



(RESEARCH ARTICLE)



PREDICTIVE VALIDITY OF NEONATAL SCREENING ASSESSMENTS FOR NEURODEVELOPMENTAL OUTCOMES IN PRETERM INFANTS: A PROSPECTIVE COHORT STUDY FROM EASTERN INDIA

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World Journal of Biology Pharmacy and Health Sciences, 2026, 27(03), 185–193

Publication history: Received on 10 August 2026; revised on 29 September 2026; accepted on 30 September 2026

Article DOI: <https://doi.org/10.30574/wjbphs.2026.27.3.0491>

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ABSTRACT

Background: Preterm birth is a leading cause of long-term neurodevelopmental impairment, and India carries the largest absolute burden of preterm births worldwide. Early neonatal and early-infancy screening could direct scarce early-intervention resources, but the predictive validity of these tools has not been examined in Eastern Indian populations.

Objective: To evaluate the predictive validity of the General Movements Assessment (GMA) and the Hammersmith Neonatal Neurological Examination (HNNE) for cognitive and motor outcomes in preterm infants, and to estimate the prevalence of neurodevelopmental delay in this population.

Methods: In this prospective observational cohort study, 80 preterm infants (gestational age 25–36 weeks; mean 30.8 ± 3.5 weeks) were recruited from NICUs and follow-up clinics in Eastern India. GMA and HNNE were performed as index tests, and the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) served as the reference standard at 18 months corrected age. Neurodevelopmental delay was defined as a cognitive or motor composite score < 85 . Sensitivity, specificity, predictive values, likelihood ratios, and area under the receiver operating characteristic curve (AUC) were calculated; Spearman correlation and logistic regression examined associations.

Results: Neurodevelopmental delay was present in 40 infants (50.0%); 25 (31.3%) had moderate-to-severe delay (composite < 70). Abnormal GMA (poor repertoire, cramped-synchronized, or absent fidgety movements) predicted delay with a sensitivity of 95.0% and specificity of 95.0% (AUC = 0.950). An HNNE global score ≤ 68 showed a sensitivity of 92.5% and specificity of 97.5% (AUC for the continuous score = 0.979). HNNE scores correlated strongly with Bayley-III cognitive ($\rho = 0.92$) and motor ($\rho = 0.93$) composites (both $p < .001$). Cramped-synchronized or absent fidgety movements identified moderate-to-severe delay with 96.0% sensitivity and 100% specificity. Neonatal sepsis was the only independent clinical predictor of delay (adjusted OR = 10.61, 95% CI 2.54–44.35).

Conclusion: GMA and HNNE showed high predictive validity for 18-month neurodevelopmental outcomes in preterm infants from Eastern India. Both tools are low-cost and suitable for triaging infants to early intervention in resource-constrained settings, although external validation in larger multicentre cohorts is required.

Keywords: Preterm Infant; General Movements Assessment; Hammersmith Neonatal Neurological Examination; Bayley-III; Neurodevelopmental Outcome; Predictive Validity

1 INTRODUCTION

Preterm birth, defined by the World Health Organization as birth before 37 completed weeks of gestation, affected an estimated 13.4 million live births in 2020, and India contributes the largest absolute number of preterm births of any country (Ohuma et al., 2023; Blencowe et al., 2013). Improvements in neonatal intensive care have increased survival, but survivors remain at substantially elevated risk of cerebral palsy (CP), cognitive delay, language impairment, and later learning difficulties (Pascal et al., 2018; Pierrat et al., 2017; Johnson & Marlow, 2017). Indian cohorts report neurodevelopmental impairment in a substantial proportion of very-low-birth-weight and preterm survivors at 12–24 months corrected age (Mukhopadhyay et al., 2010; Oommen et al., 2019; Murki et al., 2020).

