Review Article

Indian Journal of Maternal-Fetal and Neonatal Medicine
Volume 3 Number 1, January - June 2016
DOI: http://dx.doi.org/10.21088/ijmfnm.2347.999X.3116.5

Predictors of Outcome in High Risk Neonates

Suchit Tamboli*, Ram Dhongade, Sunil Mhaske***, Liza Bulsara****, R.B. Kothari*****

Author's Affiliation:
*Director, Chiranjiv Clinic and Child Development Center 3783, Ghumare lane, Ahmednagar, ** Director Shaishav Clinic Lakshmi Road Opposite Vijay Talkies, Pune. *** Professor & Head, ***Resident,*****Associate Professor, Department of Paediatrics, PDVVPF's Medical College, Ahmednagar.

Reprint Request:
Suchit Tamboli, Asso. Prof, Department of Paediatrics, PDVVPF's Medical College, Vilad Ghat, Ahmednagar, Maharashtra 414111
E-mail: tamboli.k@gmail.com

Abstract

High risk neonate is at risk for neonatal mortality and morbidity. Short term outcome are predicted by combination of BPD, PDA, IVH, PVL, RDS, NEC etc. For better neonatal long term outcome recognition of high risk pregnancy, prevention of preterm births, increase transport facilities and multidisciplinary early intervention is necessary.

Keywords: High Risk Neonate; Predictors of Outcome; Early Intervention; Prevention of Preterm Birth; Transport to Level 3 Prenatal Centre; Multidisciplinary Team.

More and more smaller and sicker neonates are surviving over the past three decades with improved treatment modalities. Concurrent advances in reproductive technology have resulted in increasing numbers of preterm and multiple births. These high risk neonates account for infant mortality and morbidity and evidence shows that despite the neonatal interventions very low birth weight (VLBW) remain at a substantial risk for long-term morbidity including cerebral palsy, mental retardation, developmental delay, school problems, behavioral issues, growth failure and overall poor health status [1].

Outcome refers not only to initial 2 years but also includes school age, adolescence & adult life. Focus is moving from very VLBW to extremely low birth (EBLW) & now to extremely immature infants (< 25 weeks gestation) because with decreasing birth weight and gestational age more severe and different morbidities have become apparent [2].

Last two decades have seen tremendous interest in neonatal intensive care all over India but sadly very little attention has been paid to less glamorous care such as systematic follow up of high risk infants. Some of the most elegantly done follow up studies in India are 'Pune Children's Studies' by Chaudhari et al on children born in late eighties [3]. However neonatology in India has taken great strides in last 10 years and hence there is a need to continue to correlate neonatal risk factors and interventions with long term outcomes to help us improve our strategies and also understand cost-efficacy of this expensive care. This article is an overview of predictors of long term outcome of a high risk neonate who is exposed to perinatal stress.

Antenatal Predictors

Ultrasound and Doppler Examination

Abdominal circumference below fifth percentile predicts immediate outcome. The best antenatal predictor of poor outcome was abnormal venous flow, based on the DV Doppler. At five years of age 54% of children born after raised umbilical /cerebral or U/C ratio were functioning below the expected level, compared to 20% of children born with normal U/C ratio. There is association between abnormalities in the fetal aorta Doppler studies and minor neurological disability[4].

Maternal Diseases and Antenatal Steroids

Preterm born to mother with preeclampsia do better because they have less IVH and PVL but in

contrast preterm infant exposed to chronic choriamniotis and elevated pro-inflamatory cytokines in amniotic fluid have increased risk of PVL and Cerebral Palsy [5]. Single dose of antenatal steroids is well known to prevent RDS however fetal exposure to multiple/weekly courses of steroids is known to result into smaller head size [6]. Multiple prenatal factors like infection, metabolic, anoxia, toxic, genetic, infarction etc may result into spastic Cerebral Palsy.

Natal Predictors

Birth Asphyxia

Drage et al. found that 5 minutes Apgar score gave a better prediction for neurological abnormality later on and post asphyxial encephalopathy grade III could predict significant morbidity and sequelae among survivors. An interesting finding from a large prospective NCPP study at USA and case control study done at western Australia have conclusively shown that not more than 10% of cerebral palsy cases were at best related to birth asphyxia. Sigmund Freud who suggested that the baby may have asphyxia primarily because of a prenatal structural or metabolic insult to the baby 's brain and that asphyxia is only a middle episode of a long drama starting with intrauterine asphyxia and presenting with a low Apgar score and neurological deficit later on [7].

