Research Paper

Preterm General Movements in Prediction of Neurodevelopmental Disability and Cerebral Palsy at Two Years: *A Prospective Cohort Study*

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ABSTRACT

Background: A neurological assessment before discharge from the NICU would enable early targeted intervention to mitigate the risk and severity of cerebral palsy (CP) and neurodevelopmental disability.

Objective: To assess the accuracy of general movements (GM) in the preterm and fidgety movement periods in predicting neurodevelopmental disability and cerebral palsy in very preterm infants (≤32 weeks gestational age) at 18-24 months corrected gestational age.

Study design: Prospective cohort study

Participants: One hundred and seventy very preterm infants, mean (SD) gestation 29.8 (1.32) weeks, and birthweight 1215 (226) g.

Outcomes: Infants underwent GM assessments in the preterm period (31-36 weeks post-conception age and fidgety movement period (8-18 weeks post term age). Neurodevelopmental outcomes were assessed in 127 children using the Griffiths Mental Developmental Scales-2.

Results: Nine children had neurodevelopmental disability (two infants with cerebral palsy and seven with global developmental delay. The relative risk (95% CI) for neurodevelopmental disability was 1.46 (0.31-6.89) with preterm movements and 6.07 (0.97 – 38.05) with fidgety movements. Sensitivity and specificity values for the prediction of neurodevelopmental disability were 33% and 64% in the preterm period and 25% and 92% in the fidgety movement period, respectively. The sensitivity and specificity values for prediction of CP were 50% and 63% in the preterm period and 100% and 93%in the fidgety movement period, respectively.

Conclusion: Preterm movements showed lower sensitivity and specificity than fidgety movements in predicting later CP and neurodevelopmental disability in preterm infants.

Keywords: *Developmental delay, Fidgety movements, Follow up care, Prognosis.*

Neurodevelopmental outcomes in preterm and very low birth weight infants have improved in recent decades, but they remain at risk of developing cerebral palsy (CP) as well as cognitive, language, visual perceptual, sensory, attention, and learning difficulties[1]. Early detection of these complications can mitigate the risk of adverse motor and developmental outcomes, decrease secondary complications and improve caregiver well-being [2].

General Movements (GMs) are spontaneous movements that can be detected from early fetal life until 4-5 months of post-term age [3]. The general movements assessment (GMA) has a high predictive ability for neurodevelopmental disability particularly cerebral palsy in preterm and term infants with risk factors [4]. General movements are classified into three types as preterm movements (28 to 36- 38 weeks post-conceptional age), writhing movements (36- 38 until 46- 52 weeks post-conceptional age), and fidgety

movements (FMs) (46-52 till 54-58 weeks post-conceptional age) [5]. The absence of core characteristics like adequate complexity, variability, and fluency of normal GMs are associated with adverse neurological outcomes [6,7]. The predictive ability of the GMA is superior to cranial ultrasound, neurological assessment, and comparable to MRI [8]. The sensitivity and specificity of FMs is the highest, followed by writhing movement in predicting CP [9], but accuracy is lower for non-CP adverse outcomes [10]. Assessment of GMs before-term has been studied less robustly [11], with studies of preterm movements reporting low specificity values [9].

The follow-up rates of high-risk infants remain poor in India [12]. Reported barriers to follow-up in low and middle- income countries (LMIC) include financial constraints for transportation and perceived wellness of the infant [13]. GMA can be a useful tool for neurological assessment in resource-limited settings where expensive neuro-imaging is not easily available.

The objective of this study was to assess the sensitivity and specificity of preterm movements in predicting neurodevelopmental disability and cerebral palsy in a cohort of very preterm infants. This was compared to the sensitivity and specificity of fidgety movements in predicting neurodevelopmental disability and cerebral palsy in the same cohort. Neurodevelopmental disability was assessed using a standardized developmental assessment at 18-24 months corrected gestational age. Video recordings of the preterm movements and the fidgety movements were performed following Prechtl standards [4].

METHODS

This prospective cohort study enrolled very preterm infants (gestational age <32 weeks, calculated based on the date of the last menstrual period) admitted to the neonatal intensive care unit of a large tertiary health center in Southern India. Informed consent was obtained from either of the parents and the study was approved by the Institutional Review Board.

Very preterm infants with major congenital anomalies incompatible with survival, those whose parents were unwilling to come for follow up and those who were on the ventilator or were sedated (could not undergo the video recordings of the GMs) were excluded. The mother's antenatal, and perinatal history and infants' details were collected from medical records. Participants for this study were recruited from September, 2013 to August, 2015; follow-up assessments were done from June, 2015 to January, 2018.

