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Original Research

Value of General Movements Assessment in Predicting Neuromotor Development Outcomes in Neonates with Neonatal Respiratory Distress Syndrome: A Prospective Cohort Study

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Abstract

Background: General movements assessment (GMA) is a non-invasive tool for early assessment of neonatal spontaneous movements. This study aimed to assess the effectiveness of GMA in predicting the neuromotor development outcomes of high-risk infants with neonatal respiratory distress syndrome (NRDS). **Methods**: The results of GMA at different phases in 80 children with NRDS expected to be born between September 2020 and July 2021 were collected, and the neuromotor development outcomes were verified by Peabody Developmental Motor Scales-2 (PDMS-2) follow-up from March 2022 to May 2022. The study used the screening method and the Chi-square test to analyze the predictive value of different phases of GMA. **Results**: The GMA writhing movements phase showed an accuracy of 70.00%, a sensitivity of 82.76%, a specificity of 62.75%, a positive predictive value of 55.81%, a negative predictive value of 86.49%, a Youden index of 0.46, and a positive likelihood ratio of 2.22. The GMA fidgety movements phase showed an accuracy of 95.00%, a sensitivity of 96.55%, a specificity of 94.12%, a positive predictive value of 90.32%, a negative predictive value of 97.96%, a Youden index of 0.91, and a positive likelihood ratio of 16.42. The differences between the specificity, accuracy and negative predictive values of GMA were statistically different ($\chi^2_2 = 9.600$, $p_2 < 0.005$; $\chi^2_3 = 17.316$, $p_3 < 0.005$; $\chi^2_5 = 10.268$, $p_5 = 0.001$), while no statistically significant differences were found in the comparison of sensitivity and positive predictive values ($p_1 = 1.000$; $\chi^2_4 = 2.690$, $p_4 = 0.101$). **Conclusions**: GMA has a favorable predictive value for neuromotor development outcomes in children with NRDS. **Clinical Trial Registration**: ChiCTR2200061223.

Keywords: general movements assessment; neonatal respiratory distress syndrome; Peabody Developmental Motor Scales-2; neuromotor development

1. Introduction

With the rapid development of perinatal medical technology and the generation-by-generation renewal of medical emergency equipment in neonatal intensive care units, the survival rate of high-risk infants is improved and the incidence of neonatal respiratory distress syndrome (NRDS) is significantly increased [1]. Preterm infants are more susceptible to NRDS compared to non-preterm newborns, and the frequency of NRDS can reach 7.8% for non-preterm infants with a gestational age of more than 37 weeks [2,3]. Children with NRDS frequently experience increased dyspnea, cyanosis, shortness of breath, respiratory failure (in extreme situations) due to pulmonary surfactant shortage, alveolar atrophy damage, and easily interrupted alveolar surface tension and pulmonary compliance balance [4].

In China, the incidence rate of newborn growth retardation in China is estimated to be between 6% and 8%. One of its notable symptoms is neuromotor dysfunction caused by brain damage. Research has revealed that NRDS is an independent risk factor for extra-uterine growth retardation in infants and children [5,6]. NRDS poses an increased risk of long-term neurodevelopmental disorders [7], and a higher potential for complications such as periventricular white matter softening, nontraumatic intraventricular hemorrhage, and even cerebral palsy in children [8]. Thygesen *et al*. [9] showed that the prevalence of cerebral palsy (CP) in children with NRDS is about 1.9%, which is about four times higher than that in children without NRDS. Cerebral palsy is commonly diagnosed in children between the ages of 12 and 24 months. Delayed diagnosis and intervention may result in missing the optimal plastic stage of the brain, which can adversely impact the effectiveness of treatment [10,11].

