Follow-Up Study On Physical And Neurodevelopmental Outcomes In Extremely Preterm Infants At The Corrected Age Of 12 Months

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Abstract

Objective: This study aimed to investigate the physical and neurological outcomes of extremely preterm infants (EPIs) at the corrected age of 12 months, to provide the basis for parents and doctors to make treatment decisions.

Methods: The follow-up data of EPIs who survived and were discharged from Women's Hospital of Nanjing Medical University during 2018–2020 were analyzed. The weight, length, and head circumference by age were recorded and compared with those of term infants to investigate the catch-up growth of EPIs. Children at 12 months' corrected age were assessed using the Gesell Developmental Scale. The relationship of basic data with the catch-up growth and nervous system development was also discussed.

Results: In total, 70 infants were included in this study. At the 1-year visit, the EPIs were larger than the 50th percentile for weight, length, and head circumference (HC) of the World Health Organization Child Growth Standards. The percentages of catch-up in weight, length, and HC were all greater than 50%. Our multivariate logistic regression showed that the higher the weight gain in the first year of life (OR = 1.45, 95% CI: 1.04–2.03, $P = 0.03$), the higher the body length gain (OR = 5.72, 95% CI: 1.08–30.21, $P = 0.04$), the higher the birth weight (OR = 1.03, 95% CI: 1.01–1.02, $P = 0.01$), and the higher the weight gain (OR = 1.32, 95% CI: 1.09–1.61, $P = 0.01$), which would induce the catch-up growth of EPIs. Furthermore, after 1 year of follow-up, the proportions of mild-to-moderate abnormal development quotient (DQ) in the five functional domains were all greater than 10%. Hence, the early catch-up growth was beneficial for neurodevelopment.

Conclusions: Close developmental surveillance is of great significance in improving the long-term quality of life of EPIs.

Introduction

Prematurity was defined according to the World Health Organization (WHO) report, which classifies extremely preterm infants (EPIs) as individuals born before 28 weeks of gestational age. The medical treatment and diagnosis capacity for EPIs significantly improved, and the survival rate of EPIs substantially increased owing to the rise and development of perinatal medicine, as well as the markedly improved technical levels in neonatal intensive care units (NICUs) [1,2]. According to the WHO, it is estimated that China has the second-highest number of premature births in the world [3]. EPIs account for about 4.1% of all preterm births. However, it must be considered that EPIs are a different group in terms of their anatomical and physiological maturity, where the risk of adverse outcomes is the highest [4,5]. Therefore, it is important to emphasize the care of EPIs around prognosis rather than the survival rate.

Understanding the effects of the neurodevelopment of EPIs for both families and services that provide care are necessary. Developmental follow-up for EPIs should be an integral part of their clinical care. A detailed neurodevelopmental assessment gives families specific information for supporting their child's development through anticipatory guidance, as well as a pathway to early intervention following the identification of any delay or disability. At a service level, understanding the effect of EPIs on developmental outcomes is needed to evaluate and inform ongoing clinical practice and to counsel families.

Although efforts have been made in China to improve the survival rate of EPIs, few comprehensive clinical analyses on EPIs have been conducted, and large-sample clinical data to analyze the growth of EPIs and the main neurodevelopment-related factors are lacking. The present study aimed to assess the physical and neurological prognoses of EPIs, providing the basis for parents and doctors to make treatment decisions.

Methods

The study was approved by the Institutional Review Board of Nanjing Maternity and Child Health Care Hospital. Written informed consent was obtained from all the patients' families before their participation.

The primary study sample consisted of EPIs treated at the NICU in Women's Hospital of Nanjing Medical University between January 2018 and October 2020 ($n = 160$). The exclusion criteria for the study included severe congenital malformation ($n = 11$); death before the age of 1 year ($n = 29$); infants with incomplete medical records ($n = 25$); infants with suspected genetic, metabolic, or chronic disease ($n = 12$); and those with growth and developmental follow-ups at some other hospital ($n = 13$). The final study sample consisted of 70 preterm infants. Children were stratified according to the gestational age at birth (GA): 24–25+6 weeks, 26–26+6 weeks, and 27–27+6 weeks; and birth weight: <1000 g (VLBW) and 1000–1500 g (ELBW).

