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Assessment of neurodevelopmental outcomes in preterm infants using risk stratification score

Nikita Deepak Nemadi[1], Sharanagouda Patil[1], Arundhati Patil[1], Roopa Mangshetty[1]

[1]Department of Paediatrics, Mahadevappa Rampure Medical College Kalaburagi, Kalaburagi, Karnataka, India.

***Corresponding author:**
Nikita Deepak Nemadi, Department of Paediatrics, Mahadevappa Rampure Medical College Kalaburagi, Karnataka, India.

nikitanemadi312@gmail.com

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ABSTRACT

Objectives: Preterm birth, defined as delivery occurring before 37 weeks gestation, poses a significant public health challenge, as an increasing number of infants who survive face neurodevelopmental disabilities. Preterm infants face various health challenges, including anaemia, hyperbilirubinaemia, feeding and respiratory difficulties, retinopathy and intracranial haemorrhage, which often lead to long-term cognitive, learning and behavioural impairments due to structural brain abnormalities. (1) To study risk stratification tools based on intrauterine and neonate insult. (2) To study and predict major neuro-developmental disability like cerebral palsy, mental retardation, blindness, deafness at 1 year of age.

Material and Methods: The study included 30 preterm infants, categorised by risk levels, after obtaining ethical clearance and parental consent. Developmental follow-up assessments were adjusted for prematurity and conducted using tools such as the Amiel-Tison angle (ATA), scarf sign, Denver developmental screening test (DDST) and Vineland social maturity scale (VSMS). Visual and hearing assessments were checked for retinopathy and deafness. Primary outcomes at 1 year included death or major neurodevelopmental delays, such as cerebral palsy, mental impairment, blindness and profound hearing loss.

Results: In this study of 30 preterm infants, 83% weighed over 1.5 kg with a mean birth weight of 1.73 kg, and amongst those under 1.5 kg, 80% had abnormal developmental outcomes. The mean gestational age was 32 ± 1 weeks. Major neurodevelopmental delays (NDD), including cerebral palsy and global developmental delay, was observed in 16.6% of the infants, while 30% experienced minor NDD. Preterms with major NDD had higher intervention needs, with 40% requiring positive pressure ventilation and intubation, and 20% requiring chest compressions, 26.6% having abnormal ATAs. Statistically significant perinatal risk factors for poor neurodevelopmental outcomes included extreme prematurity (≤32 weeks), birth weight (<1.7 kg), need for resuscitation and prolonged ventilation (>7 days).

Conclusion: The study identified extreme prematurity, low birth weight, need for resuscitation and prolonged ventilation as key predictors of poor neurodevelopmental outcomes in preterm infants. Infants were stratified into low and high-risk groups to plan follow-up intensity and early intervention. Tools such as ATA, DDST, and VSMS aid in the early detection of neurodevelopmental disabilities, emphasising the importance of standardised follow-up programmes in neonatal units to improve outcomes for high-risk infants.

Keywords: Preterm birth, Neuro-development outcome, Amiel-Tison angle, Denver developmental screening test, Vineland social maturity scale

INTRODUCTION

Preterm birth, defined as delivery before 37 weeks of gestation, presents a major public health challenge, with many surviving infants facing neurodevelopmental disabilities.[1] Despite

advancements in neonatal intensive care unit technology that has improved survival rates and reduced severe neonatal complications, the risk of neurodevelopmental and behavioural impairments remains significant.[1] Prematurity and low birth weight are leading causes of neonatal mortality worldwide, particularly in low-income regions such as Asia and sub-Saharan Africa[1]. These conditions contribute to a range of complications, including anaemia, hyperbilirubinaemia, respiratory issues, and intracranial haemorrhage, which can lead to long-term neurological and developmental challenges.[2] India, with the highest number of preterm births globally, is addressing this issue through the implementation of the World Health Organization-recommended guidelines, including antenatal corticosteroids, tocolytics, magnesium sulphate and Kangaroo Mother Care.[3] While survival rates have improved, preterm infants remain at high risk for conditions such as cerebral palsy, cognitive and motor impairments and sensory deficits.[3] Early identification and intervention, supported by structured follow-up programmes, are essential to mitigate these risks and improve outcomes for these vulnerable infants.[2]

MATERIAL AND METHODS

Methods of collection of data

Study design

Prospective observational study.