Early developmental intervention after discharge improves cognitive outcomes in infancy and preschool years, and its benefit is greatest when commenced during the period of maximal neuroplasticity (Spittle et al., 2015; Orton et al., 2024). International guidelines therefore recommend that infants at high risk of CP and developmental disability be identified as early as possible so that intervention can begin before six months corrected age (Novak et al., 2017; Morgan et al., 2021). In low- and middle-income settings, where follow-up capacity is limited, a reliable early screening step is essential for directing therapy resources to the infants who need them most.

Two neurological assessments are particularly suited to this purpose. Prechtl's General Movements Assessment (GMA) is a non-invasive, observation-based evaluation of spontaneous movement quality; absent fidgety movements at 3–5 months post-term and cramped-synchronized movements are among the strongest early predictors of CP (Prechtl et al., 1997; Einspieler & Prechtl, 2005; Bosanquet et al., 2013; Kwong et al., 2018), and abnormal general movements are also associated with later cognitive dysfunction (Einspieler et al., 2016). The Hammersmith Neonatal Neurological Examination (HNNE) is a structured bedside examination of tone, posture, reflexes, movement, and behaviour with published reference data for preterm infants at term-equivalent age (Dubowitz et al., 1998; Dubowitz et al., 2005; Ricci et al., 2008). Both tools require minimal equipment and have been recommended for early detection in resource-limited settings (Noble & Boyd, 2012; Juneja et al., 2022).

Despite this evidence, most validation studies originate from high-income countries or tertiary centres with different sociodemographic profiles. Indian data are few and largely from Southern and Western India (John et al., 2022; Kadam et al., 2023), and no study has evaluated the predictive validity of these screening tools among preterm infants in Eastern India, where disparities in neonatal follow-up services persist (Bora & Saikia, 2018). This study was designed to address this gap by evaluating the predictive validity of GMA and HNNE for cognitive and motor outcomes, estimating the prevalence of neurodevelopmental delay, and identifying clinical risk factors associated with adverse outcome in preterm infants from Eastern India.

2 METHODS

2.1 Design and Setting

This was a prospective observational cohort study reported in accordance with the STROBE statement and the STARD 2015 guidelines for diagnostic accuracy studies (von Elm et al., 2007; Bossuyt et al., 2015). Ethical approval was obtained from the Institutional Ethics Committee before recruitment. Participants were recruited from Neonatal Intensive Care Units (NICUs) and neonatal follow-up clinics of public and private hospitals in Eastern India. Written informed consent was obtained from a parent or legal guardian of every infant.

2.2 Participants

Infants born before 37 completed weeks of gestation who were admitted to a participating NICU and survived to discharge were enrolled consecutively. Exclusion criteria were major genetic syndromes or congenital malformations, postnatally acquired brain injury (such as trauma or meningitis), and loss to follow-up before the outcome assessment. Infants were withdrawn if consent was revoked or if follow-up data were incomplete. A standardized case report form recorded gestational age, birth weight, sex, mode of delivery, 5-minute Apgar score, and culture-proven or clinically diagnosed neonatal sepsis.

2.3 Index Tests

2.3.1 General Movements Assessment (GMA)

General movements were video-recorded in the preterm/writhing period and again in the fidgety period at 12–16 weeks post-term age, and classified by a trained assessor using Prechtl's method (Einspieler et al., 2004). Each infant was assigned a final category: normal, poor repertoire (PR), cramped-synchronized (CS), or absent fidgety movements (F–). For analysis, GMA was dichotomized in two ways: any abnormal pattern (PR, CS, or F–) and definitely abnormal pattern (CS or F–).

2.3.2 Hammersmith Neonatal Neurological Examination (HNNE)

The HNNE was administered before hospital discharge at or near term-equivalent age and yielded a global score, with higher scores indicating a more optimal neurological status (Dubowitz et al., 1998; Ricci et al., 2008). The GMA and HNNE assessors were blinded to each other's findings.

