International Journal of Scientific Reports
Khalifa AKA. Int J Sci Rep. 2015 May;1(1):3-21
http://www.sci-rep.com

pISSN 2454-2156 | eISSN 2454-2164

DOI: http://dx.doi.org/10.18203/issn.2454-2156.IntJSciRep20150195

Review Article

Management of neonatal hazards in intensive care units: a review

Amany K. A. Khalifa*

Department of Pediatrics, Ain Shams University, Cairo, Egypt

Received: 19 April 2015
Accepted: 25 April 2015

***Correspondence:**
Dr. Amany K. A. Khalifa,
E-mail: ammanykhalifa@gmail.com

ABSTRACT

The study aims at reviewing the neonatal morbidity and their management with a closer look to the intensive care units. The critical situation of high-risk infants, including preterm or within serious medical conditions, has been highlighted and elaborated. The management of every pertinent condition was accordingly detailed.

Keywords: Neonatal hazards, High-risk infants, Neonatal management

INTRODUCTION

An outline of the high-risks that tackle the neonates and management of each were comprehensively reviewed. This concise review elaborates the most frequent pathoses that encounter a significant risk on neonates.

For example, sepsis is one of the commonest morbidities in high-risk infants which is none significantly related to prenatal care, mode of delivery, gender, gestational age, different modes of ventilation and surgical interventions but highly related to duration of hospital admission. Phototherapy alone was the primary management in all cases of neonatal jaundice supported by exchange transfusion in 4.6% of jaundiced cases.

MATERIALS AND METHODS

For the risk that are usually encountered in the neonates, databases of Medline, PubMed, Google scholar were searched under the following key terms: neonatal hazards, neonatal morbidity, high risks in neonatal intensive care unit, and management of neonatal hazards. The research results were revised and scrutinized to extract a simple review for the average practitioner.

DISCUSSION

While high infant mortality rates were recognized by the British medical community at least as early as the 1860s, modern neonatal intensive care is a relatively recent advance. It was not until 1965 when the first American Newborn Intensive Care Unit (NICU) was opened in New Haven, Connecticut and in 1975 the American Board of Pediatrics established sub-board certification for neonatology.[1]

This entry gives the number of deaths of infants under one year old in a given year per 1000 live births in the same year; included is the total death rate, and deaths by sex, male and female. This rate is often used as an indicator of the level of health in a country.[2]

The statistical rate of infant death during the first four weeks after live birth, expressed as the number of such deaths per 1000 live births in a specific geographic area or institution in a given time.[3] According to Campbell et al, the Neonatal Mortality Rate (NMR) was 25 per 1000 live births. Half the deaths occurred in the first two days of life. Neonatal causes of death were pre-maturity (39%), asphyxia (18%), infections (7%), congenital malformation (6%) and unclassified (29%).[4]

Gestational age or birth weight aside, the high-risk neonate is defined as a newborn whose chance of morbidity or mortality is greater-than average. It is usually secondary to abnormal circumstances which are concomitant with the delivery events as well as the adjustment to extrauterine existence. The high-risk period begins at the time of viability up to 28 days after birth and evinces imminent threats upon life and health either in the prenatal, perinatal, or postnatal periods.[4]

Classification according to birth weight

1. Extremely Low Birth Weight:

An Extremely Low Birth Weight (ELBW) is the birth weight of an infant which measures less than 1000g. Most extremely low birth weight infants are also the youngest of premature newborns, usually born at 27 weeks' gestational age or even younger.[5]

Survivability correlates with gestational age for infants who are Appropriate for Gestational Age (AGA). In 2002, the first-year survival rate was 13.8% for infants with a birth weight of less than 500 g, 51% for infants with a birth weight of 500-749 g, and 84.5% for infants with a birth weight of 750-1000 g. Infants with ELBW are more susceptible to enormous complications of premature birth, both in the immediate neonatal period and after discharge from the nursery. However, the mortality rate has diminished with the use of surfactants, the proportion of surviving infants with severe sequelae, such as chronic lung disease, cognitive delays, cerebral palsy, and neurosensory deficits (i.e., deafness and blindness), has not diminished yet. In the same vein, improved neurodevelopmental outcomes have been reported in a few small studies, such improvement has not been globally observed.[6]

Children of extremely low birth weight have relatively higher rates of developing chronic conditions, compared with their peers with normal weight. These conditions include asthma, cerebral palsy, and visual disability, as well as poorer cognitive ability, academic achievement, motor skills, and social adaptive functioning. Since children of extremely low birth weight encompass less than 1% of babies, the societal impact is not that catastrophic in contrast to the tragedy of the pathetic hosting families.[7] Congenital infection is, however, the major cause of death in extremely low birth weight infants.[8]

2. Very low birth weight:

Very Low Birth Weight (VLBW) is a term used to describe babies who are born weighing less than 1500 grams (3 pounds, 4 ounces). Only a few babies, 1.5 percent, are born this tiny. However, the overall rate of very low birth weight babies in the US is increasing. This is primarily due to the greater numbers of multiple birth babies who are more likely to be born early and weight less.[9] The primary causes of VLBW are premature birth (born <37 weeks gestation, and often <30 weeks) and intrauterine growth restriction (IUGR), usually due to problems with placenta, maternal health, or to birth defects, other factors that can contribute to the risk of VLBW include:

Race: African-American babies are twice as likely as Caucasian to be VLBW, Age: Teen mothers (especially if <15 years old) have a much higher risk of having VLBW infant.

Multiple birth: More than 50% of twins and other multiple gestations are VLBW.

Maternal health: Women exposed to drugs, alcohol, and cigarettes and Mothers of lower socioeconomic status.[10] The rate of very low birth weight was highest among babies born to mothers aged 45-54 years (3.6 percent). Mothers under 15 years of age also had high rates of very low birth weight (3.0 percent.) The rate was lowest among mothers aged 25-29 years (1.3 percent).[11]

Long-term outcome: VLBW infants are at high risk for cerebral palsy, developmental delay, mental retardation, visual problems (including blindness), hearing impairment, chronic lung disease and SIDS.[10]

3. Low Birth Weight:

Low Birth Weight (LBW) has been defined by the World Health Organization (WHO) as weight at birth of less than 2500 grams (5.5 pounds). There is significant variation in the incidence of low birth weight across regions. South Asia has the highest incidence, with 31 per cent of all infants with low birthweight, while East Asia/Pacific has the lowest, at 7 per cent. India is home to nearly 40 per cent of all low-birthweight babies in the developing world. In sub-Saharan Africa 14 per cent and in the Middle East/North Africa 15 per cent of infants are born with low weight [12]. (Risk factors for LBW: Birth spacing <36 months, maternal height 145 cm, pre-delivery weight 55 kg, pregnancy weight gain 6 kg, exposure to tobacco, inadequate antenatal care maternal hypertension, low socio-economic status, maternal anemia and less maternal education were associated with delivery of a low birth weight infants Conditional logistic regression analysis showed that significant risk factors associated with low birth weight were inadequate antenatal care (ANC).[13]

LBW is the most significant factor contributing to neonatal mortality and morbidity. There is higher risk of asphyxia, sepsis, hypothermia, and feeding problems, in these neonates. Common illnesses tend to be more severe and last longer in this group apart from immediate problems, LBW neonates are prone to long-term disorders like infections, malnutrition, and neurodevelopment disabilities.[14]

4. Macrosomia:

The term is used to describe a newborn with an excessive birth weight. However; there is no general agreement about what the weight limit should be. In various studies, birth weights above 4000, 4200 and 4500 g were used as definitions of newborn macrosomia. The most accepted definition is a birth weight greater than 4000g.[15]

The causes of fetal macrosomia may be divided into non-modifiable and modifiable factors. Genes would be considered non-modifiable. The other factors that may be considered non-modifiable include fetal sex, parity, maternal age and maternal height. Modifiable factors include mainly pre-gestational maternal anthropometric characteristics, maternal nutritional intake, gestational weight gain, level of physical activity, smoking, and metabolic parameters, especially those related to maternal glucose metabolism.[16]

Fetal risks associated with macrosomia include birth trauma (3-7%), including shoulder dystocia (9.2-24%), brachial plexus injuries (1-4%), perinatal asphyxia, and death (0.4%), neonatal risks associated with macrosomia include hypoglycemia (50%), hematological disturbances (i.e., polycythemia) and electrolyte disturbances (up to 50%). In addition, a macrosomic birth is also associated with longterm health risks for the newborn.[17]

Classification according to size for gestational age

1. Small for gestational age (SGA):

Small for gestational age babies are those who are smaller in size than normal for the baby's sex and gestational age, most commonly defined as a weight below the 10^{th} percentile for the gestational age. The diagnosis of SGA should be based on accurate anthropometry at birth including weight, length, and head circumference.[18]

The Ponderal Index (PI) is a measure of leanness of a person, calculated as a relationship between mass and height. An infant may be small at birth because of genetic factors. Nongenetic factors that can restrict intrauterine growth usually are not apparent before 32 to 34 weeks of gestation; these factors include placental insufficiency from maternal disease involving the small blood vessels (as in preeclampsia, primary hypertension, renal disease, or long-standing diabetes); placental involution accompanying postmaturity; and infectious agents such as cytomegalo virus, rubella virus, or toxoplasma gondii. An infant may also be SGA if the mother is an opioid or cocaine addict or a heavy user of alcohol or, to a lesser degree, if she smoked cigarettes during pregnancy.[19]

These infants, who were designated "small for gestational age", had more frequent problems with perinatal depression (asphyxia), hypothermia, hypoglycemia, polycythemia, long-term deficits in growth, and neurodevelopmental handicaps and higher rates of fetal and neonatal mortality.[20]

2. Large for Gestational Age (LGA):

Large for gestational age is defined as a birth weight greater than the 90^{th} percentile for age. However, it has been suggested that the definition be restricted to infants with birth weights greater than the 97^{th} percentile (2 standard deviations above the mean) as this more accurately describes infants who are at greatest risk for perinatal morbidity and mortality.[21]

Common causes of a fetus or infant who is large for gestational age other than genetic factors are: Gestational diabetes and prolonged pregnancy. Common complications include the following: Excess amount of red blood cells polycythemia, low blood sugar levels (hypoglycemia), lung problems, increased risk of birth injuries.[22]

3. Intrauterine Growth Restriction (IUGR):

Intrauterine growth restriction is the inability of a fetus to maintain its expected growth along a standardized curve regardless of whether this growth falls below the 10^{th} percentile. Thus, the IUGR fetus may be growth-restricted but not "small for gestational age". Fetal growth at less than the 5th percentile should be considered absolute IUGR and investigations and management must be initiated immediately.[23]

4. Causes of Intrauterine Growth Restriction:

Maternal causes of IUGR include the following: Chronic hypertension, pregnancy-associated hypertension, cyanotic heart disease, class F or higher diabetes, hemoglobinopathies, autoimmune disease, protein-calorie malnutrition, smoking, substance abuse, uterine malformations, thrombophilias, prolonged high-altitude exposure. Placental or umbilical cord causes of IUGR include the following: Twin-to-twin transfusion syndrome, placental abnormalities, chronic abruption, placenta previa, abnormal cord insertion, cord anomalies and multiple gestations.[24]

