ORIGINAL ARTICLE

Postnatal Growth at 64 Weeks Postmenstrual Age in Preterm Infants Delivered at ≤ 34 Weeks' Gestation: A Single Center Study

Apoorva Kutar,[1] Padmasani Venkat Ramanan,[1] Elizabeth Kandathil Eapen[2]

[1]Department of Pediatrics, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India
[2]Department of Pediatrics, Sree Mookambika Institute of Medical Sciences, Kulasekharam, Kanyakumari, Tamil Nadu, India

ABSTRACT

Objective: To study the postnatal growth at 64 weeks postmenstrual age (PMA) in preterm neonates born at ≤ 34 weeks gestational age.

Methods: A cross-sectional study was conducted between August, 2019 and November, 2021, wherein, we took anthropometric measurements of neonates (delivered at ≤ 34 weeks' gestation) at 64 (± 2) weeks PMA. The rapidity of postnatal growth was categorized according to change in the *z*-score of anthropometric measures, viz, weight-for-age, length-for-age and head circumference-for-age, between birth and 64 weeks PMA. For each of the growth parameters, growth rate was categorized according to the change in *z*-score (*z*-score at 64 weeks PMA minus *z* score at birth) as slow (< –0.67), acceptable (–0.67 to < 0.67), and rapid (≥ 0.67).

Results: Out of the 156 preterm neonates evaluated, weight gain was slow, acceptable and rapid in 95 (60.8%), 45 (28.9%), and 16 (10.3%), respectively. Length gain was slow, acceptable, and rapid in 87 (55.7%), 49 (31.4%), and 20 (12.9%) infants, respectively. Likewise, Head circumference gain was slow, acceptable and rapid in 103 (66.5%), 42 (26.5%), and 11 (7.0%) infants, respectively. The risk [aOR 995% CI)] for slow weight gain increased with early initiation of complementary feeding [8.0 (3.5 - 18.0)] and decreased with a longer duration of EBF [0.4 (0.6 - 0.2), $P < 0.001$]. The risk for rapid weight gain also decreased with the longer duration of EBF [0.27 (0.5 - 0.1), $P < 0.001$]. Gestational age < 32 weeks ,weight for gestation at birth, and re-hospitalization following discharge were the other key factors influencing the growth rate

Conclusion: Among babies born preterm (≤ 34 weeks), more than half had slow gain in weight, length and head circumference. EBF till 6 months corrected age was protective against slow and rapid weight gain.

Keywords: *Exclusive breast feeding, Prematurity, Weight gain*

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INTRODUCTION

Around 11% of live births globally and 13% in India are preterm [1,2]. The postnatal growth rate in preterms has not been well studied, even though it has important clinical implications. Rapid somatic growth may increase the risk of metabolic dysfunction while slow growth leads to adverse psychomotor and neurocognitive outcomes, undernutrition and increased risk of infections [3-5]. Optimal postnatal growth is one that follows the trajectory of the intrauterine growth curve and maintains the same centiles as those at birth [6]. The aim of this study was to assess the growth rate in preterms infants, born at ≤ 34 weeks' gestation, at 64 weeks postmenstrual age (PMA) and to identify the factors influencing the same.

Correspondence to: Dr Padmasani Venkat Ramanan, Professor, Department of Pediatrics,
Sri Ramachandra Medical College and Research Institute, Chennai, Tamil Nadu 600116, India.
padmasani2001@yahoo.com
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METHODS

This cross-sectional study was done in a tertiary care hospital in South India, between August, 2019 and November, 2021, after obtaining approval of the institutional ethics committee and written informed consent from the parents. Infants who were born preterm (gestational age ≤ 34 weeks) and who were attending the well-baby clinic, were enrolled at 64 (± 2) weeks PMA (6 months corrected age, CA). Infants with congenital malformations, chronic systemic illnesses, those separated from the mother, and those with any acute illness at the time of evaluation were excluded. The maternal details including antenatal and sociodemographic data and neonate's anthropometric measurements at birth were noted from the hospital records. Details of any medical illness following discharge from the neonatal intensive care unit (NICU) were also retrieved from records.

