

Influence of high-risk factors on early neurodevelopmental outcome of high-risk newborns and role of follow up compliance

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Aims and Objective: Influence of high-risk factors on early Neurodevelopmental and Neuromotor outcome at 3 months of corrected age and role of continued Newborn follow up care. **Participants:** All high-risk newborn discharged from tertiary care level NICU were enrolled for study at discharge. **Method:** In this prospective observational study, the influences of various sociodemographic factors as prematurity, birth weight, maternal education, family size, clinical profile, sociodemographic factors, parity, feeding patterns and follow up compliance on the neuro developmental outcome at 1 and 3 months of corrected age were studied. **Results:** Prematurity, ELBW and VLBW infants, Male infants, Low socioeconomic status, disease-causing CNS injury (Severe Birth asphyxia, meningitis), poor maternal education, mixed and top feeding, longer duration of NICU stay, poor follow-up attendance and compliance were significantly($p < 0.05$) associated with poor neurodevelopmental outcome at 1 and 3 month of corrected age. **Conclusion:** Collaborative efforts shall be made to educate the parents of high-risk newborns towards the need and importance of neonatal follow-up and early stimulation and intervention therapy to decrease the future neurodevelopment abnormality. Special attention shall be given to premature LBW infants of the less-educated mother, of poor socioeconomic status and residing in distant rural areas having poor access to specialized center-based services.

Keywords: Collaborative, Influences, Neurodevelopment

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Introduction

Advances in Perinatal care and the establishment of improved neonatal services have increased the survival rates of many high-risk newborns in developing countries. Development delay is anticipated in these babies and its early recognition is important, so as to provide early interventional services. As per NFHS 4 infant mortality is 41/1000 live birth and more so higher in rural areas 46 in comparison to urban areas 29 per 1000 live birth. Prematurity (35%), Birth Asphyxia (20%) sepsis (20%) are the major causes of mortality [1].

And a larger proportion of infants who survive have a higher risk of abnormal development in comparison to normal newborn [2]. Parents of the developmentally delayed child also have a poor quality of life, mental burnout, and poor mental health in comparison to others. It also has a detrimental effect on other siblings in the family and the overall growth of a Nation [3,4].

This study was conducted to see the influence of various risk factors on the early neurodevelopmental outcome and their correlation with poor follow up compliance, in order to improve newborn follow up services and to improve early identification and early intervention programs to these high-risk newborns.

Aims and Objective

Influence of high-risk factors on early Neurodevelopmental and Neuromotor outcome at 3 months of corrected age and role of continued Newborn follow-up care

Material and Method

This was a prospective observational follow-up study conducted at Shyam Shah Medical College and associated Gandhi memorial hospital Rewa, Madhya Pradesh, India. on High-risk Newborns discharged from NICU at NFC (Newborn Follow-up Clinic) over the 1-year period. All high risk newborn as LBW infants of weight < 1800gm and/or gestation <35 weeks, SGA/IUGR, severe birth asphyxia, mechanical ventilation for >24 Hr, shock requiring vasopressor support, culture-positive sepsis, meningitis, seizures, significant pathological NNH, major congenital malformation, IEM, congenital infection and babies with abnormal neurological examinations at discharge were enrolled for study,

Newborns expired, referred and lost to follow-up during the study period were excluded. Follow up visits were scheduled as per NNF guidelines at 2, 6, 10, 14 weeks of postnatal age, 3 months 6 months [5].

At discharge and follow up, detailed history and examination were done to assess Growth, feeding, and neurodevelopment. Data were collected and recorded on predesigned Pro-forma. Parents were counseled and educated regarding home-based Early Stimulation therapy to all infants at risk for abnormal neurodevelopment and showing abnormal neurological examination on discharge.

During hospitalization, and after discharging early Stimulation therapy was given by parents themselves under supervised education in the pediatric department, it included different domains of intervention: Motor, Visual, Auditory, Tactile(relational) and environmental [6].