5. Asymmetric versus symmetric growth retardation:

Most growth retarded infants have asymmetric growth restriction. First there is restriction of weight and then length, with a relative "head sparing" effect. This asymmetric growth is more commonly due to extrinsic influences that affect the fetus later in gestation, such as preeclampsia, chronic hypertension, and uterine anomalies.[10] Postnatal growth after IUGR depends on cause of growth retardation, postnatal nutritional intake, and social environment. Symmetric growth retardation affects all growth parameters. In the human brain, most neurons develop prior to the 18th week of gestation. Early gestational growth retardation would be expected to

affect the fetus in a symmetric manner, and thus have permanent neurologic consequences for the infant. Examples of etiologies for symmetric growth retardation include genetic or chromosomal causes, early gestational intrauterine infections (TORCH) and maternal alcohol use.[10]

6. Complications of IUGR:

Fetal distress, hypoxia, acidosis and low APGAR Score at birth, increased perinatal morbidity and mortality, grade 3-4 intraventricular haemorrhage, necrotizing enterocolitis, bronchopulmonary dysplasia, metabolic disturbances, polycytemia hypothermia, impaired cognitive function and cerebral paresis.[25]

Classification according to gestational age

The Ballard maturational assessment, Ballard score, or Ballard scale is a commonly used technique of gestational age assessment. It assigns a score to various criteria, the sum of all of which is then extrapolated to the gestational age of the baby. These criteria are divided into Physical and Neurological criteria. This scoring allows for the estimation of age in the range of 26 weeks - 44 weeks. The New Ballard Score is an extension of the above to include extremely pre-term babies i.e. up to 20 weeks. The scoring relies on the intra-uterine changes that the fetus undergoes during its maturation. Whereas the neurological criteria depend mainly upon muscle tone, the physical ones rely on anatomical changes.[26]

1. Prematurity

Prematurity is a term used to describe when a baby is born early. Most pregnancies last around 40 weeks but some are shorter and some are longer. Babies that are born between 37 weeks and 42 weeks are called full term. Babies that are born before 37 weeks are called premature or preterm. They are affectionately known as "preemies".[27]

Late preterm infants are born at a gestational age between 34 weeks, and 36 weeks and 6 days. They have higher morbidity and mortality rates than term infants (gestational age ≥37 weeks) due to their relative physiologic and metabolic immaturity, even though they are often the size and weight of some term infants.[28] Late preterm term has replaced near term to describe this group of infants, since near term incorrectly implies that these infants are "almost term" and only require routine neonatal care.[29]

Preterm babies are higher for black infants (18%) and Native Americans (14%) than for Hispanics (12%), whites (11%) and Asians (10%). Black infants were two times more likely than Asian infants to be born premature, and prematurity is the leading cause of infant death for black infants.[30]

Infants born at 34 0/7 to 36 6/7 weeks' gestation compared with term infants experience more difficulties with feeding (32% versus 7%), hypoglycemia (16% versus 5%), jaundice (54% versus 38%), temperature instability (10% versus 0%),apnea (w6% versus 0.1%), and respiratory distress (29% versus 4%) Late preterm infants also receive intravenous fluids (27% versus 5%), evaluations for sepsis (37% versus 13%), and mechanical ventilation (3.4% versus 0.9%) more often than their term counterparts. Late preterm infants are 3.5 times more likely to have two or more of these problems than term infants.[31] There are some known risk factors for premature birth. But even if a woman does everything "right" during pregnancy, she still can have a premature baby.

The predisposing risk factors include:

- Carrying more than one baby (twins, triplets, quadruplets or more).
- Having a previous preterm birth.
- Problems with the uterus or cervix.
- Chronic health problems in the mother, such as high blood pressure, diabetes, and clotting disorders.
- Certain infections during pregnancy.
- Cigarette smoking, alcohol use, or illicit drug use during pregnancy.

The risk of complications increases directly with immaturity.[32] Thus, infants who are extremely premature, born at or before 25 weeks of gestation, have the highest mortality rate (approximately 50 %) and if they survive, are at the greatest risk for severe impairment. Complications of the premature infant are divided into short-term complications (e.g., respiratory and cardiovascular complications), which occur in the neonatal period, and long-term sequelae (e.g., neurodevelopmental disabilities such as cerebral palsy) in patients who survive and are discharged from the neonatal intensive care unit Short-term complications increase the risk of long-term sequelae.[33]

2. Postterm:

Postmaturity is when a baby has not yet been born after 42 weeks of gestation, two weeks beyond the normal 40. Post-term, postmaturity, prolonged pregnancy and post-dates pregnancy all refer to postmature birth.[19]

In the United States, postterm births have decreased from 11 percent of all births in 1990 to 5.5 percent of births in 2009; the decline in postterm births is due to the increase in the induction of labor of pregnancies at 41 weeks of due to an effort to avoid the delivery of postterm infants.[34]

In a population-based Norwegian study, the reported incidence of postterm deliveries was 7.6 percent from 1989 to 1999.[35] The causes of post-term births are idiopathic. But post-mature births are more likely when the mother has experienced a previous post-mature birth. Due dates are easily miscalculated when the mother is unsure of her last menstrual period. When there is a miscalculation, the baby could be delivered before or after the expected due date. Post-mature births can also be attributed to irregular menstrual cycles.[19]

Perinatal mortality (defined as stillbirths plus early neonatal deaths) at 42 weeks of gestation is twice that at 40 weeks (4-7 vs. 2-3 per 1,000 deliveries, respectively) and increases 4-fold at 43 weeks and 5- to 7-fold at 44 weeks. These data also demonstrate that, when calculated per 1000 ongoing pregnancies, fetal and neonatal mortality rates increase sharply after 40 weeks.[36] A number of key morbidities are greater in infants born to postterm pregnancies as well as pregnancies that progress to and beyond 41 0/7 weeks gestation including meconium and meconium aspiration, neonatal academia, low APGAR scores, macrosomia, and, in turn, birth injury.[37]

PROBLEMS OF HIGH RISK NEONATES

Respiratory distress of newborn

1. Transient tachypnea of newborn:

Transient tachypnea of the newborn (TTN, TTNB, or "Transitory tachypnea of newborn") is a respiratory problem which can be manifested in the newborn shortly after delivery. Amongst causes of respiratory distress in term neonates, it is the commonest, It consists of a period of rapid breathing (higher than the normal range of 40-60 times per minute).[38]

Physical findings include tachypnea with variable grunting, flaring, and retracting. The infant is often described as having "quiet" tachypnea. Extreme cases may exhibit cyanosis. A study investigating the risk factors for duration of tachypnea in patients with transient tachypnea of the newborn reported that peak respiratory rate of more than 90 breaths per minute during the first 36 hours of life was associated with prolonged tachypnea lasting more than 72 hours.[39]

2. Respiratory Distress syndrome of newborn:

Infant Respiratory Distress Syndrome (IRDS), also called neonatal respiratory distress syndrome or respiratory distress syndrome of newborn, previously called Hyaline Membrane Disease (HMD), is a syndrome in premature infants caused by developmental insufficiency of surfactant production and structural immaturity in the lungs. It can also result from a genetic problem with the production of surfactant associated proteins.[40]

Infant respiratory distress syndrome affects about 1% of newborn infants and is the leading cause of death in preterm infants the incidence decreases with advancing gestational age, from about 50% in babies born at 26-28 weeks, to about 25% at 30-31 weeks.[41]

The greatest risk factor for respiratory distress syndrome is prematurity, although the syndrome does not occur in all premature newborns. Other risk factors include maternal diabetes, cesarean delivery, and asphyxia.[42]

The symptoms usually appear within minutes of birth, although they may not be seen for several hours. Symptoms may include: Bluish color of the skin and mucus membranes (cyanosis), brief stop in breathing (apnea), decreased urine output, grunting, nasal flaring, rapid breathing, shallow breathing, shortness of breath and grunting sounds while breathing, unusual breathing movement and drawing back of the chest muscles with breathing.[43]

Other complications may include: intraventricular hemorrhage of the newborn, pulmonary hemorrhage (sometimes associated with surfactant use), Broncho-pulmonary dysplasia, delayed mental development and mental retardation associated with brain damage or bleeding, Retinopathy of prematurity and blindness.[44]

3. Bronchopulmonary dyspalsia (BPD):

This recently introduced definition uses oxygen dependency at 36 weeks PMA, total duration of oxygen supplementation, positive pressure requirements and gestational age of the infant to delineate the three degrees of severity, mild, moderate and severe (mild BPD: need for supplemental oxygen 28 days, but not at 36 weeks; moderate BPD: need for supplemental oxygen 28 days and <30% at 36 weeks and severe BPD: need for supplemental oxygen 28 days, and >30% at 36 weeks and/or positive pressure at 36 weeks).[45]

Risk of bronchopulmonary dysplasia is more anticipated when birth weight decreases. Figures for incidence vary depending on criteria used. A study found that approximately half of all admissions, weighing <1,250 g, to a UK neonatal intensive care unit developed BPD.[46]

Babies who have had BPD are at a greater risk for repeated respiratory infections, such as pneumonia, bronchiolitis, and Respiratory Syncytial Virus (RSV) that require a hospital stay. Many of the airway (bronchiole) changes in babies with BPD will not go away. Other potential complications in babies who have had BPD are: Developmental problems (cerebral palsy), poor growth and pulmonary hypertension.[47]

4. Meconium aspiration syndrome (MAS):

Meconium aspiration syndrome (alternatively "Neonatal aspiration of meconium") is a medical condition affecting

newborn infants. It occurs when meconium is evident in their lungs during or before delivery. Meconium is the first stool of an infant, composed of materials ingested during the time the infant spends in the uterus.[48]

In the industrialized world, meconium in the amniotic fluid can be detected in 8-25% of all births after 34 weeks' gestation. Of those newborns with meconium-stained amniotic fluid, approximately 10% develop MAS. But In developing countries with less availability of prenatal care and where births are common home, incidence of MAS is thought to be higher and is associated with a greater mortality rate.[49]

The mortality rate of meconium-stained infants is considerably higher than that of non-stained infants; meconium aspiration used to account for a significant proportion of neonatal deaths. Residual lung problems are rare but include symptomatic cough, wheezing, and persistent hyperinflation for up to 5-10 year. The ultimate prognosis depends on the extent of Central Nervous System (CNS) injury from asphyxia and the presence of associated problems such as pulmonary hypertension.[50]

High risk infants may be identified by fetal tachycardia, bradycardia or absence of fetal accelerations upon CTG in utero, at birth the infant may look cachexic and show signs of yellowish meconium staining on skin, nail and the umbillical cord, these infants usually progress onto Infant Respiratory distress syndrome within 4 hours.[51]

Neonatal hypothermia

Neonatal hypothermia is defined as an abnormal thermal state in which the newborn's body temperature drops below 36.5 1°C (97.7 1°F). Progressive reduction in body temperature leads to adverse clinical effects ranging from mild metabolic stress to death.