Long-term neuromotor developmental abnormalities have an extremely negative impact on children's normal life, learning, and physical and mental health, and are accompanied by high social costs [6]. Consequently, it is essential to recognize aberrant development in children with NRDS as soon as possible and to establish early intervention. With the use of general movements assessment (GMA), a non-invasive neurodevelopmental diagnostic method, it is possible to identify early abnormalities

and to avoid long-term developmental consequences [12]. The prognostic usefulness of GMA for neuromotor development outcomes in children with NRDS has yet to be examined in the literature. Accordingly, this study aimed to establish a theoretical foundation for the importance of early GMA competency development in children with NRDS. Toward that end, 80 live-born children diagnosed with NRDS were recruited and screened. Individual neuromotor development outcomes were then analyzed.

2. Materials and Methods

2.1 Participants

This prospective cohort study recruited 80 infants diagnosed with NRDS at Xuzhou Central Hospital who were expected to be delivered between September 2020 and July 2021. We contacted the infant's guardians via phone numbers, WeChat, and QQ, and have obtained the consent of the guardian. In the study, GMA outcomes were recorded, and their corrected neuromotor developmental outcomes were evaluated between 1 and 1.5 years of age at the outpatient clinic of the Department of Pediatric Rehabilitation at Xuzhou Central Hospital. Subjects had to concurrently satisfy all inclusion, and none of the exclusion, criteria. This research was approved by the Medical Ethics Committee of Xuzhou Rehabilitation Hospital of Xuzhou Medical University (NO: XK-LW-20220319-002).

Inclusion criteria:

(1) Conformity with the diagnostic criteria of neonatal respiratory distress syndrome in the guidebook, European Consensus Guidelines on the Management of Neonatal Respiratory Distress Syndrome in preterm infants [13];

(2) One or more GMAs for each of the writhing movements (term to corrected 48 weeks of age) and the fidgety movements (FMs) (corrected 49–55 weeks of age) phase;

(3) The guardians of the children provided signed informed consent.

Exclusion criteria:

(1) Doubt regarding the mother's last menstruation period;

(2) Metabolic disorders were genetically transmitted via relatives of the children;

(3) Central dyskinesia caused by progressive and degenerative neurological and muscular diseases due to craniocerebral trauma, brain tumors, and other maladies;

(4) Children received orthopedic surgery within the first half year;

(5) Children received injections of botulinum toxin within the prior six months;

(6) Children did not cooperate with follow-up or follow-up outcome was unclear.

2.2 Evaluation Tools

2.2.1 General Movements (GMA)

Standard digital camera unit, iVMS-4200 Client monitoring software, evaluating bed, thermometer, and heater are included in the evaluation unit (Shanghai Fury Industrial Development Co., Ltd. Shanghai, China). The assessment room temperature was set between 28 and 30 degrees Celsius. The camera was positioned 1.5 meters away from the bed and at 45 degrees (inclined down); the appropriate size was selected according to the infant's weight. The infant was placed in the center of the GMA bed, exposing the head, neck, upper limbs, and lower limbs. The initial and follow-up assessments were carried out by two pediatricians with GMA training, using the iVMS-4200 Client monitoring software to monitor the infants' triggered spontaneous movements for 10–20 minutes while awake and while showing no signs of emotional distress, such as screaming or hiccups. In case of disagreement, a third senior GMA-qualified professional reviewed the case and rendered a final evaluation.

Writhing movements and FMs phase assessment results were recorded. The results of the writhing movements evaluation included normal writhing movements (N), poor repertoire (PR), cramped-synchronized (CS) and chaotic (Ch). The results of FMs included the presence of FMs (F+), sporadic FMs (F±), absence of FMs (F–), and abnormal FMs (AF). If numerous examinations were conducted during the writhing phase, the most recent assessment result within eight weeks of the full term was recorded as the writhing phase assessment result, where N was the normal outcome and PR, CS, and Ch were noted as abnormal. The GMA evaluation results between 9 and 15 weeks after full term were considered for analysis. If the fidgety movements phase was assessed more than once, normal fidgety movements were documented as F± (within the second month after term) and F+ (at least once). F– and F± (not appearing in the second month after term) were recorded as aberrant. If the infant evaluated only once, the result of this evaluation shall prevail.