2.4 Reference Standard

Neurodevelopmental outcome was assessed at 18 months corrected age with the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III), which yields cognitive and motor composite scores (mean 100, SD 15) (Bayley, 2006). Assessors were blinded to the index-test results. Because the Bayley-III is known to underestimate delay relative to earlier editions, a composite score < 85 (-1 SD) was used to define neurodevelopmental delay, and < 70 (-2 SD) to define moderate-to-severe delay (Anderson et al., 2010). The primary outcome was delay in either the cognitive or motor domain.

2.5 Statistical Analysis

Analyses were performed in Python (SciPy, statsmodels, scikit-learn). Continuous variables are presented as mean $\pm$ SD or median (interquartile range), and categorical variables as n (%). Differences across GMA categories were tested with the Kruskal–Wallis test with Bonferroni-corrected pairwise Mann–Whitney U tests, and categorical associations with the chi-square or Fisher's exact test. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratios were calculated with Wilson 95% confidence intervals (Trevethan, 2017). Discriminative ability of the continuous HNNE score was quantified by the AUC with 2,000-sample bootstrap 95% confidence intervals, and the optimal cut-off was identified with the Youden index (Youden, 1950). Spearman's correlation coefficient (ρ) assessed the relationship between HNNE and Bayley-III scores. Univariable and multivariable logistic regression estimated odds ratios (OR) for clinical predictors of delay. Statistical significance was set at $p < .05$.

3 RESULTS

All 80 enrolled infants completed the 18-month Bayley-III assessment and were included in the analysis. The cohort had a mean gestational age of 30.84 ± 3.47 weeks (range 25–36) and mean birth weight of 1851.3 ± 261.7 g; 17 infants (21.3%) were extremely preterm (< 28 weeks), 28 (35.0%) very preterm (28–31 weeks), and 35 (43.8%) moderate-to-late preterm (32–36 weeks). Sex was evenly distributed (40 male, 40 female), 51 (63.8%) were delivered by caesarean section, 56 (70.0%) had a 5-minute Apgar score < 7 , and 25 (31.3%) had neonatal sepsis. Half of the cohort ($n = 40$) had normal general movements (Table 1).

Table 1: Baseline Characteristics and Outcome Scores by GMA Category (Mean $\pm$ SD or n [%])

Variable	Total $n=80$	Normal $n=40$	PR $n=16$	CS $n=12$	F– $n=12$	p
Gestational age, weeks	30.84 ± 3.47	32.40 ± 2.98	30.00 ± 3.98	28.33 ± 1.56	29.25 ± 3.41	$< .001$
Birth weight, g	1851.3 ± 261.7	1916.2 ± 230.8	1827.9 ± 286.3	1675.5 ± 187.7	1842.0 ± 325.4	.031
Sex, M/F	40/40	22/18	6/10	5/7	7/5	.559
Caesarean delivery	51 (63.8)	26 (65.0)	9 (56.3)	8 (66.7)	8 (66.7)	.918
Apgar score (5 min)	5.46 ± 1.83	6.32 ± 1.79	4.94 ± 1.77	3.92 ± 0.67	4.83 ± 1.40	$< .001$
Neonatal sepsis	25 (31.3)	2 (5.0)	5 (31.3)	7 (58.3)	11 (91.7)	$< .001$

HNNE global score		62.78 ± 13.21	73.50 ± 2.58	63.94 ± 3.28	45.25 ± 3.25	43.00 ± 4.71	< .001
Bayley-III cognitive composite	cognitive	80.73 ± 16.85	94.60 ± 5.20	79.50 ± 5.72	59.42 ± 7.01	57.42 ± 7.74	< .001
Bayley-III motor composite	motor	81.24 ± 17.83	95.18 ± 6.95	82.75 ± 6.23	57.50 ± 5.20	56.50 ± 6.24	< .001

Note. PR = poor repertoire; CS = cramped-synchronized; F- = absent fidgety movements. p values from Kruskal–Wallis (continuous) or chi-square (categorical) tests across the four GMA categories.