Study setting

Department of Paediatrics, Basaveshwar Teaching and General Hospital, Kalaburagi and Sangameshwar teaching and general hospital Kalaburagi. Attached to Mahadevappa Rampure Medical College, Kalaburagi.

Sample size: 30

Using the formula, $n = Z^2PQ/d^2$ where,

n = sample size, Z =confidence interval, P = Prevalence, Q = 1-P, d = error rate

P = 6.5% Q = 93.5

d^2 = permissible error was 10%

Sample size (n) = $Z^2{}_aPQ/d^2$

= $(1.96)^2 \times 6.5 \times 93.5/(10)^2$

= 23.34

Round figure sample size n =30

Study duration

August 01, 2022, to March 31, 2024 (20 months).

Inclusion criteria

1. Preterm babies <34 weeks
2. Both inborn and outborn babies are referred in the first 48 hours.

Exclusion criteria

1. Preterm >34 weeks of gestation
2. Preterm infants with congenital malformation requiring major surgeries, dysmorphism, intrauterine infections

Table 1: Demographics and perinatal factors.

Parameter	Category	No. of patients	Percentage
Gender	Female	11	36.7
	Male	19	63.3
Birth weight (kg)	≤1.50	5	16.7
	>1.50	25	83.3
Gestational Age (weeks)	≤32	7	23.3
	>32	23	76.7
Mode of delivery	LSCS	12	40.0
	NVD	18	60.0
Place of delivery	BTGH	14	46.7
	PVT	3	10.0
	STGH	13	43.3
Antenatal risk factors	Abnormal NST	1	3.3
	DC twins	1	3.3
	Eclampsia	2	6.7
	MC twins	2	6.7
	Oligohydramnios	1	3.3
	Overt DM, G. HTN	1	3.3
	Pre-eclampsia	1	3.3
	Uteroplacental insufficiency	1	3.3
	Severe pre-eclampsia	2	6.7
	No risk factors	18	60.0
Steroid coverage	Completed	17	56.7
	Not given	7	23.3
	Partial	6	20.0
Need for resuscitation	Chest compression	1	3.3
	Intubation	2	6.6
	PPV	3	10.0
	No resuscitation	24	80.0
Need for ventilation	HFNC	1	3.3
	NIV	18	60.0
	Short ventilation	7	23.3
	Ventilation >7 days	2	6.7
	No ventilation	2	6.7

NVD: Normal vaginal delivery, PPV: Positive pressure ventilation, LSCS: Lower segment cesarean section, BTGH: Basaveshwar teaching and general hospital, STGH: Sangameshwar teaching and general hospital, PVT: Private hospital, NST: Non stress test, DC: Dichorionic, MC: Monochorionic, DM: Diabetes Mellitus, G.HTN: Gestational hypertension, HFNC: High flow nasal cannula, NIV: Non invasive ventilation

Table 2: Risk stratification score.

	Mild risk	Moderate risk	Severe risk
Gestation	33–34 weeks	30–32 weeks	<30 weeks
Birth weight	>1501 g	1251–1500 g	<1250 g
Intrauterine insults		Maternal fever	Severe maternal pre-eclampsia
		Abnormal non-stress test	Monochorionic
		Premature rupture of membranes	Chorioamnionitis twins/triplets/higher order
		Dichorionic twins	Abruption of placenta
Antenatal steroids	Complete	Incomplete course or <24 h from last dose	No antenatal steroids
Need for resuscitation at birth		Need for resuscitation-positive pressure ventilation	Extensive resuscitation -chest compressions, Adrenaline
Hypoglycaemia		Asymptomatic	Symptomatic
Shock	Nil	Saline bolus	Inotropes
Neonatal jaundice			Requiring exchange transfusion / Bilirubin induced neurological dysfunction

3. Transferred to another hospital before completion of the care
4. Babies collapse during the first 48 hours of life.

Methodology

Following approval from the Institutional Ethical Committee and obtaining informed consent from the parents, 30 subjects were selected for the study based on inclusion criteria. A questionnaire was developed to gather participant information, including demographic data, birth details and associated risk factors [Table 1]. The infants were then categorised into mild, moderate, or severe risk groups according to the risk score [Table 2].

