

Poor Head Growth Is Associated with Later Mental Delay among Vietnamese Preterm Infants: A Follow-up Study

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ABSTRACT

Background: Preterm infants in low- and middle-income countries are at high risk of poor physical growth, but their growth data are still scarce.

Objectives: To describe the growth of Vietnamese preterm infants in the first 2 years, and to compare with references: World Health Organization (WHO) child growth standards, and healthy Southeast Asian (SEA) infants. Further, to assess the association between growth in the first year and neurodevelopment at 2 years corrected age (CA).

Methods: We conducted a cohort study to follow up preterm infants discharged from a neonatal intensive care unit for 2 years. Weight, length and head circumference (HC) were measured at 3, 12 and 24 months CA. Neurodevelopment was assessed using Bayley Scales of Infant and Toddler Development—3rd Edition at 24 months CA.

Results: Over 90% of the cohort showed catch-up weight at 3 months CA. Weight and length were comparable to healthy SEA but were lower than WHO standards. HC was significantly smaller than those of WHO standards with HC Z-scores steadily decreasing from -0.95 at 3 months CA to -1.50 at 24 months CA. Each one decrement of HC Z-score from 3 to 12 months CA was associated with nearly twice an increase in odds of mental delay at 24 months CA (odds ratio 1.89; 95% confidence interval 1.02–3.50).

Conclusion: Vietnamese preterm infants exhibited early catch-up weight but poor head growth, which was associated with later delays in mental development. Our findings support the importance of HC measures in follow-up for preterm infants.

KEYWORDS: growth, preterm, neurodevelopment, head circumference, low-resource settings, , South East Asia

INTRODUCTION

Poor physical growth, defined as underweight (weight for age < -2 SDs), stunting (length or height for age < -2 SDs) or wasting (weight for height/length < -2 SDs), remains a public health challenge worldwide [1]. Approximately 300 million children under 5 years of age are underweight or stunted, mainly in low- and middle-income countries (LMICs) [2]. The risk of poor growth may be higher in preterm infants (born < 37 completed weeks of gestation) whose growth is impeded by premature organs, lower nutrient reserves and unfavorable extrauterine environment [3]. In resource-limited settings, preterm infants may be more vulnerable due to deprived living conditions including inadequate nutrition intake, high prevalence of infectious diseases and contaminated environments [4]. The limited data indicate that preterm infants in LMICs do not meet the same growth trajectories as full-term counterparts and show reduced catch-up growth [5]. Further, follow-up programs for preterm infants, if available at all, may not be standardized to early identify growth and nutrition problems.

Poor physical growth in infancy is likely to be associated with neurodevelopment in later childhood [6, 7]. The critical time for growth in length and weight associated with later neurodevelopment was found to be the first year of life [8–10]. Whereas the critical time for growth in head size linked to later neurodevelopment seems to continue up to 2 years [11]. Head size is in proportion with the brain volume and its neuronal and neuroglial constituents; hence, head size growth is a promising indicator of neurodevelopment [12–14]. Specifically, a study has demonstrated that head size at birth was related to motor function, while head growth during the pre-school age was related to intellectual and language performances [15].

World Health Organization (WHO) child growth chart is the gold standard and has been universally employed as a reference in over 120 countries [16]. However, it has a potential bias due to limited geographical scope with data derived from six countries,

only: Brazil, Ghana, India, Norway, Oman, and the USA [17]. For preterm infants, a postnatal growth chart has recently been published by Villar *et al.* [18] but only covered the first 6 months of corrected age (CA). These limitations call for further investigations into the growth of preterm infants in different geographic regions and ethnic origins. A recent series of studies has provided more insight into the physical growth of healthy children in the Southeast Asian (SEA) region including Vietnam, showing lower growth patterns of weight and height compared with the WHO standards [19, 20].

In Vietnam as in other LMICs, the improvements in neonatal care have resulted in an increasing number of preterm infants being able to survive and be discharged home. However, the standard follow-up programs for these infants are still lacking, which may hamper the optimal on-going care. When the study was conducted in Children's Hospital 1 (CH1), one visit was scheduled within a few days after discharge for all preterm infants to ensure the transition from hospital to home and to address any remaining parental concerns. The follow-up was not in place but was planned individually depending on the postnatal complications and family resources. In the dawn of advanced neonatal care, preterm infants, particularly those discharged from intensive care, are likely to be at high risk of poor growth due to biological and environmental predisposition. However, little is known about the growth of preterm infants in Vietnam and other LMICs.

Therefore, in this cohort study, we explored growth in the first 2 years of life among Vietnamese preterm infants discharged from neonatal intensive care. Firstly, we described growth in raw measures, in Z-scores derived from WHO standards and percentages of poor growth. Secondly, we compared the growth measures in our cohort with those from WHO standards and healthy infants in the SEA region. Thirdly, we examined the association between growth Z-scores of length and head circumference (HC) in the first year and neurodevelopment at 2 years.