2.2.2 Peabody Developmental Motor Scales-2 (PDMS-2)

PDMS was published in 1983 by Folio and Fewell, renowned experts in child development assessment and intervention in the United States. It was applied in China in 2006 and proved to have good reliability and validity both at home and abroad [14,15]. Rehabilitation therapists with specialized training in operating PDMS-2 were used in the current investigation. This scale contains two subassessment units, namely the gross motor assessment unit and the fine motor assessment unit, which can comprehensively evaluate the outcome of neuromotor development in children aged 0–72 months. A total of six functional areas include: posture, reflex, movement, grasping, physical manipulation, and visuomotor integration. According to the spontaneous willingness and movement completion degree, each assessment was divided into 3 grades: 0, 1, and 2, which could be converted into gross motor quotient (GMQ), fine motor quotient (FMQ), and total motor quotient (TMQ). Subjects were graded according to these scores.

2.3 Diagnostic Criteria for Neuromotor Development Outcomes

2.3.1 Cerebral Palsy

The Chinese Guidelines for Rehabilitation of Cerebral Palsy (2022) [16] was used as the gold standard for the diagnosis of cerebral palsy, whereby the child's motor pattern is aberrant throughout the follow-up of neuromotor development outcomes, and clinical neurological examinations render a diagnosis of cerebral palsy (CP).

2.3.2 Neuromotor Development Delay

PDMS-2 grading is poor (GMQ and/or FMQ scores 70–79) or very poor (GMQ and/or FMQ scores 35–69), and the possibility of cerebral palsy is ruled out on clinical neurological examination.

2.3.3 Normal Developmental Outcome

Normal development outcome was measured as: child with PDMS-2 follow-up assessment score $\geq$80 without abnormal movement pattern.

2.4 Statistical Analysis

All data were analyzed by SPSS 26.0 software (SPSS Inc, Chicago, IL, USA), and non-normally distributed information was expressed using Median (M) (P25, P75). Data were described by frequency, percentage, and descriptive statistical analysis. The McNemar test was used for comparing the otherness of predictive values at a different phase, with differences of a p-value < 0.05 considered statistically significant.

3. Results

3.1 Predicted Outcomes and Follow-Up Results of Neuromotor Development in 80 Children

The follow-up outcome of 80 children was evident. The newborn general information is shown in Table 1. The median Apgar 1-min and Apgar 5-min scores were 8.00 (7.00, 9.00) and 9.00 (8.00, 9.00). The median birth weight was 1935.00 (1407.50, 2740.00) g, with a weight range of 590–4500 g. The median gestational age at birth was 33.43 (31.68, 37.18) weeks, with a gestational age range of 26.43–40.43 weeks. The mean follow-up month age was 14.3 $\pm$ 1.76 months. The specific assessment of various phases of GMA and neuromotor follow-up outcomes are shown in Table 2.

3.2 Evaluation Index of Screening Results at Different Phases of GMA

3.2.1 Writhing Movements Phase Evaluation Index of Screening Results

Of the 80 children, 37 had an evaluated outcome of N, 38 had an evaluated outcome of PR, 5 had an evaluated outcome of CS, 37 had a normal (–) outcome and 43 were abnormal (+). The writhing phase showed a sensitivity of 82.76% (24/29), a specificity of 62.75% (32/51), a positive predictive value of 55.81% (24/43), a negative predictive value of 86.49% (32/37), a Youden index of 0.46, and a positive likelihood ratio of 2.22, with the moderate agreement (Table 3).

3.2.2 Fidgety Movements Phase Evaluation Index of Screening Results

Of the 80 children, 50 had an assessment outcome of F+, 25 had an assessment outcome of F$\pm$, 5 had an assessment outcome of F–, 50 had a normal (–) and 30 had an abnormal (+) assessment outcome during the fidgety movements phase of the GMA. The phase of the fidgety movements showed a sensitivity of 96.55% (28/29), a specificity of 94.12% (48/51), a positive predictive value of 90.32% (28/31), a negative predictive value of 97.96% (48/49), a Youden index of 0.91, and a positive likelihood ratio of 16.42. There was a high degree of consistency (Table 4).

