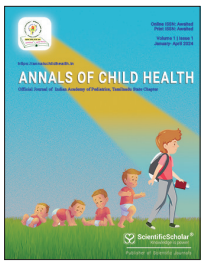
ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

https://annalschildhealth.in/

Annals of Child Health

Article in Press



Original Article

Prevalence and Risk Factors of Developmental Delay among High-risk Preterm NICU Graduates – A Cross-Sectional Study

Dhakshinamurthy ArvindKrishna[1], Sridevi A. Naaraayan[2], Krishnaswami Devi Meenakshi[3]

[1]Department of Pediatrics, ACS Medical College and Hospital, [2]Department of Pediatrics, Institute of Child Health and Hospital for Children, Madras Medical College, [3]Department of Pediatrics, Kilpauk Medical College, Chennai, Tamil Nadu, India.

***Corresponding author:**
Krishnaswami Devi Meenakshi, Department of Pediatrics, Kilpauk Medical College, Chennai, Tamil Nadu, India.

drdevi_1804@yahoo.in

Received: 08 June 2024
Accepted: 03 December 2024
EPub Ahead of Print: 24 January 2025
Published:

DOI
10.25259/ACH_14_2024

Quick Response Code:

ABSTRACT

Objectives: Preterm and low birth weight neonates are vulnerable to developing neurodevelopmental handicaps more frequently compared to their term counterparts. Neurodevelopmental delay is multifactorial and is likely a consequence of an immature brain, perinatal risk factors, and environmental exposures. The study objective was to determine the prevalence of developmental delay in high-risk preterm infants and also to determine the risk factors for delay in development.

Material and Methods: The study was an analytical cross-sectional study conducted in the Department of Pediatrics of a tertiary care medical college hospital from October 2021 to October 2022. Infants born as high-risk preterm neonates who required neonatal intensive care unit (NICU) stay in the early neonatal period were included in the study at the corrected age of 1 year after informed parental consent. Infants whose parents did not consent to the study were excluded from the study. Details of maternal, neonatal, and perinatal risk factors were noted in a pro forma. All infants included in the study were part of the follow-up program in the high risk newborn follow-up clinic and were assessed for growth and development periodically. A detailed neurological examination was done. During the follow-up of high-risk neonates, clinical assessment tools like Amiel-Tison angles were used. Details regarding the passive tone and active tone were documented in the follow-up card and reviewed. Early intervention was planned if tone abnormalities were identified. Developmental screening was done using the Trivandrum developmental screening test. Only trivandrum developmental screening test (TDSC) was used in screening, and confirmatory tests such as Bayley and developmental assessment scale for Indian infants (DASII) were not used in the study center. Although TDSC is not a confirmatory test, in a resource-limited setting, it may help to identify infants with delays in development early and refer them to a higher center. The prevalence of developmental delay was expressed in proportion with a 95% confidence interval (CI). Risk factors were determined by bivariate, followed by multivariate logistic regression analysis. $P < 0.05$ was considered significant.

Results: The present study included infants who were high-risk preterm NICU graduates, of whom 57.2% were male. 22.7% of neonates had birth weight <1750 g. The prevalence (95% CI) of developmental delay was 18 % (12.2–27.6%). There were 18% neonates with gross motor delay, 13% with delay in fine motor development, 18% with delayed language development, and 14% with delay in social and adaptive milestones. By multivariate analysis, it was found that among the neonatal risk factors, apnea and birth weight <1.75 kg were independent risk factors for developmental delay.

Conclusion: High-risk preterm NICU graduates are at risk of neurodevelopmental delay, and we observed an 18% prevalence of delay. Periodic follow-up and early intervention of babies with risk factors such as apnea and birth weight <1.75 kg is necessary.

