

Editorial - Educational

Challenges in Neonatology and Ethical Considerations

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Neonatology is a subspecialty of pediatrics, which has technologically advanced in the past 40 to 50 years. "Neonatology" and "Neonatologist" were first introduced in 1960¹. The first Sub-Board Examination and the first meeting in Neonatal-Perinatal Medicine were held in 1975¹. Medical care of an infant within the first twenty-eight days of life (a neonate) is provided in the neonatal intensive care units (NICU). The patients of NICU include preterm infants, acutely ill-term infants and infants with congenital anomalies. One of the great challenges in neonatology is managing smaller premature babies^{2,3,4}.

Gestational Age and Viability

Gestational age is expressed in weeks. Term gestation is 40 completed weeks. A preterm infant is born before 37 weeks, and an extremely preterm (EP) infant is born at less than 28 weeks. These babies pose a great challenge in neonatal medicine, but the most challenging are babies born at 23 and 24 weeks of gestation⁴.

The World Health Organization (WHO) defines viability as the gestational age at which the chances of survival are greater than 50% with or without medical care; it is approximately 24 weeks of gestation in developed high-income countries and 34 weeks in low-income countries. The biological criteria consider the maturity of the fetus, especially the lungs. Lung maturity is the major limiting factor for survival. The surfactant appears at 22 to 23 weeks of gestation. It is at this gestational age when infants might be able to survive^{5,6}.

Although the survival of the smallest babies has improved over the years, there is a growing concern regarding the associated increase in survivors with disabilities^{7,8}.

When an infant is born less than 28 weeks, two important factors are to be considered: if the baby would survive and what is the long-term risk?

Neonatal Survival

In the 1960's, the reported survival rate of infants born below 1kg and before 30 weeks of gestation was approximately 5%; these infants were considered non-viable⁹. There is continued improvement of medical care, such as the introduction of Continuous Positive Airway Pressure (CPAP), mechanical ventilation strategies, the use of exogenous surfactant, antenatal steroids and the avoidance of postnatal steroids¹⁰. The data from

Europe, Australia and the UK for infants born in the 1990's at less than 26 weeks of gestation reveals survival rate of 50% to 80% and as high as 40% at 23 weeks of gestation¹¹. Studies from USA and Canada showed similar trends; a 1kg baby who had a reported mortality risk of more than 90% in the 1960's, had a survival rate of more than 90% in the 1990's. Babies with birth weights less than 750g had a reported survival rate of more than 50% in the 1990's¹². Epicure study performed in the UK and Ireland on babies born in 1995 and 2006 revealed improved survival in extremely preterm infants, including infants born at 23 weeks of gestation. Studies from Sweden, US, Australia and France reported similar improved survival rates. Sweden has reported the best survival rates of more than 50% even in babies born at 23 weeks of gestation. Studies performed from 1984 to 2004 of more than 14,000 extremely low-birth-weight (ELBW) infants reveals improved survival. The age of viability as defined by 50% survival rate has gone down from 25 weeks of gestation in 1990's to 24 weeks of gestation in early 2000^{10,13-16}.

Long-Term Outcome

Preterm infants are at risk of short-term neonatal complications during NICU stay, such as early onset sepsis (EOS), intraventricular hemorrhage (IVH), late onset sepsis (LOS) necrotizing enterocolitis (NEC), periventricular leukomalacia (PVL), retinopathy of prematurity (ROP) and chronic lung disease (CLD). There is also an increased risk of subsequent neurological deficits, such as cerebral palsy, cognitive delay/mental retardation, visual and hearing deficits, inattention, behavioral disorders and poor performance at school^{10,17,18}. Early neurodevelopmental assessments are performed from 1.5 to 3 years using various Infant Development scales (Bayley or Griffiths); the later assessments are performed at 5 to 18 years using various cognitive tests^{10,19}. Various studies report composite outcomes and classify them as mild, moderate and severe. A severely disabled child is highly dependent, has severe cerebral palsy, could not walk, has extreme learning difficulties and is blind or has a severe sensorineural hearing loss. A moderately disabled child is reasonably independent, has cerebral palsy but can walk, has moderate learning difficulties and vision impairment or sensorineural hearing loss correctable with aids. A mildly disabled child is independent, has mild neurological abnormalities without major functional problems and might have mild learning difficulties and hearing impairment or eye problems (refractive errors, squints) that do not need aids²⁰.

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Studies from Australia, Europe and the UK on neurodevelopment outcome of extremely preterm infants born in the 1990's reveal that approximately 20% to 35% of survivors have substantial (moderate to severe) disabilities¹¹.

Epicure studies included more than 500 surviving extremely preterm babies born in 1995 and more than 1,000 surviving babies born in 2006 at less than 28 weeks. The comparison of neurodevelopment assessment at three years of age between the two cohorts reveal that a higher proportion of extremely preterm babies born at gestational ages of 24 and 25 weeks now survive without a disability. There was an increased survivors' rate with disabilities by 2.6%, but there was improved survival without disabilities (15% in babies born at 25 weeks and 10% in babies born at 24 weeks). The improvement was not significant in babies born at 22 to 23 weeks. A significant number of babies born in 2006 had either mild or no impairment at three years²¹. A study including 700 infants born at less than 27 weeks from 2004 to 2007 performed a neurodevelopmental assessment at 2.5 years of age and revealed that 11% of extremely preterm children were severely disabled compared to 0.3% in term infants. However, no gestational age was spared; 42% of the extreme preterm infants and 78% of term infants had no disability. Morbidities and neurodevelopmental outcomes improve with each week of gestation. Overall, 73% of these babies had mild or no disability. The risk of moderate to severe disabilities had improved with increasing gestational age (60% in babies born at 22 weeks, 51% in 23 weeks; 34% in 24 weeks, 27% in 25 weeks and less than 20 % in 26 weeks)^{17,20}.