Prolonged, unrecognized cold stress may divert calories to produce heat, impairing growth. Neonates respond to cooling by sympathetic nerve discharge of norepinephrine in the brown fat and by lipolysis followed by oxidation or re-esterification of the fatty acids that are released. These reactions produce heat locally, and a rich blood supply to the brown fat helps transfer this heat to the rest of the neonate's body. This reaction increases the metabolic rate and O2 consumption 2- to 3-fold. Thus, in neonates with respiratory insufficiency cold stress may also result in tissue hypoxia and neurologic damage. Additionally, hypothermia can result in hypoglycemia, metabolic acidosis, and death.[52]

An early sign of hypothermia is feet that are cold to the touch. If prolonged hypothermia, the baby becomes less active, suckles poorly, impaired feeding and has a weak cry. In severely hypothermic babies the face and extremities may develop a bright red color. The baby becomes lethargic and develops slow, shallow and irregular breathing and a slow heartbeat. Low blood sugar and metabolic acidosis, generalized internal bleeding (especially in the lungs) and respiratory distress may occur. Such a level of hypothermia is very dangerous and unless urgent measures are taken, the baby will not make it.[53]

Congenital malformations

Congenital anomalies, congenital abnormalities, birth defects and congenital malformations are all terms used to describe developmental disorders of the embryo and fetus. There are several hundred separate anomalies which fall under these headings including structural, functional, metabolic and hereditary conditions. However, there is no single universally accepted system of classification of anomalies or indeed a single agreed definition of what constitutes a congenital anomaly. About 3% of newborns have a "major physical anomaly", meaning a physical anomaly that has cosmetic or functional significance.[53]

Congenital anomalies involving the brain are the largest group at 10 per 1000 live births, compared to heart at 8 per 1000, kidneys at 4 per 1000, and limbs at 1 per 1000. All other physical anomalies have a combined incidence of 6 per 1000 live births. Congenital anomalies of the heart have the highest risk of death in infancy, accounting for 28% of infant deaths due to congenital anomaly, while chromosomal anomalies and respiratory anomalies each account for 15% and brain anomalies about 12%.[54]

Genetically, congenital anomalies clone inheritance of abnormal genes from the parents, as well as new mutations in one of the germ cells that gave rise to the fetus. Environmentally, causes of congenital anomalies are referred to as teratogenic. Teratogens can include dietary deficiencies, toxins, or infections. For example, dietary deficiency of maternal folic acid is associated with spina bifida. Ingestion of harmful substances by the mother (e.g., alcohol, mercury, or prescription drugs such as phenytoin) can cause recognizable combinations of birth defects. Several infections which a mother can contract during pregnancy can also be teratogenic. These are referred to as the TORCH infections.[54]

Neonatal infections

Neonatal sepsis is any infection involving an infant during the first 28 days of life. Neonatal sepsis is also known as "sepsis neonatorum". The infection may involve the infant globally or may be limited to just one organ (such as the lungs with pneumonia). It may be acquired prior to birth (intrauterine sepsis) or after birth (extrauterine sepsis). Viral (such as herpes, rubella [German measles]), bacterial (such as group B strep) and more rarely fungal (such as Candida) causes may be implicated.[55]

Neonatal sepsis may be categorized as early-onset or late-onset. Of newborns with early-onset sepsis, 85% present

within 24 hours, 5% present at 24-48 hours, and a smaller percentage present within 48-72 hours. Onset is most rapid in premature neonates. Early-onset sepsis is associated with acquisition of microorganisms from the mother. Transplacental infection or an ascending infection from the cervix may be caused by organisms that colonize the mother's genitourinary tract; the neonate acquires the microorganisms as it passes through the colonized birth canal at delivery. The microorganisms most commonly associated with early-onset infection include the following: Group B Streptococcus (GBS), Escherichia coli, Coagulase-negative Staphylococcus, Haemophilus influenzaeand Listeria monocytogenes.[56]

Late-onset sepsis occurs at 4-90 days of life and is acquired from the caregiving environment. Organisms that have been implicated in causing late-onset sepsis include the following: Coagulase-negative Staphylococcus, Staphylococcus aureus, E. coli, Klebsiella, Pseudomonas, Enterobacter, Candida, GBS, Serratia, Acinetobacte and Anaerobes.[57]

Neonatal sepsis screening: DLC showing increased numbers of polymorphs, DLC: band cells >20%, increased haptoglobins, micro ESR (Erythrocyte Sedimentation Rate) titer >55 mm, gastric aspirate showing >5 polymorphs per high power field, newborn CSF (Cerebro Spinal Fluid) screen: showing increased cells and proteins, suggestive history of chorioamnionitis, PROM (Premature Rupture Of Membranes),Culturing for microorganisms from a sample of CSF, blood or urine, is the gold standard test for definitive diagnosis of neonatal sepsis. This can give false negatives due to the low sensitivity of culture methods and because of concomitant antibiotic therapy. Lumbar punctures should be done when possible as 10-15% presenting with sepsis also have meningitis, which warrants an antibiotic with a high CSF penetration.[58]

Hyperbilirubinemia and jaundice

Jaundice is a yellow discoloration of the skin and eyes caused by hyperbilirubinemia (elevated serum bilirubin concentration). The serum bilirubin level required to cause jaundice varies with skin tone and body region, but jaundice usually becomes visible on the sclera at a level of 2 to 3 mg/dL (34 to 51 μmol/L) and on the face at about 4 to 5 mg/dL (68 to 86 μmol/L). With increasing bilirubin levels, jaundice seems to advance in a head-to-foot direction, appearing at the umbilicus at about 15 mg/dL (258 μmol/L) and at the feet at about 20 mg/dL (340 μmol/L). Slightly more than half of all neonates become visibly jaundiced in the first week of life.[59]

Approximately 85%of all term newborns and most premature infants develop clinical jaundice. Also 6.1% of well term newborns have a maximal serum bilirubin level >12.9 mg/dl. A serum bilirubin level >15 mg/dl is found in 3%of normal term babies. Physical examination is not a reliable measure of serum bilirubin.[60]

1. Physiological jaundice:

Physiological jaundice results from increased erythrocyte breakdown and immature liver function. Physiological jaundice may be evident at two or three days old, begins to disappear towards the end of the first week and has resolved by day TEN. The bilirubin level does not usually rise above 200 μmol/Land the baby remains well. However the bilirubin level may go much higher if the baby is premature or if there is increased red cell breakdown as frequently seen in extensive bruising, and cephalhaematoma.[61]

2. Pathological jaundice:

Features of pathologic jaundice include the appearance of jaundice within 24 hours after birth, a rapidly rising total serum bilirubin concentration (increase of more than 5 mg per dL per day), and a total serum bilirubin level higher than 17 mg per dL in a full-term newborn. Other features of concern include prolonged jaundice, evidence of underlying illness, and elevation of the serum conjugated bilirubin level to greater than 2 mg per dL or more than 20 percent of the total serum bilirubin concentration. Pathologic causes include disorders such as sepsis, rubella, toxoplasmosis, occult hemorrhage, and erythroblastosis fetalis.[61]

3. Breast-feeding and jaundice:

Exclusively breast-fed infants have a different pattern of physiological jaundice as compared to artificially fed babies. Jaundice in breast-fed babies usually appears between 24-72 hours of age, peaks by 5-15 days of life and disappears by the third week of life. They have also been reported to have higher bilirubin levels. Decreased frequency of breast-feeding is associated with exaggeration of physiological jaundice. Encouraging a mother to breastfeed her baby at least 10-12 times per day would be helpful in the management of jaundice in a term healthy baby.[62]

4. Breast milk jaundice:

Breast milk jaundice tends to run in families. It occurs equally often in males and females and affects 0.5% to 2.4% of all newborns. Breast milk jaundice is long-term jaundice in an otherwise healthy, breast-fed baby. It develops after the first week of life and continues up to the sixth week of life. It is probably caused by factors in the breast milk that block certain proteins in the liver that break down bilirubin.[63]

Perinatal asphyxia

Perinatal asphyxia is the neurological condition that results when a newborn infant is deprived of oxygen long enough to cause damage. If an infant fails to establish adequate, sustained respiration after birth, the infant is said to have perinatal asphyxia. The term "perinatal"

refers to that period of time either during or close to the time of delivery. Other terms used for perinatal asphyxia include intrapartum asphyxia or birth asphyxia. If the cause of the oxygen deprivation is not corrected, the organs, the brain in particular, may be damaged, sometimes irreparably.[64]

Perinatal asphyxia and resulting Hypoxic Ischemic Encephalopathy (HIE) occur in 1 to 3 per 1000 births in the United States. Higher rates occur in developing countries with limited diagnostic and interventional resources. Worldwide, 10% to 60% of infants who develop HIE will die and at least 25% of the survivors will have long-term neurodevelopmental sequelae. Hypoxic ischemic encephalopathy is the primary cause of 15% to 28% of cerebral palsy among children.[65]

Acute hypoxic brain injury in a neonate can occur for a variety of reasons. Any condition that leads to decreased oxygen supply (hypoxia) and decreased blood supply to the brain (ischemia) can lead to this condition. Acute perinatal events such as placental abruption, umbilical cord prolapsed, uterine rupture, tight nuchal cord, or an acute blood loss are risk factors.[66]

Birth trauma

Birth trauma is defined as an injury sustained by the neonate during the process of labour and delivery. It usually results from trauma sustained during a difficult delivery or secondary to obstetric manipulation of the fetus to allow for delivery.[67]

Birth injuries account for fewer than 2% of neonatal deaths. From 1970-1985, rates of infant mortality due to birth trauma fell from 64.2 to 7.5 deaths per 100000 live births, a remarkable decline of 88%. This decrease reflects, in part, the technologic advancements that allow today's obstetrician to recognize birth trauma risk factors using ultrasonography and fetal monitoring prior to attempting vaginal delivery. The use of potentially injurious instrumentation, such as midforceps rotation and vacuum delivery, has also declined. The accepted alternative is a cesarean delivery.[68]

The main types of birth trauma: birth trauma of the skull and brain, spine, the internal organs (liver, spleen, adrenal glands, etc., various bones of a skeleton (collarbone, the hip bone, etc.), brachial plexus, etc. The most frequent generic traumatic injuries of skull and brain, which not only can lead to death, but also accompanied by lesions of the Central nervous system, leading to disability and delay of mental development.[69]

Bleeding disorders

Bleeding syndromes in the newborn are rare, but they may be life-threatening and demand immediate attention. Results of an initial coagulation evaluation often can direct the clinician toward diagnostic possibilities, as can the degree of illness manifested by the infant. Among the potential causes of neonatal bleeding are platelet disorders, neonatal hemophilia and other congenital clotting factor deficiencies, vitamin K deficiency syndromes, liver failure, and disseminated intravascular coagulation. Depending on the cause, platelet or protein concentrates may be used for transfusion therapy.[70]