Keywords: Premature birth, Neonatal intensive care unit, Developmental disabilities

INTRODUCTION

Preterm refers to live births before 37 completed weeks of gestation and is categorized as extreme preterm (<28 weeks), very preterm (28 to <32 weeks), and moderate-to-late preterm (32–37 weeks) based on the gestational age. An estimated 13.4 million babies were born before completing 37 weeks of gestation in the year 2020.[1] The rates of preterm births vary in different countries and range from 4% to 16%. Complications related to preterm birth are a leading cause of death among children under 5 years of age and were responsible for approximately 90000 deaths in the year 2019. The survival rates also vary with countries, and only half of the babies born at or <32 weeks gestation in low-income countries survive in contrast to high-income countries where almost all babies in this category survive.[2]

India is a major contributor to global preterm birth, with nearly one in six live births being preterm. However, the prevalence of preterm birth is unevenly distributed within states of India, ranging from 9% to 16%.[3] Studies from low and middle-income countries have reported that preterm births are at higher risk for neonatal mortality compared with full-term births.[3] Similar observations have been made in some Indian studies. Among those preterm babies who survive, disabilities such as hearing deficit, visual problems, and learning disabilities are common.[2,4,5]

Preterm and low birth weight neonates have better survival with advances in neonatal care. However, they are vulnerable to developing neurodevelopmental handicaps more frequently compared to their term counterparts.[6] Studies have shown that gestational age, birth weight, need for cardiopulmonary resuscitation at birth, mechanical ventilation, neonatal morbidities like bronchopulmonary dysplasia, necrotizing enterocolitis, sepsis, and duration of hospital stay were the common factors that influenced the neurodevelopmental outcome of neonatal intensive care unit (NICU) graduates.[7]

Although the risk of significant neurodevelopmental delay is high in extreme prematurity, it has been observed that moderate to late preterm neonates who require NICU care are also at risk.[8] Preterm neonates have differences in neurological status, intellectual functioning, school performance, and behavior when compared to term neonates. Although severe handicaps can be picked up by 2 years of age, longer follow-up can identify subtle changes in behavior, motor coordination, visual motor integration, and perception.[9] The study objective was to determine the prevalence of developmental delay in high-risk preterm NICU graduates and to determine the risk factors for developmental delay in them.

MATERIAL AND METHODS

This study was an analytical cross-sectional study conducted in the department of pediatrics of a tertiary care medical college hospital from October 2021 to October 2022. The study was commenced after obtaining approval from the Institutional ethics committee (Study ID 609/2021, meeting held on October 07, 2021). Infants born as high-risk preterm neonates who required NICU stay in the early neonatal period were included in the study at a corrected age of 1 year. The study participants were all infants who were born as preterm neonates and who required NICU stay in the early neonatal period. All preterm neonates with gestational age <37 weeks and any birth weight category who survived till 1 year of age were included. The birth weight of the neonates was recorded from the documents. The discharged neonates were followed up in the high-risk newborn out patient (OP) from where the infants were enrolled into the study at a corrected age of 1 year.

Infants whose parents did not consent to the study were excluded from the study. The sample size was calculated from a previous study, which reported a 24% prevalence of neurodevelopmental delay among preterm at 1-year follow-up with an error margin of 8% to calculate a 95% confidence interval (CI), and the sample size was calculated to be 110.[10]

The infants were included in the study after obtaining informed parental consent. Details of maternal, perinatal, and neonatal risk factors were noted from the child's NICU discharge summary in a structured pro forma. All the admitted preterm neonates undergo an ultrasonogram cranium as a routine in the NICU both during the stay and also before discharge. The details of the sonogram were available in the discharge summary.

All infants included in the study were part of the follow-up program in the high-risk newborn follow-up clinic and were assessed for growth and development periodically. A detailed neurological examination was done. During the follow-up of high-risk neonates, clinical assessment tools like Amiel-Tison angles were used. Details regarding the passive tone and active tone were documented in the follow-up card and reviewed.

Developmental screening was done using the Trivandrum developmental screening test. Only TDSC was used in screening, and confirmatory tests were not used in the study center. Although TDSC is not a confirmatory test, in a resource-limited setting, it may help to identify infants with delays in development early and refer them to a higher center.

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences version 24. The prevalence of developmental delay was expressed as a proportion with 95% CI. Risk factors were determined by bivariate, followed by multivariate logistic regression analysis. In the study, $P < 0.05$ was considered significant.