The information regarding the perinatal and neonatal period was obtained by a systematic examination of the participants' medical records, including personal health booklets, hospital discharge notes, and follow-up or outpatient information notes.

Physical measurement

The physical traits recorded were HC, body length, and body weight, which were measured three times during the first year after birth. Adequate catch-up growth was defined as a body weight reaching the 25th percentile of the corrected age for the appropriate-for-gestational-age children [6].

Neurological developmental assessment

Neurobehavioral development for infants at the corrected age of 12 months was assessed using the Gesell Developmental Scale (GDS), which contained five subscales of gross motor, fine motor, adaptive behavior, language, and social behavior. Infant development was assessed using the development quotient (DQ) according to the following criteria: normal ($DQ \geq 85$), borderline ($75 \leq DQ < 85$), and abnormal ($DQ < 75$).

Statistical analysis

Data were double entered, verified for accuracy, and analyzed using SPSS 21.0. All results were expressed as mean values $\pm$ standard deviation. Differences in population rates between the two or more groups were evaluated using the chi-squared test. Data were evaluated using analysis of variance or *t* test for comparisons between groups. The logistic regression analysis was used to determine the factors for catch-up growth. $P < 0.05$ indicated a statistically significant difference.

Results

Physical growth

The study involved 70 VLBW/ELBW EPIs, including 30 VLBW with a mean gestational age of (25.13 ± 0.77) weeks and a mean birth weight of (838.17 ± 91.35) g, and 40 ELBW with a mean gestational age of (26.63 ± 0.58) weeks and a mean birth weight of (1143.01 ± 108.84) g; the differences between the two groups were statistically significant ($P < 0.05$). The singleton and twin birth cases in VLBW and ELBW groups were 21 and 9, and 35 and 5, respectively, but no statistically significant differences were found between the two groups ($P > 0.05$). The natural labor in the VLBW and ELBW groups was 25 and 28, respectively; statistically significant differences were found between the two groups ($P < 0.05$) (Table 1).

Table 1 A completion of the clinical data in the two groups

	VLBW(n=30case)	ELBW(n=40case)	t/ c2	p
GA(weeks)	25.13 $\pm$ 0.77	26.63 $\pm$ 0.58	-9.17	0.01
Sex	male(16)	male(25)	0.59	0.44
	female(14)	female(15)		
multiple birth	singleton21	singleton35	3.28	0.07
	twins9	twins5		
Fertilization way	natural conception20	natural conception24	0.33	0.56
	assisted reproductive technology(ART)10	ART16		
Delivery modes	natural labor25	natural labor28	0.06	0.005
	cesarean section5	cesarean section12		
Birth weight(g)	838.17 $\pm$ 91.35	1143.01 $\pm$ 108.84	-9.87	0.01
Birth body length(cm)	32.33 $\pm$ 2.68	35.63 $\pm$ 2.70	-5.06	0.01
Birth head circumference(cm)	23.52 $\pm$ 1.37	25.86 $\pm$ 1.12	-6.24	0.01
Apgar's score	Apgar's score $\leq$ 3(4)	Apgar's score $\leq$ 3(5)	9.93	0.007
	4~7(18)	4~7(10)		
	$\geq$ 8(8)	$\geq$ 8(25)		
Mother's height before pregnancy(cm)	160cm 3	160cm 10	1.29	0.255
	$\geq$ 160cm 27	$\geq$ 160cm 30		
growth rate of weight ^a (g/day)	30.76 $\pm$ 5.97	30.16 $\pm$ 7.93	0.34	0.72
growth rate of body length ^b (cm/month)	2.96 $\pm$ 0.92	3.10 $\pm$ 0.62	-0.79	0.43
growth rate of head circumference ^c (cm/month)	1.21 $\pm$ 0.27	1.44 $\pm$ 0.38	-2.78	0.007

^agrowth rate of weight: the weight gain rate from 1 to 3 months of life ^bgrowth rate of body length: the body length gain rate from 1 to 3 months of life ^cgrowth rate of HC: the HC gain rate from 1 to 3 months of life.