Postnatal Predictors

Birth Weight

Birth weight > 800 grams seems to be one of the good predictors of intact survival. However the developmental outcome of ELBW infant is determined by a complex interaction of medical and environmental factors acting on the developmentally vulnerable premature brain. 7-17 % has neuro sensory impairment and 13-37 % delays in cognitive function and also quite high rate of behavioral problems. Since 2000 there is net increase in survivors without impairment however the rates of subnormal cognitive function continue to remain unchanged. VLBW and ELBW children have more respiratory illnesses leading to hospital readmissions and other health problems in initial years but those extremely premature entering adulthood showed no significant differences between the ELBW adults and term-born controls with regards to rates of high school graduation, college enrollment permanent employment and independent living status.

Prematurity

The greater the immaturity and the lower the birth weight, the greater the likelihood of intellectual and neurologic deficit. 50% of 500-750g infants have a significant neurodevelopmental impairment (blindness, deafness, mental retardation , cerebral palsy.)

With increasing gestational age, survival rates increase to approximately 15% at 23 wk, 56% at 24 wk, and 79% at 25%. The survival of infants <24wk gestation , weighing <750g with a 1- min Apgar score <3 is 30% . These infants are also at risk for poor neuro developmental outcome. Birth-weight – specific neonatal diseases such as grade III IVH , severe group B streprococcal pneumonia, and pulmonary hypoplasia also contribute to a poor outcome.

Cerebral Palsy

Children with 'transient dystonia' had an excess of school problems at a mean age of 6.7 years [8].

The developmental outcome of ELBW infant is determined by a complex interaction of medical and environmental factors acting on the developmentally vulnerable premature brain. 7-17 % has neuro sensory impairment and 13-37 % delays in cognitive function. Disability rate as high as 49 % is reported [9]. Spastic diplegia is most commonly associated with pre-term birth.

Cerebral Palsy is caused by not only prematurity or low birth weight but a series of life threatening medical events. Spastic Cerebral Palsy is caused by prenatal factors like infection, metabolic, anoxia, toxic, genetic, infarction. Ataxic cerebral palsy is caused by perinatal cause such as anoxia. Atonic cerebral palsy is caused by post natal factors such as toxin , trauma, infection [7].

Many surviving LBW infants have hypotonia before 8 mo corrected age, which improves by the time they are 8 mo-1yr old. This transient hypotonia is not a poor prognostic sign [10].

School age outcome of premature children consists of significantly poorer intelligence, achievement & higher rates of behavioral problem. These scores are directly proportional to the degree of immaturity. Problems can be poor vocabulary skill, significant delay in reading, spelling and mathematics. The problems that appear to be related to academic failures include deficits in attention; memory and behavior are affected in preterm, ELBW babies.

Hypoxic Ischemic Encephalopathy

Ataxic cerebral palsy is caused by perinatal cause

such as anoxia. It causes severe motor disability. They have poor score on cognitive, neuropsychological, educational and behavioral assessments even with no functional motor deficit; memory and attention or executive functions were impaired in severe groups. There is difficulty with language, spelling, letter recognition, visual and short term memory. ELBWchildren perform poorly on tests of visual-motor performance but are closer to controls on measures of language.[9]

Hearing Impairment

Hypoxia damages the hair cells of the cochlea and hearing impairment is often due to hypoxia ischemia.[9]

Seizures

HIE grade III is associated with seizures and is a bad prognostic factor for long term intact neurology.

IVH, PVL

Although incidence of periventricular hemorrhage has decreased, the rates of PVL remained unchanged thus leading to adverse neurological outcome. Isolated visual impairment can rarely be seen as a consequence of PVL.

RDS, BPD, PDA

Complications of RDS like asphyxia, cardiac arrest affect neurodvelopmental outcome. RDS may be associated with PDA. Delayed closure of the PDA is associated with hypoxia, acidosis, increased pulmonary pressure secondary to vasoconstriction, systemic hypotension, immaturity, and local release of prostaglandins, which dilate ductus. There is a relationship between early adrenal insufficiency ,ductal patency , airway inflammation and the development of BPD. VLBW infants with PDA are at increased risk of more prolonged and more severe RDS , bronchopulmonary dysplasia and death due to progressive respiratory failure. Although 85 to 90 % of all infants surviving RDS after requiring ventilatory support with respirators are normal , the outlook is much better for those weighing more than 1500 gm. The long term prognosis for normal pulmonary function in most infants surviving RDS is excellent. Survivors of severe neonatal respiratory may have significant pulmonary and neurodelopmental impairment . Somehow pulmonary hemorrhage does not seem to be associated with increased long term morbidity.