Detailed neurological examination of high-risk newborn infants was done at 1 month and 3 months corrected postnatal age, Upto 1month RENAS scale of neonatal neurobehavioral examination and between 1 - 3 months of age and beyond neurodevelopment and tone was assessed by DDST-II and Amiel Tison method respectively.

Renasc Scale is a modified form of Brazelton's Neonatal Behavioural Assessment Scale(NBAS)[7] is easily administrable, making it suitable for busy setting, it consists of 10 items each has 5 scores, it was recorded as abnormal if the score was < 2 in any item or a total score was < 20.

DDST-II: is a simple, clinically useful tool for early detection of serious development delays in apparently normal infants and children(asymptomatic but having perineal risk factors) from 1 month to 6 yr of age, confirming suspicions with the objective tool and in monitoring children with development problems, serially. It consists of 125 items in 4 development domains, each item has 25th., 50th, 75th, and 90th mark. Infant age is plotted by age line in the chart in each domain.

The test was interpreted normally if the child was able to pass 3 items on the left side of age line(above 75% mark) and the maximum number of 1 cautions (age line falls between 75th and 90th and child fails or refuses that item) and abnormal if the child fails an item that falls on Left side of age line at 90% mark and has 2 or more cautions [8].

Amiel Tison method [9] is a screening test for neuromotor assessment, the predictive value of this test at 3 months examination for normal outcomes at 12 months is 93%. hypertonia or hypotonia was defined by measuring adductor, popliteal, ankle dorsiflexion, and scarf sign. Hypertonia in the upper and lower limb is defined when the tested angle is restricted on less than age-specific norms. Adductor and popliteal angles are best studied Age-specific norms angles for Amiel Tison tone assessment

| Months | 3 | 6 | 9 | 12 |
|-----------------|--------|--------|---------|---------|
| Adductor angle | 40-80 | 70-110 | 100-140 | 130-150 |
| Popliteal angle | 80-100 | 90-120 | 110-160 | 150-170 |

Influence of various factors as prematurity, birth weight, maternal education, family size, disease profile, sociodemographic factors, parity, feeding patterns, duration of NICU stay, no of followup visits and followup compliance were assessed to see the effect on the early neurodevelopmental outcome at 1 and 3 months of corrected age. Abnormal neurodevelopment outcome variables for this study were defined by Abnormal DDST results at 1 month and Abnormal DDST results or abnormal tone at 3 months.

Statistical Analysis: data was analyzed using software SPSS 23 for windows. Univariate and bivariate analysis was carried out using the two-tailed Fisher exact test or chi-square test for categorical variables. Critical levels of significance of the results were considered at a 0.05 level i.e. $P < 0.05$ was considered significant. And $p < 0.0001$ was considered highly significant. This study was given ethical clearance by SSMC ethical comity and written consent was taken from parents of the high-risk newborn before enrolment for this study.

Results

Total of 150 newborns was enrolled for study at the time of discharge from NICU, 140 newborns were examined at 1 month (corrected for prematurity) and 10 were lost to followup, a total of 98 newborns were followed up to 3 months of corrected age and assessed for development, rest were lost to followup.

Table-1: Neurodevelopmental outcome at 1 month of corrected age n=140.