Bleeding in neonates may present with oozing from the umbilicus or stump, cephalhaematoma, bruising more than that anticipated after delivery, bleeding from peripheral venipuncture or procedure sites, bleeding into scalp, bleeding following circumcision, petechiae, intracranial haemorrhage, bleeding from mucous membranes and unexplained anaemia and hypotension.[71]

Table 1: Causes of neonatal bleeding.[10]

Category	Incidence
Platelet disorders, (Thrombocytopenia) (Platelet count <150 x 109/L)	1-4% of term newborns, 40-72% of sick preterms and 25% of ICN admissions; of these, 75%present before age 72 h
Impaired platelet function	Rare
Coagulation protein disorders	X-linked recessive: Hemophilia A (Factor VIII) and Hemophilia B (Factor IX), Autosomal recessive (rare): Factors V, VII, X, XI, XII, XIII, afibrinogenemia
Acquired deficiencies	Vitamin K deficiency
Combined platelet and coagulation factor disorders:	Most commonly DIC and hepatic dysfunction
Disorders of vascular integrity	Hemangiomas or vascular malformations

Metabolic disorders

1. Hypoglycemia:

Estimates of the incidence of hypoglycemia in the newborn depend both on the definition of the condition and the methods by which blood glucose concentrations are measured. The overall incidence has been estimated at 1 to 5 per 1000 live births, but it is higher in at-risk populations. For example, 8% of large-for-gestational-age infants (primarily infants of diabetic mothers (IDMs) and 15% of preterm infants and infants who have intrauterine growth retardation (IUGR) have been reported as having hypoglycemia; the incidence in the entire population of “high-risk” infants may be as high as 30%.[72]

Hypoglycemia in the first few days after birth is defined as blood glucose <40 mg/dL. In preterm infants, repeated blood glucose levels below 50 mg/dL may be associated with neurodevelopmental delay.[10] Delay in treatment may

lead to significant neurologic consequences, such as permanent brain damage or even death.[73]

Different conditions are in association with neonatal hypoglycemia including decreased substrate availability such as inborn errors, prematurity and intra-uterine growth retardation; hyperinsulinemia for example in infants of diabetic mother, islet cell hyperplasia, erythroblastosis fetalis, exchange transfusion, Beckwith-Wiedemann Syndrome, maternal β-mimetic tocolytic agents, high umbilical arterial catheter and abrupt cessation of intravenous glucose; other endocrine abnormalities such as pan-hypopituitarism, hypothyroidism and adrenal insufficiency; increased glucose utilization for example in cold stress, increased work of breathing, sepsis and perinatal asphyxia; and miscellaneous conditions such as polycythemia, congenital heart disease and central nervous system abnormalities.[74]

2. Hypocalcemia:

Hypocalcemia is a serum total Ca concentration <8 mg/dL (<2 mmol/L) in term infants or <7 mg/dL (<1.75 mmol/L) in preterm infants. It is also defined as an ionized Ca level <3.0 to 4.4 mg/dL (<0.75 to 1.10 mmol/L), depending on the method (type of electrode) used.[59]

2.1 Early onset neonatal hypocalcemia:

This condition is fairly common and seen within the first 3-4 days of life in following clinical settings: prematurity, preeclampsia, infant of diabetic mother, perinatal stress/ asphyxia, maternal intake of anticonvulsants (phenobarbitone, phenytoin sodium), maternal hyperparathyroidism and Iatrogenic (alkalosis, use of blood products, diuretics, phototherapy, lipid infusions.[75]

2.2 Late-onset hypocalcemia:

Late-onset hypocalcemia is common in neonates, frequently associated with seizures or tetany. It is often attributed to transient hypoparathyroidism. Late-onset hypocalcemia in neonates is mostly a sign of coexisting vitamin D deficiency and hypomagnesemia. These neonates are readily managed with therapy of limited duration, and neonates presenting with tetany or seizures due to hypocalcemia are unlikely to benefit from neuroimaging studies.[76]

3. Inborn errors of metabolism:

Single gene defects result in abnormalities in the synthesis or catabolism of proteins, carbohydrates, fats, or complex molecules. Most are due to a defect in an enzyme or transport protein, which results in a block in a metabolic pathway. Effects are due to toxic accumulations of substrates before the block, intermediates from alternative metabolic pathways, defects in energy production and use caused by a deficiency of products beyond the block, or a combination of these metabolic deviations. Nearly every metabolic disease has several forms that vary in age of onset, clinical severity, and, often, mode of inheritance.[77]

Severe illness in the newborn, regardless of the underlying cause, tends to manifest with non-specific findings, such as poor feeding, drowsiness, lethargy, hypotonia and failure to thrive. IEM should be considered in the differential diagnosis of any sick neonate along with common acquired causes such as sepsis, hypoxic-ischemic encephalopathy, duct-dependent cardiac lesions, congenital adrenal hyperplasia and congenital infections. clinical pointers towards an underlying Inborn Errors of Metabolism (IEM) include: Deterioration after a period of apparent normalcy, parental consanguinity, Family history of neonatal deaths rapidly progressive encephalopathy and seizures of unexplained cause Severe metabolic acidosis, persistent vomiting, peculiar odor and acute fatty liver or HELLP.[77]

Inborn errors of metabolism can affect any organ system and usually affect multiple organ systems manifestations vary from those of acute life threatening disease to subacute progressive degenerative disorders. Categories of IEM are as follows: Disorders of protein metabolism (aminoacidopathies, organic acidopathies, urea cycle defects). Disorder of carbohydrate metabolism (Carbohydrate intolerance disorders, glycogen storage disorders, disorders of gluconeogenesis and glycogenolysis), lysosomal storage disorders (Gaucher's disease, Niemann-Pick disease), disorder of lipid metabolism (fatty acid oxidation defects) mitochondrial disorders (e.g. Kearns-Sayre syndrome), peroxisomal disorders (e.g. Zellweger syndrome, adrenoleucodystrophy) and trace metal disorders (e.g., Menke's Kinky Hair syndrome, and Wilson's disease).[78]

Retinopathy of prematurity

Retinopathy Of Prematurity (ROP), previously known as retrolental fibroplasia, is an eye disease that affects prematurely-born babies. It is thought to be caused by disorganized growth of retinal blood vessels which may result in scarring and retinal detachment. ROP can be mild and may resolve spontaneously, but it may lead to blindness in serious cases. As such, all preterm babies are at risk for ROP, and very low birth weight is an additional risk factor. Both oxygen toxicity and relative hypoxia can contribute to the development of ROP.[79]

In the United States, the incidence of ROP in premature infants is inversely proportional to their birth weight. Fielder studied infants weighing less than 1700 g and noted development of ROP in 51%.In general, more than 50% of premature infants weighing less than 1250 g at birth show evidence of ROP, and about 10% of the infants develop stage III of ROP.[80] In 1995, Retinopathy

of prematurity accounted for 10.6% of cases of blindness in children in schools for the blind in South Africa.[81]

Hearing loss

The incidence of hearing loss in neonates is 2 - 4 cases in every 1000 live births. Hearing loss, especially in mild and moderate forms, may not be recognized before the second year, but may produce great defects in conversational abilities.[82]

MANAGEMENT OF HIGH RISK NEONETES

History

Review the relevant maternal and newborn baby history prior to commencing the examination It is important to review: maternal: medical and obstetric history, including: medications (prescribed and recreational), results of maternal and fetal investigations, family history, social history and newborn baby: mode of birth, resuscitation at birth, medication since birth vitamin K, Hepatitis B, observations since birth temperature, weight, urine, meconium and feeding since birth.[83]

Examination

The routine newborn assessment should include an examination for size, macrocephaly or microcephaly, changes in skin color, signs of birth trauma, malformations, evidence of respiratory distress, level of arousal, posture, tone, presence of spontaneous movements, and symmetry of movements. Total and direct bilirubin levels should be measured in newborns with jaundice, and a complete blood count should be obtained in those with pallor or a ruddy complexion. Infants with chest abnormalities may need to be evaluated for Poland's syndrome or Turner's syndrome. Murmurs in the immediate newborn period are usually innocent and represent a transition from fetal to neonatal circulation. Because cyanosis is primarily secondary to respiratory or cardiac causes, affected newborns should be evaluated expeditiously, with the involvement of a cardiologist or neonatologist.[84]

Investigations for specific diseases

1. Neonatal sepsis

In spite of the isolation of microorganisms from blood, CSF or urine remains the gold standard for definitive diagnosis. Nonspecific laboratory investigation for the diagnosis of invasive bacterial infections remain the most important diagnostic aid for the management of septic neonates.[85]

Laboratory investigations for diagnosis of neonatal sepsis

- Specific laboratory tests: blood, CSF and urine culture, direct visualization of bacteria (gram stain), detection of bacterial antigens and PCR.
- Hematological investigations: white blood cell count, total and differential, platelet count.
- Biochemical investigations: C-reactive protein (CRP), procalcitonin, ESR and other acute phase reactants (haptoglobin).
- Cytokines and receptors: IL-1, IL-6, IL-8 and IL-10).

2. Perinatal asphyxia:

Neonatal investigations contribute to diagnostic and prognostic accuracy. Umbilical arterial and venous blood at birth, and samples from the newborn infant in the first hour or two after birth (although subject to various false-positive and false-negative results and difficulties of interpretation), are useful for the diagnosis of HIE. Pertinent brain imaging and electroencephalography have important diagnostic and prognostic roles in HIE. Other causes of neonatal encephalopathy should be excluded

3. Inborn errors of metabolism:

3.1 First line investigations (metabolic screen):

The following tests should be obtained in all babies with suspected IEM: Complete blood count: (neutropenia and thrombocytopenia seen in propionic and methylmalonic academia), arterial blood gases and electrolytes blood glucose, plasma ammonia (Normal values in newborn: 90-150 g/dl or 64-107 mol/L), arterial blood lactate (Normal values: 0.5-1.6 mmol/L), Liver function tests, urine ketones, urine reducing substances, Serum uric acid (low in molybdenum cofactor deficiency).

3.2 Second line investigations (ancillary and confirmatory tests):

These tests need to be performed in a targeted manner, based on presumptive diagnosis reached after first line investigations as Gas chromatography mass spectrometry (GCMS) of urine- for diagnosis of organic acidemias [86].

4. Hyperbilirubinemia:

Classically, a total serum bilirubin level is the only testing required in a moderately jaundiced infant who presents on the second or third day of life and is otherwise well. Further investigation is essential for any baby who is also unwell, presents in the first 24 hours or has prolonged (after 10 days) jaundice [87].