NEC: Premature infants with NEC who require surgical intervention or who have concomitant bacterimia are at increased risk for adverse growth and neurodevelopmental outcome. [10]

Hyperbilirubinemia

Disruption of the blood brain barrier by disease, asphyxia, and maturational changes in blood brain barrier permeability affect risk. The precise blood level above which free bilirubin is toxic for an individual infant is unpredictable ,the duration of exposure needed to produce toxic effects is unknown .The more the preterm the infant the greater the susceptibility to kernicterus. The commonest outcome known is athetoid cerebral palsy.

Renal Injury in Asphyxiated Newborn

Oliguria in the perinatal period is a sensitive indicator of infants at risk for long term neurologic deficits. Oliguria was significantly associated with clinical signs of HIE, including seizures, death and long term neurological deficits.

Sepsis

There is association between infection and brain injury, including severe intraventricular hemorrhage and periventricular leukomalacia. This leads to poor neurodevelopmental outcome. Elevated peripheral neutrophil counts in the first 96 h of life in term infants with HIE may contribute to abnormal neurodevelopmental outcome. Neonatal infections among ELBW infants are associated with poor neurodevelopmental and growth outcomes in early childhood. [11] Atonic cerebral palsy is caused by post natal factors such as toxin ,trauma, infection.

Hypoglycemia

Both premature and full term infants are at risk for serious neurodevelopmental deficits from equally low glucose levels .The risk is related to the depth and duration of hypoglycemia.Early diagnosis and treatment of neonatal hypoglycemia is crucial to prevent future neurological sequelae. Even in the absence of gross hypoglycemic encephalopathy it can be cause of epilepsy even in full term babies due to delayed feeding which has been elegantly described by Udani et al Aggressive correction of hypoglycemia is more important in presence of additional perinatal risk factors. [12,13]

Treatment Modalities in a High Risk Neonate

Surfactant Treatment

In surfactant treated neonates moderate and severe pulmonary haemorrhage is associated with an increased risk of death and short term morbidity. Long term morbidity not affected.

Role of Ventilation

The prognosis of ELBW with 'protected long term' Ventilation remains grim. Those intubated have diminished survival and high rates of impairment. Parents of these infants should be informed of changes in prognosis as the time of ventilation increases. Severe hyperoxaemia and severe hypocapnia were associated with adverse outcome in infants with post-asphyxial HIE. During the first hours of life, oxygen supplementation and ventilation should be rigorously controlled [14].

Early HFOV when used with a lung recruitment strategy in combination with surfactant replacement may ameliorate acute neonatal lung injury that predisposes some preterm infants to develop chronic lung diseases [15].

Role of Inhaled Nitric Oxide

The results of NO inhalation are very promising. Use of NO has improved neurodevelopmantal outcomes at two years of age. Inhaled nitric oxide decrease the risk of chronic lung disease and death, as well as of severe intraventricular hemorrhage or periventricular leukomalacia [16].

Hyperoxia

Exposure to the extra uterine environment to high inspired oxygen concentrations produces cellular damage due to free radicle release and is a well known cause of retinopathy of prematurity (ROP), however lower the gestational age, lower the birth weight, and the sicker the infant add to the risk is for ROP.

Environment, Socioeconomic Status, Parental Education and Nutrition, As Predictors of Outcome

While under nutrition is harmful, over nutrition seems to harm lower birth weight in adult life. Studies all over suggest, that environment certainly contributes in the long run which has been shown by Dr Chaudhari et al in her "Pune children Studies-Biology vs Environment". Bavdekar et al from Pune have shown that a combination of small size at birth, followed by accelerated weight gain during childhood appeared to be responsible for an increased risk of insulin resistance in prepubertal children consistent with earlier findings by Barker et al. Combination of perinatal risk factors and non optimal rearing conditions can lead to poor developmental outcome, where as good rearing conditions can ameliorate the risk. Low social class is a frequently used index of non optimal rearing environment because of the associated social and economic disadvantages. Poor social class is powerful determinant of intellectual status in preterm infants.