3.3 Statistical Variability Analysis of the Predictive Value of Different Phases of GMA in Children with NRDS

Significant differences in the specificity, accuracy, and negative predictive value of the GMA writhing movements phase assessment were found when compared with the fidgety movements phase assessment ($\chi^2_2 = 9.600$, $p_2 < 0.005$, $\chi^2_3 = 17.316$, $p_3 < 0.005$, $\chi^2_5 = 10.268$, $p_5 = 0.001$). Comparing sensitivity and positive predictive value in the phase of the writhing movements, no significant significance was found ($p_1 = 1.000$, $\chi^2_4 = 2.690$, $p_4 = 0.101$) (Table 5).

4. Discussion

NRDS is a common neonatal condition that can lead to significant morbidity and long-term developmental delays. Studies have shown that the incidence of CP in children with NRDS is about four times higher than in children without NRDS [9]. Therefore, the impact of NRDS on neurodevelopmental outcomes in infants and children cannot be ignored, especially for low-and-middle income countries [17,18]. The age range of 0–2 years is a critical period of rapid brain development. Human brain development is a complex dynamic evolutionary process that is precisely regulated during this sensitive period. Specifically, during this time, the neurons and synapses of the brain undergo rapid growth and remodeling. Interventions during this phase can take advantage of the brain's greater plasticity and regulation abilities [10]. This study verified the accuracy and importance of the two-phase GMA for predicting neurodevelopmental outcomes in children with NRDS and provided a theoretical basis for early assessment and clinical intervention.

In this study, the follow-up outcomes of 80 children with NRDS were: five children with cerebral palsy (6.25%), 24 children with neuromotor retardation (30.00%), and 51 children with normal neuromotor development (63.75%). Our assessment was based on an epi-

Table 1. Newborn general information description (n = 80).

Variables	Class	N	Cum. No.	%	Cum.%
Newborn					
Embryonic age	<37 weeks	60	60	75.00	75.00
	37–40 weeks	20	80	25.00	100.00
Birth weight	Low birth weight	59	59	73.75	73.75
	Normal birth weight	20	79	25.00	98.75
	Macrosomia	1	80	1.25	100.00
Gender	Male	45	45	56.25	56.25
	Female	35	80	43.75	100.00
NRDS grading	Grade I	52	52	65.00	65.00
	Grade II	25	77	31.25	96.25
	Grade III	3	80	3.75	100.00
Neonatal Intensive Care Unit	Yes	38	38	47.50	47.50
	No	42	80	52.50	100.00
Periventricular leukomalacia	Yes	3	3	3.75	3.75
	No	77	80	96.25	100.00
Intracranial hemorrhages	Yes	8	8	10.00	10.00
	No	72	80	90.00	100.00
Surfactant therapy	Yes	75	75	93.75	93.75
	No	5	80	6.25	100.00
Mechanical ventilation	Yes	33	33	41.25	41.25
	No	47	80	58.75	100.00
Parturient					
Advanced maternal age (>35 years old)	Yes	22	22	27.50	27.50
	No	58	80	72.50	100.00
Education of mother	Specialty or below	65	65	81.25	81.25
	Undergraduate	12	77	15.00	96.25
	Higher	3	80	3.75	100.00
Conception method	*In vitro* fertilization-embryo transfer	14	14	17.50	17.50
	Conceived naturally	66	80	82.50	100.00
Delivery method	Vaginal delivery	28	28	35.00	35.00
	Cesarean	52	80	65.00	100.00
Chorioamnionitis	Yes	59	59	73.75	73.75
	No	21	80	26.25	100.00
Gestational hypertension	Yes	29	29	36.25	36.25
	No	51	80	63.75	100.00
Gestational diabetes	Yes	18	18	22.50	22.50
	No	62	80	77.50	100.00
HELLP syndrome	Yes	2	2	2.50	2.50
	No	78	80	97.50	100.00
Spontaneous onset of labor	Yes	57	57	71.25	71.25
	No	23	80	28.75	100.00
Premature rupture of membranes	Yes	46	46	57.50	57.50
	No	34	80	42.50	100.00
Hormone therapy	Yes	69	69	86.25	86.25
	No	11	80	13.75	100.00

NRDS, Neonatal Respiratory Distress Syndrome; HELLP, Hemolysis Elevated Liver Enzymes Low Platelets.