5. Bleeding disorders (coagulopathy):

Laboratory investigation should include an activated partial thromboplastin time (APTT), prothrombin time

(PT) (or more commonly international normalized ratio (INR) to standardize for different reagents) and complete blood count with platelet count. Additionally, all sick newborns should have fibrinogen and Fibrin Degradation Products (FDP) measured. (Fibrinogen concentrations may be normally less in premature babies, and FDP may be increased with liver disease or after blood transfusion as well as with Disseminated Intravascular Coagulopathy (DIC). Blood should preferably be taken from a venous site.[88]

6. Respiratory distress syndrome:

Blood gases: respiratory and metabolic acidosis along with hypoxia. Metabolic acidosis results from poor tissue perfusion, pulse oximetry is used as a non-invasive tool to monitor oxygen saturation, which should be maintained at 90-95%, chest X-ray, monitor full blood count, electrolytes, glucose, renal and liver function, echocardiogram: diagnosing patent ductus arteriosus (PDA), determine the direction and degree of shunting, making the diagnosis of pulmonary hypertension and excluding structural heart disease and Cultures to rule out sepsis [89].

GENERAL GUIDELINES

Neonatal resuscitation

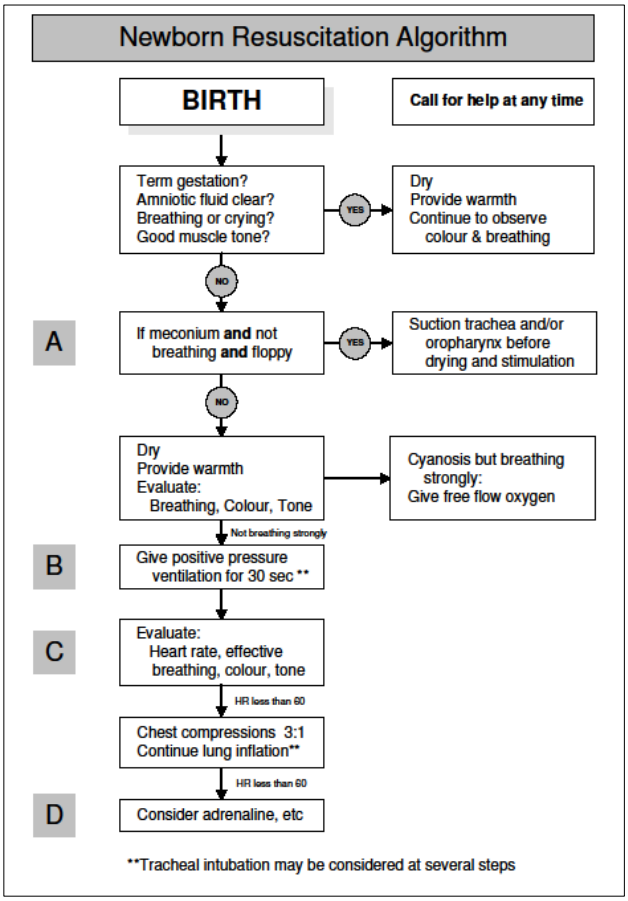

Figure 1: Neonatal resuscitation algorithm.

Table 2: The APGAR score.

Sign	Score 0	Score 1	Score 2
Heart rate	Absent	<100/min	>100/min
Respiration	Absent	Weak	Good cry
Muscle tone	Flaccid	Some flexion	Well flexed
Reflexes	No response	Grimace	Cough/sneeze
Color	Bale/Blue	Blue extremities	Completely pink

Newborn stabilization

The program known as S.T.A.B.L.E. (Sugar and Safe Care, Temperature, Airway, Blood, Lab work, Emotional Support) is widely recognized worldwide. It was developed to improve the quality of care in infants before and during transport as well as to reduce neonatal complications due to inadequate neonatal transport. The high number of infants whose health status deteriorates during transport prompted us to collaborate in the organization of a neonatal transport system that would allow the transport of patients from the birth center or first contact to our neonatal intensive care unit in a safe and organized manner.[90]

Safe neonatal transport

Safe neonatal transport is an integral part of the regionalization program. Its main objective is to lower the morbidity and mortality in this group of patients.[91]

Paramedics, nurses, respiratory therapists, nurse practitioners, and physicians have the role of rapidly stabilizing critically ill newborn patients for immediate transfer. The services of a specialized neonatal transport team have been shown to be associated with reductions in hypothermia and acidosis, as well as with reduced mortality in low birth weight infants.[92]

Ground ambulance

This mode of transport is used for relatively short-distance transport (up to 25 miles) when surface transportation is more efficient and often more rapid than air transport. It must also be used when climactic conditions preclude air transport.

Advantages include the following:

- Lowest transport costs.
- Relative immunity to weather.
- Transport vehicles may be equipped as a specialty vehicle exclusively for pediatric and/or neonatal patients.
- Ground units may be equipped to simultaneously transport 2 patients in the event of twin or higher-order multiple transport requests.
- Comparatively roomy interior space allowing for improved patient access.

Disadvantages to the use of ground ambulances include the following:

- Slowest mode of transport while en route and Necessity of physically securing neonatal incubator inside the transport vehicle and ensuring that neonatal-specific equipment is available if the ambulance is not dedicated to neonatal transport.

Others include Rotor-wing aircraft (helicopter) transport and fixed-wing aircraft (airplane) transport.

The neonatal transport team members must be equipped by all necessary facilities for transporting the infants. This includes, among others, a specially equipped incubator, specialty ventilator, medications, and other equipment that serves as a traveling NICU. Complete care of the infant can be performed from the isolette and support systems which must be available to the transport team.[93]

MANAGEMENT OF SPECIAL MEDICAL PROBLEMS

Neonatal sepsis

Treatment begins with careful monitoring of the infant's vital signs and regulation of the thermal environment. Supportive therapy for a septic infant starts with the administration of oxygen when respiratory distress or hypoxia becomes present. The infant may also need more invasive respiratory support such as continuous positive airway pressure (CPAP) or to be placed on a ventilator if they are suffering from apneic episodes. Infants who are sick may also develop electrolyte abnormalities. These infants will need careful, ongoing monitoring and adjustment of the fluid and electrolyte balance, especially when the infants are Nil Per Os (NPO).[94]

Antibiotic therapy is continued for 7 to 21 days if the cultures are positive, or it is discontinued in 3 days if cultures are negative. The infant's outcome is variable. Before the availability of antibiotics, mortality rates for infected infants were greater than 95%. In the 1970s and 1980s, the mortality rate decreased to 20% to 40%. Today, with the use of antibiotics along with early recognition and supportive care, mortality has reduced to 13% to 45%, depending on the causative agent.

However, approximately 1500 neonates in the United States still die annually from systemic infections. Prolonged antibiotic therapy poses additional hazards for affected infants. Antibiotics predispose the infant to growth of resistant organisms and superinfections from fungal agents such as candida. The nurse must be alert for signs of such complications

Therapy with intravenous immune globulin had no effect on the outcomes of suspected or proven neonatal sepsis.

Neonatal hypoglycemia:[10]

- Glucometer reading >40 mg/dL and infant is feeding normally: follow usual nursery protocol.
- Glucometer reading 20-40 mg/dL, infant is term and is able to feed: feed 5 mL/kg of D5W and Repeat blood glucose or glucometer 20 min after feeding.
- Glucometer reading: <20 mg/dL or<40 mg/dL and NPO or preterm or <40 mg/dL after feeding or<40 mg/dL and symptomatic: give IV bolus of 2-3 mL/kg of D10W, Begin continuous infusion of D10W at 4-6 mg/kg/min, If infant of diabetic mother, begin D10W at 8-10 mg/kg/min (100-125 cc/kg/d), Repeat blood glucose in 20 min and pursue treatment until blood sugar >40 mg/dL.
- For persistent hypoglycemia despite above measures: increase rate of glucose infusion stepwise in 2 mg/kg/min increments up to 12-15 mg/kg/min glucose. Use increased volume with caution in infants where volume overload is a concern.
- Maximal concentration of glucose in peripheral IV is D12.5.If infant requires IV dextrose concentrations >12.5%, insert central venous catheter.

If hypoglycemia is diagnosed in an infant younger than 3 months, surgical intervention may be necessary. Surgical exploration usually is undertaken in severely affected neonates who are unresponsive to glucose and somatostatin therapy. Near-total resection of 85-90% of the pancreas is recommended for presumed congenital hyperinsulinism, which is most commonly associated with an abnormality of beta-cell regulation throughout the pancreas. Risks include the development of diabetes

Neonatal hypocalcemia

Patients at increased risk of hypocalcemia (prophylactic):Preterm infants (≤32 weeks), sick infants of diabetic mothers and those with severe perinatal asphyxia should receive 40 mg/kg per day of elemental calcium (4 mL/kg/day of 10% calcium gluconate) for prevention of early onset hypocalcemia.

Patients diagnosed to have asymptomatic hypocalcemia (on screening) asymptomatic: should receive 80-mg/kg/day elemental calcium (8 mL/kg/day of 10% calcium gluconate) for 48 hrs.

Patients diagnosed to have symptomatic hypocalcemia: These patients should receive a bolus dose of 2 mL/kg/dose diluted 1:1 with 5% dextrose over 10 min under cardiac monitoring.

When there is severe hypocalcaemia with poor cardiac function, calcium chloride 20 mg/kg may be given through a central line over 10-30 min. This should be

followed by a continuous IV infusion of 80 mg/kg/day elemental calcium for 48 h. The treatment of late onset hypocalcemia is specific to etiology and may in certain diseases be life-long.[95]

Perinatal asphyxia (hypoxic ischemic encephalopathy)

Delivery room management follows standard Neonatal Resuscitation Program (NRP) guidelines. Close attention should be paid to appropriate oxygen delivery, perfusion status, and avoidance of hypoglycemia and hyperthermia.[96]

Most infants with severe hypoxic-ischemic encephalopathy need ventilatory support during first days of life. Therefore, the role of mechanical ventilation is to maintain the blood gases and acid-base status in the physiological ranges and prevent hypoxia, hyperoxia, hypercapnia, and hypocapnia. Hypocapnia in particular may lead to severe brain hypoperfusion and cellular alkalosis and has been associated with worse neurodevelopmental outcomes. Of note, recent evidence indicates that increased FiO2 in the first 6 hours of life is a significant risk factor for adverse outcomes in infants with hypoxic-ischemic encephalopathy treated with hypothermia therapy.[97]

Studies indicate that a mean blood pressure above 35-40 mmHg is necessary to avoid decreased cerebral perfusion. Hypotension is common in infants with severe hypoxic-ischemic encephalopathy and is due to myocardial dysfunction, capillary leak syndrome, and hypovolemia. Because of the concern for acute tubular necrosis and syndrome of inappropriate antidiuretic hormone secretion, fluid restriction is typically recommended for these infants until renal function and urine output can be evaluated.[98] Hyperthermia has been shown to be associated with increased risk of adverse outcomes in neonates with moderate-to-severe hypoxic-ischemic encephalopathy.[99]