| | Variables | N | Abnormal (41) | % 29 | P value | OR | Univariate 95%CI Lower Upper | |
|----------------------|---------------|-----|---------------|------|----------------------------|------|------------------------------|-------|
| Gestational age | <34 weeks | 53 | 19 | 35.8 | prematurity $p=0.05$ | 2.6 | 0.9 | 7.4 |
| | 34-37 weeks | 35 | 6 | 17.1 | | | | |
| | >37 weeks | 52 | 16 | 30.7 | | | | |
| birth weight | <1.5kg | 34 | 14 | 41.1 | $p^* < 0.05$ VLBW vs LBW | | | |
| | 1.4-2.5 kg | 65 | 15 | 23 | | | | |
| | >2.5 kg | 41 | 12 | 29.2 | | | | |
| SEX | M | 85 | 30 | 35.2 | $p^* = 0.01$ | 2.67 | 1.2 | 5.92 |
| | F | 65 | 11 | 16.9 | | | | |
| locality | Rural | 112 | 35 | 31 | $p > 0.06$ | | | |
| | Urban | 38 | 10 | 26 | | | | |
| SES | UM | 16 | 4 | 25 | U vs L and M= $p^* > 0.05$ | | | |
| | LM | 85 | 23 | 27 | | | | |
| | Lower | 39 | 14 | 35.8 | | | | |
| Feeding | EBF | 92 | 22 | 23.9 | $p^* = 0.08$ | | | |
| | Mixed and top | 48 | 19 | 39.5 | | | | |
| Maternal education | >HS | 63 | 23 | 36.5 | $p^* = 0.06$ | | | |
| | | 77 | 18 | 23.3 | | | | |
| NICU stay | <14 days | 58 | 10 | 17.2 | $p^* < 0.006$ | 0.34 | 0.15 | 0.77 |
| | >14 days | 82 | 31 | 37 | | | | |
| Family size | Primi | 81 | 16 | 19.7 | $p^* = 0.003$ | 0.33 | 0.15-0.71 | |
| | Multi | 59 | 25 | 42.3 | | | | |
| Follow up compliance | Non compliant | 53 | 22 | 41.5 | $p^* < 0.05$ | 2.53 | 1.2 | 5.358 |
| | compliant | 87 | 19 | 21.8 | | | | |

| | | | | | | | | |
|------------|------------|----|----|------|------------------------------|------|-----|------|
| Co-morbidi | RDS | 30 | 9 | 30 | p*=<0.001 HIE and meningitis | 0.14 | 0.5 | 0.42 |
| | NNH | 34 | 7 | 20 | | | | |
| | NNS | 62 | 10 | 16.1 | | | | |
| | HIE | 27 | 13 | 48.1 | | | | |
| | Meningitis | 32 | 12 | 37.5 | | | | |

Prematurity, VLBW, male sex, infant of rural locality, of poor SES, top-fed, less educated mother, longer NICU stay, multiparity, poor NICU follow-up, and presence of comorbid conditions as HIE and meningitis were associated with neurodevelopmental outcome at 1 month of corrected age.

Table-2: Neurodevelopmental outcome at 3 months of corrected age n-98.

| | Variables | N | Neuro- development | | p* | OR/CI | Neuromotor (Tone) | | p* |
|---------------------|---------------|----|--------------------|-------|-----------------------------|------------------|-------------------|------|----------------------------|
| | | | Abnormal(21 %) | % | | | Abnormal-14 % | % | |
| GA | <34WK | 31 | 11 | 31 | p*=<0.05 | 5.1CI (1.2-20) | 5 | 12.1 | p=>0.05 |
| | 34-37WK | 31 | 3 | 9 | | | 2 | 9 | |
| | >37 WK | 36 | 7 | 19.4 | | | 7 | 19.4 | |
| BW | <1.5kg | 26 | 9 | 34.6 | p*=<0.05(SGAVs AGA) | | 2 | 7 | p=0.05 |
| | 1.4-2.5 kg | 44 | 5 | 11.36 | | | 5 | 11 | |
| | >2.5 kg | 28 | 7 | 25 | | | 7 | 25 | |
| SEX | M | 53 | 15 | 28.3 | p*=<0.05 | 2.5CI 0.9-7.3 | 10 | 15.8 | p=>0.05 |
| | F | 45 | 6 | 13.3 | | | 4 | 12.9 | |
| locality | Rural | 66 | 15 | 22.7 | p>0.05 | | 11 | 16.6 | p=>0.05 |
| | Urban | 32 | 6 | 18.7 | | | 3 | 9 | |
| SES | UM | 12 | 2 | 16.6 | p*=<0.05 UM vs L | | 1 | 14.2 | p=0.05 |
| | M | 60 | 10 | 16.6 | | | 9 | 16.9 | |
| | Lower | 26 | 9 | 34.6 | | | 4 | 10.5 | |
| Feeding | EBF | 65 | 10 | 15.3 | p*=<0.03 | 0.03CI 0.36-0.13 | 5 | 7 | p=0.01 |
| | Mixed and top | 33 | 11 | 33.3 | | | 9 | 27.2 | |
| Maternal education | >HS | 36 | 6 | 16.6 | p>0.05 | | 5 | 13.8 | p=>0.05 |
| | | 62 | 15 | 24.1 | | | 9 | 14.5 | |
| NICU stay | <14 Days | 48 | 3 | 6.2 | p*=<0.001 | 0.11CI 0.03-0.4 | 3 | 6.2 | p=<0.05 |
| | >14 days | 50 | 18 | 36 | | | 11 | 22 | |
| Family size | Primi | 67 | 13 | 19.4 | p*=>0.05 | | 8 | 11 | p=>0.05 |
| | Multi | 31 | 8 | 25.8 | | | 6 | 19.3 | |
| followup compliance | non compliant | 30 | 12 | 40 | p*=<0.004 | 4.3CI 1.5-12.03 | 8 | 26.6 | p=<0.004 |
| | compliant | 68 | 9 | 13.2 | | | 6 | 8.8 | |
| Morbidities | RDS | 22 | 7 | 31 | p*=<0.05 HIE and meningitis | | 3 | 13 | p=<0.05 HIE and meningitis |
| | NNH | 24 | 4 | 16.6 | | | 4 | 16.6 | |
| | NNS | 42 | 4 | 9 | | | 3 | 7.14 | |
| | HIE | 27 | 10 | 37 | | | 7 | 25.9 | |
| | meningitis | 24 | 7 | 29.1 | | | 5 | 20.8 | |