3.1 Prevalence of Neurodevelopmental Delay

Neurodevelopmental delay (cognitive or motor composite < 85) was present in 40 infants (50.0%), and moderate-to-severe delay (< 70) in 25 (31.3%). Cognitive delay affected 36 infants (45.0%; 23 [28.8%] < 70) and motor delay 36 infants (45.0%; 24 [30.0%] < 70). Delay was more frequent with decreasing gestational age: 15/17 (88.2%) extremely preterm, 14/28 (50.0%) very preterm, and 11/35 (31.4%) moderate-to-late preterm infants ($\chi^2 = 14.77$, $p < .001$). Sex ($p = .50$) and mode of delivery ($p = .64$) were not associated with delay.

3.2 Screening Findings and Outcome

Bayley-III scores declined in a graded manner across GMA categories (Figure 1). Infants with normal general movements had mean cognitive and motor composites above 94, whereas every abnormal category averaged below the delay threshold. Pairwise comparisons showed that the normal group differed from each abnormal group, and poor repertoire differed from both cramped-synchronized and absent fidgety movements on HNNE, cognitive, and motor scores (all Bonferroni-adjusted $p < .001$); cramped-synchronized and absent fidgety groups did not differ ($p = 1.00$).

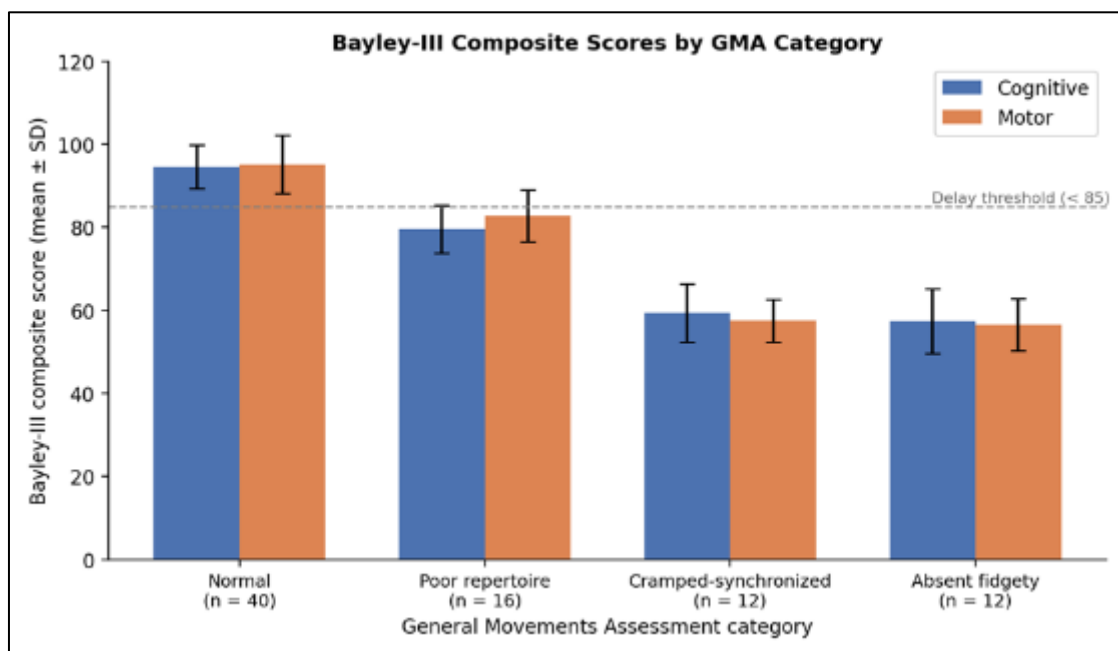


Figure 1: Bayley-III Cognitive and Motor Composite Scores (Mean ± SD) by GMA Category

HNNE global scores correlated strongly with Bayley-III cognitive ($p = 0.92$) and motor ($p = 0.93$) composites (both $p < .001$). Weaker correlations were observed for gestational age (cognitive $\rho = 0.41$; motor $\rho = 0.47$), 5-minute Apgar score ($\rho = 0.45$; 0.48), and birth weight ($\rho = 0.23$, $p = .042$; 0.29 , $p = .009$).