The recruited infants underwent preterm movement assessment, fidgety movement assessment and neurodevelopmental assessment between 18- 24 months [14]. General movements were classified as normal or abnormal by the primary investigator, who had Advanced Certification by the General Movement Trust.

All infants were started on an early intervention program prior to NICU discharge. Follow-up visits at the High-risk infant clinic were advised once every 3 months until 18 months corrected gestational age when the formal neurodevelopmental assessment was performed.

The Neurodevelopmental assessments were performed between corrected age of 18 and 24 months using the Griffiths Mental Developmental Scales – 2nd edition (GMDS) [15] by a certified psychologist who

was blinded to the medical history and the GMA results. The GMDS has five domains: locomotor, personal and social skills, hearing and language, eye-hand coordination, and performance. A sub-quotient is obtained in each domain, the average of which is the general quotient (GQ) that is considered as the indicator of the child's overall development. Normal GQ has a mean (SD) of 100 (12); and a cut-off score of ≤ 76 (<-2SD) indicates neurodevelopmental disability. The mean (SD) normative GQ in Indian infant aged 16-24 months was 104 (9.4) [16]. Cerebral Palsy was diagnosed if the child has abnormalities in posture and tone and classified using the Gross Motor Function Classification System by the developmental pediatrician who was also unaware of the GMA results.

The sample size was calculated using the agreement method. With reference to a study by Mutlu, et al. [17], the agreement between general movements and neurological assessment was found to be 0.78. Assuming a sample agreement of 0.78, a population agreement of 0.50 and prevalence of severe developmental delay as 17 % [12], the sample size was calculated as 139. Estimating a 20% loss to follow up it was decided to recruit 166 infants.

Statistical analysis: Data were analyzed using the SPSS package for Windows, version 21.0 (SPSS Inc). Fisher's exact test or Chi-square was used to compare categorical data and independent sample t-test was used to compare continuous data. Relative risk was calculated to predict neurodevelopmental disability. Sensitivity, specificity, positive, and negative predictive values were calculated using the Medcalc software [18].

RESULTS

The flow of the study is shown in **Fig. 1**. There were no significant differences in demographic characteristics, neonatal morbidities and prevalence of abnormal general movements between the 127 infants who completed the final neurodevelopmental assessment and the 43 infants who did not come for the assessment (**Web Table I**).

The mean (SD) gestational of the cohort was 29.8 (1.32) weeks, and birth weight was 1215 (226) grams. The mean (SD) age at preterm movement assessment was 34.4 (1.0) weeks post conceptional age and at assessment of the fidgety movements was 11.9 (2.1) weeks post-term age.

The mean (SD) GQ was 95 (12). 118 (93%) children had normal neurodevelopmental outcomes. Nine children (7%) had neurodevelopmental disability that included seven (5.5%) children with global developmental delay and two (1.57%) children with CP (one had GMFCS level V and the other had GMFCS level III). **Table I** shows the baseline characteristics of the 127 children who completed the final neurodevelopmental assessment.

Table II shows the sensitivity, specificity, and predictive values of GMs in in two time periods for predicting neurodevelopmental disability and cerebral palsy. The RR (95% CI) of preterm movements and fidgety movements for the prediction of neurodevelopmental disability was 1.45 (0.31, 6.89) (P=0.69), and 6.07 (0.97-38.05) (P=0.082), respectively. Specificity values are high during the fidgety movement period for

prediction of neurodevelopmental disability and cerebral palsy. Sensitivity and specificity of preterm movements for the prediction of cerebral palsy were 50% and 63%, respectively while of fidgety movements for CP were 100% and 94%, respectively.

The index child classified as GMFCS level V had poor repertoire GMs in preterm period, followed by absent FMs); while the child with CP classified as GMFCS level III had normal preterm, but abnormal FMs.

DISCUSSION

This study looked at the value of preterm movements and fidgety movements in predicting neurodevelopmental disability (including cerebral palsy) at 18-24 months gestational age in very preterm babies. The incidence of CP was 1.57% that was consistent with results obtained from an earlier cohort from this Institution [16]. The preterm movements had poor sensitivity and specificity values for the prediction of neurodevelopmental disability and CP in this study, unlike two earlier studies [8,18]. However, longitudinal studies have shown that abnormal preterm movements normalize with brain maturation resulting in normal fidgety movements in these infants with normal neurodevelopmental outcomes. This implies that abnormal preterm movements are associated with acute perinatal complications which resolve with maturity of the central nervous system [11,19,20]. Preterm movements may have poor association with outcomes like minor neurological impairments, coordination problems, and fine manipulative disability at school age and puberty [21–23].