METHODS

Settings

Our cohort study was conducted at the Neonatal Intensive Care Unit (NICU) at Children's Hospital 1 in Ho Chi Minh City, Vietnam. The study hospital is one of two major tertiary centers responsible for intensive care of newborns in the South of Vietnam. The 30-bed NICU has 1200 admissions annually, of which the vast majority are transferred from obstetrical care facilities and a few are directly admitted from home via the emergency room ([Supplementary Appendix](#)). The criteria for NICU admission are also described in detail in the [Supplementary Appendix](#).

Participants

All preterm newborns discharged from the NICU between July 2013 and September 2014 were eligible for enrolment if they fulfilled the inclusion criteria: <37 completed weeks of gestation at birth and age at admission <29 days. Exclusion criteria were congenital brain malformation and chromosome anomaly. Gestational age (GA) was defined as completed weeks of gestation and was determined using one of the three following methods in order of priority: antenatal ultrasound before 20 weeks of gestation, the last menstrual day or clinical examination applying the New Ballard Score [21]. Newborns were classified by GA as extremely/very preterm (EVP, GA < 32 completed weeks) and moderate/late preterm (MLP, GA 32–36 completed weeks). Small for gestational age (SGA) was defined as birth weight (BW) <10th percentile for GA [22]. CA in months was calculated by subtracting the weeks remaining to complete 40 weeks from the chronological age [23].

Data collections

Demographic characteristics including gender, living place, primary caregiver, maternal factors (age, educational level and occupation) and ethnicity were obtained in caregiver interviews. Clinical characteristics including GA, BW, multiple birth, length of hospital stay, mechanical ventilation, sepsis and surgery were obtained from chart review ([Supplementary Appendix](#)). Data on feeding practices were collected at follow-up.

Infants were followed up at 3, 12 and 24 months CA. At each visit, anthropometric measures were

determined twice by the principal investigator and nurses. Weight was measured using digital electronic scales (brand name SECA and LAICA) accurate to the nearest 5 g with infants in light clothing and without shoes. Recumbent length was measured using a horizontal infant ruler accurate to the nearest 1 mm with the infant's head held by one observer and fixed by a flat vertical board, and both legs extended and held by a second observer. Occipital-frontal HC was measured using a non-stretchable encircling tape (brand name SECA) accurate to the nearest 1 mm in the largest circumference. These measures were converted to standardized Z-scores (WAZ: weight for age, LAZ: length for age and HCZ: HC for age) using WHO growth standards for infants by gender and age from birth to 2 years [17]. Poor growths including underweight, stunting and microcephalus were defined as WAZ, LAZ and HCZ < -2.0, respectively. Catch-up growth was defined as reaching a growth measure of greater than -2 SDs of WHO growth standards [24].

At 24 months CA, neurodevelopmental performances were assessed using subtests of Bayley Scales of Infant and Toddler Development - 3rd Edition (Bayley-III) including cognitive, receptive and expressive language, fine and gross motor. The Bayley-III was translated and was adapted for use in Vietnamese children [25]. Scale scores were combined to generate composite scores. Mental delay was defined as cognitive composite scores <76.4 (<-2 SDs) or language composite scores <72.1 (<-2 SDs). Motor delay was defined as motor composite scores <78.2 (<-2 SDs). These cut-off points were derived from a reference of healthy Vietnamese children. Details of 2-year neurodevelopment of preterm infants in the cohort are reported elsewhere [25, 26].

Statistical analyses

The outliers of growth measures were checked before the data were combined with the dataset of Bayley-III scores [26]. Skewness and kurtosis were calculated to identify the distribution characteristics of growth variables ([Supplementary Appendix](#)). Growth Z-scores were calculated by using the mean and standard deviation of WHO growth standards according to gender and completed months of age

(e.g. infant at 11 months 29 days CA was considered 11 months CA) [17]. The percentages of poor growth were reported according to age and gender including underweight, stunting and microcephaly. The growth measures were compared with those of WHO child growth standards, and healthy SEA infants (South-East Asian Nutrition Surveys, SEANUTS) [19, 20] according to age and gender using Student's *t*-test.

To examine the association between neurodevelopment and growth measures, we used logistic regression analysis with selected variables: LAZ and HCZ at 3 months CA, the Z-scores changes from 3 to 12 months CA. Weight and its growth were not chosen due to the fluctuation of weight following morbidities and altered feeding practices in infancy, unlike a steady growth of length and head size. The outcomes of interest included mental and motor delays. However, due to a small number of infants with motor delay (i.e. five infants in the impaired group), we only report here the analysis of the mental outcome and growth. The association was adjusted for gender and GA and presented as adjusted odds ratios (ORs) with 95% confidence interval (CI). All statistical analyses were performed two-tailed using R-software 3.5.0 and the level of statistical significance was set at $p < 0.05$.

Ethics

Our study was approved by the Institutional Review Board of Children's Hospital 1 and written parental consent was obtained for each study participant.

RESULTS

In the study period, 294 infants (all out-born) were admitted to the unit, 255 were discharged alive, and 211 (83%) were followed up at least once in the first 2 years. Infants who were followed up or were lost to follow-up or died are illustrated in Fig. 1. The follow-up rates increased from 179/252 (71%) at 3 months to 178/247 (72%) at 12 months and 184/243 (76%) at 24 months. The mean (SD) BW and GA of followed-up infants were 1767 (475) g and 31.6 (2.4) weeks compared with 1877 (473) g and 32.7 (2.4) weeks of those who were lost to follow-up.

