RESEARCH PAPER

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

HIMA B JOHN,[1] SAMUEL P OOMMEN,[2] T O SWATHI,[2] MANISH KUMAR,[1] RAGNHILD STOEN,[3] LARS ADDE[4]

From [1]Department of Neonatology, and [2]Developmental Pediatrics Unit, Christian Medical College, Vellore, Tamil Nadu, India; [3]St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway; [4]Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway.

Correspondence to: Dr Samuel P Oommen, Professor, Developmental Pediatrics Unit, Department of Pediatrics, Christian Medical College, Vellore 632 004, Tamil Nadu. devpaed@cmcvellore.ac.in

Received: May 10, 2022; Initial review: June 07, 2022; Accepted: August 01, 2022.

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.*

Published online*:** August 20, 2022; ***PII: S097475591600443

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 move- ment in predicting CP [9], but accuracy is lower for non-CP adverse outcomes [10]. Assessment of GMs beforeterm has been studied less robustly [11], with studies of preterm movements reporting low specificity values [9].

Invited Commentary: Pages 755- 56.

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 neuroimaging may not be 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 neuro-developmental 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 neuro-developmental disability. The mean (SD) normative GQ in Indian infants aged 16-24 months was 104 (9.4) [16]. Cerebral palsy was diagnosed if the child has abnormalities in posture and tone, and was classified using the Gross Motor Function Classification System (GMFCS) 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, and 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 age of the cohort was 29.8 (1.32) weeks, and birth weight was 1215 (226) g. The mean (SD) age at preterm movement assessment was 34.4 (1.0) weeks post conceptional age and at assessment of the fidgety movements, it 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 two time periods for predicting

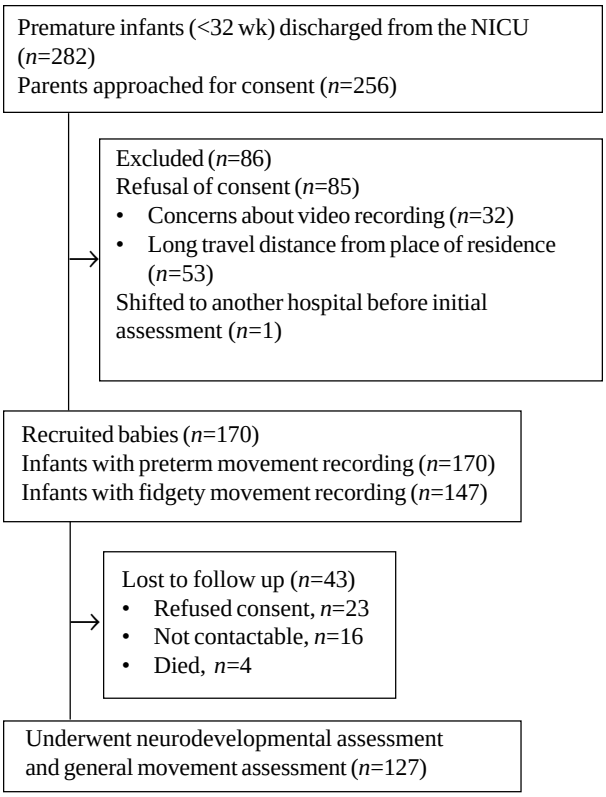

Fig. 1 Flow of the study

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

Table I Association of Antenatal and Neonatal Complications With Neurodevelopmental Outcomes

Complications	*Neurodevelopmental outcome*	
	Normal (n=118)	*Abnormal (n= 9)*
Female	48 (40)	3 (33)
Gestational age, wk[a]	29.9 (1.29)	29.38 (1.67)
Birth weight, g[a]	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 [mean (SD) 6(13) days]; late cranial ultrasound was done between day 21 to day 80 of life [mean (SD) 44 (11) days].

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.

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

	Preterm general Movements (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.

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 environ- ment 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.

Acknowledgements: Dr Grace Rebekah, for her assistance with statistical analysis, Ms Indira Balan and Ms. Meenakshi Papanasam who helped in organizing follow up appointments for this study, and Mr Selvakumar G for his technical support.

Ethics clearance: IEC, Christian Medical College, Vellore; No. 8390, dated Sept 09, 2013.

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

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.

Funding: Fluid Research Grant of Christian Medical College, Vellore; *Competing interests*: None stated.