Conclusion

Short term outcome and 2 years outcome are predicted by combination of BPD, PDA, IVH, PVL, RDS, NEC etc. The more the diagnoses an infant has the more severe those diagnoses the more likely that infant show adverse response on assessment at 18 to 24 months. Early outcomes do not reliably predict school age performance, behavioral problems, specific learning disabilities etc and studies have shown adverse outcomes have remained unchanged over last 2 decades. Therefore the need for a multidisciplinary follow up clinic under guidance of a neonatologist cannot be overemphasized which should be explained to the parents during discharge planning from NICU. Early interventions in such clinics are aimed at minimum disability and can rehabilitate the child but can not give cure. Therefore enhancing the recognition of high risk pregnancies, developing strategies to prevent preterm births, increasing maternal transports to level III prenatal centers, improving neonatal transport facilities to ensure prevention of hypoxemia and hypoglycemia and broadening the scope and availability of prenatal care to periphery will lead to better neonatal long term outcome. More attention may be paid to hypo/hyper oxemia and also hypocarbia and better infection control. Areas of research include usage of nitric oxide, optimal nutrition and early intervention programs for rehabilitation of children with adverse outcomes.

References

1. Deanne Wilson – Costello; Is there evidence that long term outcomes have improved with intensive care?; Seminars in Fetal & Neonatal Medicine. 2007; 12: 344-354.
2. Saroj Saigal, Peter Rosenbaum; What matters in the long term : Reflections on the context of adult outcomes versus detailed measures in childhood ; Seminars in Fetal & Neonatal Medicine. 2007; 12:

415–422.

3. Sudha Chaudhari, Madhumati otiv, Anjali Chitale , Mahendra Hoge , Anand Pandit, Anjali mote ; Pune Low Birth Weight Study – Cognitive Abilities and Educational Performance at Twelve years; Indian pediatrics. 2004; 41: 12.
4. Andrew C.G Breeze, Christoph C. Lees; Prediction and perinatal outcomes of fetal growth restriction; Seminars in Fetal & neonatal Medicine. 2007; 12: 383–397.
5. Editorials; Predictors of outcomes in preterm infants: Which ones and when? ; The journal of Pediatrics. Feb. 2001; 138(2): 153-155.
6. Bonanno C, Fuchs k. Wapner RJ. ; Single versus repeat courses of antenatal steroids to improve neonatal outcomes : risks and benefits; Obstet Gynecol Surv. 2007 Apr; 62(4): 261-71.
7. Nair MKC,Pejavar RK.Birth asphyxia and cerebral palsy;Child development 2000 and beyond;prism books. 2000; 9-14.
8. Joe Fawke.Neurological outcomes following preterm birth; Seminars in Fetal & Neonatal Medicine. 2007; 12: 374-382.
9. Rennie J.M., Cornelia F. Hagmann N.J. Robertson; outcome after intrapartum hypoxic ischaemia at term; Seminars in Fetal & Neonatal Medicine. 2007; 12; 398-407.
10. Kliegman.Beherman.Jenson.Stanton; The new born infant; Nelson Textbook of Pediatrics ; Elsevier. 2007; 1: 679-713.
11. Adams-CI, Stoll BJ. Neonatal infection and long-term neurodevelopmental outcome in the preterm infant; Curr Opin Infect Dis. 2006 Jun; 19(3): 290-7.
12. YalnizogluD,HaliloguG ,Turanli G.Neurological outcome in patients with MRI pattern of damage typical for neonatal hypoglycemia ;Brain development. 2007 June; 29(5): 285-92.
13. Udani V.Pediatric epilepsy-an Indian perspective; Indian JPediatr. 2005 Apr; 72(4): 309-13.
14. Klinger , J. Beyene , P. shah, M. Periman ; Do hyperoxaemia and hypocapnia add to the risk of brain injury after intrapartum asphyxia ? ; Arch. Dis. child. Fetal Neonatal Ed. 2005; 90; 49-52.
15. Dale R. Gerstmann, Kari wood , Annie Miller , Mike Steffen, Bob Ogden, Stephen D. Minton ; Childhood Outcome After Early High – Frequency Oscillatory Ventilation for Neonatal Respiratory Distress Syndrome ; Pediatrics. Sept. 2001,108(3): 617-623.
16. Aren K.L . Mestan , Jeremy D. Marks , Kurt Hecox, Dezheng Huo, Michael D. Schreiber ; Neurodevelopmental Outcomes of premature infants treated with inhaled nitric oxide ; N. Engl J Med. 2005; 353: 23:32.