The included neonates were categorized according to the World Health Organization (WHO) classification based on gestational age as extremely preterm (24 wk to 27 wk + 6d), very preterm infants (28 wk to 31 wk + 6d), and moderately preterm (32 wk to 33 wk + 6d). Feeding details including the duration of exclusive breastfeeding (EBF) and the time of initiation of complementary feeds were collected by interviewing the mother. Complementary feeding (CF) was defined as food other than breast milk and formula. Socioeconomic status (SES) was classified using the modified Kuppusamy classification [7]. Anthropometric measurements were performed using standard techniques. Weight (g) was recorded using a calibrated weighing machine accurate to 5g, length (cm) and head circumference (cm) were measured to the nearest 1mm, using an infantometer and a non-stretchable measuring tape, respectively. Intraobserver variations were minimized by repeated measurements and taking the average of three readings. The *z*-scores of weight-for-age (WAZ), length-for-age (LAZ), and head circumference-for-age (HCZ) at birth and 64 weeks PMA were calculated using the Intergrowth-21st Standard Application [8].

Staying with the original centile was taken as acceptable growth, i.e., no catch-up/ down. A change of more than 0.67 in the z-score between two time-points during infancy represents crossing two major percentiles (5th, 10th, 25th, 50th, 75th, 90th and 95th) on the growth chart [9]. Thus, for each of the growth parameters, the growth rate was categorized according to the change in *z*-score (*z*-score at 64 weeks PMA minus *z*-score at birth) as slow (<– 0.67), acceptable (–0.67 to < 0.67), and rapid (≥ 0.67) [9]. The nutritional status was described as underweight and stunted when WAZ and LAZ were less than –2, respectively. Factors affecting postnatal growth rate, were further analyzed.

The sample size was calculated based on the estimated prevalence (19%) of slow growth in a population of term babies evaluated at 8 months [10] as no published data was available for preterm babies at 64 weeks PMA. With a 5% precision and 95% confidence interval, the minimum sample size was calculated to be 137 subjects.

Statistical analysis: This was performed using the Statistical Package for Social Science Program, IBM SPSS 17.0 version. Categorical variables were expressed as frequency and percentage, and continuous variables were expressed as mean (SD) or median (IQR). Multinomial regression analysis was done to find out the association between variables and outcomes. $P < 0.05$ was considered significant.

RESULTS

A total of 156 infants, born at gestational age ≤ 34 weeks, were evaluated at 64 weeks (± 2) PMA. The baseline characteristics of the study population and feeding practices at discharge from the NICU are described in **Table I**. The mean (SD) gestational age was 30.98 (2.0) weeks. The mean (SD) weight (g), length (cm), and head circumference (cm) at birth were 1514 (451.2), 39.61 (3.71) and 28.8 (2.9), respectively.

The median (IQR) length of NICU stay was 15.5 (1, 98) days. Enteral feeding had been started within 72 hrs of birth in 152 (97.4%) neonates, and 74 (47.4%) had reached full oral feeds within seven postnatal days. At the time of discharge from the hospital, 31.4% were on EBF and 138 (67.5 %) infants were getting some breast milk.

Following discharge from NICU, 30 (19.2%) preterms had been hospitalized at least once. The indications for hospitalization were febrile episodes (76.6%), diarrheal illnesses (50%), acute respiratory infections (43.3%) and Corona virus disease (COVID-19) (6.6%).

At 64 weeks (± 2) PMA, 15 (9.7%) were underweight, 36 (23.0%) stunted and 48 (30.8%) with HCZ of < –2. In terms of change in WAZ, 95 (60.8%) had slow weight gain, 45 (28.9%) had acceptable weight gain, and 16

Table I Baseline Parameters at Birth for Preterm Infants Enrolled in the Study (*n* = 156)

Variables	*n* (%)
Gestational age	
< 28 wk	10 (6.4)
28 to 31 wk + 6/7 d	71 (45.5)
32 to 34 weeks	75 (48.1)
Male gender	78 (50).
Birth order	
First born	118 (75.6)
Second born	35 (22.4)
Twin deliveries	54 (34.6)
Cesarean delivery	115 (73.7)
Anthropometry	
Weight-for-age *z*-score < -2	11 (7.0)
Length-for-age *z*-score < -2	16 (10.2)
Head circumference-for-age *z*-score < -2	13 (8.3)
Feeding at discharge from the neonatal intensive care unit	
Exclusive breast milk	49 (31.4)
Mixed feeding	89 (57.0)
Exclusive formula	18 (11.5)

Values expressed as n (%)

(10.3%) had rapid growth. In terms of change in LAZ, 87 (55.7%) had slow length gain, 49 (31.4%) had acceptable length gain and 20 (12.9%) had rapid length gain. In terms of change in HCZ, 103 (66.5%) had a slow increase 42 (26.5%) had an acceptable increase in and 11 (7.0%) had a rapid increase in head circumference.