Prematurity, VLBW, infant of poor SES, top-fed, longer NICU stay, poor NICU follow-up, and presence of comorbid conditions as HIE and meningitis were associated with poor neurodevelopmental outcome at 3 months of corrected age (p=<0.05)

Prematurity, ELBW and VLBW infants, Male infants, Low socioeconomic status, disease-causing CNS injury (Severe Birth asphyxia, meningitis), poor maternal education, mixed and top feeding, longer duration of NICU stay, poor followup attendance and compliance were significantly (p=<0.05) associated

With poor neurodevelopmental and neuromotor outcome at 1 month and 3 month of corrected age.

Discussion

Optimal neurological, neurobehavioral and neurodevelopment Outcome of NICU graduate is

One of the major challenges. Early gestational age and low birth weight are the most significant predictors of poor long-term neurological outcome. Structural changes of the brain, infection, male gender and neonatal intensive care unit course are important factors affecting the adverse outcome. The outcome of premature birth can vary widely, spanning completely normal development to severe neurologic deficits, with most children showing mild to moderate cognitive delay and increased incidence of neuropsychiatric conditions such as anxiety, attention deficit hyperactivity, and autism spectrum disorders.

In this study, 29% of infants had abnormal neurobehavioral status when examined at 1 month corrected age and 21% at 3 months. VLBW and preterm had a higher incidence of the abnormal neurobehavioral score (46%) than Full-term at 1 month and 3 months (40%). Very preterm and late preterm both are known independent significant risk factors for poor outcomes at 3 months age and have poor neurodevelopment outcomes than full-term infants [11].

A similar observation was also observed in other studies that moderate and late preterm children show developmental delay when compared to full-term newborns, and Prematurity and low birth weight infants also had abnormal scores on measures of behavior problems, school readiness, and IQ through 4.5 years of age [12].

According to literature pathophysiology of abnormal development in these newborns is caused by the immaturity of the brain, as the Immature brain reacts to perinatal insults by long-lasting adaptations which include increased neurogenesis as well as delayed neuronal and glial maturation. Delayed maturation of neurons and glial cells is thought to be responsible for most of the developmental and cognitive deficits [10].