REFERENCES

1. Pascal A, Govaert P, Oostra A, Naulaers G, Ortibus E, Van den Broeck C. Neurodevelopmental outcome in very pre-term and very-low-birthweight infants born over the past decade: A meta-analytic review. Dev Med Child Neurol. 2018;60:342-55.
2. Novak I, Morgan C, Adde L, et al. Early, accurate diagnosis and early intervention in cerebral palsy: Advances in diag-nosis and treatment. JAMA Pediatr. 2017;171:897-907.
3. Prechtl HF. General movement assessment as a method of developmental neurology: New paradigms and their consequences. Dev Med Child Neurol. 2001;43:836-42.
4. Einspieler C, Prechtl HF. Prechtl's assessment of general movements: A diagnostic tool for the functional assessment of the young nervous system. Ment Retard Dev Disabil Res Rev. 2005;11:61-7.
5. Einspieler C, others. Prechtl's method on the qualitative assessment of general movements in preterm, term and young infants. Mac Keith Press London, UK; 2004.
6. Noble Y, Boyd R. Neonatal assessments for the preterm infant up to 4 months corrected age: A systematic review. Dev

Med Child Neurol. 2012;54:129–39.
7. Spittle AJ, Doyle LW, Boyd RN. A systematic review of the clinimetric properties of neuromotor assessments for pre-term infants during the first year of life. Dev Med Child Neurol. 2008;50:254-66..
8. Manacero SA, Marschik PB, Nunes ML, Einspieler C. Is it possible to predict the infant's neurodevelopmental out-come at 14 months of age by means of a single preterm assess- ment of general movements?. Early Hum Dev. 2011;88:39-43.
9. Kwong AKL, Fitzgerald TL, Doyle LW, et al. Predictive validity of spontaneous early infant movement for later cerebral palsy: A systematic review. Dev Med Child Neurol. 2018;60:480-9.
10. Stahlmann N, Härtel C, Knopp A, et al. Predictive value of neurodevelopmental assessment versus evaluation of general movements for motor outcome in preterm infants with birth weights <1500 g. Neuropediatrics. 2007;38:91-9.
11. Olsen JE, Brown NC, Eeles AL, et al. Trajectories of general movements from birth to term-equivalent age in infants born < 30 weeks' gestation. Early Hum Dev. 2015;91:683-8.
12. Mukhopadhyay K, Malhi P, Mahajan R, Narang A. Neuro-developmental and behavioral outcome of very low birth weight babies at corrected age of 2 years. Indian J Pediatr 2010;77:963-7.
13. Milambo JPM, Cho K, Okwundu C, et al. Newborn follow-up after discharge from a tertiary care hospital in the Western Cape region of South Africa: A prospective observational cohort study. Glob Health Res Policy. 2018;3:1-7.
14. John HB, Oommen SP, Kumar M. Trajectories of general movements in very preterm infants: An experience from South India, a prospective cohort study. Current Medical Issues. 2022;20:16-21.
15. Griffiths R. Griffiths mental development scales extended revised manual. Firenze: Giunti Organizzazioni Speciali. 2006.
16. Oommen SP, Santhanam S, John H, et al. Neuro-develop-mental outcomes of very low birth weight infants at 18-24 months, corrected gestational age in a tertiary health centre: a prospective cohort study. J Trop Pediatr. 2019;65:552-60.
17. Mutlu A, Livanelioglu A, Korkmaz A. Assessment of general movements in high-risk infants by Prechtl analysis during early intervention period in the first year of life. Turkish J Pediatr. 2010;52:630-37.
18. Schoonjans F. MedCalc's Diagnostic test evaluation calculator. MedCalc n.d. Accessed June 20, 2018. Available from: *https:// www.medcalc.org/calc/diagnostic _test.php*
19. Kodric J, Sustersic B, Paro-Panjan D. Assessment of general movements and 2.5 year developmental outcomes: Pilot results in a diverse preterm group. Eur J Paediatr Neurol. 2010;14:131-7.
20. Albers S, Jorch G. Prognostic significance of spontaneous motility in very immature preterm infants under intensive care treatment. Biol Neonate. 1994;66:182-7.
21. Zahed-Cheikh M, Brévaut-Malaty V, Busuttil M, et al. Comparative analysis of perinatal and postnatal factors, and general movement in extremely preterm infants. Brain Dev. 2011;33:656-65.
22. Einspieler C, Marschik PB, Milioti S, Nakajima Y, Bos AF, Prechtl HFR. Are abnormal fidgety movements an early marker for complex minor neurological dysfunction at puberty? Early Hum Dev. 2007;83:521–5.
23. Bruggink JL, Einspieler C, Butcher PR, Van Braeckel KN, Prechtl HF, Bos AF. The quality of the early motor reper-toire in preterm infants predicts minor neurologic dysfunc-tion at school age. J Pediatr. 2008;153:32-9.
24. Groen SE, De Blécourt AC, Postema K, Hadders-Algra M. General movements in early infancy predict neuromotor development at 9 to 12 years of age. Dev Med Child Neurol. 2005;47:731-8.
25. Kwong AKL, Fitzgerald TL, Doyle LW, Cheong JLY, Spittle AJ. Predictive validity of spontaneous early infant movement for later cerebral palsy: A systematic review. Dev Med Child Neurol. 2018;60:480-9.