At the 1-year visit, the EPIs included in this study were larger than the 50th percentile for weight, length, and HC of the WHO Child Growth Standards. At the corrected age of 3 and 6 months, rapid growth was most pronounced. It showed a steady upward trend and then decreased slightly over the remaining months, especially in terms of body length and HC (Table 2).

Table 2 Physical growth (mean $\pm$ SD) at different ages by infant sex

	corrected GA	male	percentile	female	percentile
		Mean±SD		Mean±SD	
Weight (kg)	3	6.67±1.13	P ₅₀ ~P ₇₅	6.63±0.71	P ₇₅ ~P ₈₀
	6	8.33±1.59	P ₅₀ ~P ₇₅	8.20±0.85	P ₇₅ ~P ₈₀
	12	9.65±1.72	P ₅₀ ~P ₇₅	8.91±1.64	P ₅₀ ~P ₇₅
body length (cm)	3	61.22±2.87	P ₂₅ ~P ₅₀	61.68±2.80	P ₇₅ ~P ₈₀
	6	68.12±3.04	P ₅₀ ~P ₇₅	68.66±2.85	P ₈₀ ~P ₉₅
	12	74.82±3.10	P ₂₅ ~P ₅₀	74.39±3.66	P ₅₀ ~P ₇₅
head circumference (cm)	3	40.47±1.22	P ₂₅ ~P ₅₀	40.00±1.09	P ₅₀ ~P ₇₅
	6	43.44±1.30	P ₅₀ ~P ₇₅	42.62±1.10	P ₅₀ ~P ₇₅
	12	45.44±1.28	P ₂₅ ~P ₅₀	44.49±1.94	P ₂₅ ~P ₅₀

As shown in Table 3, the percentage of catch-up in weight in the VLBW group was 28%, 26%, and 32%, the percentage of catch-up in weight in the ELBW group was 33%, 31%, and 31%; however, no statistically significant differences were found between the two groups ($P > 0.05$). The percentage of catch-up in body length in the VLBW group was 25%, 23%, and 25%, and the percentage of catch-up in body length in the ELBW group was 33%, 28%, and 29%, but no statistically significant differences were observed between the two groups ($P > 0.05$). The percentage of catch-up in HC in the VLBW group was 30%, 26%, and 27%, and the percentage of catch-up in HC in the ELBW group was 32%, 27%, and 29%; the differences between the two groups were statistically significant at corrected 12 months ($P < 0.05$) (Table 3).

Table 3 Completion of catch-up growth

		corrected age (month)					
		3		6		12	
weight	VLBW	28%	total(61%)	26%	total(57%)	32%	total(63%)
	ELBW	33%		31%		31%	
body length	VLBW	25%	total(58%)	23%	total(51%)	25%	total(54%)
	ELBW	33%		28%		29%	
head circumference	VLBW	30%	total(62%)	26%	total(53%)	25%*	total(56%)
	ELBW	32%		27%		31%*	

* $\chi^2=0.39$, $p=0.05$.

The logistics regression analysis was performed assuming whether suitable catch-up growth could be achieved as the dependent variable. It was conducted with sex, multiple birth, GA, birth weight, birth body length, birth HC, mother's height before pregnancy, Apgar's score, growth rate of weight, growth rate of body length, and growth rate of HC as independent variables. The assigned values of the multivariate regression variables are shown in Table 4.