These early assessments have high specificity, but have a modest sensitivity to predict future outcomes. In Epicure study, the majority (86%) of the babies with severe disability at 30 months remained severely or moderately disabled at six years with few exceptions which improved to mild and no disability. Infants with moderate, mild or no disability showed a similar trend; some conditions are becoming worse and very few are improving²². The disadvantage continues through childhood and adolescence^{4,23}.

A study in 1997 assessed very preterm infants at the age of 5 years and found that 41% of extremely preterm infants received specialized care compared to 16% term infants; 13% to 21% had severe cognitive delay compared to 3% in the term controls. Mild cognitive delay was also higher in the extremely preterm group (40% compared to 12%)²⁴. At eight years, 91% of these infants were in regular school and 9% went to special school compared to 94% term controls who went to normal school. The special care needs at school increased from 41% at five years to 65% at eight years²³. They continue to use more health or educational resources in middle childhood²⁵. They are also at increased risk of various mental health problems in later years, such as low IQ, inattention, emotional and behavioral problems along with other psychiatric illnesses compared to the term born controls⁴. These subtle disabilities are common even in infants reported to have a normal neurodevelopmental function at 1 to 3 years of age¹⁹.

Early neurodevelopment outcome at 2 to 3 years of life is influenced by short-term complications of prematurity, such as IVH and CLD, whereas the important factors that affect the long-term outcome in school-age were the parents and the family²⁷.

Controversies with Assessments

Early neurodevelopmental assessment has high specificity but low sensitivity in identifying later school-age cognitive deficit. They may not necessarily reflect longer term outcomes. Many infants who had no impairments at 2 to 3-year assessment had the lower end of the normal cognitive function. They continued to be at a disadvantage compared to their term counterparts. The neuropsychological disorders (behavioral, conduct, inattention, learning difficulties, school failure and psychiatric illnesses) often occur in surviving extremely low-birth-weight infants (<1000 grams). Various studies have used different denominators which make these percentages confusing and unreliable. Some have used NICU admission, live birth while some have used total infants followed-up. One of the biggest confounders is the time lag in reporting these outcomes. There is a gradual evolution of neonatal care over the last 3 to 4 decades. The outcome assessments may be less relevant for current care practices^{19,27,28}.

Ethical Consideration

The ethical question to consider is should we continue providing neonatal intensive care to all the extreme preterm infants despite the high risk and poor long-term outcome? Ethics in medicine are influenced by several factors²⁹. There are two philosophies of care; a traditional "disease-oriented" philosophy that believes in the "sanctity of life" and aims at preserving life at any cost and a "person-oriented" philosophy, which considers the "quality of life" and view some impairments as a fate worse than death⁵.

The "sanctity of life" believes life is sacred. Letting the patient die in view of the bad outcome is considered unethical³⁰. The supporters of the "sanctity of life" concept argue that the definition of quality of life is highly subjective. An infant may suffer from varied severity of neurological problems; these may be acceptable by some and unacceptable by others³¹. It is difficult to predict and challenging to stipulate "good or bad" or "acceptable or unacceptable" outcomes. The "sanctity of life" concept supporters do not see any moral difference between normal and disabled people. They proclaim that all humans must be treated alike. Doctors, nurses and parents should not simply let babies die because of the fear of disabilities³⁰. Parents and survivors (disabled people) have more positive outlooks regarding the quality of life. Disabled people have reported that they are satisfied and happy with their lives^{30,32}.

The "person oriented" approach believes in the "quality of life" as the main influencing factor. They believe in the de-escalation of intensive care and shifting to palliative care in individuals where a meaningful survival is not possible³¹. The "quality of life" supporters believe that prolonging life in certain sick infants is inhumane, particularly when death seems imminent, treatment is proving futile and there is no hope for a meaningful survival. It delays the course of dying, prolongs suffering and shows disrespect to the patient³³⁻³⁵.

In neonatology, the "sanctity of life" proposition (disease-oriented) is often reasoned out for "quality of life" judgments (person oriented). This is a sensitive issue and debatable area.

Decision-Making in the NICU

Decision making in a NICU is a challenge; it is not always possible to predict the mortality and determine the risk of impairments^{30,36}. Obstetricians and neonatologists have a tendency to misjudge the mortality and disability risks in extremely preterm infants⁷. The uncertainty regarding intact survival may cause a delay in initiating or providing suboptimal care, thus may reduce the probability of an impairment-free survival. An aggressive and prompt resuscitation and subsequent intensive care improve not only survival, but also intact survival in these tiny babies⁷. A baby should not be taken as a mere percentage, but as an individual human being and must be given a fair chance to receive required care³³. There may be a time during the subsequent course in the NICU when the continuation of intensive care may not be appropriate and palliative care to relieve pain and other distressing symptoms seems reasonable. This is usually performed in a severely ill baby, where no treatment choice is being effective and death is imminent. It is also considered in cases where meaningful survival is not possible, such as in a pre-viable infant (under 24 weeks) when a child has developed severe bilateral grade 4 intraventricular hemorrhage, severe birth asphyxia, progressive neuromuscular paralysis, anencephaly or a serious genetic condition like trisomy 13 and 18^{5,30}.

Counseling of the parents should be guided by the most pertinent and recent literature while acknowledging that it may not always be possible to ascertain the extent of impairments in an individual baby³⁷.

Once a consensus is achieved, and a decision is made to de-escalate the treatment in a baby with no prospect of meaningful survival, palliative care must be considered. The main focus should be to provide as much comfort as possible, mainly pain relief³⁰.

Children at risk of disabilities who are discharged from the NICU require proper follow-up. They and their families require access to all the support services for disabled people³⁰.

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