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Original Research Article

Neurodevelopmental outcomes in high-risk infants at 12 months: a prospective observational study from Western India

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ABSTRACT

Background: Objectives of the study were to evaluate neurodevelopmental outcomes at 12 months corrected age in high-risk neonates using developmental assessment scales for Indian infants (DASII) and correlate findings with neonatal morbidities.
Methods: This prospective observational study was conducted at a tertiary care hospital in Rajkot, India, involving 88 high-risk infants admitted to the neonatal intensive care unit (NICU). After discharge, follow-up was done at 3, 6, 9, and 12 months corrected age. Developmental assessments (DASII), brainstem evoked response audiometry (BERA) for hearing, and retinopathy of prematurity (ROP) screening were performed. The primary outcome of the study was the proportion of high-risk infants with neurodevelopmental delay at 12 months corrected age, as assessed by the DASII, specifically focusing on mental and motor developmental quotients (MeDQ and MoDQ) <70.
Results: Of 88 infants, 76 completed follow-ups. Developmental delay was seen in 31.6%. MeDQ <70 in 14.5%, MoDQ <70 in 21.1%, any degree of hearing loss in 25%, and ROP requiring treatment in 2.6%. Prematurity, sepsis, and hypoglycaemia were key morbidities associated with poor outcomes.
Conclusions: High-risk infants remain vulnerable to neurodevelopmental delays. Early screening and structured follow-up are essential in Indian settings.

Keywords: High-risk infants, DASII, Prematurity, Developmental delay, India, Neonatal outcome

INTRODUCTION

Despite significant improvements in neonatal survival, neurodevelopmental impairments remain prevalent among high-risk infants globally. Prematurity, low birth weight (LBW), perinatal asphyxia, and neonatal sepsis remain major contributors to long-term developmental challenges. Globally, preterm birth affects approximately 15 million infants annually, with India accounting for the highest burden, contributing nearly 3.5 million cases per year.[1] The implications are severe, as preterm and LBW infants are at increased risk for cognitive impairment, motor disabilities, cerebral palsy, hearing loss, and visual impairment.[2]

Early childhood represents a critical window for neurological development. The vulnerability of the developing brain to insults during this sensitive period underscores the importance of structured follow-up and timely intervention.[3] Early interventions have proven effective in improving outcomes in high-income countries, where structured neurodevelopmental follow-up programs are standardized.[4] However, in low- and middle-income countries, including India, such services remain fragmented and underdeveloped due to resource constraints and limited infrastructure.[5]

The developmental assessment scale for Indian infants (DASII), standardized specifically for the Indian pediatric population, provides a robust framework for monitoring developmental trajectories in early childhood.[6] However, longitudinal data on the use of DASII from public hospitals, particularly in semi-urban and rural areas, remains limited.[7] This study aims to bridge this gap by

evaluating the neurodevelopmental outcomes of high-risk neonates using DASII at 12 months corrected age, exploring the associations with common neonatal morbidities.

METHODS

This hospital-based prospective observational analytical study was conducted over a two-year period from November 2015 to October 2017 at the Department of Pediatrics, P. D. U. Government Civil Hospital, Rajkot, a tertiary care public teaching hospital in Western India. The study enrolled high-risk neonates admitted to the NICU, defined by the presence of one or more of the following: preterm birth (<37 weeks gestation), low birth weight (<2500 g) and associated morbidities, birth asphyxia with hypoxic ischemic encephalopathy grade II/III, culture proven as well as clinical sepsis, symptomatic hypoglycemia, neonatal jaundice requiring double volume exchange transfusion, or neonatal seizures. Infants with major congenital anomalies, chromosomal abnormalities, or whose parents refused follow-up were excluded. A total of 88 neonates were recruited, of which 76 completed the scheduled follow-up assessments and were analyzed for primary outcome. Follow-up evaluations were conducted at 3, 6, 9, and 12 months corrected gestational age. Growth was monitored using standard anthropometric measurements. Neurodevelopmental assessment was performed at 12 months using the DASII, providing both mental developmental quotients (MeDQ) and motor developmental quotients (MoDQ). The Amiel-Tison neurological examination was used for tone assessment. Auditory screening was done using brainstem evoked response audiometry (BERA) at 3 months of age. Retinopathy of prematurity (ROP) screening commenced at 3 weeks of postnatal age and was carried out as per national guidelines. The primary outcome of the study was the proportion of infants with MeDQ or MoDQ below 70. Secondary outcomes included milestone delays, hearing loss, ROP requiring treatment, and their associations with neonatal morbidities.