This study reiterated the strong psychometric properties of fidgety movements for the prediction of CP, in concurrence with published literature [6,7,24], that illustrate its usefulness in predicting CP.

While CP, a motor disorder, was predicted accurately by GMA, neurodevelopmental disability was less accurately predicted. This may be accounted for by the general quotient of the Griffith scale that is a composite of the child's abilities domains that include language, eye hand coordination and personal social skills. A child with poor language or personal-social abilities (to which the environment is a major contributor), but good motor abilities, would be classified as having a neurodevelopmental disability, but may have had normal fidgety movements.

The assessors of the neurodevelopmental outcomes were blinded to the infants' GM results which reduced the chance for bias. This study showed that abnormal fidgety movements were highly predictive of CP. This makes it a very useful and single tool to predict neurodevelopmental outcomes by trained assessors. Moreover, since parents are likely to stop bringing infants for follow up after the first few months; assessment of infants using GMs can be a very useful tool in the NICU for counseling parents.

There were a few limitations in this study. As the study was done in a tertiary institution with adequate facilities for assessment and follow up, generalizability of results to the community should be done with caution. The scoring for GMs in this study was done by a single observer, as there was no other trained assessor limiting the measurement of interrater reliability for assessment. There was a significant drop-out of

about 25% (43 of 170 infants) who despite our best efforts did not complete the follow up which could have influenced the final results.

To conclude, this paper reiterates the utility of fidgety movements in the prediction of CP, while preterm movement assessments have limited use in prediction of neurodevelopmental disability or CP.

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Contributors: HB: conceptualized and designed the study, was involved in data collection and analysis, interpretation and conclusion, prepared and revised the manuscript; SPO, RS, LA: involved in study design, supervised data acquisition and analysis, interpretation of data and critical revision of the manuscript; STO: involved in data collection and critical revision of the manuscript. MK: involved in data acquisition and interpretation, guided and critically revised the final manuscript.

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Note: Additional material related to this study is available with the online version at www.indianpediatrics.net.

WHAT IS ALREADY KNOWN?

- Fidgety movements have superior psychometric properties for prediction of Cerebral Palsy.

WHAT THIS STUDY ADDS?

- Preterm general movement assessment had limited utility in predicting neurodevelopmental disability or cerebral palsy.
- The utility of fidgety movements was predominantly in predicting cerebral palsy.

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Table I Association of Antenatal and Neonatal Complications With Neurodevelopmental Outcomes

Complications	*Neurodevelopmental outcome*	
	Normal (N=118) (n,%)	*Abnormal (N= 9) (n,%)*
Female	48 (40)	3 (33)
Gestational age,[a] *(wk)*	29.9 (1.29)	29.38 (1.67)
Birthweight,[a] *(g)*	1219 (229)	1157 (179)
Birth weight *z*-score <-2SD	1(0.8)	0
Length *z*-score <-2SD	15 (13)	0
Head circumference *z*-score <-2SD	8 (7)	0
Normal delivery	41 (35)	5 (56)
Multifetal pregnancy	37 (31)	6 (67)
PIHP	32 (27)	5 (55)
No antepartum steroids (*n*=121)	16 (14)	1 (11)
Perinatal asphyxia	4 (3)	0
Pneumonia	5 (5)	0
Bronchopulmonary dysplasia	19 (16)	0
Hyaline membrane disease[b]	41 (35)	7 (78)
Invasive ventilation	20 (17)	0
Septicemia	10 (8)	0
Necrotizing enterocolitis	2 (2)	0
Early major brain lesion[c] (*n*=120)	4 (4)	0
Late major brain lesion[c] (*n*= 122)	12 (10)	3 (37)

Data expressed as n (%) or [a]mean (SD). PIHP – Pregnancy induced hypertension. [b]P=0.026. [c]Major brain lesion was defined as Grade 3 or 4 IVH or PVL using Papile grading using ultrasound findings for intraventricular hemorrhage and de Vries classification using ultrasound findings for periventricular leukomalacia. Early cranial ultrasound was done between day 1 to day 20 of life (m 6, sd 3); late cranial ultrasound was done between day 21 to day 80 of life (M 44, SD 11)