Table 1 presents the demographic and clinical characteristics by gender. These characteristics were similar between boys and girls, except for twin births being more frequent among girls (23%) compared with boys (12%). Among studied infants, 100/211 (47%) were EVP and 111/211 (53%) were MLP. The SGA infants accounted for 6% of the cohort (9/134 boys and 3/77 girls). At 3 months CA, 41/211 (19%) infants were exclusively breastfed, 82/211 (39%) were fed by both breastmilk and formula and 88/211 (42%) were only formula fed.

Table 2 shows growth measures, growth Z-scores and the percentages of poor growth (underweight, stunting and microcephaly) grouped by gender. At 3 months CA, catch-up weight was seen in 102/111 (92%) boys and 61/68 (90%) girls, and catch-up length was seen in 95/111 (86%) boys and 57/68 (84%) girls. At 12 months CA, boys had higher percentages of poor growth than girls in all three measures (underweight, boys vs. girls: 9% vs. 0%; stunting, boys vs. girls: 13% vs. 3%; microcephaly, boys vs. girls: 36% vs. 14%), but the distribution was comparable at 24 months CA.

Figure 2 shows the pattern of growth measures plotted against data extracted from WHO growth standards [17], and healthy SEA infants [19, 20]. Compared with WHO standards, our data showed significantly lower growth measures except for comparable weight at 3 months CA (both boys and girls). HCs of our preterm infants were significant smaller at all three time points for both girls and boys. Compared with healthy SEA infants (SEANUTS data), our weight and length measures were comparable at 12 months CA but significantly higher at 24 months CA (Supplementary Table SA).

Among 184 preterm infants assessed by Bayley-III at 24 months CA, we included 143 infants with completed data for examining the association between growth measures and mental performance. There were 31/143 (22%) infants classified as moderate/severe mental delay at 24 months CA. Using logistic regression adjusted for gender and GA, we found that the decrement in HCZ from 3 to 12 months CA was significantly associated with an increase in odds of mental delay (OR 1.89, 95% CI 1.02–3.50). Specifically, each one decrement in HCZ in the first year was associated with nearly twice an

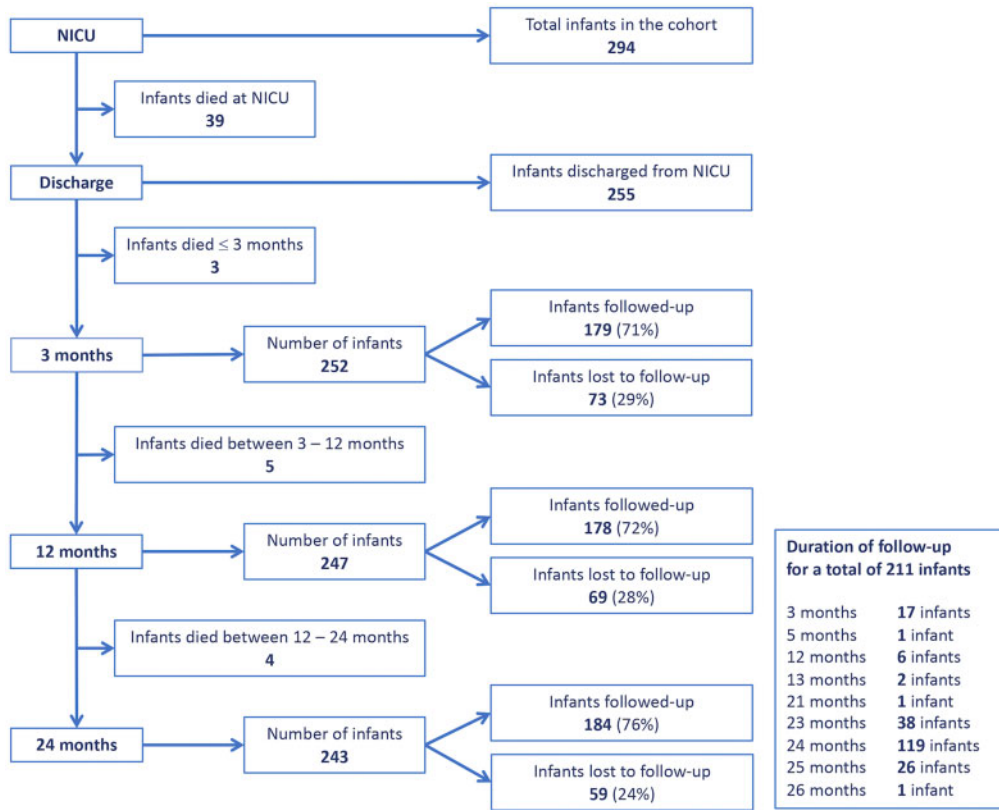


FIG. 1. Flowchart of Vietnamese preterm infants followed up from NICU discharge to 24 months corrected age. Among 178 participants at 12 months, 165 infants were examined at 11 or 12 completed months, 12 infants were examined at 10, 13 or 14 completed months and 1 infant was examined at 19 completed months. Among 184 participants at 24 months, 176 infants were examined at 23 or 24 completed months, 7 infants were examined at 22 or 25 completed months and 1 infant was examined at 20 completed months. All age is corrected age.

increase in odds of mental delay at 24 months CA as shown in Fig. 3.