Statistical analysis

Data were entered in Microsoft Excel and analyzed using IBM statistical package for the social sciences (SPSS) statistics version 26. Descriptive statistics were used to summarize demographic and clinical characteristics. Categorical variables were compared using Chi-square or Fisher's exact test. Odds ratios (OR) with 95% confidence intervals were calculated to examine associations between specific morbidities and developmental delays. A p value <0.05 was considered statistically significant.

Human ethics declaration

All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration, as revised in 2013. The study was approved by the Institutional Ethics Committee.

RESULTS

A total of 88 high-risk neonates were enrolled in the study. Of these, 3 (3.4%) infants died post-discharge and 9 (10.2%) were lost to follow-up. Final neurodevelopmental evaluation at 12 months corrected age was completed for 76 infants (86.4%).

The cohort comprised 46 males (52.6%) and 42 females (47.4%). A majority were preterm (60.2%), and low birth weight (LBW) was observed in 64.7% of infants, including 29.5% with very low birth weight (VLBW) and 3.4% with extremely low birth weight (ELBW). The most frequent neonatal morbidities were prematurity (60.2%), sepsis (28.4%), birth asphyxia with HIE-II/III (19.3%), hypoglycemia (8%), seizures (4.5%), and jaundice requiring double volume exchange transfusion (DVET, 4.5%) (Table 1).

Table 1: Baseline characteristics of high-risk neonates (n=88) enrolled in the neurodevelopmental outcome study.

Variables	Number (%)
Sex	
Male	46 (52.3)
Female	42 (47.7)
Gestation	
Term	35 (39.8)
Preterm	53 (60.2)
Birth weight	
Normal	31 (35.2)
LBW	28 (31.8)
VLBW	26 (29.5)
ELBW	3 (3.4)
Sepsis	25 (28.4)
Birth asphyxia with HIE-II/III	17 (19.3)
Jaundice requiring DVET	4 (4.5)
Neonatal seizures	4 (4.5)
Hypoglycemia	8 (9.1)

LBW=low birth weight, VLBW=very low birth weight, ELBW=extreme low birth weight, DVET=double volume exchange transfusion, HIE-hypoxic ischemic encephalopathy. Data presented as number and percentage

At 12 months corrected age, 24 infants (31.6%) had developmental delay in at least one domain. Specifically, 11 infants (14.5%) had a MeDQ <70, and 16 infants (21.1%) had a MoDQ <70, as assessed by the DASII. Milestone delays were observed in nearly one-third of the cohort. Hearing loss, as detected by BERA, was seen in 25% of infants, while 2.6% required treatment for ROP.

Analysis of associations between neonatal morbidities and outcomes revealed that birth asphyxia (HIE) was associated with the highest burden of adverse outcomes,

with 47% of affected infants exhibiting both MeDQ and MoDQ <70, and 67% showing some degree of hearing loss. Neonatal sepsis, the most common morbidity, was linked to MoDQ <70 in 7 cases and milestone delay in 8 infants. Symptomatic hypoglycaemia also emerged as a strong contributor, with 50% of affected infants showing both MeDQ and MoDQ <70. Seizures and jaundice requiring DVET were associated with developmental impairments and hearing loss, though in fewer cases (Table 2 and Figure 1).

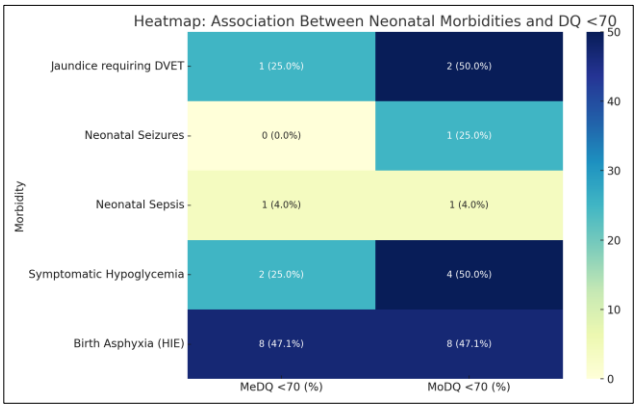

Figure 1: Heat map showing the strength of association between neonatal morbidities and developmental delay at 12 months. Color intensity represents proportion of infants with MeDQ or MoDQ <70.