Our multivariate logistic regression analysis showed that the higher weight gain rate from 1 to 3 months of life (OR = 1.45, 95% CI: 1.04–2.03, $P = 0.03$) would induce catch-up growth of EPIs of weight, the higher body length gain rate from 1 to 3 months of life (OR = 5.72, 95% CI: 1.08–30.21, $P = 0.04$) would induce catch-up growth of EPIs of body length, and the higher birth weight rate (OR = 1.03, 95% CI: 1.01–1.02, $P = 0.01$) and the higher weight gain rate from 1 to 3 months of life (OR = 1.32, 95% CI: 1.09–1.61, $P = 0.01$) would induce catch-up growth of EPIs of HC (Table 5).

Table 4 Assigned values of the multivariate regression variables

Factors	assigned values
sex	1=male 2=female
multiple birth	1= singleton 2= twin
GA	numerical variable
Birth weight	numerical variable
Birth body length	numerical variable
Birth head circumference	numerical variable
Mother's height before pregnancy	1=<160cm, 2= $\geq$ 160cm
Apgar's score	1=Apgar's score $\leq$ 3 2=4~7 3= $\geq$ 8
Fertilization way	1= Natural conception 2= ART
Delivery modes	1= Natural labor 2= Cesarean section
growth rate of weight	numerical variable
growth rate of body length	numerical variable
growth rate of head circumference	numerical variable

Table 5 A multivariate logistic analysis of the catch-up growth of the EPIS

	Factors	B	SE	Wald c2	P	OR(95%CI)
weight	growth rate of weight	0.37	0.17	4.82	0.03	1.45 1.04 2.03
body length	growth rate of body length	1.74	0.85	4.22	0.04	5.72 1.08 30.21
head circumference	birth weight	0.01	0.01	7.04	0.01	1.03 1.01 1.02
	growth rate of weight	0.28	0.10	8.03	0.01	1.32 1.09 1.61

Neurological development

Using GDS, the proportion of mild-to-moderate abnormal DQ of adaptability, gross motor movement, fine movement, language, and personal social contact at the corrected age of 12 months was 17.1%, 12.9%, 15.7%, 20.9%, and 14.3%, respectively. Further, 10.2% were scored > 85 in all the five functional areas (Table 6). The factors that influenced DQ were also investigated.

The effect of catch-up growth on DQ was studied for infants who had recently completed their bodily catch-up growth. The results indicated that the CG group of weight had significantly higher DQ scores compared with the NO-CG group in gross motor movement domains. Also, the CG group of body length had significantly higher DQ scores than the NO-CG group in adaptability and fine movement domains. However, the CG group of HC showed no significant difference compared with the NO-CG group in any of the domains (Table 7).

Table 6 Results of GDS at the corrected age of 12 months

Functional domains	Normal	Borderline	Abnormal
Adaptability	41.4%	41.5%	17.1%
Gross motor movement	48.6%	38.5%	12.9%
Fine movement	40.0%	44.3%	15.7%
Language	31.4%	47.7%	20.9%
Personal social contact	45.7%	40.0%	14.3%

Table 7 A comparison of DQ of the EPIS of the catch-up growth in the two groups

		Adaptability			Gross motor movement			Fine movement			Language		
		mean±SD	t	p	mean±SD	t	p	mean±SD	t	p	mean±SD	t	p
weight	CG	82.21±7.63	-0.45	0.65	88.86±4.10	-3.15	0.008	83.62±8.32	-0.55	0.58	80.25±9.40	-0.23	0.81
	NO-CG	82.90±8.50			82.90±8.50			85.43±7.45			81.14±9.70		
body length	CG	83.09±9.10	2.06	0.04	83.54±8.51	0.09	0.92	85.06±8.54	3.13	0.003	80.15±10.29	-0.31	0.75
	NO-CG	79.81±4.61			83.38±5.25			79.56±5.25			81.00±6.15		
head circumference	CG	82.34±7.60	-0.008	0.99	82.73±8.64	-1.55	0.07	83.34±7.96	-0.93	0.35	79.54±9.36	-1.44	0.16
	NO-CG	82.36±7.66			86.57±6.43			85.64±9.22			83.57±9.46		