DISCUSSION

Our study provides detailed data on the physical growth of 211 Vietnamese preterm infants in need of neonatal intensive care. Although the growth measures were consistently lower than WHO standards throughout the first 2 years, the majority showed catch-up growth as early as 3 months CA, in line with previous findings [24]. Approximately 10–15% of our infants remained underweight or stunted at 3 months CA, but these percentages decreased in the follow-up period, similar to a report by Barros *et al.* [27]. Hence, these low percentages of poor growth are encouraging in the context of high prevalence of

stunting (28%) and underweight (17%) among children in LMICs worldwide [4]. The improvement in living conditions, including nutrition supplies and accessible healthcare, following the recent development of Vietnam from a low-income to a middle-income country, is likely to have contributed to these results. However, WHO and UNICEF reported stunting among 25% and underweight among 14% of Vietnamese children in 2015 (<https://data.unicef.org/topic/nutrition/malnutrition>). This contrast to our findings could be explained by our selected cohort from mainly urbanized settings as opposed to countrywide data from WHO and UNICEF.

Further, caregivers are likely to pay special attention to nutrition and healthcare needs to their assumedly vulnerable preterm infants. Interestingly,

Table 1. Demographic and clinical characteristics of Vietnamese preterm infants followed-up during 2 years after NICU discharge

Characteristics	N (%) or Mean (SD)		
	Gender		Total (n = 211)
	Boys (n = 134)	Girls (n = 77)	
Birth weight (g), mean (SD)	1796 (444)	1715 (523)	1767 (475)
Gestational age (weeks), mean (SD)	31.7 (2.4)	31.6 (2.5)	31.6 (2.4)
Gestational age distribution, n (%)			
<28 weeks	6 (4)	6 (8)	12 (6)
28 to <32 weeks	56 (42)	32 (42)	88 (42)
32 to <34 weeks	42 (31)	20 (26)	62 (29)
34 to <37 weeks	30 (22)	19 (25)	49 (23)
Multiple births (all twins), n (%)	16 (12)	18 (23) [†]	34 (16)
Living in the city of study-site, n (%)	34 (25)	14 (18)	48 (23)
Mother age at birth (years), mean(SD)	28.5 (5.7)	29.2 (6.3)	28.8 (5.9)
Maternal education, ^a n (%)			
Elementary school or less	45 (34)	26 (34)	71 (34)
High school (junior or senior)	73 (54)	44 (57)	117 (55)
College or higher level	16 (12)	7 (9)	23 (11)
Maternal occupation, n (%)			
Skilled job ^b	22 (16)	16 (21)	38 (18)
Housewife	39 (29)	22 (29)	61 (29)
Farmer	13 (10)	13 (17)	26 (12)
Others ^c	60 (45)	26 (34)	86 (41)
Primary care by parents, ^d n (%)	120 (90)	71 (92)	191 (91)
Ethnic minority (non-Kinh), ^e n (%)	2 (1)	2 (3)	4 (2)
Length of stay (days), median (IQR)	33 (29)	35 (34)	34 (31)
Mechanical ventilation, n (%)	66/133 (50)	40/77 (52)	106/210 (50)
Surgery, ^f n (%)	19/133 (14)	17/77 (22)	36/210 (17)
Sepsis, n (%)	82/132 (62)	58/77 (75)	140/209 (67)
Positive blood culture	15 (18)	11 (19)	26 (19)
Negative blood culture ^g	67 (82)	47 (81)	114 (81)

Of note, data on income status were not available due to indeterminate responses from parents' perspective. Because of rounding, percentages may not total 100.

NICU, neonatal intensive care unit.

^aEducational system consists of the basic education and the higher education. Twelve-year basic education includes 5 years in elementary school, 4 years in junior high school and 3 years in senior high school. The higher education includes college, undergraduate and postgraduate education in the universities.

^bSkilled job refers to professional and intellectual work.

^cOther jobs refer to unskilled labor and shopkeeper.

^dOther primary caregivers were grandparents or other relatives.

^eEthnic minority includes Khmer, Chinese.

^fSurgery includes repairs of congenital malformations (26), volvulus from intestinal malrotation (1), peritonitis due to gastrointestinal perforation (5), patent ductus arteriosus ligation (4).

^gSuspected sepsis based on clinical signs and biomarkers for septicemia.