To further quantify these associations, an odds ratio analysis was conducted. The odds ratio analysis demonstrated a strong and statistically significant association between certain neonatal morbidities and neurodevelopmental delays at 12 months corrected age. Infants with hypoxic ischemic encephalopathy (HIE) had markedly increased odds of both cognitive (MeDQ <70; OR: 5.80, p=0.010) and motor delay (MoDQ <70; OR: 8.00, p=0.003), indicating a substantial impact on overall development. Symptomatic hypoglycaemia was also significantly linked with poor outcomes, with odds ratios of 8.44 for MeDQ <70 and 6.89 for MoDQ <70 (p<0.05), suggesting it is a critical, yet potentially modifiable, risk factor. Neonatal sepsis showed a significant association with MoDQ <70 (OR: 3.48, p=0.033), though its association with MeDQ <70 was not statistically significant. While neonatal seizures and jaundice requiring DVET showed elevated odds for developmental delays, these did not reach statistical significance, likely due to smaller sample sizes. These findings underscore the importance of targeted surveillance and early interventions for infants with HIE, hypoglycaemia, and sepsis, given their strong associations with neurodevelopmental impairments (Table 3 and Figure 2).

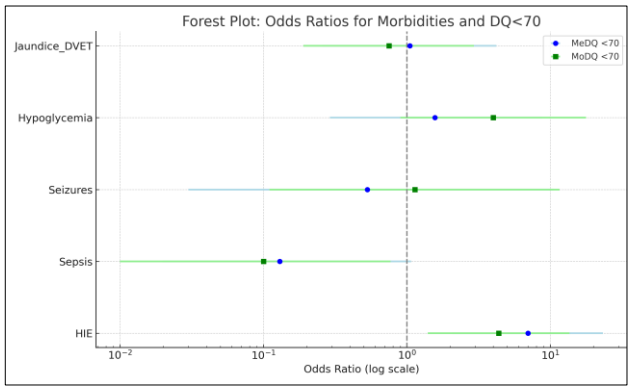

Figure 2: Forest plot of odds ratios. Forest plot of odds ratios (with 95% confidence intervals) for the association of major neonatal morbidities with neurodevelopmental delay (MeDQ <70 and MoDQ <70) at 12 months corrected age. The plot highlights the stronger association of HIE and hypoglycemia with both developmental domains.

These findings support the role of specific morbidities-particularly birth asphyxia, sepsis, and hypoglycaemia, as important contributors to adverse neurodevelopmental outcomes in high-risk neonates.

Table 2: Association between selected neonatal morbidities and developmental delays (MeDQ <70 and MoDQ <70) at 12 months corrected age.

Morbidity	MeDQ <70 (%)	P value (MeDQ)	MoDQ <70 (%)	P value (MoDQ)
Jaundice requiring DVET	25.0	0.56	50.0	0.22
Neonatal seizures	0.0	1.0	25.0	1.00
Neonatal sepsis	4.0	0.03	4.0	0.01
Symptomatic hypoglycemia	25.0	0.63	50.0	0.07
Birth asphyxia (HIE-II/III)	47.1	0.002	47.1	0.02

MeDQ=Mental developmental quotient, MoDQ=motor developmental quotient, DVET=double volume exchange transfusion, HIE-hypoxic ischemic encephalopathy. Data presented as percentage of affected infants with Fisher's exact test p value <0.05 as significant

Table 3: Odds ratios for morbidities associated with MeDQ and MoDQ <70.

Morbidity	OR (95% CI) (MeDQ<70)	P value (MeDQ)	OR (95% CI) (MoDQ <70)	P value (MoDQ)
HIE	7.0 (2.10–23.32)	0.002	4.37 (1.40–13.62)	0.01
Sepsis	0.13 (0.02–1.07)	0.06	0.1 (0.01–0.77)	0.03

Continued.