Table 2. The constituent ratio of neuromotor development outcomes in children [n (%)].

	Writhing movements			Fidgety Movements		
	N	PR	CS	F+	F±	F–
Cerebral palsy	1 (2.70)	1 (2.63)	3 (60.00)	0 (0)	1 (3.85)	4 (80.00)
Develop retardation	4 (10.81)	19 (50.00)	1 (20.00)	1 (2.04)	22 (84.61)	1 (20.00)
Develop normally	32 (86.49)	18 (47.37)	1 (20.00)	48 (97.96)	3 (11.54)	0 (0)
Total	37 (100.00)	38 (100.00)	5 (100.00)	49 (100.00)	26 (100.00)	5 (100.00)

N, normal writhing movements; PR, poor repertoire; CS, cramped-synchronized; F+, presence of fidgety movements; F±, sporadic FMs; F–, absence of FMs; FMs, fidgety movements.

Table 3. Writhing phase predicted outcome *vs.* PDMS-2 outcome (n).

GMA predicted outcome	Neuromotor developmental outcomes		Total
	(+) [b]	(–)	
(+) [a]	24	19	43
(–)	5	32	37
Total	29	51	80

(+) [a] was the writhing phase assessment abnormality; (+) [b] includes neuromotor development delay and CP; PDMS-2, Peabody Developmental Motor Scales-2; GMA, general movements assessment; CP, cerebral palsy.

Table 4. Fidgety phase predicted outcome *vs.* PDMS-2 outcome (n).

GMA predicted outcome	Neuromotor developmental outcomes		Total
	(+) [b]	(–)	
(+) [a]	28	3	31
(–)	1	48	49
Total	29	51	80

(+) [a] was the fidgety phase assessment abnormality; (+) [b] includes neuromotor development delay and CP; PDMS-2, Peabody Developmental Motor Scales-2; GMA, general movements assessment; CP, cerebral palsy.

Table 5. Comparison each phase predictive validity of GMA.

GMA evaluation phase	Writhing movements	Fidgety movements	χ^2	*p*-value
Sensitivity	82.76%	96.55%	-	1.000
Specificity	62.75%	94.12%	9.600	<0.005
Accuracy	70.00%	95.00%	17.316	<0.005
Positive predictive value	55.81%	90.32%	2.690	0.101
Negative predictive value	86.49%	97.96%	10.268	0.001

GMA, general movements assessment.

demiological study that calculated the overall incidence of CP to be approximately 2.11 per 1000 [19]. Among the five children with CP up to 80% of the GMA evaluation results were CS and F–. White lung is an important manifestation of respiratory impairment in children with NRDS. An unexpected finding was that four children with confirmed CP had white lung. We speculate that these children may have suffered from more severe asphyxia and hypoxia secondary to NRDS. Brain cells are extremely sensitive to hypoxia, which severely affects the formation and maturation of normal synapses during brain development in children with NRDS. In the later follow-up, neurological examination showed different degrees of brain tissue structure injury, mainly periventricular leukomalacia or basal ganglia injury. In this study, CS and F– had the highest predictive value for cerebral palsy. Kwong *et al*. [20] assessed spontaneous movements in high-risk children and similarly validated the predictive value of CS and F– for developmental outcomes. Among the 24 children with motor retardation, 21 demonstrated low frequency and amplitude of normal movements in multiple assessments of the phase of the fidgety movements; two children had F+ results in the phase of the fidgety movements but were not followed up with multiple GMA and did not undergo early intervention; and one child had CS and F– results in the GMA and did not later develop into CP.