Table II Accuracy of General Movements During Preterm and Fidgety Movement Age for the Prediction of Neurodevelopmental Disability and Cerebral Palsy

	Preterm general Movement (n=127)	*Fidgety movements (n=118)*
Neurodevelopmental disability		
Sensitivity	33.33 (7.49-70.07)	25.00 (3.19- 65.09)
Specificity	64.41 (55.07- 73.00)	92.73 (86.17- 96.81
PPV	5.83 (2.33- 13.86)	18.51 (5.44- 47.29)
NPV	93.60 (90.03- 95.94)	94.93 (92.59- 96.55)
Cerebral palsy		
Sensitivity	50 (1.26- 98.74)	100 (15.81- 100)
Specificity	63.69 (55.93- 70.96)	93.79 (88.54-97.12)
PPV	1.60 (0.40- 6.20)	16.02 (9.20- 26.42)
NPV	99.08 (96.40-99.77)	100

Data expressed as value (95% CI). PPV – positive predictive values; NPV – negative predictive value.

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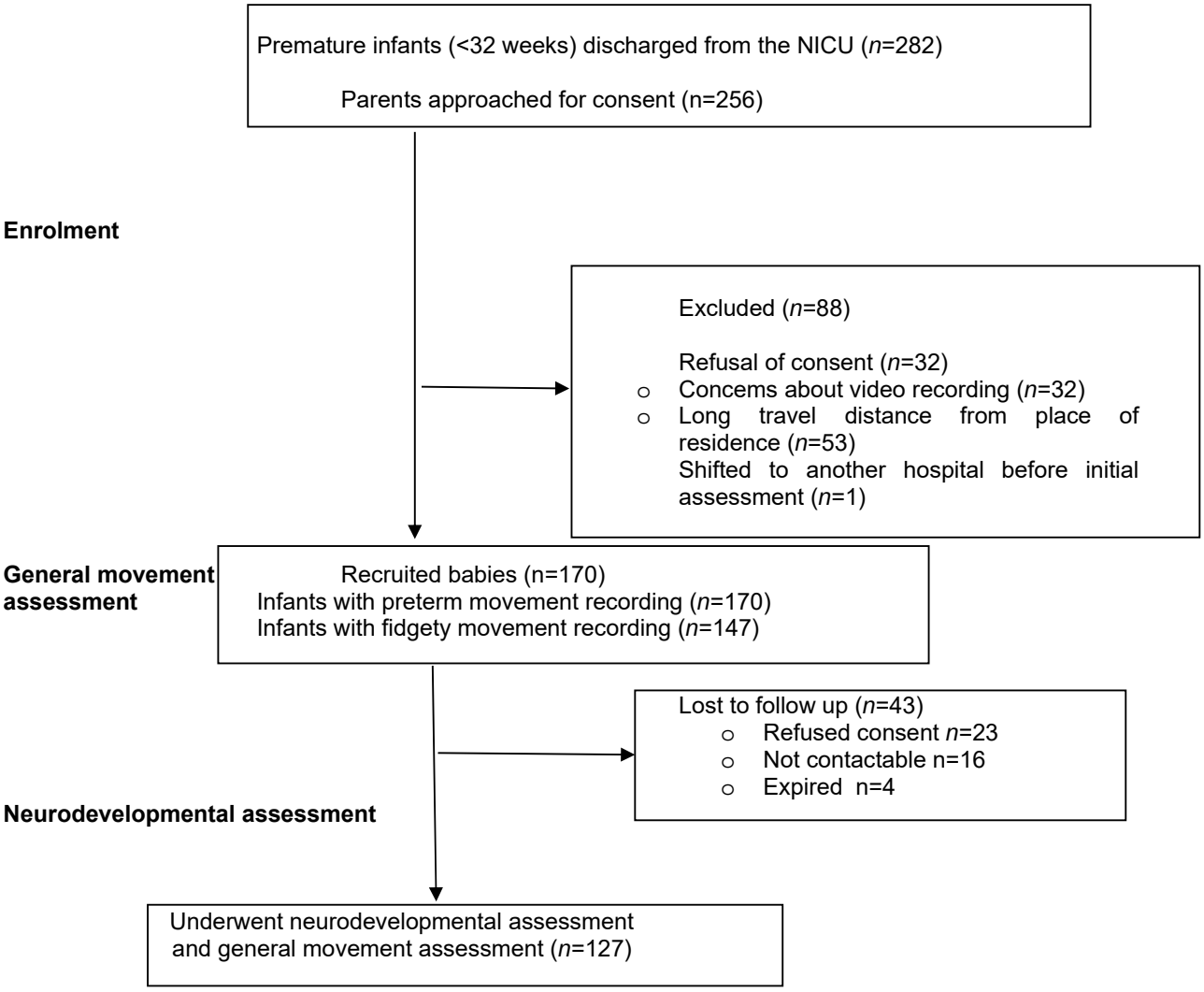