Hypoxic-ischemic encephalopathy is the most common cause of seizures in the neonatal period. Seizures are generally self-limited to the first days of life but may significantly compromise other body functions, such as maintenance of ventilation, oxygenation, and blood pressure, even asymptomatic electrographic seizures, may contribute to brain injury and increase the risk of subsequent epilepsy. Current therapies available to treat neonates with seizures include phenobarbital, phenytoin, and benzodiazepines. Phenobarbital has been shown to be effective in only 29-50% of cases.[100]

Extensive experimental data suggest that mild hypothermia (3-4°C below baseline temperature) applied within a few hours (no later than 6 h) of injury is neuroprotective.[101] herapeutic hypothermia when applied within 6 hours of birth and maintained for 48-72 hours is a promising therapy for mild-to-moderate cases of hypoxic-ischemic encephalopathy Two methods have been used in clinical trials: selective head cooling and whole body cooling. Rewarming is a critical period. In clinical trials, rewarming was carried out gradually, over 6-8 hours.[102]

Neonatal jaundice

Phototherapy, intravenous immune globulin (IVIG), and exchange transfusion are the most widely used therapeutic modalities in infants with neonatal jaundice. Phototherapy is the primary treatment in neonates with unconjugated hyperbilirubinemia.and phototherapy is very safe and may have no serious long-term effects in neonates.[103]

Exchange transfusion became the second-line treatment when phototherapy failed to control serum bilirubin levels. However, data have shown that treatment with IVIG in infants with Rh or ABO isoimmunization can significantly reduce the need for exchange transfusions.[104] At the author's institution, a tertiary center where exchange transfusions used to be frequent, only 0-2 such procedures per year are performed, and IVIG has replaced exchange transfusion as the second-line treatment in infants with isoimmune jaundice.[105]

The guidelines of AAP (2004) suggest a dose range for IVIG of 500-1000 mg/kg in infants with breast milk jaundice, interruption of breastfeeding for 24-48 hours and feeding with breast milk substitutes often help reduce the bilirubin level. Evidence suggests that simple expedient of supplementing feeds of breast, milk with 5 mL of a breast milk substitute, reduces the level and duration of jaundice in breast milk–fed infants. Because this latter intervention causes less interference with the establishment of the breastfeeding dyad, Kumral et al. prefer the use this approach to complete interruption of breast feeding in most cases.[106]

Respiratory distress syndrome

The advent of surfactant therapy has reduced the mortality rate from respiratory distress syndrome by approximately 50%. Neonates with respiratory distress syndrome who require assisted ventilation with a FIO2 of more than 0.40 should receive intratracheal surfactant as soon as possible, preferably within 2 hours after birth. Early surfactant therapy in tiny neonates followed by rapid extubation to nasal CPAP decreased the need for and duration of mechanical ventilation and decreased the rate of pulmonary air leakage and 28-day mortality compared with selective surfactant therapy in respiratory distress syndrome followed by ventilation and Because surfactant protects the immature lungs, several investigators have recommended its prophylactic use after resuscitation in extremely premature neonates (<27 weeks' gestation).[107]

High-Frequency Oscillatory Ventilation (HFOV) has a frequency range of 10-15 Hz. Early in its use, high-

HFOV was found to be clearly superior to conventional ventilation. In one clinical trial, prophylactic HFOV reduced chronic lung disease.[108]

Bronchopulmonary dysplasia (BPD)

Management of BPD in the NICU requires a multimodal approach including adequate nutrition, careful fluid management, effective and safe pharmacotherapy, and respiratory support aiming at minimal lung injury. Among pharmacological interventions, caffeine has the best risk-benefit profile.

Postnatal corticosteroids should be reserved to ventilated infants at highest risk of BPD who cannot be weaned from the ventilator. Several ongoing randomized controlled trial are evaluating optimal oxygen saturation targets in preterm infants whilst the most beneficial respiratory support strategy to minimize lung injury remains unclear and requires further investigation.

Meconium aspiration syndrome

If the baby is not vigorous (defined as depressed respiratory effort, poor muscle tone, and/or heart rate < 100 beats/min): Use direct laryngoscopy, intubate, and suction the trachea immediately after delivery. Suction for no longer than 5 seconds. If no meconium is retrieved, do not repeat intubation and suction. If meconium is retrieved and no bradycardia is present, reintubate and suction. If the heart rate is low, administer positive pressure ventilation and consider suctioning again later. If the baby is vigorous (defined as normal respiratory effort, normal muscle tone, and heart rate >100 beats/min): Do not electively intubate, clear secretions and meconium from the mouth and nose with a bulb syringe or a large-bore suction catheter.[109]

Surfactant therapy is now commonly used to replace displaced or inactivated surfactant and as a deterrent to remove meconium. Although surfactant use does not appear to affect mortality rates, it may reduce the severity of disease, progression to extracorporeal membrane oxygenation (ECMO), and decrease length of hospital stay. Studies are ongoing to evaluate the potential role of pulmonary lavage with surfactant.[110]

For treatment of persistent pulmonary hypertension of the newborn (PPHN), inhaled nitric oxide is the pulmonary vasodilator of choice. Oxygen is also a potent pulmonary vasculature vasodilator. Phosphodiesterase inhibitors, including sildenafil and milrinone, are being increasingly used as adjunctive therapies for PPHN.[111]

Extracorporeal membrane oxygenation is used if all other therapeutic options have been exhausted. Although effective in treating meconium aspiration syndrome, ECMO is associated with a high incidence of poor neurologic outcomes.[112]

DISCHARGE PLANNING

Discharge planning has been described as 'the development of an individualized discharge plan for the patient prior to leaving hospital, with the aim of containing costs and improving patient outcomes'

It is a crucial component of making the transition from the acute care setting to the home A transition is considered 'a passage or movement from one state, condition, or place to another that may create a period of vulnerability associated with changes in health status, role relations, expectations, or abilities'.[113]

The infant is considered ready for discharge if, in the judgment of the responsible physician, the following have been accomplished:

- A sustained pattern of weight gain of sufficient duration has been demonstrated.
- Adequate maintenance of normal body temperature.
- Established competent feeding by breast or bottle without cardiorespiratory compromise.
- Appropriate immunizations have been administered.
- Appropriate metabolic screening has been performed.
- Hematologic status has been assessed.
- Nutritional risks have been assessed.
- Hearing evaluation and funduscopic examinations have been completed. Neuro developmental and neurobehavioral status has been assessed and demonstrated to the parents.
- Plans for follow-up monitoring and treatment have been instituted.
- Family and Home Environmental Readiness and Community and Health Care System Readiness should be assessed.

DEVELOPMENTAL OUTCOME

Neonatal intensive care and rapid improvements in technology are associated with improved survival of critically ill newborn and preterm infants. Survival rates have increased to 93% for VLBW infants, 85% for ELBW infants and about 50% for infants weighing 501 to 750 g.[114]

With decreasing mortality, morbidity rates have remained stable. At highest risk for unfavorable outcomes are preterm infants compromised during the neonatal period by respiratory distress syndrome, bronchopulmonary dysplasia, necrotizing enterocolitis (NEC), sepsis, anemia, Intra Ventricular Hemorrhage (IVH), hydrocephalus, meningitis, or seizures.[115]

A greater incidence of Cerebral Palsy (CP), attention deficit hyperactivity disorder, visual-motor deficits, mild to severe cognitive disabilities, hearing loss, speech and language impairment, and neuromotor problems has been reported in outcome studies of preterm infants.[116] The

goal of early diagnosis of hearing loss is to acheive better verbal and social communication. Delayed diagnosis may have a negative impact on the patient's verbal, educational, psychological and socioeconomic abilities. It is universally accepted that screening for hearing loss in neonates is crucial.[117]

The incidence of hearing loss in neonates who were in the NICU for more than 48 hours was about 2-4%. Patients hospitalized in the NICU must be screened for hearing loss, because these neonates probably have more problems and multiple risk factors, such as prematurity, low birth weight, use of ototoxic drugs and mechanical ventilation.[118]

Hearing loss incidence in neonates hospitalized in the NICU who had primary pulmonary hypertension and underwent extractorporeal membrane oxygenation was 20 - 25%. Severe hyperbilirubinemia causes hearing loss. When indirect bilirubin passes the blood brain barrier, it will be deposited in the basal ganglia, and also in the vestibulo-cochlear nucleus. It has been reported that 33% of newborns with blood bilirubin levels of 15 - 25 mg/dl had loss of wave complexes IV and V in Auditory Brainstem Response (ABR).[119]

CONCLUSION

There are many neonatal hazards that might jeopardize and threaten the lives of neonates. Such hazards have been increasing recently. The management starts with expecting the unexpected and taking all the necessary precautions before and after delivery. By viewing the high risks, it is rational to conclude that maternal good health and perfect care can minimize the anticipated hazards. When risks occur, the practitioner is updated with the ideal procedures in our concise review.

ACKNOWLEDGMENTS

I would like to sincerely thank Dr. Maged Zakaria for helping me design this review. My acknowledgment extends to my dear friends; Dr. Mona Saber and Dr. Manar Montaser for their guidance and support.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Patti J. Thureen, Marianne S. Anderson, William W. Hay. The small-for-gestational age infant neo reviews. Am Acad Pediatr. 2001;2(6):139-49.
2. CIA World Factbook. Egypt infant mortality rate, 2011. Available at: http://www.indexmundi.com/egypt/infant_mortality_rate.html.
3. Mosby's Medical Dictionary. The free dictionary: infant mortality, 2009. Available at: http://medicaldictionary. The free dictionary.com/infant+mortality.
4. Campbell O, Gipson R, el-Mohandes A, Issa AH, Matta N, Mansour E, et al. The Egypt national perinatal/neonatal mortality study 2000. J Perinatol. 2004;24(5):284-9.
5. Martin JA, Kung HC, Mathews TJ, Hoyert DL, Strobino DM, Guyer B, et al. Annual summary of vital statistics: 2006. Pediatrics. 2006;121(4):788-801.
6. Subramanian K, Ted Rosenkrantz. Transient tachypnea of the new-born, 2012. Available at: http://emedicine.medscape.com/article/976914-overview.
7. Mayor S Extremely low birth weight is linked to risk of chronic illness BMJ. 2005;331(7510):180.
8. Hodgman JE, Barton L, Pavlova Z, Fassett MJ. Infection as a cause of death in the extremely-low-birth-weight infant. J Matern Fetal Neonatal Med. 2003;14(5):313-7.
9. Freeman VA. Very low birth weight babies delivered at facilities for high risk neonates. Final Rep. 2010 Apr;8:1-41.
10. William H. Tooley; Intensive Care Nursery House Very low and extremely low birth weight infants. In: William H. Tooley, eds. Staff Manual. California: The Regents of the University of California; 2004: 66-68.
11. Matthews TJ, MacDorman MF. Infant mortality statistics from the 2006 period linked birth/infant death data set. National vital statistics reports. In: Matthews TJ, MacDorman MF, eds. A Report. bHyattsville, MD: National Center for Health Statistics; 2010;58(17)1-20.
12. United Nations Children's Fund and the World Health Organization (UNICEF & WHO). Low birthweight. In: WHO, eds. Country, Regional and Global Estimates. New York and Geneva: UNICEF and WHO; 2004: 2-3.
13. Mumbare S, Maindarkar G, Darade R, Yenge S, Tolani MK, Patole K. Maternal risk factors associated with term low birth weight neonates. Indian Pediatr. 2012;49(1):25-8.
14. Gupta RK. Care of low birth weight neonates, from the department of pediatrics. ASCOMS, Sidhra Jammu-J&K-India. 2008;10(4):158-9.
15. Akin Y, Cömert S, Turan C, Piçak A, Ağzikuru T, Telatar B. Macrosomic newborns: a 3-year review. Turk J Pediatr. 2010;52(4): 378-83.
16. Henriksen T. The macrosomic fetus: a challenge in current obstetrics. Acta Obstet Gynecol Scand. 2008;87:134-45.
17. Lindsay CA. Pregnancy complicated by diabetes mellitus. In: Martin RJ, Fanaroff AA, Walsh MC, eds. Fanaroff and Martin's Neonatal-Perinatal Medicine. Diseases of the Fetus and Infant. 8th ed. Philadelphia: Mosby Elsevier; 2006: 326-327.
18. Carlo WA. Large for gestational age infants. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, eds. Nelson Textbook of Pediatrics. 19th ed.