RESULTS

The present study included infants who were high-risk preterm NICU graduates, of whom 57.2% were males and 42.8% were females. 22.7% of infants had birth weight <1750 g, while 77.3% weighed more than 1750 g at birth. All preterm neonates who were included in the study were also part of the retinopathy of prematurity screening program, which is an ongoing program till the age of 1 year. As the birth weight cut-off used in retinopathy of prematurity (ROP) screening is 1750 g, the same cut-off was used to study the risk of developmental delay.

The prevalence (95% CI) of developmental delay was 18% (12.2–27.6% [Table 1]). There are, 18% of infants with gross motor delay, 13% with delay in fine motor development, 18% with delayed language development, and 14% with delay in social and adaptive milestones. Among the 20 infants with developmental delay, there were 13 infants with global developmental delay, motor and language delay in 1 infant, language and social delay in 2 infants, isolated language delay in 1 infant, and isolated motor delay in 3 infants.

Among the maternal and perinatal risk factors, it was observed that gestational diabetes was present in 25.4%, pregnancy-induced hypertension in 28.1%, antepartum hemorrhage in 2.7%, multiple gestation in 15.4%, and lower segment cesarean section (LSCS) in 48% of neonates. The prevalence of developmental delay was lower among neonates of mothers with gestational diabetes (14.3% vs. 19.5%) [Table 2].

The prevalence of developmental delay was higher among neonates of mothers with risk factors such as pregnancy-induced hypertension (22.6% vs. 16.5%), antepartum hemorrhage (33% vs. 17.8%), and multiple gestation (29.4% vs. 16.1%). Among the neonatal risk factors, 10% had apnea, 58% had respiratory distress syndrome, 25.4% had sepsis, 1% had an intraventricular hemorrhage, 65.4% were administered oxygen, and 7.2% were given blood transfusion. No formal illness severity scores were used in the study population. However, many of the variables usually used in severity scores were periodically assessed during the stay in the NICU.

Table 1: Basic demographic details of the study population.

Risk factor	Frequency	Percentage
Gender		
Male	63	57.27
Female	47	42.73
Gestational age		
28–32weeks	38	34.55
32–36weeks	72	65.45
Birth weight		
<1.75 kg	25	22.73
>1.75 kg	85	77.27

The prevalence of developmental delay was higher among neonates with birth weight <1.75 kg (48% vs. 9.4%), gestational age between 28 and 32 weeks (36.8% vs. 8.3%), who had apnea (63.6% vs. 13.1%), respiratory distress syndrome (RDS) (31% vs. 3.8%), and sepsis (39.3% vs. 11%) [Table 3].

The bivariate analysis identified birth weight <1.75 kg, gestational age of 28–32 weeks, neonatal morbidities such as apnea, respiratory distress syndrome, and sepsis, and interventions such as oxygen therapy and blood transfusion as risk factors for developmental delay, which is shown in Table 4. Multivariate logistic regression revealed birth weight <1.75 kg in the neonatal period to be an independent risk factor, which is depicted in Table 5.

DISCUSSION

The present study was conducted on infants who were admitted to our NICU; the NICU is a 40 bedded unit with 3195 admissions during the study period. It is a predominantly intramural unit, with the majority of the neonates being delivered in the hospital. During the study period, there were 137 deaths, which amounted to a death rate of 4.3%. The present study revealed a prevalence of developmental delay of 18% among the high-risk preterm NICU graduates. Assessment of these infants showed that motor delay was more common than delay in social and adaptive development. Language delay was the least common morbidity encountered. Delays in language and social milestones were considered if the infant did not develop the age-appropriate milestones in these domains. As the study was done at the corrected age of 12 months, the delay in language and social milestones was considered if the infants had not developed the early milestones in the language and social domains.

Apnea in the neonatal period and birth weight <1.75 kg were significant risk factors for developmental delay.