Complementary feeding had been introduced before six months CA in 103 (66.1%) infants. The earliest age of introducing of CF was 3 months CA, and the median (IQR) CA at the time of starting CF was 5 (4, 7) months. The median (IQR) duration of EBF (months) was significantly lesser in the slow [3 (2, 4)] and rapid weight gain groups [2.5 (2, 3)] as compared to the acceptable weight gain [6 (5, 6)] group. The median (IQR) CA in months at which CF was initiated was significantly lower in the slow weight gain group [4 (4, 5)] as compared to rapid weight gain [6 (5,6)] and acceptable weight gain [6 (5, 6)] groups. The comparative features of infants with slow and rapid weight gain are depicted in **Table II** with 'acceptable gain' taken as the reference.

The risk of slow weight gain was more among the extremely and very preterm infants. The risk for slow weight gain increased with early initiation of complementary feeding [aOR 995% CI) 8.0 (3.5, 18.0), $P < 0.001$] and decreased with a longer duration of EBF [aOR (95% CI) 0.4 (0.6, 0.2), $P < 0.001$]. The risk for rapid weight gain also decreased with the longer duration of EBF [aOR (95% CI) 0.27 (0.5, 0.1), $P < 0.001$]. Thus, exclusive breastfeeding till 6 months CA was shown to protect against both slow and rapid weight gain. The risk factors associated with slow and rapid weight gain are shown in **Table III**.

DISCUSSION

The change in *z*-score between two time-points is the most objective method of assessing the growth trajectory of an infant. In our study a majority of preterms had slow growth for all the three growth parameters, viz, WAZ, LAZ, and HCZ, in the first six months of infancy. Being small for gestation age (SGA), having a birth weight < 1500g and post-NICU discharge hospitalization were associated with rapid growth while the introduction of complementary feeds before 6 months CA was associated with slow growth. A shorter duration of EBF was associated with both slow and rapid growth.

Previous studies have reported that preterm neonates with gestational age closer to term had faster weight gain [9,11]. Some previous studies have also noted that catch-up in appropriate for gestation age (AGA) and large for gestation age (LGA) preterms occurs early, while it occurs only by two years CA in infants born preterm SGA [9]. However, one study reported significantly higher weight growth velocities in SGA and AGA infants as compared to LGA infants when assessed at 40 weeks PMA [12]. Twin birth has been reported to be associated with faster postnatal weight gain [16]. We found no association probably because the assessment was done at an earlier age in our study.

There are no guidelines on the ideal duration of EBF in preterms and the prevalence of EBF till 6 months CA among preterms has been previously reported to be 35.3% [13] which is similar that in the current study (33.9%) There are few previous studies on the relationship between EBF and growth in preterms. In preterm infants (27-34 weeks gestation), the recommended growth velocity of 10-15 g/kg/day can be achieved using unfortified expressed breastmilk with higher feeding volumes of 200 mL/kg/d [14].

Usually, the absence of illness improves growth. The association of postdischarge hospitalization with rapid growth noted in our study could be due to the opportunity to interact with health care professionals and correct inappropriate feeding practices [15].

Table II Characteristics of Infants with Acceptable, Rapid or Slow Weight Gain

	Acceptable weight gain (n = 45) Group I	*Rapid weight gain (n =16) Group II*	*Slow weight gain (n = 95) Group III*
Birth weight (g)[a,d,,f]	1482.9 (411.2)	1206.8 (252)	1580.8 (474.7)
Gestational age (wk)[c]	32 (33, 30)	33 (32.75, 33)	31 (28.5, 32)
Male[b]	18 (40%)	6 (37.5%)	54 (56.8%)
Weight at 64 wk (±2) postmenstrual age[a,e]	7018.2 (828)	6848.7 (805.5)	6730.2 (802)
Weight gain (g)[a,e,,f]	5535.2 (630.4)	5641.8 (645.4)	5149.4 (740)
Gain in length (cm)[a]	24.3 (3.5)	23.9 (2.5)	24 (4.5)
Gain in head circumference (cm)[a,d,]	12.06 (2.9)	13.0 (1.2)	11.8 (3.0)
Age at initiation of complementary feeds (mo)[a,e,,f]	5.6 (0.6)	5.8 (0.8)	4.5 (0.8)