Philadelphia, Pa: Saunders Elsevier; 2011: Chap 91.4.
19. Kendig JW. Postmature infant. The Merck Manuals Online Medical Library, 2007. Available at: http://www.merck.com/mmpe/sec19/ch272/ch272f.html. Retrieved 2008-10-06.
20. Thureen PJ, Anderson MS, Hay WW. The small-for-gestational age infant neo reviews. Am Acad Pediatr. 2001;2(6):139-49.
21. Xu H, Simonet F, Luo ZC. Optimal birth weight percentile cut-offs in defining small- or large-for-gestational-age. Acta Paediatr. 2010;99:550.
22. Carlo WA. Large for gestational age infants. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, eds. Nelson Textbook of Pediatrics. 19th ed. Philadelphia, Pa: Saunders Elsevier; 2011: Chap 91.4.
23. Divon MY, Ferber A. Fetal growth restriction: etiology [electronic version], 2007. Available at: http://www.uptodateonline.com.
24. Severi FM, Rizzo G, Bocchi C, D'Antona D, Verzuri MS, Arduini D. Intrauterine growth retardation and fetal cardiac function. Fetal Diagn Ther. 2000;15(1):8-19.
25. Axt-Fliedner R, Schwarze A, Nelles I, Altgassen C, Friedrich M, Schmidt W, et al. The value of uterine artery Doppler ultrasound in the prediction of severe complications in a risk population. Arch Gynecol Obstet. 2005;271(1):53-8.
26. Ballard JL, Novak KK, Driver M. A simplified score for assessment of fetal maturation of newly born infants. J Pediatr. 1979;95(5 Pt 1):769-74.
27. Kimberly G. Lee. Committee on Obstetric Practice, American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 379. Management of delivery of a newborn with meconium-stained amniotic fluid. Obstet Gynecol. 2007;110:739.
28. Escobar GJ, McCormick MC, Zupancic JA, Coleman-Phox K, Armstrong MA, Greene JD, et al. Unstudied infants: outcomes of moderately premature infants in the NICU. Arch Dis Child Fetal Neonatal Ed. 2006 Jul;91(4):F238-44.
29. Raju TN, Higgins RD, Stark AR, Leveno KJ. Optimizing care and outcome for late-preterm (near-term) infants: a summary of the workshop sponsored by the National Institute of Child Health and Human Development. Pediatrics. 2006;118:1207-14.
30. National Center for Health Statistics. Final natality data, 2009. Available at: www.marchofdimes.com/peristats. Accessed February 2009.
31. Engle WA, Kominiarek MA. Late preterm infants, early term infants, and timing of elective deliveries section of neonatal-perinatal pediatrics. Clin Perinatol. 2008;35:325-41.
32. Institute of Medicine (IOM). Preterm Birth: causes, consequences, and prevention. In: IOM, eds. IOM Report. Washington, D.C.: National Academies Press; 2006.
33. Boyle EM, Poulsen G, Field DJ, Kurinczuk JJ, Wolke D, Alfirevic Z, et al. Effects of gestational age at birth on health outcomes at 3 and 5 years of age: population based cohort study. BMJ. 2012;344:e896.
34. Martin JA, Hamilton BE, Ventural SJ, Osterman MJ, Kirmeyer S, Mathews TJ, et al. Births: final data for 2009. Natl Vital Stat Rep. 2011;60:1.
35. Nakling J, Backe B. Pregnancy risk increases from 41 weeks of gestation. Acta Obstet Gynecol Scand. 2006;85:663.
36. Resnik R. Fetal macrosomia: 3 management dilemmas. J Fam Pract. 2003;5(12)28-36.
37. American College of Obstetricians and Gynecologists (ACOG). Antenatal corticosteroid therapy for fetal maturation. In: ACOG, eds. ACOG Committee Opinion, Number 273, May 2002. America: ACOG; 2005.
38. Lissauer T, Clayden A. Transitory tachypnea of newborn. In: Lissauer T, Clayden A, eds. Illustrated Textbook of Paediatrics. 3rd ed. US: Mosby/Elsevier; 2007: 162
39. Kasap B, Duman N, Ozer E, Tatli M, Kumral A, Ozkan H. Transient tachypnea of the newborn: predictive factor for prolonged tachypnea. Pediatr Int. 2008;50(1):81-4.
40. Miller-Keane, Benjamin F. Miller, Marie T. O'Toole. Miller-Keane encyclopedia & dictionary of medicine, nursing and allied health. In: Miller-Keane, Benjamin F. Miller, Marie T. O'Toole, eds. A Book. 7th ed. Philadelphia: Saunders; 2003.
41. Rodriguez RJ, Martin RJ and Fanaroff AA. Respiratory distress syndrome and its management. In: Fanaroff, Martin eds. Neonatal-Perinatal Medicine: Diseases of the Fetus and Infant. 7th ed. St. Louis: Mosby; 2001: 1001-1011.
42. Qiu X, Lee SK, Tan K, et al. Comparison of singleton and multiple-birth outcomes of infants born at or before 32 weeks gestation. Obstet Gynecol. 2008;111:365-371.
43. Cloherty JP, Eichenwald EC, Stark AR. Manual of neonatal care, North American. In: Cloherty JP, Eichenwald EC, Stark AR, eds. A Book. 6th ed. Philadelphia: Williams and Wilkins Lippincott; 2007.
44. Cloherty J, Stark A, Eichenwald E. Manual of neonatal care. In: Cloherty J, Stark A, Eichenwald E, eds. A Book. 6th ed. Philadelphia: Lippincott, Wilkins and Williams; 2008.
45. Palta M, Sadek-Badawi M, Evans M, Weinstein MR, McGuinnes G. Functional assessment of a multicenter very low-birth-weight cohort at age 5 years: new-born lung project. Arch Pediatr Adolesc Med. 2000;154:23-30.
46. Panickar J, Scholefield H, Kumar Y, Pilling DW, Subhedar NV. Atypical chronic lung disease in preterm infants. J Perinat Med. 2004;32(2):162-7.

47. Cowie RL, Murray J and Becklake MR. Disorders of the intrathoracic airways. In: Mason RJ, Broaddus VC, Martin TR, eds. Murray and Nadel's Textbook of Respiratory Medicine. 5th ed. Philadelphia, Pa: Saunders Elsevier; 2010: Chap 44.
48. Klingner MC, Kruse J. Meconium aspiration syndrome: pathophysiology and prevention. J Am Board Fam Pract. 1999;12(6):450-66.
49. Clark MB. Meconium aspiration syndrome, 2009. Available at: http://emedicine.medscape.com/article/974110-overview.
50. Cheng Y, Nicholson J, Nakagawa S, Bruckner TA, Washington AE, Caughey AB. Perinatal outcomes in low-risk term pregnancies: do they differ by week of gestation? Am J Obstet Gynecol. 2008;199(4):370.3e1-7.
51. Dargaville PA, Copnell B. The epidemiology of meconium aspiration syndrome: incidence, risk factors, therapies, and outcome. Pediatrics. 2006;117(5):1712.
52. Kendig James W. Postmature infant. The Merck Manuals Online Medical Library, 2007. Available at: http://www.merck.com/mmpe/sec19/ch272/ch272f.html. Accessed 06 October 2008.
53. Haobijam J. Hypothermia and its management in new-born, 2013. Available at: http://e-pao.net/epSubPageExtractor.asp?src=education.Health_Issue.Hypothermia_and_its_management.
54. Kumar Abbas, Fausto. TORCH infections. In: Kumar Abbas, Fausto, eds. Robbins and Cotran's Pathologic Basis of Disease. 7th ed. Philadelphia: Saunders; 2009: 470.
55. Mersch J. Neonatal sepsis (Sepsis neonatorum), 2009. Available at: medicine.net. Accessed 3 April 2009.
56. Klinger G, Levy I, Sirota L, Boyko V, Reichman B, Lerner-Geva L, et al. Epidemiology and risk factors for early onset sepsis among very-low-birth weight infants. Am J Obstet Gynecol. 2009;201(1):38.e1-6.
57. van den Hoogen A, Gerards LJ, Verboon-Maciolek MA, Fleer A, Krediet TG. Long-term trends in the epidemiology of neonatal sepsis and antibiotic susceptibility of causative agents. Neonatology. 2009 Jul;97(1):22-8.
58. Carr R, Brocklehurst P, Doré CJ, Modi N. Granulocyte-macrophage colony stimulating factor administered as prophylaxis for reduction of sepsis in extremely preterm, small for gestational age neonates (the PROGRAMS trial): a single-blind, multicentre, randomised controlled trial. Lancet. 2009;373(9659):226-33.
59. Jospe N. Neonatal hyperbilirubinemia. In: Jospe N, eds. A Merck Manual of Patient Symptoms Podcast. US: Merck; 2009.
60. Georgy ML, Martin CR, Clothery JP. Neonatal hyperbilirubinemia. In: Georgy ML, Martin CR, Clothery JP, eds. Manual of Neonatal Care. US: Merck; 2011.
61. Dennery PA, Seidman DS, Stevenson DK. Neonatal hyperbilirubinemia. N Engl J Med. 2001;344:581-90.
62. Gartner LM, Herschel M. Jaundice and breast-feeding. Pediatr Clin North Am. 2001;48:389-99.
63. Preer GL, Philipp BL. Understanding and managing breast milk jaundice. Arch Dis Child Fetal Neonatal Ed. 2011;96(6):461-6.
64. [Laciou-Petruccell A. Perinatal asphyxia. New York, NY: Vantage Press; 2006. Available at: http://www.pediatrics.emory.edu/divisions/neonatology/dpc/asphyx1.html.
65. Wyatt JS, Gluckman PD, Liu PY, Azzopardi D, Ballard R, Edwards AD, et al. Determinants of outcomes after head cooling for neonatal encephalopathy. Pediatrics. 2007;119:912-921.
66. Rutherford MA, Azzopardi D, Whitelaw A, Cowan F, Renowden S, Edwards AD, et al. Mild hypothermia and the distribution of cerebral lesions in neonates with hypoxic-ischemic encephalopathy. Pediatrics. 2005;116:1001-6.
67. Parker LA. Early recognition and treatment of birth trauma: injuries to the head and face. Adv Neonatal Care. 2005;5(6):288-97.
68. Moczygemba CK, Paramsothy P, Meikle S, Kourtis AP, Barfield WD, Kuklina E, et al. Route of delivery and neonatal birth trauma. Am J Obstet Gynecol. 2010;202(4):361.e1-6.
69. Beck CT. Birth trauma and its sequelae. J Trauma Dissociation. 2009;10(2):189-203.
70. Manco-Johnson MJ. Bleeding disorders in the neonate. Neo Rev. 2008;9:162-9.
71. Christensen. Hematologic problems of the neonate. In: Christensen, eds. A Book. 1st ed. Philadelphia: W.B. Saunders Company; 2000.
72. McGowan JE. Neonatal hypoglycemia. Pediatr Rev. 1999;20:6.
73. Sperling MA, Menon RK. Differential diagnosis and management of neonatal hypoglycemia. Pediatr. Clin North Am. 2004;51:703-23.
74. Gomella TM, Cunningham F. Eyal. Neonatology: management, procedures, on-call problems, diseases and drugs. In: Gomella TM, Cunningham F. Eyal, eds. A Book. 6th ed. New York: McGraw-Hill Professional; 2009.
75. Jain A, Agarwal R, Sankar MJ, Deorari AK, Paul VK. Hypocalcemia in the newborn. Indian J Pediatr. 2010;77(10):1123-8.
76. Thomas TC, Smith JM, White PC, Adhikari S. Transient neonatal hypocalcemia: presentation and outcomes. Pediatrics. 2012;129(6):e1461-7.
77. Sharma S, Kumar P, Agarwal R, Kabra M, Deorari AK, Paul VK. Approach to inborn errors of metabolism presenting in the neonate. Indian J Pediatr. 2008;75(3):271-6.
78. Rao AN, Kavitha J, Koch M, Suresh Kumar V. Inborn errors of metabolism: review and data from a tertiary care center. Indian J Clin Biochem. 2009;24(3):215-22.