3.3 Predictive Validity of GMA and HNNE

Any abnormal GMA predicted neurodevelopmental delay with a sensitivity and specificity of 95.0% each (Table 2). The continuous HNNE score showed excellent discrimination (AUC = 0.979, 95% CI 0.948–1.000), with an optimal Youden cut-off of ≤ 68 (sensitivity 92.5%, specificity 97.5%). Cramped-synchronized or absent fidgety movements were highly specific: no infant with either pattern had a normal outcome, and these patterns identified 24 of 25 infants with moderate-to-severe delay. The two tools agreed closely ($\kappa = 0.95$); all 38 infants with HNNE ≤ 68 also had abnormal GMA, so combining the tests did not improve accuracy over GMA alone.

Table 2: Predictive Validity of Neonatal Screening Assessments for 18-Month Neurodevelopmental Outcome

Index test	Outcome	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	LR+ / LR-	AUC
GMA any abnormal	Any delay	95.0 (83.5–98.6)	95.0 (83.5–98.6)	95.0 (83.5–98.6)	95.0 (83.5–98.6)	19.00 / 0.05	0.950
GMA any abnormal	Cognitive delay	100.0 (90.4–100.0)	90.9 (78.8–96.4)	90.0 (76.9–96.0)	100.0 (91.2–100.0)	11.00 / 0.00	0.955
GMA any abnormal	Motor delay	94.4 (81.9–98.5)	86.4 (73.3–93.6)	85.0 (70.9–92.9)	95.0 (83.5–98.6)	6.93 / 0.06	0.904
GMA CS or F–	Any delay	60.0 (44.6–73.7)	100.0 (91.2–100.0)	100.0 (86.2–100.0)	71.4 (58.5–81.6)	— / 0.40	0.800
GMA CS or F–	Moderate-to-severe delay	96.0 (80.5–99.3)	100.0 (93.5–100.0)	100.0 (86.2–100.0)	98.2 (90.6–99.7)	— / 0.04	0.980
HNNE ≤ 68	Any delay	92.5 (80.1–97.4)	97.5 (87.1–99.6)	97.4 (86.5–99.5)	92.9 (81.0–97.5)	37.00 / 0.08	0.979*
HNNE ≤ 68	Cognitive delay	97.2 (85.8–99.5)	93.2 (81.8–97.7)	92.1 (79.2–97.3)	97.6 (87.7–99.6)	14.26 / 0.03	0.996*
HNNE ≤ 68	Motor delay	94.4 (81.9–98.5)	90.9 (78.8–96.4)	89.5 (75.9–95.8)	95.2 (84.2–98.7)	10.39 / 0.06	0.973*

Note. Delay = Bayley-III composite < 85; moderate-to-severe delay = < 70. CS = cramped-synchronized; F– = absent fidgety movements; PPV/NPV = positive/negative predictive value; LR = likelihood ratio (— = not estimable because specificity was 100%). *AUC of the continuous HNNE score; other AUCs refer to the dichotomized test.