To account for prematurity, developmental follow-up assessments were age-corrected based on the expected date of delivery, using a full correction method. This adjustment ensured that developmental milestones were assessed relative to the infant's expected developmental timeline, considering their prematurity. Tone abnormalities were evaluated every 3 months using the Amiel-Tison angle (ATA) and scarf sign.[1] The Denver developmental screening test (DDST) was administered at 2, 4, 8 and 12 months to assess major milestone achievements [Table 3].[4]

At 12-month corrected gestational age, the Vineland social maturity scale (VSMS) was used to assess the infants' intelligence quotient (IQ).[5] In addition, visual assessments were conducted to screen for retinopathy of prematurity[6] and hearing assessments were performed to detect any hearing impairments.[7]

At the end of 1 year, the outcomes were categorised into primary and secondary outcomes. Primary outcomes were defined as death before 12 months post-discharge or major neurodevelopmental delays, such as cerebral palsy, mental impairment, blindness, or profound hearing loss.[8] Secondary outcomes included normal development or minor neurodevelopmental disabilities, such as refractive errors or squints, impaired hearing not requiring assistive devices, growth delays and delays in achieving milestones in two or fewer domains [Table 4].[7]

Table 3: Neurodevelopmental outcomes and risk factors.

Parameter	Category	No. of patients	Percentage
Neurodevelopmental outcome	Major NDD	5	16.6
	Minor NDD	9	30.0
	Normal	16	53.4
NEC	Stage 2	3	10.0
	No NEC	27	90.0
Shock	Inotropes	10	33.3
	Saline bolus	7	23.3
	No shock	13	43.3
Seizures/ encephalopathy	Yes	1	3.3
	No	29	96.7
Intraventricular Haemorrhage (IVH)	Grade 4	1	3.3
	Grade 3	1	3.3
	Grade 1	1	3.3
	Normal	27	90.0
ROP	Early stage 2	5	16.7
	Stage 1	1	3.3
	Normal	24	80.0
BERA	Bilateral mild SNHL	1	3.3
	Left mild SNHL	1	3.3
	Normal	28	93.3
AT angle	Abnormal	8	26.6
	Normal	22	73.4

AT: Amiel-Tison, NEC: Necrotising Enterocolitis, ROP: Retinopathy of prematurity, BERA: Brainstem evoked response audiometry, SNHL: Sensorineural hearing loss, NDD: Neurodevelopmental delay

RESULTS

This study includes neurodevelopmental outcomes of 30 early preterm babies followed up till 1 year of age with various assessments and investigations.

This study examined the neurodevelopmental outcomes of 30 early preterm infants followed until 1 year of age. It found that lower birth weight and earlier gestational age were significantly associated with higher rates of neurodevelopmental delays (NDD). Specifically, 80% of infants weighing <1.5 kg and 86% of those born at or before 32 weeks had abnormal developmental outcomes. The need for resuscitation at birth, particularly the use of positive pressure ventilation and intubation, was also significantly linked to major NDD. A clinical risk score based on gestational age, birth weight, need for resuscitation, and ventilation was developed, which successfully stratified infants into low- and high-risk groups for major NDD. The low-risk group had a 42.3% incidence of NDD, while the high-risk group had a 75% incidence.

Table 4: Neurodevelopmental delay and IQ distribution.

Parameter	Category	No. of patients	Percentage
Developmental delay (DDST)	Fine motor delay	2	6.7
	GDD	6	20.0
	Gross motor delay	2	6.6
	Language delay	2	6.7
	No delay	18	60.0
IQ (VSMS)	Average	23	76.7
	Below average	4	13.3
	Borderline	2	6.7
	Mild intellectual disability	1	3.3
Clinical risk score for NDD	Low risk (0–1)	26	86.6
	High risk (≥2)	4	13.4

IQ: Intelligence quotient, VSMS: Vineland social maturity scale, DDST: Denver developmental screening test, GDD: Global developmental delay, NDD: Neurodevelopmental delays