Morbidity	OR (95% CI) (MeDQ<70)	P value (MeDQ)	OR (95% CI) (MoDQ <70)	P value (MoDQ)
Seizures	0.53 (0.03–10.56)	0.68	1.14 (0.11–11.61)	0.91
Hypoglycemia	1.57 (0.29–8.61)	0.60	4.0 (0.90–17.75)	0.07
Jaundice_DVET	1.05 (0.26–4.21)	0.95	0.75 (0.19–2.93)	0.68

MeDQ=Mental developmental quotient, MoDQ=motor developmental quotient, DVET=double volume exchange transfusion, HIE-hypoxic ischemic encephalopathy. Data presented as odd's ratio with 95% confidence interval with p value

DISCUSSION

Our findings of significant developmental delays in approximately one-third of high-risk infants at 12 months align with existing literature, reinforcing the global evidence that neonatal complications adversely impact long-term outcomes.[8,9] Prematurity, birth asphyxia, and neonatal sepsis emerged as significant predictors of developmental impairments, supporting previous studies highlighting these as major risk factors.[7,10] With therapeutic hypothermia in today's era, we can significantly improve neurodevelopmental outcomes in neonates with moderate-to-severe HIE.[11]

Notably, our study identifies a strong association between symptomatic hypoglycaemia and developmental impairments, highlighting the critical need for aggressive management and close monitoring of glucose levels in neonates. Recent research suggests even transient neonatal hypoglycaemia can have lasting cognitive and motor sequelae, reinforcing the importance of vigilant monitoring and early intervention strategies.[12]

Similarly, our results indicating significant developmental impairment in infants with neonatal seizures emphasize the necessity for early neurological surveillance. Neonatal seizures are known to indicate underlying neurological pathology and are linked to subsequent motor and cognitive deficits.[13] Therefore, structured neurodevelopmental screening programs are imperative for early identification and intervention, thereby potentially reducing the burden of disability.[9]

Our findings underscore the importance of systematic follow-up programs that include developmental screening tools such as DASII, vision and hearing assessments, and targeted interventions. This comprehensive approach is particularly relevant in resource-constrained settings like India, where structured follow-up programs can dramatically improve outcomes by facilitating early diagnosis and timely management.[6,14]

Moreover, the significant association between hearing loss and neonatal sepsis found in our study highlights the importance of integrating regular hearing evaluations into neonatal follow-up programs.[15] Infections in early neonatal life can also trigger neuroinflammatory cascades, influencing long-term neurodevelopmental trajectories.[16] Early identification and management of hearing impairment are essential for optimizing language, cognitive, and social development.[4]

This study presents prospective, systematically collected follow-up data on high-risk neonates from a public sector tertiary care hospital in Western India, a region where such data remains sparse. The use of DASII, a tool standardized for Indian children, enhances the cultural and contextual relevance of neurodevelopmental assessment in this cohort. A comprehensive, multidimensional evaluation was performed at multiple time points, including structured developmental screening, auditory evaluation using BERA, and ROP screening, allowing for a robust appraisal of neurodevelopmental and sensory outcomes. The study included a wide range of common neonatal morbidities, facilitating analysis of their relative impact on developmental outcomes.

Limitations

Limitations of our study include a single-center public hospital study, which may limit the generalizability of findings to other regions or private-sector populations. The sample size, while adequate for primary analysis, was relatively small for subgroup comparisons, limiting statistical power. Total loss to follow-up (10.2%) and post-discharge mortality (3.4%) could introduce attrition bias, particularly if those infants had worse outcomes. Larger-scale longitudinal studies are needed to better characterize developmental trajectories and optimize screening and intervention strategies.

CONCLUSION

High-risk infants, particularly those born preterm or affected by significant neonatal morbidities such as sepsis, birth asphyxia, and hypoglycaemia, are at considerable risk of neurodevelopmental delays at 12 months corrected age. Structured follow-up utilizing standardized assessment tools like DASII, coupled with routine vision and hearing screenings, is essential to mitigate long-term disabilities. Given India's high neonatal morbidity burden, expanding neurodevelopmental surveillance and intervention programs within public health infrastructure should be a national priority to improve long-term outcomes.

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