3.4 Clinical Risk Factors

Infants with neonatal sepsis had lower cognitive (64.80 ± 14.59 vs 87.96 ± 12.25) and motor (64.20 ± 14.39 vs 88.98 ± 13.32) composites than those without sepsis (both $p < .001$), and 22/25 (88.0%) developed delay compared with 18/55 (32.7%) without sepsis ($\chi^2 = 18.85$, $p < .001$). In univariable analysis, gestational age, Apgar score, and sepsis were associated with delay (Table 3). In the multivariable clinical model, only sepsis remained an independent predictor (adjusted OR = 10.61; model AUC = 0.80). When the HNNE score was added, it was the only significant predictor (adjusted OR per 5 points = 0.007, 95% CI 0.0003–0.17, $p = .002$) and model AUC increased to 0.99. GMA could not be entered into the regression because of quasi-complete separation (only 2 of 40 infants with normal GMA had delay).

Table 3: Logistic Regression for Clinical Predictors of Neurodevelopmental Delay

Predictor	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
Gestational age (per week)	0.79 (0.68–0.91)	.001	0.79 (0.55–1.14)	.202
Birth weight (per 100 g)	0.86 (0.72–1.02)	.081	1.32 (0.91–1.92)	.142
Apgar score, 5 min (per point)	0.66 (0.50–0.87)	.003	0.86 (0.50–1.48)	.579
Neonatal sepsis (yes vs no)	15.07 (3.98–57.07)	< .001	10.61 (2.54–44.35)	.001

Note. Outcome = Bayley-III cognitive or motor composite < 85. Adjusted model includes all four predictors (likelihood-ratio $p < .001$; McFadden pseudo- $R^2 = 0.25$).

In summary, half of the cohort showed neurodevelopmental delay at 18 months corrected age. Both GMA and HNNE identified affected infants with high accuracy, cramped-synchronized and absent fidgety movements marked the most severely affected infants, and neonatal sepsis was the strongest clinical risk factor.

4 DISCUSSION

This study found that two low-cost neonatal and early-infancy screening tools, the GMA and the HNNE, predicted 18-month cognitive and motor outcomes in preterm infants from Eastern India with high accuracy. Half of the cohort had neurodevelopmental delay, and neonatal sepsis emerged as the strongest clinical risk factor. These findings support the use of structured neurological screening before and shortly after NICU discharge to prioritize infants for early intervention in resource-constrained settings.

4.1 Predictive Validity of the General Movements Assessment

The high specificity of cramped-synchronized and absent fidgety movements in this cohort is consistent with the established evidence base, in which absent fidgety movements show pooled sensitivity above 95% and specificity close to 90% for later CP (Bosanquet et al., 2013; Kwong et al., 2018) and form part of the recommended pathway for early CP diagnosis (Novak et al., 2017). The graded decline in Bayley-III scores from normal through poor repertoire to cramped-synchronized and absent fidgety movements mirrors the Australian very-preterm cohort of Spittle et al. (2013), in which abnormal general movements were associated with poorer motor and cognitive outcomes at 2 and 4 years. The strong association with cognitive outcome also supports evidence that general-movement quality reflects the integrity of wider cortical-subcortical networks rather than motor pathways alone (Hadders-Algra, 2004; Einspieler et al., 2016).

The sensitivity observed for any abnormal GMA was higher than that reported in the South Indian cohort of John et al. (2022), where fidgety-period assessment predicted CP with 100% sensitivity but broader neurodevelopmental disability with only 25% sensitivity. That study used the Griffiths scales with a lower disability threshold and had a low event rate (9 of 127 children), whereas the present cohort had a higher-risk profile and used a Bayley-III threshold of < 85. The findings are also consistent with Kadam et al. (2023), who showed that GMA findings in Indian preterm infants were associated with developmental quotients at 1 year. Taken together, these data suggest that GMA performs in Indian populations comparably to high-income settings when assessors are trained in Prechtl's method (Juneja et al., 2022).

