includes:

- Thermal regulation
- Oxygen therapy and assisted ventilation
- Treating patent ductus arteriosus
- Fluid and electrolyte therapy
- Nutrition
- Treating hyperbilirubinemia
- Preventing infection
- Immunization at the right time

Long-term problems of prematurity

Premature infants are vulnerable to a wide spectrum of morbidity. Though severe morbidity occurs in a smaller percentage, the exact prevalence of lesser morbidity is not known. The various long-term problems include:

- Developmental disability which may include cerebral palsy, mental retardation, hearing loss, visual impairment
- Retinopathy of prematurity
- Chronic lung disease
- Poor growth
- Increased rates of postneonatal illness and hospitalization
- Increased frequency of congenial anomalies
- Increased risk of child abuse and neglect

Intrauterine growth retardation

Intrauterine growth retardation is seen in infants who are small for gestational age. There is no uniform consensus regarding the definition for an infant that is small for

their gestational age. Most define it as a two standard deviation below the mean for gestational age or below the tenth percentile.

Risk factors

About one third of infants who are born with low birth weight are said to be small for gestational age. The various risk factors are:

Maternal factors

The maternal factors include:

- Toxemia of pregnancy
- Hypertension
- Renal disease
- Hypoxemia due to high altitude, cyanotic cardiac disease or pulmonary disease
- Malnutrition
- Sickle cell anemia
- Drugs like narcotics, alcohol, cigarettes, cocaine
- Genetic size
- Collagen vascular disease
- Diabetes mellitus
- Postmaturity
- Multiple gestation
- Antiphospholipid antibodies

Placental factors

The placental factors include:

- Decreased placental weight
- Decreased placental cellularity
- Decreased placental surface area
- Villous placentitis
- Placental infarction

- Placental tumors
- Placental separation
- Twin transfusion syndrome

Fetal factors

The fetal factors include:

- Constitutional
- Chromosomal disorders including trisomies
- TORCH infection
- Congenital anomalies
- Radiation
- Multiple gestation
- Pancreatic aplasia
- Insulin deficiency
- Insulin like growth factor I deficiency

Management

The management of small for gestational age infants starts from the antenatal period itself. During antenatal checkup when IUGR is detected all steps should be taken to find out the cause. All relevant investigations should be performed, which includes:

- Serial ultrasonic examination
- Nonstress testing
- Oxytocin challenge testing
- Biophysical profile

Sometimes early delivery is advocated though the fetus is premature. This is done when the risk of staying in utero is higher than early delivery. The factors include:

- Arrest of fetal growth
- Fetal distress
- Pulmonary maturity near term in a mother with hypertension

If there is poor placental flow then the fetus should be delivered by Caesarian section as the fetus may not tolerate labor.

Fetal distress, perinatal depression, meconium aspiration, hypoxia and hypothermia are known to occur in small for gestational age (SGA) infants. All these should be anticipated and trained staff and equipment should be kept ready to treat these problems. It is always better to deliver these SGA infants in centers which have all the facilities to treat these problems.

After the infant is born and if the cause of IUGR is still not known, then necessary steps should be taken to find the cause. These include:

- Examination of the newborn – The weight and length of the newborn is measured and the ponderal index is calculated.

$$\text{Ponderal index} = \text{Weight in grams} \times 100 / \text{Length in centimeters}$$

If the ponderal index is less than 2 it indicates symmetric IUGR. Symmetric IUGR occurs when the growth of the fetus is affected during the first trimester and the causes include chromosomal disorders, genetic malformation, severe maternal hypertension and infections. If the ponderal index is more than 2.5 it indicates asymmetric IUGR. Asymmetric IUGR occurs when the growth of the fetus is affected later in the pregnancy and the causes include maternal malnutrition and maternal vascular diseases like pre-eclampsia and hypertension. The outcome is poor in symmetric IUGR.

- Examination of the placenta – Placental infarction and infection can lead to IUGR and hence the placental has to be examined when an IUGR baby is born.
- Screening for congenital infections – TORCH can lead to IUGR. About 60% of the infants with congenital rubella infection are IUGR infants. About 40% of the babies infected with cytomegalovirus are born with intrauterine growth retardation.

Complications of IUGR

IUGR infants are prone for a diverse group of complications. These include:

- Congenital anomalies – These include cardiac anomalies and microcephaly. Most of these occur due to chromosomal anomalies or TORCH infection.
- Perinatal depression
- Meconium aspiration –It occurs in 5-15% of births and usually occurs in term and post-term infants. IUGR is common in post-term infants.
- Pulmonary hemorrhage – It is the presence of red blood cells in air spaces, interstitial spaces or both. Positive pressure ventilation is required to treat infants with this complication.
- Persistent pulmonary hypertension – This occurs in term and post-term infants after birth asphyxia, meconium aspiration pneumonia, group B streptococcal sepsis, hyaline membrane disease, hypoglycemia, polycythemia and pulmonary hypoplasia due to diaphragmatic hernia, amniotic fluid leak, oligohydramnios, or pleural effusions. The symptoms closely resemble that of congenital heart disease.
- Hypothermia – Hypothermia occurs due to poor subcutaneous fat and decreased brown fat.
- Hypoglycemia – Hypoglycemia occurs due to decreased glycogen store and poor synthesis.
- Hypocalcemia
- Hyponatremia
- Polycythemia – It is defined as venous hematocrit of over 65%. This occurs due to fetal erythropoiesis secondary to chronic intrauterine hypoxia.

Special considerations

Feeding with milk should be started at 1 hour of age and should be continued every 2-3 hours. If oral feeding is not tolerated, gavage or intravenous feeding should be done. SGA infants require more calories than AGA infants. During the first few days the serum concentration of sodium, calcium and glucose should be monitored. Blood glucose should be monitored every 2-4 days. Serum calcium is monitored especially in infants who are asphyxiated or premature.

The long-term problems of IUGR infants include:

- Poor postnatal growth
- Neurologic handicaps
- Developmental handicaps

These long term problems could be either due to growth retardation or due to the underlying causes like chromosomal abnormalities. IUGR babies have less mortality rates when compared to preterm AGA babies. But the morbidity at 1 year of age is higher.

These handicaps occur even in the absence of chromosomal abnormalities. These are commonly encountered in proportional IUGR infants and in those infants who have suffered perinatal asphyxia and hypoglycemia. SGA have less risk of neonatal death compared to premature AGA of same birth weight but a greater risk of morbidity at one year of age.

IUGR usually recurs. So it is important to efficiently manage subsequent pregnancies. The various recommendations are:

- The mother should be cared for by personnel experienced with high risk pregnancies
- The health of the mother and fetus should be assessed throughout pregnancy by ultrasonic and non-stress tests
- Early delivery should be considered if fetal growth is poor.

Reference

1. Nelson Textbook of Pediatrics – 17th Edition
2. Manual of Neonatal Care – 4th Edition