Values expressed as [a]mean (SD), [b]n (%), [c]median (IQR). P value < 0.05 between [d] Group I and II; [e] Group I and III; [f] Group II and III

Table III Risk Factors for Slow and Rapid Weight Gain in Preterm Infants (≤34 week) at 6 Months Chronological age using Acceptable Growth as Reference

Variables	*Slow weight gain (n = 95)*			*Rapid Weight Gain (n = 16)*			*Acceptable Weight Gain (n = 45)*
	n (%)	*Adjusted OR (95% CI)*	*P value*	*n (%)*	*Adjusted OR(95% CI)*	*P value*	*n (%)*
GA < 28 wk	10 (100%)	16.2 (0.9, 289.9)	0.05	0	2 (0.03, 108.3)	0.07	0
GA 28 wk to 31wk +6d	50 (70.4%)	2.1 (1.0, 4.4)	0.04	3 (4.2%)	0.3 (0.08, 1.3)	0.1	18 (25.3%)
GA 32 wk to 33 wk +6d	35 (41.6%)	-	-	13 (17.3 %)	-		27 (36%)
Complementary feeds initiated before 6 mo CA	80 (77.6%)	8.0 (3.5, 18.0)	< 0.001	5 (4.8%)	0.6 (0.2, 2.2)	0.5	18 (17.4%)
Duration of exclusive breastfeeding (mo)[a]	3 (2, 4)	0.4 (0.6, 0.2)	<0.001	2.5 (2, 3)	0.27 (0.5, 0.1)	<0.001	6 (6,5)
Duration of exclusive breastfeeding till 6 mo CA	15 (31.2%)	0.6 (0.02, 0.16)	<0.001	0	-	<0.001	33 (68.7%)
Birthweight < 1500 g	45 (54.2%)	-	-	14 (16.8%)	4.2 (50.6, 0.35)	0.25	24 (28.9%)
SGA at birth	2 (8.3%)	5.9 (48.3, 0.72)	0.09	14 (58.4%)	0.21 (0.30, 0.001)	0.005	08 (33.3%)
One or more Post NICU hospitalization	16 (53.3%)	-	-	7 (23.4%)	0.3 (3.7, 0.2)	0.3	7 (23.3%)
Infant formula use	59 (67%)	0.4 (1.3, 0.15)	0.14	14 (15.9%)	0.1 (1.9, 0.01)	0.14	15 (17.1%)
Human Milk Fortifier	67 (60.3%)	0.8 (1.7, 0.3)	0.64	14 (12.7%)	0.2 (1.4, 0.05)	0.12	30 (27.0%)

Values expressed as n (%) or [a]median (IQR). CA Chronological age, GA Gestational age, NICU Neonatal intensive care unit, DR Odds ratio, SGA Small for gestational age

One limitation of this study is its cross-sectional nature. Longitudinal follow-up of infants from birth would give a better understanding of the growth pattern. Also, details about the infant feeding practices were collected from the mother only at one point of time. Recall bias is a possibility. The role of micronutrients deficiency and maternal factors were not explored.

Majority of preterm infants with gestational age 34 weeks or lower had slow growth at 64 weeks PMA. Appropriate infant feeding practices for preterm infants and close long-term follow-up are necessary to promote optimal growth.

Ethics clearance: No IEC-NI/19/JUL/70/60 dated Dec 27, 2019.

Contributors: AK, PVR, EKE: Study design; AK: Data collection, statistical analysis, manuscript writing; PVR: Study design, developed the methodology, supervised data collection, data interpretation and editing of manuscript; EKE: Critical inputs to the methodology, manuscript editing; All authors read and approved the final manuscript.

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WHAT THIS STUDY ADDS?

- Majority of preterm (≤ 34 weeks gestational age) infants have slow growth when assessed at six months corrected age.
- Exclusive breastfeeding till six months corrected age in infants delivered preterm (≤ 34 weeks) protects against both rapid and slow growth rate.

Available from: *https://intergrowth21.tghn.org/standards-tools/*

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