Table 2. Growth measures and growth delay by age and gender for 211 Vietnamese preterm infants^a

	Weight			Length			Head circumference		
	Measures (g), mean (SD)			Measures (cm), mean (SD)			Measures (cm), mean (SD)		
	Boys	Girls	Total	Boys	Girls	Total	Boys	Girls	Total
3 months	6270 (1050)	5640 (950)	-	60.2 (3.2)	58.8 (3.1)	-	39.4 (1.5)	38.2 (1.4)	-
12 months ^b	8950 (1320)	8510 (1210)	-	73.9 (3.3)	72.9 (2.7)	-	43.8 (1.4)	43.2 (1.2)	-
24 months ^c	11 460 (1530)	10 910 (1750)	-	85.1 (3.4)	83.9 (3.3)	-	45.9 (1.4)	45.2 (1.4)	-
	Z-scores, ^d mean (SD)			Z-scores, mean (SD)			Z-scores, mean (SD)		
	Boys	Girls	Total	Boys	Girls	Total	Boys	Girls	Total
3 months	-0.15 (1.40)	-0.28 (1.28)	-0.20 (1.36)	-0.60 (1.62)	-0.50 (1.49)	-0.56 (1.57)	-0.88 (1.24)	-1.05 (1.15)	-0.95 (1.21)
12 months ^e	-0.54 (1.24)	-0.22 (1.15)	-0.42 (1.21)	-0.42 (1.46)	-0.14 (1.09)	-0.31 (1.34)	-1.61 (1.09)	-1.09 (0.87)	-1.42 (1.04)
24 months ^f	-0.43 (1.13)	-0.27 (1.24)	-0.37 (1.17)	-0.75 (1.13)	-0.53 (1.03)	-0.67 (1.10)	-1.59 (0.98)	-1.32 (0.97)	-1.50 (0.98)
	Underweight, <i>n</i> (%)			Stunting, <i>n</i> (%)			Microcephaly, <i>n</i> (%)		
	Boys	Girls	Total	Boys	Girls	Total	Boys	Girls	Total
3 months	9/111 (8)	7/68 (10)	16/179 (9)	16/111 (14)	11/68 (16)	27/179 (15)	16/111 (14)	13/68 (19)	29/179 (16)
12 months ^g	10/110 (9)	0/67(0)	10/177 (6)	14/110 (13)	2/67 (3)	16/177 (9)	40/110 (36)	9/66 (14)	49/176 (28)
24 months ^h	8/117 (7)	2/65 (3)	10/182 (5)	18/117 (15)	7/65 (11)	25/182 (14)	42/117 (36)	14/66 (21)	56/183 (31)

^aParticipants include 134 boys and 77 girls. Some infants did not show up at early visits (i.e. 3 or 12 months) but came at later visits (i.e. 12 or 24 months).

^bData from 165 infants at 12 ± 1 months CA including 104 boys and 61 girls.

^cData from 176 infants at 24 ± 1 months CA including 113 boys and 63 girls.

^dZ-scores were calculated using mean and SD of WHO child growth standards according to age and gender, wherein, completed month of age was used.

^eData from 177 infants including 110 boys and 67 girls from 10 to 14 completed months CA.

^fData from 183 infants including 117 boys and 66 girls from 22 to 25 completed months CA.

^gData from 177 infants with available Z-scores above.

^hData from 183 infants with available Z-scores above.