79. Phelps DL. Retinopathy of prematurity: history, classification, and pathophysiology. Neo Rev. 2001;2(7):e153-66.
80. Bashour M. Retinopathy of prematurity, 2012. Available at: http://emedicine.medscape.com/article/1225022-overview.
81. Varughese S, Gilbert C, Pieper C, Cook C. Retinopathy of prematurity in South Africa: an assessment of needs, resources and requirements for screening programmes. Br J Ophthalmol. 2008;92(7):879-82.
82. Kenna M, Behrman RE, Kliegmen R. Nelson textbook of pediatrics. In: Kenna M, Behrman RE, Kliegmen R, eds. 16th ed. Philadelphia: Saunder's Company; 2000: 1940-1949.
83. Levene MI, Tudehope DI, Sinha S. Examination of the newborn. In: Essential Neonatal Medicine. 4th ed. Australia: Blackwell Publishing; 2008: 25-34.
84. Fuloria M, Kreiter S. The new-born examination: part I. Emergencies and common abnormalities involving the skin, head, neck, chest, and respiratory and cardiovascular systems. Am Fam Physician. 2002;65(1):61-8.
85. Chirico G, Loda C. Laboratory aid to the diagnosis and therapy of infection in the neonate. Pediatr Rep. 2011;3(1):e1.
86. Sharma S, Kumar P, Agarwal R, Kabra M, Deorari AK, Paul VK. Approach to inborn errors of metabolism presenting in the neonate. Indian J Pediatr. 2010;75(3):271-6.
87. Hansen TWR, Itani O, Windle ML. Neonatal jaundice, 2012. Available at: http://emedicine.medscape.com/article/ 974786-overview.
88. Mcmillan DD, Wu J. Approach to the bleeding newborn. Paediatr Child Health. 1998;3(6):399-401.
89. Pramanik AK, Rosenkrantz T, David AC. Respiratory distress syndrome, 2006. Available at: http://emedicine.medscape.com/article/976034-overview.
90. Verónica RM, Gallo LL, Medina DR, De la Torre MG, Mancilla J-L, Amezcua MM, et al. Safe neonatal transport in the State of Jalisco: Impact of the S.T.A.B.L.E. program on morbidity and mortality. Bol Med Hosp Infant Mex. 2011;68(1):31-5.
91. Yeager SB, Horbar JD, Greco KM, Duff J, Thiagarajan RR, Laussen PC. Pretransport and posttransport characteristics and outcomes of neonates who were admitted to a cardiac intensive care unit. Pediatrics. 2006;118:1070-7.
92. Chen P, Macnab AJ, Sun C. Effect of transport team interventions on stabilization time in neonatal and pediatric interfacility transports. Air Med J. 2005;24(6):244-7.
93. Carell M. Children's hospital at Vanderbilt 2200 children's way Nashville. TN. 2012;37232(615):936-1000.
94. Bellig L. Neonatal sepsis. Emedicine, 2004. Available at: http://www.emedicine.com/ped.topic2630.htm. Accessed 12 July 2004.
95. Jain A, Agarwal R, Sankar MJ, Deorari AK, Paul VK. Hypocalcemia in the newborn. Indian J Pediatr. 2010;77(10):1123-8.
96. Ten VS, Matsiukevich D. Room air or 100% oxygen for resuscitation of infants with perinatal depression. Curr Opin Pediatr. 2009;21(2):188-93.
97. Sabir H, Jary S, Tooley J, Liu X, Thoresen M. Increased Inspired oxygen in the first hours of life is associated with adverse outcome in newborns treated for perinatal asphyxia with therapeutic hypothermia. J Pediatr. 2012;161(3):409-16.
98. Kecskes Z, Healy G, Jensen A. Fluid restriction for term infants with hypoxic-ischaemic encephalopathy following perinatal asphyxia. Cochrane Database Syst Rev. 2005;(3):CD004337.
99. Laptook A, Tyson J, Shankaran S, McDonald S, Ehrenkranz R, Fanaroff A, et al. Elevated temperature after hypoxic-ischemic encephalopathy: risk factor for adverse outcomes. Pediatrics. 2008;122(3):491-9.
100. Miller SP, Weiss J, Barnwell A, Ferriero DM, Latal-Hajnal B, Ferrer-Rogers A, et al. Seizure-associated brain injury in term newborns with perinatal asphyxia. Neurology. 2002;58(4):542-8.
101. Gunn AJ, Gunn TR. The 'pharmacology' of neuronal rescue with cerebral hypothermia. Early Hum Dev. 1998;53(1):19-35.
102. Shankaran S, Pappas A, Laptook AR, McDonald SA, Ehrenkranz RA, Tyson JE, et al. Outcomes of safety and effectiveness in a multicenter randomized, controlled trial of whole-body hypothermia for neonatal hypoxic-ischemic encephalopathy. Pediatrics. 2008;122(4):e791-8.
103. Atkinson LR, Escobar GJ, Takyama JI, Newman TB. Phototherapy use in jaundiced newborns in a large managed care organization: do clinicians adhere to the guideline. Pediatrics. 2003;111:555.
104. Gottstein R, Cooke RW. Systematic review of intravenous immunoglobulin in haemolytic disease of the newborn. Arch Dis Child Fetal Neonatal Ed. 2003;88(1):6-10.
105. Huizing K, Roislien J, Hansen T. Intravenous immune globulin reduces the need for exchange transfusions in Rhesus and AB0 incompatibility. Acta Paediatr. 2008;97(10):1362-5.
106. Kumral A, Ozkan H, Duman N, Yesilirmak DC, Islekel H, Ozalp Y. Breast milk jaundice correlates with high levels of epidermal growth factor. Pediatr Res. 2009;66(2):218-21.
107. Engle WA, Kominiarek MA. Late Preterm infants, early term infants, and timing of elective deliveries section of neonatal-perinatal pediatrics. Clin Perinatol. 2008;35:325-41.
108. Truffert P, Paris-Llado J, Escande B, Magny JF, Cambonie G, Saliba E, et al. Neuromotor outcome at 2 years of very preterm infants who were treated

with high-frequency oscillatory ventilation or conventional ventilation for neonatal respiratory distress syndrome. Pediatrics. 2007;119:e860-5.
109. Kattwinkel J, Perlman JM, Aziz K, Colby C, Fairchild K, Gallagher J, et al. Neonatal resuscitation: 2010 American Heart association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Pediatrics. 2010;126(5):1400-13.
110. El Shahed AI, Dargaville P, Ohlsson A, Soll RF. Surfactant for meconium aspiration syndrome in full term/near term infants. Cochrane Database Syst Rev. 2007;18(3):CD002054.
111. Abman SH, Kinsella JP. Inhaled nitric oxide therapy for pulmonary disease in pediatrics. Curr Opin Pediatr. 1998;10(3):236-42.
112. Kugelman A, Gangitano E, Taschuk R, Garza R, Riskin A, McEvoy C, et al. Extracorporeal membrane oxygenation in infants with meconium aspiration syndrome: a decade of experience with venovenous ECMO. J Pediatr Surg. 2005;40(7):1082-9.
113. Weiss M, Johnson NL, Malin S, Jerofke T, Lang C, Sherburne E. Readiness for discharge in parents of hospitalized children. J Pediatr Nurs. 2008;23(4):282-95.
114. Msall ME, Tremont MR. Functional outcomes in self-care, mobility, communication, and learning in extremely low-birth weight infants. Clin Perinatol. 2000;27(2):381-401.
115. McGrath MM, Sullivan MC, Lester MC. Longitudinal neurologic follow-up in neonatal intensive care unit survivors with various neonatal morbidities. Pediatrics. 2000;106(6):1397-405.
116. van Baar AL, van Wassenaer AG, Briet JM, Dekker FW, Kok JH. Very preterm birth is associated with disabilities in multiple developmental domains. Pediatr Psychol. 2005;30(3):247-255.
117. Welzel-Muler K, Stephan K, Nekahem D, Hirst-Stadlmann. A, Weichbold V. Hearing screening: normal newborn nursery versus neonatal intensive care unit. Int Pediatr. 2001;16(1):1-3.
118. Lutman ME, Davis AC, Fortnum HM, Wood S. Field sensitivity of targeted neonatal hearing screening by transientevoked otoacoustic emissions. Ear Hear. 1997;18(4):256-76.
119. Neault MW. Pediatric audiology. In: Wetmore RF, eds. Pediatric Otolaryngology, Principle and Practice. 2nd ed. New York: Thieme; 2000: 191-200.

Cite this article as: Khalifa KA. Management of neonatal hazards in intensive care units: a review. Int J Sci Rep 2015;1(1):3-21.