DISCUSSION

In our study, amongst the 30 subjects, 63% were males and 37% were females, resulting in a male-to-female ratio of 1:0.5. This ratio is comparable to the findings of Serenius *et al.*[1] and Sujatha *et al.*[2] both reported a ratio of 1:0.8. The incidence of major NDD in our cohort was 16.6%, which aligns closely with the 20% reported by Jain *et al.*,[3] though it is higher than the 6.2% observed by Sujatha *et al.* [Table 5].[2]

The mean birth weight of preterm neonates in our study was 1.73 kg, which is higher than the values reported by Longo *et al.*[9] and Serenius *et al.*[1] However, our findings are consistent with those of Patel *et al.*[10] and Sujatha *et al.*[2] reported similar mean birth weights around 1.4 kg. The mean gestational age in our study was 32 ± 1 weeks, which is consistent with the findings of Patel *et al.*[10] and Sujatha *et al.*[2] In contrast, Serenius *et al.*[1] reported a lower mean gestational age of 25 ± 1 weeks.

Antenatal risk factors were present in 40% of cases in our study, a lower proportion compared to the 70.5% reported by Sujatha *et al.*[2] Antenatal steroid coverage in our cohort was 76.7%, which was the lowest compared to the higher coverage rates reported by Sujatha *et al.*,[2] Serenius *et al.*,[1] and Longo *et al.*[9] Furthermore, 60% of the deliveries in our study were normal vaginal deliveries, a higher proportion compared to the 19% reported by Longo *et al.* [Table 6].[9]

In terms of neonatal interventions, 20% of the preterm neonates in our study required resuscitation at birth, which is lower than the 75% reported by Longo *et al.*[9] However, the requirement for ventilation was higher in our study at 93%, compared to the lower rates reported by Sujatha *et al.*[2] and Longo *et al.*[9]

Table 5: Demographic and neonatal characteristics.

Study	Place	Sample size	Male/female ratio	Major NDD (%)	Mean GA (weeks)	Mean birth weight (kg)
Longo *et al.* (2019)[9]	Italy	502	1:1.04	10.7	29±2	1.11
Serenius *et al.* (2013[1]	Sweden	456	1:0.8	7.0	25±1	0.8
Sujatha *et al.* (2016)[2]	Kerala	225	1:0.8	6.2	30±2	1.42
Jain *et al.* (2020)[3]	Gujarat	62	1:1.2	20.9	-	-
Patel *et al.* (2017)[10]	-	-	-	-	31±2	1.45
Present Study (2024)	Kalaburagi	30	1:0.5	16.6	32±1	1.73

NDD: Neurodevelopmental delay, GA: Gestational Age

Table 6: Antenatal risk factors, delivery mode, resuscitation and ventilation.

Study	Antenatal risk factors	Steroids (%)	NVD	Resuscitation required	Ventilation (NIV+intubation)
Longo *et al.* (2019)[9]	-	88	19%	75%	51%
Serenius *et al.* (2013)[1]	-	90	-	-	-
Sujatha *et al.* (2016)[2]	70.5%	91	-	12.7%	59.2%
Present Study (2024)	40%	76.7	60%	20%	93%

NVD: Normal vaginal delivery, NIV: Non invasive ventilation

Limitation of the study

1. Single centre study and relatively small sample size
2. We did not assess the long-term impact on neurodevelopment or potential psychiatric or psychological disorders, including behavioural disorders.

CONCLUSION

Perinatal risk factors identified in the index study as poor neurodevelopmental outcome predictors were extreme prematurity that is, gestational age (≤32 weeks), birth weight, need for extensive resuscitation, and prolonged ventilation (>7 days). Babies were stratified based on these risk factors into low and high risk for major NDD at 1-year age. This will be helpful in planning the intensity of follow-up and early intervention. Parameters such as ATA, DDST, and VSMS can help in the early recognition of neuro-developmental disability. Early stratification of neonates with the possibility of abnormal outcomes can help in early intervention and moving towards an intact survival of high-risk neonates. Standardised follow-up programmes should be an integral part of every neonatal unit to improve the outcome of high-risk neonates.

Ethical approval: The research/study was approved by the Institutional Review Board at Mahadevappa Rampure Medical College Kalaburagi, number 20220796, dated July 27, 2022.
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