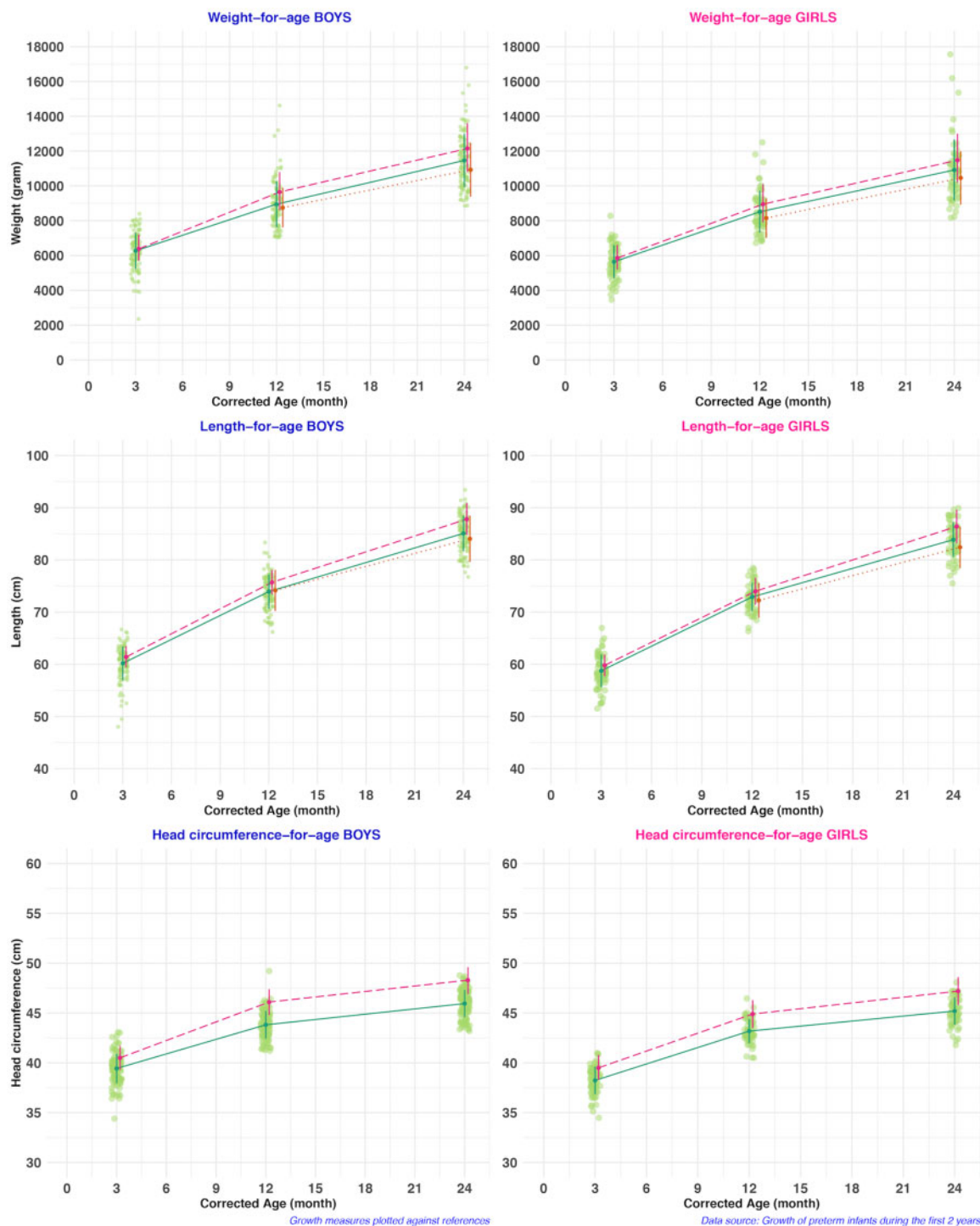


Fig. 2. Growth measures of Vietnamese preterm infants plotted against references according to gender. NICU CH1, Neonatal Intensive Care Unit at Children’s Hospital 1; SEANUT, South East Asian Nutrition Survey; WHO, World Health Organization. Light green dots represent individual measures, dark green solid lines represent growth data of preterm infants discharged from NICU CH1, pink dashed lines represent data from WHO child growth and orange dotted lines represent data of healthy Southeast Asian infants from SEANUTs.

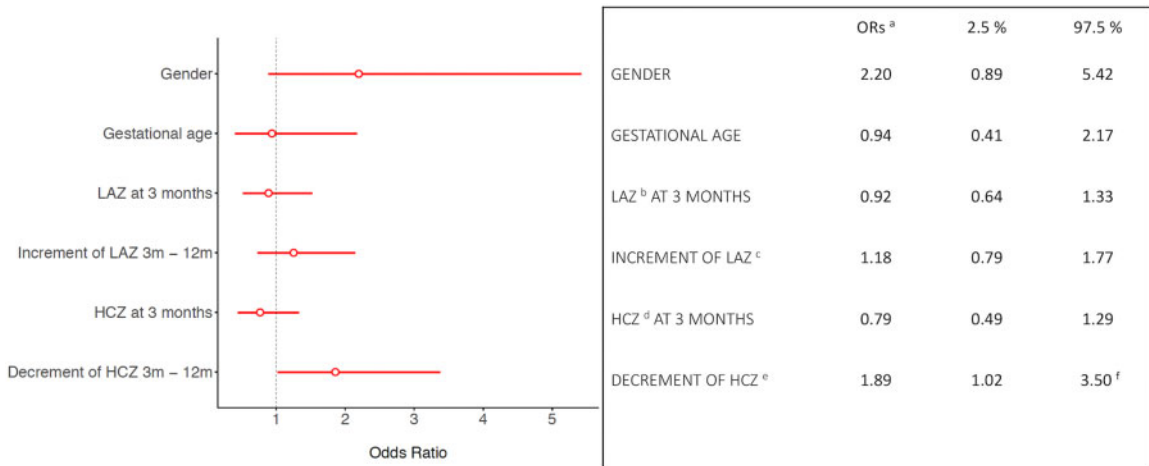


FIG. 3. The association between growth Z-scores and neurodevelopmental impairments. ^aOdds ratios estimated as follows: for gender, girls relative to boys; for GA, moderate and late preterm ($GA \geq 32$ weeks) relative to very and extremely preterm ($GA < 32$ weeks); for LAZ and HCZ, each increment in one Z-score at 3 months; for increment of LAZ and decrement of HCZ from 3 to 12 months CA, each increment and each decrement in one Z-score difference. ^bLAZ: length Z-score for age. ^cIncrement of LAZ: increment of length Z-scores from 3 to 12 months CA. ^dHCZ: head circumference Z-score for age. ^eDecrement of HCZ: decrement of head circumference Z-scores from 3 to 12 months CA. ^f p -value < 0.05 .

the patterns for weight and length growth of our infants were in line with a study of extremely preterm infants from Sweden [28]. Further, weight and length of our infants were also comparable at 12 months and even significantly higher at 24 months compared with SEA infants in the series of SEANUTS [19, 20]. This series of large scale studies were carried out on healthy infants in both rural and urban areas of four countries including Indonesia, Malaysia, Thailand and Vietnam. This indicates a seemingly normal weight and length growth of Vietnamese preterm infants. Nevertheless, HC and its growth showed an alert sign. HCZ exhibited significant faltering in the first year from -0.95 to -1.42 and a steady decrease to -1.50 at 2 years, inconsistent with other reports [29]. This downward pattern raises considerable concern as our finding also indicated that HC growth in the first year was associated with mental performance at 2 years. This association is supported by some studies [30, 31] but not by all [32]. HC growth may be improved by the supplement of nutrients [33], but more data are needed to explore this matter. Our findings highlighted the informative contribution of HC in the

routine growth measures for followed-up preterm infants, assisting in early detection of substandard mental performance.