Some improvement was observed in the data between 1 month and 3 months, and more infants were performing well at 3 months in comparison to 1 month, which can be attributed to multiple factors as early identification of risk factors, effective counseling regarding early stimulation and persistence on breastfeeding. The role of these factors is also documented in many studies and if implemented early results in a favorable outcome [13].

In this study 33.3% of infants who were >2.5 kg had abnormal muscle tone at 3 months as all of the

HIE infants were in this category and abnormal results in Neurobehavioral and development screening are more common in infants with HIE and meningitis. In the current study groups, many of the infants were having multiple risk factors, and It is also noted that infants with multiple risk factors have the worst neurodevelopment outcome [14,15].

It is seen that gender differences exist in certain neurodevelopment outcomes and are consistent with the literature [14]. According to some studies males, infants are more vulnerable when exposed to prenatal and perinatal adversities [14-17] and this has been attributed to an altered intrauterine metabolic environment [14], different times of postnatal maturation [15,16], or differences in epigenetic transmission [12]. In the current study, it was also observed that male infants continued to show significantly lower scores than females at 1 month however at 3 months results were the same as compared to females.

The strong link between maternal education and socio-economic status and compliance with the utilization of various medical services is well demonstrated [18]. The current study also observed that poor Maternal education, rural locality, large Family were associated with poor neurodevelopmental outcome at 1 and 3 months.

Poor compliance to followup was significantly contributing to poor neurodevelopment outcomes in our results, it emphasizes the importance of regular newborn followup and role of early stimulation and intervention therapy. A significant proportion (80%) of these newborns belonged to lower and middle SES, less educated mothers, rural locality and families living in the distant area and were more likely to be non-compliant to followup [19]. In this study Socioeconomic status of the family was found to significantly influence the neurodevelopment outcome at 1 month. Infants belonging to lower class showed poor neurobehavioral scores than infants of other classes ($p < 0.05$), but no significant association was observed at 3 months of as many the infants (40%) of lower SES were lost to followup.

A statistically significant link between exclusive breastfeeding and favorable outcome in neurodevelopment in comparison to infants on formula or mixed feeding was observed. Prolonged and Exclusive Breast Feeding plays an important role in early neurodevelopment and childhood cognitive outcome.

It is proved that breastfed children have significantly improved overall myelination accompanied by increased general verbal and nonverbal abilities compared to non-breast fed children [20].

Although the family size was not found to significantly affecting development at 1 and 3-months multiparous mothers were less compliant than primiparous, so were more likely to lost to followup. No significant association between maternal age and the early developmental outcome was observed in the current study. Although rural locality and lower maternal education were not significantly associated with poor outcomes in the present study, as more number of less-educated mothers of rural areas were less likely to visit follow-up clinic and were lost to followup [19].

Infants with longer duration of NICU were more likely to have poor performance at 1 and 3 months ($P < 0.001$), as many of these newborns, were having multiple risk factors and more complications than the rest of the study population so were more vulnerable to develop development problems. Collaborative efforts shall be made to educate the parents of high-risk newborns towards the need and importance of neonatal follow up as to provide early stimulation and intervention therapy to decrease the future neurodevelopment abnormality [21].

Conclusion

Close coordination with ASHA and AWW may also improve neonatal follow up in low resource settings, and they can also be trained in home-based early stimulation therapy, which is simple and easy to administer will improve neurodevelopmental outcomes in these infants.

What does this study add to the existing knowledge?

High-risk newborn follow up with early stimulation and early intervention is known to improve neurodevelopmental outcomes in Developed countries, but it is difficult to get a similar outcome in resource-poor settings due to higher rates of poor follow up compliance. The current study identified various sociodemographic factors independently causing the adverse developmental outcome.

It is recommended that Special attention shall be given to premature LBW infants of the less-educated mother, living in a rural area, poor

Socioeconomic status, and family living in distant areas having poor access to specialized center-based services so that these babies can be identified early to provide early intervention and improve developmental outcome.

Author's contributions

Dr. Jyoti Prajapati: Concept, study design

Dr. Aashish Jain: Statistical analysis

Dr. Jyoti Singh: Manuscript preparation

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