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Follow-up Studies – Beyond Survival

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Advances in antenatal medicine and neonatal intensive care, including antenatal corticosteroids, delivery room resuscitation, surfactant use, improved ventilation techniques, and nutritional management, have resulted in improved survival rates of preterm infants. The need to report follow up outcomes of babies who are born very low birth weight (VLBW) is being increasingly recognized over the last two decades [1,2]. Similar to many developed countries, survival of Indian VLBW babies is also improving. Therefore, there is a paucity of prospectively recorded developmental outcomes from India. The paper by Modi, *et al.* [3] published in this issue is a pioneering effort in this direction. The strengths of the study are detailed descriptions of care process that make it possible to compare with other centers. It would have been ideal to compare the outcomes of VLBW babies from different centers with differences in care process. Comparison with normal birth weight (NBW) babies has limited novelty. Most studies on outcomes like this one, are based on single-hospital, small cohorts and short duration of follow up. A few population cohorts with longer follow up are published [4,5] but there are very few studies from India [6]. Different authors have used different developmental assessment tools and reported normal or abnormal at varied ages thus making the comparisons difficult, hence, the fundamental interest of identifying modifiable risk factors in care process has not been served.

THE IDEAL WAY TO FOLLOW VLBW INFANTS?

An expert panel of the American Academy of Pediatrics,

National Institute of Child Health and Human Development, Vermont Oxford Network, and California Children's Service, has jointly put forward an evidence-based recommendation to assess quality of follow-up for VLBW infants [1]. The panel recommends post-discharge assessment in a total of 70 indicators in the following areas: general care, physical health, vision, hearing, speech, and language, developmental and behavioral assessment; and psychosocial issues. The panel describes in detail the areas of assessment, timing of tests and what intervention should be planned in case of a deviation from normal. National Neonatology Forum (NNF), has also outlined follow-up guidelines for neonatal intensive care unit (NICU) graduates.

IMPORTANT OUTCOME INDICATORS

Most published reports of neurodevelopmental outcome in infancy focus primarily on the incidence of severe disability, often defined as mental retardation, cerebral palsy, epilepsy, blindness, and/or moderate to severe hearing impairment. This has historically been the neurodevelopmental outcome of interest owing to the severity of the developmental impact of these severe and often combined morbidities. But, interest has shifted to the larger proportion of VLBW infants who are not severely brain injured, and their outcomes [7]. The most common impairment seen in VLBW and ELBW infants at 18 and 30 months is cognitive impairment [4]. Bayley scores of less than 70 (more than 2 standard deviations below the mean) are considered severely impaired. Reported rates of cognitive impairment throughout

childhood range from 14% to 39% at 24 weeks, 10% to 30% at 25 weeks 4% to 24% at less than 26 weeks, to 11% to 18% at less than 29 weeks [8]. At 30 months corrected age, 30% of children had impaired cognitive functioning. Additionally, although measures of intelligence in children at school-age provide a reliable assessment of general cognitive functioning, they do not identify specific learning disabilities. In addition to impairments in global cognitive functioning, more subtle cognitive impairments are often detected only by school age [4,8,9].

DURATION OF FOLLOW-UP

Most large clinical trials in the field of neonatology now include a measure of neurodevelopmental outcome, but the optimal age of assessment has not been agreed on. Due to the administrative challenges of long-term follow-up, including cost, tracking and feasibility, most authors have published data on shorter long-term outcomes (18 to 22 months corrected age). There is, now, an increasing evidence of adverse outcomes into school age and adolescence [6,7]. Development, neurological examination and vision assessment should ideally be followed till at least 5-6 years [1].

WHY FOLLOW-UP?

Recent studies support that a combination of biologic and environmental factors contribute to survival and outcome of preterm infants. Factors significantly associated with an increased likelihood of a favorable outcome for infants 22 to 25 weeks' gestation who received intensive care were higher gestational age, higher birth weight, female gender, singleton, and antenatal steroids, all factors known at birth [8]. Multiple births are an important risk factor for both death and neuro-developmental impairment among VLBW infants [8]. Common neonatal morbidities, including bronchopulmonary dysplasia (BPD), retinopathy of prematurity, necrotizing enterocolitis, and infection, have also been associated with poor cognitive function and academic abilities in infancy. Rates of neurodevelopmental impairment at 18 to 22 months corrected age is directly proportional to duration of need for mechanical ventilation in the NICU. BPD has been implicated as a risk factor for cerebral palsy in multiple studies [8]. It also has an independent negative effect on motor outcome at 3 years.

Cranial ultrasound abnormalities - periventricular leukomalacia (PVL) are the strongest predictors of

cerebral palsy. There is a 3- to 10-fold increased risk of cerebral palsy associated with cystic PVL [8]. The presence of hydrocephalus may increase the risk by 12.2 times, and the presence of PVL and hydrocephalus by 15.4 times.

It is important to recognize babies at-risk and those with modifiable factors in their health, so that outcomes can be improved. Hence, time has come when nations / regions (not just one hospital) must record outcomes of all preterm / VLBW babies till at least school age. They must also record variables likely to be associated with outcomes and care process. This will pave the way forward to improving outcomes of these at-risk babies we are saving.

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