To the caregivers, low weight at premature birth and subsequent poor growth in infancy cause considerable concerns. Further, the first 2 years of life may be critical for long-term growth and neurodevelopment [34]. A promising finding in our study is the weight and length growth comparable to the regional reference of healthy infants. But the remaining problem is the poor HC growth associated with a higher risk of mental delay. Our findings suggest that caregivers should be encouraged to support neurodevelopmental care for their preterm child in addition to physical growth. The importance of verbal interaction and playing with the children using age-appropriate toys and challenges should be emphasized as these are known to contribute to the neurodevelopment [35]. Timely support and intervention for infants at risk could be of potential importance [36]. These efforts could alleviate the effect of poor growth on neurodevelopment and should be considered in follow-up programs for preterm infants in LMICs.

A limitation of our study is the highly selected patients in the study hospital, all referred from other facilities providing obstetrical care. Further, the estimated number of preterm newborns in need of intensive care in the catchment area of the hospital greatly outnumbers those referred to our NICU. This potentially limits the generalization of our study to the overall Vietnamese preterm population. However, all the studied infants were in the most severe conditions required intensive care, therefore, it could be speculated that less severely ill preterm infants may have better growth compared with our results. Further, about a quarter of the infants and families lost to follow-up at scheduled visits possibly also caused selection bias. Another limitation is the lack of parental height data, which is related to the linear development of the infants at 2 years [37]. Moreover, despite being a useful indicator, feeding difficulty was not eligible for analysis due to considerable recall bias. On the other hand, the strength of our study is its longitudinal prospective design in which growth measurements were followed-up and repeated on a cohort of preterm infants over time. Another strong point is the vigorous approach for measurement through standard tools and methods, duplicated records and predetermined times of assessment.

CONCLUSION

In this study of Vietnamese preterm infants, weight and length growth in the first 2 years were comparable to healthy child growth in the SEA region but remained lower than the WHO standards. HC Z-scores showed significant faltering during the first 2 years. Further, HC growth was associated with neurodevelopmental outcomes. These findings emphasize the contributive importance of HC in routine growth measurement when planning to scale up standard follow-up programs for preterm infants in LMICs. The possible causal relationship and interventions to mitigate the effects of growth on neurodevelopment need to be explored further.

SUPPLEMENTARY DATA

Supplementary data are available at *Journal of Tropical Pediatrics* online.

DISCLOSURE

The authors declare no conflict of interest.

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REFERENCES

1. Victora CG, de Onis M, Hallal PC, *et al.* Worldwide timing of growth faltering: revisiting implications for interventions. *Pediatrics* 2010;125:e473–80.
2. Stevens GA, Finucane MM, Paciorek CJ, *et al.* Trends in mild, moderate, and severe stunting and underweight, and progress towards MDG 1 in 141 developing countries: a systematic analysis of population representative data. *Lancet (London, England)* 2012;380:824–34.
3. Elizabeth KE, Krishnan V, Zachariah P. Auxologic, biochemical and clinical (ABC) profile of low birth weight babies—a 2-year prospective study. *J Trop Pediatr* 2007;53:374–82.
4. Black RE, Victora CG, Walker SP, *et al.* Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet (London, England)* 2013;382:427–51.
5. Gladstone M, Oliver C, Van den Broek N. Survival, morbidity, growth and developmental delay for babies born preterm in low and middle income countries—a systematic review of outcomes measured. *PLoS One* 2015;10:e0120566.
6. Jukes M. Impact of early childhood health and nutrition on access to education in developing countries. *Paediatr Child Health (Oxford)* 2007;17:485–91.
7. Walker SP, Grantham-McGregor SM, Powell CA, *et al.* Effects of growth restriction in early childhood on growth, IQ, and cognition at age 11 to 12 years and the benefits of nutritional supplementation and psychosocial stimulation. *J Pediatr* 2000;137:36–41.
8. Ehrenkranz R. A, Dusick AM, Vohr BR, *et al.* Growth in the neonatal intensive care unit influences