Similar studies done earlier have arrived at varying prevalences of developmental delay among preterm NICU graduates, ranging from 14.6% to 50.4%.[6,11] Variation in the prevalence may be due to differences in the gestational age and morbidity pattern at the time of admission to the NICU. In countries with high neonatal mortality, a study done on preterm <32 weeks had identified a pooled estimate of 24.6% (95% CI: 15.3–33.9%) for moderate-to-severe impairment, while for mild impairment, it was 32.4% (95% CI: 15.4–49.4%).[12] Compared to earlier studies, it was observed in the present study that there was a relatively lower prevalence of developmental delay. This was probably due to higher mortality among extremely low birth weight (ELBW) and very low birth weight (VLBW) neonates in the unit as well as developmentally supportive practices in the

Table 2: Comparison of maternal risk factors among infants with delayed development and normal development.

Risk factor	Developmental delay	Development normal	Unadjusted odds ratio(95% CI)	*P*-value
Gestational diabetes				
Yes	4(14.3)	24(85.7)	0.688(0.209–2.262)	0.536
No	16(19.5)	66(80.5)		
Pregnancy-induced hypertension				
Yes	7(22.6)	24(77.4)	1.481(0.528–4.151)	0.454
No	13(16.5)	66(83.5)		
Antepartum hemorrhage				
Yes	1(33)	2(66.7)	2.316(0.200–26.866)	0.490
No	19(17.8)	88(82.2)		
Multiple gestations				
Yes	5(29.4)	12(70.6)	2.167(0.665–7.055)	0.192
No	15(16.1)	78(83.9)		

CI:Confidence interval

Table 3: Comparison of neonatal risk factors among infants with delayed development and normal development.

Risk factor	Development	
	Delay	Normal
Gender		
Male	10(15.9)	53(84.1)
Female	10(21.3)	37(78.7)
Birth weight		
<1.75 kg	12(48)	13(52)
>1.75 kg	8(9.4)	77(90.6)
Gestational age		
28–32weeks	14(36.8)	24(63.2)
32–37weeks	6(8.3)	66(91.7)
Oxygen therapy		
Yes	19(26.4)	53(73.6)
No	1(2.6)	37(97.4)
Blood transfusion		
Yes	4(50)	4(50)
No	16(15.7)	86(84.3)
Apnea		
Yes	7(63.6)	4(36.4)
No	13(13.1)	86(86.9)
RDS		
Yes	18(31)	40(69)
No	2(3.8)	50(96.2)
Sepsis		
Yes	11(39.3)	17(60.7)
No	9(11)	73(89)
IVH		
Yes	1(100)	0(0)
No	19(17.4)	90(82.6)

RDS: Respiratory distress syndrome, IVH: Intraventricular hemorrhage

unit. developmentally supportive care (DSC) was a routine practice done on all neonates admitted to the NICU. As the rates of developmental delay were lower in this study, it was postulated to be due to the regular practice employed in the NICU. However, the role of DSC was not evaluated in the study.

A study comparing the neurodevelopmental outcome of late preterm and early term babies identified predominantly gross motor delay in late preterm and fine motor delay in term neonates.[13] This was similar to our observations of predominant gross motor delay in the preterm neonates. Higher gestational age at birth and higher birth weight were associated with a lower risk of developmental delay.[14]

Neurodevelopmental delay is multifactorial and is likely a consequence of an immature brain, perinatal risk factors, and environmental exposures. In the present study, it was observed that apnea was a significant independent risk factor for developmental delay. Previous studies have observed that the number of days apnea had occurred correlated positively with neurodevelopmental impairment and increasing apnea days was found to be associated with poor neurodevelopmental outcome.[15] Delayed resolution of apnea and higher daily apnea were associated with poorer neurodevelopmental outcomes evaluated at 13 months.[16] Apnea and the associated desaturation and hypoxia are said to be the factors influencing the neurological outcome of preterm babies. However, the extent to which apnea is causative of this neurodevelopmental delay or is just associated with a background of other sequelae of prematurity remains unclear.[17]

Delay, preterm/low birth weight babies were more likely to have developmental delay compared to their term counterparts. Intellectual disability and neurodevelopmental deficits are more common in this population. Low birth weight babies have delays in gross motor, cognitive, and communication skills. Very low birth weight neonates are at high risk of developmental difficulties and poor cognitive and motor outcomes. It has been observed that even apparently normal, very low birth weight children had a greater risk of

Table 4: Bivariate analysis of risk factors and developmental delay.