4.2 Predictive Validity of the Hammersmith Neonatal Neurological Examination

The continuous HNNE score correlated strongly with both Bayley-III domains and discriminated infants with and without delay with an AUC close to 0.98. This agrees with evidence that sub-optimal HNNE findings at term-equivalent age are associated with adverse neurodevelopmental outcome (Dubowitz et al., 1998; Ricci et al., 2008) and with systematic reviews identifying structured neurological examination as one of the most informative early assessments for preterm infants (Noble & Boyd, 2012; Spittle et al., 2008). Because the HNNE can be completed at the bedside before discharge, it offers a practical first screening step, with GMA at 3–5 months post-term confirming risk. In this cohort the two tools were almost fully concordant ($\kappa = 0.95$), so the combination added no accuracy; in settings where only one is available, either appears informative.

4.3 Prevalence and Clinical Risk Factors

The 50% prevalence of delay is higher than that reported in most Indian and international follow-up cohorts (Mukhopadhyay et al., 2010; Oommen et al., 2019; Pascal et al., 2018). This likely reflects the high-risk composition of the cohort, in which 70% of infants had a low 5-minute Apgar score and nearly one-third had sepsis, as well as the use of a < 85 cut-off to compensate for the known underestimation of delay by the Bayley-III (Anderson et al., 2010). The independent association of sepsis with delay agrees with the large NICHD cohort study of Stoll et al. (2004) and with evidence that systemic inflammation contributes to white-matter injury in preterm infants. Gestational age was associated with delay in univariable analysis, consistent with prior evidence (Linsell et al., 2015), but lost significance after adjustment, suggesting that its effect is partly mediated by perinatal complications such as sepsis.

4.4 Clinical Implications and Limitations

These findings support incorporating a bedside HNNE before discharge and a GMA in the fidgety period into routine NICU follow-up in Eastern India, with referral to early intervention for infants with abnormal results (Morgan et al., 2021; Spittle et al., 2015). Both tools require minimal equipment and can be delivered by trained physiotherapists, making them feasible in district-level follow-up clinics.

Several limitations should be considered. First, the sample of 80 infants is modest, and confidence intervals around sensitivity and specificity are correspondingly wide. Second, the HNNE cut-off was derived and tested in the same sample, which is likely to overestimate accuracy; it requires external validation. Third, the Neonatal Behavioural Assessment Scale planned in the protocol was not included in this analysis. Fourth, outcome was assessed at a single time point of 18 months corrected age, which may not capture later cognitive, language, or behavioural difficulties.

(Johnson & Marlow, 2017). Fifth, recruitment from selected centres in one region limits generalizability, and quasi-complete separation prevented estimation of adjusted effects for GMA. Finally, the Bayley-III has not been normed on Indian children, and the Developmental Assessment Scales for Indian Infants could be considered in future work. Larger multicentre studies with longer follow-up, incorporating neuroimaging and language outcomes, are warranted.

5 CONCLUSION

The General Movements Assessment and the Hammersmith Neonatal Neurological Examination showed high predictive validity for cognitive and motor outcomes at 18 months corrected age in preterm infants from Eastern India. Cramped-synchronized and absent fidgety movements identified almost all infants with moderate-to-severe delay, and neonatal sepsis was the strongest independent clinical risk factor. These low-cost tools can be integrated into routine NICU follow-up to target early intervention to the infants at greatest risk, pending confirmation in larger multicentre cohorts.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Acknowledgments

The authors gratefully acknowledge the support of Maharaja Vinayak Global University, Jaipur, Rajasthan, India, and the staff of the participating NICUs and follow-up clinics. The authors thank all parents and caregivers for their participation and commitment throughout the follow-up period.

Disclosure of conflict of interest

The authors declare no conflicts of interest.

Statement of ethical approval

This study was approved by the Institutional Ethics Committee.

Statement of informed consent

Written informed consent was obtained from a parent or legal guardian of every participating infant prior to enrollment.

Data availability

The dataset analyzed during the current study is available from the corresponding author on reasonable request.

Author contributions

K.A.B. contributed to study design, data collection, statistical analysis, and manuscript drafting. M.R.S. contributed to study conception, supervision, critical revision of the manuscript, and final approval of the version submitted for publication.

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