Discussion

Currently, the birth rate of EPIs in China has increased, and the treatment success rate is significantly higher than earlier. Gestational age and weight make EPIs even more susceptible to the effects of perinatal growth retardation, unlike normal full-term infants. The perinatal growth retardation is followed by a period of catch-up growth, which usually starts in early infancy^[7]. Some previous studies suggested that achieving catch-up growth in an early stage after birth was a significant factor in long-term growth and neurodevelopment outcomes^[8, 9]. A relatively high percentage of preterm infants achieved catch-up growth during the first year of life^[10]. Although less research on the catch-up of EPIs has been conducted in China, the data from our study indicated that the weight, length, and HC all rose rapidly within the corrected age of 6 months, but the growth rate slowed down after the corrected age of 6 months. In addition, the total rates of catch-up in weight, body length, and HC all reached more than 50% at the corrected age of 3, 6, and 12 months, respectively. It was possible that EPIs benefited from the improvements in nutritional support and routine follow-up and then experienced a period of accelerated postnatal growth before the corrected age of 6 months. The peak catch-up growth rates for weight, length, and HC were noted before 6 months, which had important clinical implications. It should be noted, in terms of growth levels and catch-up growth rates, a slight downward trend was observed from 6 months, especially for HC in the VLBE group. Some of the children in this age group included those transiting from breast milk to complementary foods, which, when given, might not be adequate in terms of both nutrient content and amount of intake to meet the requirements for growth. However, to support this hypothesis, additional studies focusing not only on dietary patterns but also on other aspects of feeding habits are needed to better understand the role of early feeding habits.

Our study showed that birth weight, weight, and body length gain rates from 1 to 3 months of life were the protective factors for EPIs. Birth weight played an important role in the prognostication of growth and development of preterm infants with systemic structural and functional maturation; it is one of the main determinants of future physical and brain development. Our study suggested that the effects of early infancy weight and body length gain seemed to be conducive to catch-up growth. Hack et al., however, discussed that catch-up growth throughout infancy was associated with the measures of obesity at the age of 14 and was therefore not beneficial^[11]. A study on infants with gestational age less than 32 weeks and/or birth weight less than 1500 g and followed up over 10 years found that higher weight or height at the age of 5 years was associated with greater weight at the age of 1 year^[10].

The GDS is used to evaluate the function of the central nervous system, which consists of five domains, including the adaptive domain, gross motor domain, fine motor domain, language domain, and social domain. Preterm infants show an increased risk of adverse consequences in various aspects of the development of premature babies, especially in terms of cognitive function and language. Our study findings were consistent with previous results^[12, 13]. LBW infants are at a higher risk of growth restriction and delayed motor and language development in the later stage^[14, 15]. Early catch-up growth is beneficial for neurodevelopment^[16]. Our findings showed that the CG group of weight and body length had a higher DQ of neurological outcomes than the NO-CG group. It has been suggested that a smaller HC is related to poorer cognitive outcomes^[17], but our study investigating neurodevelopment did not find an association between catch-up growth for HC and neurocognitive outcomes. Studies have shown almost one third of EPIs with some degree of developmental delay or abnormality until the age of 2 years^[18]. This study suggested that the catch-up growth in the first year could be closely monitored to early identify impaired cognition in the high-risk preterm infants.

In conclusion, our study cohort consisted solely of EPIs, a population rarely studied previously. The EPI survival rate continues to improve with the development of neonatal medicine. The present study suggested that physical growth and neurological development remained a significant problem for prematurely born infants in the first year. Besides physical growth retardation and inability to catch up with their peers in height, weight, and HC, some EPIs are at increased risk of early developmental delays, especially in speech-language development. Further studies should aim at high-risk groups of EPIs to adopt the principle of "early detection, early intervention" to help and support in preventing or reducing the occurrence of developmental delays.

Declarations

Data availability

All datasets generated for this study are included in the manuscript and/or the supplementary files.

Ethics approval and consent to participate

The study was approved by the Institutional Review Board of Nanjing Maternity and Child Health Care Hospital. All participants provided written informed consent. All methods performed in accordance with relevant regulations and guidelines.

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

The authors declare no competing interests.