Risk factor	Developmental delay(*n*=20) *n*(%)	Development normal(*n*=90) *n*(%)	*P*-value
Gestational diabetes	4(20)	24(27)	0.536
Pregnancy-induced hypertension	7(35)	24(27)	0.454
Antepartum hemorrhage	1(5)	2(2)	0.490
Multiple gestations	5(25)	12(13)	0.192
Male newborn	10(50)	53(59)	0.467
Gestational age 28–32weeks	14(70)	24(27)	<0.001*
Birth weight<1.75 kg	12(60)	13(14)	<0.001*
Apnea	7(35)	4(4)	<0.001*
Respiratory distress syndrome	18(90)	40(44)	<0.001*
Sepsis	11(55)	17(19)	0.001*
Intraventricular hemorrhage	1(5)	0(0)	0.111
Oxygen therapy	19(95)	53(59)	0.002*
Blood transfusion	4(20)	4(4)	0.015*

*Means statistically significant *P*-value

Table 5: Logistic regression of risk factors.

Risk factor	Unadjusted OR	*P*-value	Adjusted OR	*P*-value
Gestational age 28–32weeks	6.417(2.213–18.602)	0.000*	3.036(0.317–29.064)	0.335
Birth weight <1.75 kg	8.885(3.046–25.912)	0.000*	0.057(0.005–0.693)	0.025*
Apnea	11.577(2.972–45.101)	0.000*	0.146(0.016–1.330)	0.048*
RDS	11.250(2.463–51.380)	0.000*	0.260(0.013–5.151)	0.377
Sepsis	5.248(1.879–14.656)	0.001*	1.125(0.190–6.675)	0.897
Oxygen therapy	13.264(1.700–103.473)	0.002*	1.144(0.037–35.249)	0.939
Blood transfusion	5.375(1.217–23.733)	0.015*	0.340(0.032–3.606)	0.371

*Means statistically significant *P*-value. RDS: Respiratory distress syndrome, OR: Odds ratio

delay in development when compared to those with normal birth weight. The greatest risk of delay in development was among preterm, very low birth weight babies who were appropriate for gestational age.

Limitations

A smaller sample size has resulted in a wider CI. This study, being a cross-sectional study, did not have periodic follow-up. A cohort study with a larger sample size can identify further risk factors. The data regarding growth restriction in the study population was not collected, and its association with developmental delay was not analyzed. Due to resource limitations, the study did not include developmental assessment in infants, and evaluation was limited to screening for delay.

CONCLUSION

18% of high-risk preterm NICU graduates had neurodevelopmental delay at 1 year of age, and apnea and birth weight <1.75 kg were significant independent risk factors for developmental delay in this population. Developmentally supportive newborn care should be given to all high-risk newborns during NICU stay, and all high-risk NICU graduates should receive periodic follow-up and early intervention to achieve optimal development.

Author contributions

DAK: Concept and design of study,data acquisition, interpretation of data, drafting the article, final version to be published, accountable for all aspects of work; SAN: Concept and design of study, analysis of data, interpretation of data, drafting the article, final version to be published, accountable for all aspects of work; KDM: Concept and design of study, analysis of data, interpretation of data, drafting the article, final version to be published,accountable for all aspects of work.

Ethical approval

The research/study was approved by the Institutional Review Board at Kilpauk Medical College, number 609/2021, dated 7th October 2021.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