- neurodevelopmental and growth outcomes of extremely low birth weight infants. *Pediatrics* 2006;117:1253–61.
9. Chien H-C, Chen C-H, Wang T-M, *et al.* Neurodevelopmental outcomes of infants with very low birth weights are associated with the severity of their extra-uterine growth retardation. *Pediatr Neonatol* 2018;59:168–75.
 10. Belfort MB, Rifas-Shiman SL, Sullivan T, *et al.* Infant growth before and after term: effects on neurodevelopment in preterm infants. *Pediatrics* 2011;128:e899–906.
 11. Taine M, Charles M-A, Beltrand J, *et al.* Early postnatal growth and neurodevelopment in children born moderately preterm or small for gestational age at term: a systematic review. *Paediatr Perinat Epidemiol* 2018;32:268–80.
 12. Ghods E, Kreissl A, Brandstetter S, *et al.* Head circumference catch-up growth among preterm very low birth weight infants: effect on neurodevelopmental outcome. *J Perinat Med* 2011;39:579–86.
 13. Ranke MB, Krägeloh-Mann I, Vollmer B. Growth, head growth, and neurocognitive outcome in children born very preterm: methodological aspects and selected results. *Dev Med Child Neurol* 2015;57:23–8.
 14. Neubauer V, Fuchs T, Griesmaier E, *et al.* Poor postdischarge head growth is related to a 10% lower intelligence quotient in very preterm infants at the chronological age of five years. *Acta Paediatr* 2016;105:501–7.
 15. Raz S, Newman JB, DeBastos AK, *et al.* Postnatal growth and neuropsychological performance in preterm-birth preschoolers. *Neuropsychology* 2014;28:188–201.
 16. de Onis M, Onyango A, Borghi E, *et al.* Worldwide implementation of the WHO Child Growth Standards. *Public Health Nutr* 2012;15:1603–10.
 17. World Health Organization. WHO Child Growth Standards: Length/Height-for-Age, Weight-for-Age, Head Circumference-for-Age: Methods and Development. Geneva: WHO, Dep Nutr Heal Dev, 2006.
 18. Villar J, Giuliani F, Bhutta ZA, *et al.* Postnatal growth standards for preterm infants: the Preterm Postnatal Follow-up Study of the INTERGROWTH-21st Project. *Lancet Glob Heal* 2015;3:e681–91.
 19. Rojroongwasinkul N, Bao KLN, Sandjaja S, *et al.* Length and height percentiles for children in the South-East Asian Nutrition Surveys (SEANUTS). *Public Health Nutr* 2016;19:1741–50.
 20. Sandjaja S, Poh B K, Rojroongwasinkul N, *et al.* Body weight and BMI percentiles for children in the South-East Asian Nutrition Surveys (SEANUTS). *Public Health Nutr* 2018;21:2972–81. 10.1017/S1368980018001349
 21. Ballard JL, Khoury JC, Wedig K, *et al.* New Ballard Score, expanded to include extremely premature infants. *J Pediatr* 1991;119:417–23.
 22. Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. *BMC Pediatr* 2013;13:59.
 23. Engle WA; American Academy of Pediatrics Committee on Fetus and Newborn HJ. Age terminology during the perinatal period. *Pediatrics* 2004;114:1362–4.
 24. Euser AM, de Wit CC, Finken MJJ, *et al.* Growth of preterm born children. *Horm Res Paediatr* 2008;70:319–28.
 25. Sun L, Sabanathan S, Thanh PN, *et al.* Bayley III in Vietnamese children: lessons for cross-cultural comparisons. *Wellcome Open Res* 2019;4:98.
 26. Do CHT, Kruse AY, Wills B, *et al.* Neurodevelopment at 2 years corrected age among Vietnamese preterm infants. *Arch Dis Child* 2019;105:134–140, doi:archdischild-2019-316967.
 27. Barros FC, Luis J, Rossello D, *et al.* Gestational age at birth and morbidity, mortality, and growth in the first 4 years of life: findings from three birth cohorts in Southern Brazil. *BMC Pediatr* 2012;12:685.
 28. Horemuzova E, Ámark P, Jacobson L, *et al.* Growth charts and long-term sequelae in extreme preterm infants - from full-term age to 10 years. *Acta Paediatr* 2014;103:38–47.
 29. Cockerill J, Uthaya S, Dore C, *et al.* Accelerated postnatal head growth follows preterm birth: 253. *Pediatr Res* 2005;58:398.
 30. Kan E, Roberts G, Anderson PJ, *et al.* The association of growth impairment with neurodevelopmental outcome at eight years of age in very preterm children. *Early Hum Dev* 2008;84:409–16.
 31. Rijken M, Wit JM, Le Cessie S, *et al.* The effect of perinatal risk factors on growth in very preterm infants at 2 years of age: the Leiden Follow-Up Project on Prematurity. *Early Hum Dev* 2007;83:527–34.
 32. Wood NS, Costeloe K, Gibson A T, *et al.* The EPICure study: growth and associated problems in children born at 25 weeks of gestational age or less. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F492–500.
 33. De Kieviet JF, Vuijk PJ, van den Berg A, *et al.* Glutamine effects on brain growth in very preterm children in the first year of life. *Clin Nutr* 2014;33:69–74.
 34. Schwarzenberg SJ, Georgieff MK; Committee on Nutrition Co. Advocacy for improving nutrition in the first 1000 days to support childhood development and adult health. *Pediatrics* 2018;141:e20173716.
 35. Inguaggiato E, Sgandurra G, Cioni G. Brain plasticity and early development: implications for early intervention in neurodevelopmental disorders. *Neuropsychiatr Enfance Adolesc* 2017;65:299–306.
 36. Spittle A, Orton J, Anderson PJ, *et al.* Early developmental intervention programmes provided post hospital discharge to prevent motor and cognitive impairment in preterm infants. *Cochrane Database Syst Rev* 2015;CD005495.
 37. Garza C, Borghi E, Onyango AW, *et al.*; WHO Multicentre Growth Reference Study Group. Parental height and child growth from birth to 2 years in the WHO Multicentre Growth Reference Study. *Matern Child Nutr* 2013;9:58–68.