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Author contributions

Tong M and Chi X designed the study. Wang J, Yang Y, Zhang X and Guo X carried out the study and collected data. Wang J, Zhang M and Hong Q conducted the statistical analysis and interpretation. Wang J wrote the report. Tong M and Chi X revised the report. All the authors reviewed the report and approved the final version.

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References

- [1] Choi S H, Park Y S, Shim K S, et al. Recent trends in the incidence of multiple births and its consequences on perinatal problems in Korea[J]. J Korean Med Sci, 2010,25(8):1191-1196.
- [2] Wu X P, Gu C L, Han S P, et al. A multicenter retrospective study on survival rate and complications of very preterm infants[J]. Zhongguo Dang Dai Er Ke Za Zhi, 2021,23(8):814-820.
- [3] Chawanpaiboon S, Vogel J P, Moller A B, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis[J]. Lancet Glob Health, 2019,7(1):e37-e46.
- [4] Blencowe H, Cousens S, Chou D, et al. Born too soon: the global epidemiology of 15 million preterm births[J]. Reprod Health, 2013,10 Suppl 1:S2.
- [5] Schlappach L J, Adams M, Proietti E, et al. Outcome at two years of age in a Swiss national cohort of extremely preterm infants born between 2000 and 2008[J]. BMC Pediatrics, 2012,12(1).
- [6] Danhua W, Xihong L. Recommendations for feeding preterm or low birth weight infants after hospital discharge[J]. Zhonghua Er Ke Za Zhi, 2016,54(01):6-12.
- [7] Euser A M, de Wit C C, Finken M J, et al. Growth of preterm born children[J]. Horm Res, 2008,70(6):319-328.
- [8] Knops N B, Sneeuw K C, Brand R, et al. Catch-up growth up to ten years of age in children born very preterm or with very low birth weight[J]. BMC Pediatr, 2005,5:26.
- [9] Westerberg A C, Henriksen C, Ellingvag A, et al. First year growth among very low birth weight infants[J]. Acta Paediatr, 2010,99(4):556-562.
- [10] Deng Y, Yang F, Mu D. First-year growth of 834 preterm infants in a Chinese population: a single-center study[J]. BMC Pediatrics, 2019,19(1).
- [11] Hack M, Schluchter M, Margevicius S, et al. Trajectory and correlates of growth of extremely-low-birth-weight adolescents[J]. Pediatr Res, 2014,75(2):358-366.
- [12] Adams-Chapman I, Watterberg K L, Nolen T L, et al. Neurodevelopmental outcome of preterm infants enrolled in myo-inositol randomized controlled trial[J]. Journal of Perinatology, 2021,41(8):2072-2087.

- [13] Barnes-Davis M E, Williamson B J, Merhar S L, et al. Extremely preterm children exhibit altered cortical thickness in language areas[J]. Scientific Reports, 2020,10(1).
- [14] Streimish I G, Ehrenkranz R A, Allred E N, et al. Birth weight- and fetal weight-growth restriction: impact on neurodevelopment[J]. Early Hum Dev, 2012,88(9):765-771.
- [15] Wang B, Sun J, Sun Y, et al. A clinical analysis of very and extremely low birth weight preterm infants[J]. Am J Transl Res, 2021,13(8):9395-9403.
- [16] Belfort M B, Gillman M W, Buka S L, et al. Preterm infant linear growth and adiposity gain: trade-offs for later weight status and intelligence quotient[J]. J Pediatr, 2013,163(6):1564-1569.
- [17] Yu W H, Wang S T, Chen L W, et al. Effect of first-month head-size growth trajectory on cognitive outcomes in preterm infants[J]. J Formos Med Assoc, 2022,121(1 Pt 2):367-374.
- [18] Taczała J, Latałski M, Dmoszyńska-Graniczka M, et al. Neurodevelopmental outcome and early rehabilitation of premature babies - is it needed in the first 2 years of life?[J]. Annals of Agricultural and Environmental Medicine, 2021,28(1):172-178.