Sridevi A. Naaraayan is on the Editorial Board of the Journal

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Ohuma EO, Moller AB, Bradley E, Chakwera S, Hussain-Alkhateeb L, Lewin A, *et al.* National, Regional, and Global Estimates of Preterm Birth in 2020, with Trends from 2010: A Systematic Analysis. Lancet 2023;402:1261-71.
2. Available from: https://www.who.int/news-room/fact-sheets/detail/preterm-birth [Last accessed on 2024 Jun 04].
3. Kannaujiya AK, Kumar K, Upadhyay AK, McDougal L, Raj A, James KS, *et al.* Effect of Preterm Birth on Early Neonatal, Late Neonatal, and Postneonatal Mortality in India [Published Correction Appears in PLOS Glob Public Health 2023;3:e0001806]. PLOS Glob Public Health 2022;2:e0000205.
4. Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes. Neurodevelopmental, Health, and Family Outcomes for Infants Born Preterm. In: Behrman RE, Butler AS, editors. Preterm Birth: Causes, Consequences, and Prevention. Washington, DC: National Academies Press (US); 2007. p. 11. Available from: https://www.ncbi.nlm.nih.gov/books/NBK11356 [Last accessed on 2024 Jun 01].
5. Available from: https://www.mayoclinic.org/diseases-conditions/premature-birth/symptoms-causes/syc-20376730 [Last accessed on 2024 Jun 04].
6. Chattopadhyay N, Mitra K. Neurodevelopmental Outcome of High Risk Newborns Discharged from Special Care Baby Units in a Rural District in India. J Public Health Res 2015;4:318.
7. Kang SR, Cho H. Research Trends of Follow-Up Care after Neonatal Intensive Care Unit Graduation for Children Born Preterm: A Scoping Review. Int J Environ Res Public Health 2021;18:3268.
8. Cheong JL, Doyle LW, Burnett AC, Lee KJ, Walsh JM, Potter CR, *et al.* Association Between Moderate and Late Preterm Birth and Neurodevelopment and Social-Emotional Development at Age 2 Years. JAMA Pediatr 2017;171:e164805.
9. Salt A, Redshaw M. Neurodevelopmental Follow-up after Preterm Birth: Follow up after Two Years. Early Hum Dev 2006;82:185-97.
10. Saldir M, Sarici SU, Bakar EE, Ozcan O. Neurodevelopmental Status of Preterm Newborns at Infancy, Born at a Tertiary Care Center in Turkey. Am J Perinatol 2010;27:121-8.
11. Das S, Bhattacharya M, Sanyal D, Basu S, Chatterjee A, Paul DK, *et al.* Growth and Neurodevelopmental Outcome of Neonatal Intensive Care Unit Graduates Till 1 Year at a Tertiary Care Centre in Eastern India and Identification of the Clinical and Electrophysiological Predictors of Adverse Developmental Outcome. J Pediatr Res 2017;4:155-66.
12. Blencowe H, Lee AC, Cousens S, Bahalim A, Narwal R, Zhong N, *et al.* Preterm Birth-associated Neurodevelopmental Impairment Estimates at Regional and Global Levels for 2010. Pediatr Res 2013;74 (Suppl 1):17-34.
13. Chen Z, Xiong C, Liu H, Duan J, Kang C, Yao C, *et al.* Impact of Early Term and Late Preterm Birth on Infants' Neurodevelopment: Evidence from a Cohort Study in Wuhan, China. BMC Pediatr 2022;22:251.
14. Hee Chung E, Chou J, Brown KA. Neurodevelopmental Outcomes Of Preterm Infants: A Recent Literature Review. Transl Pediatr 2020;9:S3-8.
15. Janvier A, Khairy M, Kokkotis A, Cormier C, Messmer D, Barrington KJ. Apnea is Associated with Neurodevelopmental Impairment in Very Low Birth Weight Infants. J Perinatol 2004;24:763-8.
16. Pillekamp F, Hermann C, Keller T, von Gontard A, Kribs A, Roth B. Factors Influencing Apnea and Bradycardia Of Prematurity - Implications for Neurodevelopment. Neonatology 2007;91:155-61.
17. Williamson M, Poorun R, Hartley C. Apnoea of Prematurity and Neurodevelopmental Outcomes: Current Understanding and Future Prospects for Research. Front Pediatr 2021;9:755677.

How to cite this article: ArvindKrishna D, Naaraayan SA, Devimeenakshi K. Prevalence and Risk Factors of Developmental Delay among High-risk Preterm NICU Graduates – A Cross-Sectional Study. Ann Child Health. doi: 10.25259/ACH_14_2024