Fig. 1 Flow of the study

Web Table I Definitions Used in the Study or Various Perinatal and Neonatal Variables

Perinatal asphyxia	Umbilical cord ABG or or peripheral ABG within 1 hour: pH ≤ 7.0 or ABE ≥ -12 APGAR ≤ 5 at 5 minutes History of acute perinatal event _ Intrapartum fetal distress _ Cord prolapsed _ Placental abruption _ Uterine rupture/dehiscence If outborn – resuscitated for >10 mins/did not cry at birth with signs of encephalopathy
Pneumonia	Respiratory rate > 60 and signs of respiratory distress (dyspnea, grunting, coughing, nasal flaring, irregular respirations, cyanosis, intercostal and subcostal retractions, rales and decreased breath sounds with • Fever • Associated signs of sepsis • Radiologic features: hyper expansion, atelectasis, parahilar peribronchial infiltrate, consolidation, air bronchograms, pneumatoceles, pleural effusion • Tracheal aspirates or other sites (blood, CSF, urine) culture positive
Necrotizing enterocolitis	Using modified Bell's criteria
Hyaline membrane disease	• RR > 60, grunting expiration, in-drawing of sternum, intercostal spaces and lower ribs during inspiration, cyanosis without added oxygen, • CXR characteristic of RDS, • Surfactant used (help in corroborating not diagnosing the condition) • ABG – hypoxemia, mixed metabolic and respiratory acidosis, hypercarbia
Bronchopulmonary dysplasia	Treatment with FiO2 greater than 0.21 for at least 28 days PLUS failure of room air challenge test at 36 weeks post-menstrual age Radiologic features of BPD on chest X-ray
Cranial ultrasound Major brain lesion	Grade 3 or 4 IVH or PVL defined using Papile's grading using Ultrasound findings for IVH and de Vries classification using ultrasound findings for PVL
Septicemia	Systemic signs of infection (fever, lethargy, jitteriness, poor perfusion, accompanied by bacteremia (blood culture positive)
Height, weight and head ircumference <- 2SD	*z*-scores for <- 2SD for height, weight and head circumference were calculated using the online calculator for "2013 Fenton growth charts to report percentiles and Z-scores" (*http://www.ncbi.nlm.nih.gov/pubmed/32012066*)

Web Table II Antenatal and Neonatal Characteristics of Included and Excluded Infants

Characteristics of infants	*Included (n= 127)*	*Excluded (n= 43)*	*P value*
Gestational age (wk)[a]	29.8 (1.3)	29.7 (1.3)	0.475
Birthweight (g) [a]	1215 (226)	1201(200)	0.727
SGA (Birthweight z-score <-2SD)	1 (0.8)	0	1.000
Length z-score <-2SD	15 (12)	3 (7.1)	0.566
Microcephaly (HC z-score <-2SD)	8 (6.4)	3 (7)	1.000
Female	51 (40.2)	21 (48.8)	0.373
Spontaneous vaginal delivery	46 (36)	18 (41.9)	0.586
Multifetal pregnancy	43 (34)	10 (23.3)	0.254
Pregnancy induced hypertension	37 (29.1)	14 (32.6)	0.702
At least one dose antepartum steroids	104 (86)	34 (81)	0.461
Perinatal asphyxia	4 (3.1)	1 (2.3)	1.000
Pneumonia	5 (3.9)	5 (11.6)	0.125
Necrotizing enterocolitis	2 (1.9)	0	1.000
Hyaline membrane disease	48 (37.8)	18 (41.9)	0.718
Broncho pulmonary dysplasia	19 (15)	6 (14)	1.000
CPAP and/ or ventilation	20 (15.7)	10 (23.3)	0.258
Septicemia	10 (7.9)	3 (7)	1.000
Early CUS Major brain lesion	4 (3.3)	2 (4.8)	0.650
Late CUS Major brain lesion	15 (12.3)	4 (10)	0.784
Normal preterm general movements	82 (64.6)	26 (60.5)	0.714

Values in no. (%) or [a]mean (SD). CUS= Cranial ultrasound, SGA= Small for gestational age.