The results of our trial show that both phases of GMA had good predictive value for motor developmental outcomes in children at risk for NRDS, but the specificity, accuracy, and negative predictive value of the fidgety movements phase were statistically different from that of the phase of the writhing movements. Further, the predictive value of the phase of the fidgety movements was better than that of the phase of the writhing movements. Huisenga *et al*. [21] demonstrated that the fidgety movements phase of GMA in children undergoing surgery for complex congenital heart disease in the neonatal period is more informative than the writhing movements phase. The results of the GMA fidgety movements assessment are of great value in various types of high-risk children, such as those born prematurely [22] and those undergoing *in vitro* fertilization-embryo transfer [23]. The results of the two-phase persistent abnormal GMA predict a high risk of neuromotor developmental delay and even cerebral palsy in high-risk children. A standardized tool assessment and neurological examination can determine the neuromotor developmental outcome of children and provide early scientific intervention for children at high risk of abnormal assessment. This should improve neurodevelopmental plasticity and the neuromotor developmental outcome of children, while reducing the anxiety of children's guardians.

GMA has a high predictive value for the developmental outcome of children at risk for NRDS. It is important to evaluate GMA in children with NRDS and provide early intervention, especially in the fidgety movements phase. Pediatricians must further increase their vigilance and awareness of the importance of GMA screening in children with full-term NRDS, to expand the application of GMA and optimize the neuromotor developmental outcome of children with NRDS.

4.1 Limitations

This study has certain limitation. As a single-center trial, the selected data may be significantly representative of the broader population. Although most babies were assessed multiple times in different phases of the GMA follow-up, there were still a few cases where children had only one assessment in each. Therefore, there may be some slight differences in the eventual GMA results of these children. Further, the follow-up time of children in this study was limited, and there was a lack of more standardized assessment tools to support the data. Finally, gestational age is an important factor for the prevalence of NRDS children. The study did not classify premature and non-premature children according to the gestational age of the enrolled children, so a more detailed analysis of gestational age is lacking.

4.2 Future Directions

To make the experimental data more substantive and representative, multi-center trials are necessary to expand the inclusion of NRDS children with more detailed GMA results, and to explore the predictive value of GMA for NRDS children with different gestational ages. The follow-up time must also be extended. The neurological, psychological, intellectual, motor and social behaviors of the children must be evaluated comprehensively and systematically by standardized assessment tools.

5. Conclusions

This study is the first in China to investigate the predictive value of GMA for neuromotor development outcomes in children with NRDS. Guardians should pay attention to the neuromotor development outcomes of children while heeding the prognostic outcomes of NRDS, so as to prevent long-term developmental disabilities caused by NRDS and its severe sequelae. The study also provides a theoretical basis for early intervention of NRDS children with poor neuromotor development outcomes, to help children reach the milestone of normal growth and development; in so doing, the study's finding and recommendations improve the overall health level of Chinese children.

Abbreviations

NRDS, neonatal respiratory distress syndrome; GMA, general movements assessment; PDMS-2, Peabody Developmental Motor Scales-2; GMQ, gross motor quotient; FMQ, fine motor quotient; TMQ, total motor quotient; N, normal writhing movements; PR, poor repertoire; CS, cramped-synchronized; Ch, chaotic; FMs, fidgety movements; F+, presence of fidgety movements; F±, sporadic fidgety movements; F–, absence of fidgety movements; AF, abnormal fidgety movements; CP, cerebral palsy.

Availability of Data and Materials

The data supporting this study is available on reasonable request from the corresponding author.

Author Contributions

The authors confirm their contribution to the paper as follows: study conception and design: HW, CS; data collection: HW, CS; analysis and interpretation of results: MZ, PL, WC; draft manuscript preparation: HW. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This research was approved by the Medical Ethics Committee of Xuzhou Rehabilitation Hospital of Xuzhou Medical University (NO: XK-LW-20220319-002). Informed consent was obtained from the guardians of all par-

ticipants involved in the study. Written informed consent was also obtained from the guardians to publish this paper.

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Conflict of Interest

The authors declare no conflict of interest.

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