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Original Article

Growth of premature neonates admitted in a level III neonatal unit

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ABSTRACT

Problem considered: The gold standard for postnatal growth for preterm neonates is their intrauterine growth standard. Extra uterine growth restriction (EUGR) implies weight less than minus 2 Z scores at discharge.¹

Methods: A prospective observational study of preterm neonates admitted at the level III neonatal unit of a tertiary care teaching hospital. Growth parameters (weight, length and head circumference) were recorded on admission, during hospitalization, at discharge and at term gestation. Z scores were calculated using Fenton's growth charts.^{13,14} Growth velocity was calculated for weight, length and head circumference (HC).

Results: The incidence of EUGR was 64.8% at discharge and 76.8% at term. Mean Z scores for weight, length and head circumference in neonates with EUGR and without EUGR were -1.36 ± 0.80 vs -0.40 ± 0.63 ($p = 0.000$), -1.21 ± 1.27 vs -0.38 ± 0.90 ($p = 0.000$), -1.35 ± 1.04 vs -0.44 ± 1.02 ($p = 0.000$) respectively at birth, -2.84 ± 0.60 vs -1.38 ± 0.79 ($p = 0.000$), -1.92 ± 1.26 vs -0.85 ± 0.88 ($p = 0.000$), & -1.85 ± 1.10 vs -0.88 ± 1.11 ($p = 0.000$) respectively at discharge & -2.84 ± 1.18 vs -2.44 ± 1.16 ($p = 0.102$), -2.44 ± 1.33 vs -1.95 ± 1.29 ($p = 0.071$) & -2.03 ± 1.14 vs -1.28 ± 1.61 ($p = 0.005$) respectively at term.

Mean growth velocities for neonates with EUGR and without EUGR were 7.98 ± 4.63 vs 10.85 ± 5.53 g/kg/day ($p = 0.120$) for weight, 0.65 ± 0.24 vs 0.72 ± 0.37 cm/week ($p = 0.924$) for length and 0.43 ± 0.14 vs 0.41 ± 0.15 cm/week ($p = 0.439$) for head circumference at discharge and 12.99 ± 8.54 vs 12.70 ± 7.58 g/kg/day ($p = 0.924$), 0.72 ± 0.35 vs 0.62 ± 0.22 cm/week ($p = 0.145$) and 0.49 ± 0.16 vs 0.43 ± 0.14 cm/week ($p = 0.048$) respectively for weight, length and head circumference at term.

Conclusion: About two third premature neonates at discharge and three fourths at term had EUGR. Growth velocity for HC was significantly more in neonates with EUGR by term gestation indicating a brain sparing effect.

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1. Introduction

Prematurely born neonates face a number of problems and extra uterine growth restriction (EUGR) is one of them. EUGR is defined as weight less than 10th percentile or minus 2 Z score (3rd centile) of intrauterine growth expectation at discharge.¹ A large multicentric study in UK revealed EUGR to be a universal phenomenon in preterm infants.² Moreover the number of preterms whose weight is below 10th centile increases between birth and hospital discharge.³ Birth weight and postnatal growth adversely influence cognitive development and intelligent quotient.^{4–6}

Though a number of studies have been done on growth outcome of preterm babies during childhood and adolescence^{7–10} only a few have focused on immediate growth failure after discharge from nursery.⁶ Indian studies on EUGR are few & recent ones include only very low birth weight (VLBW) babies.^{11,12} Since 30–40% of neonates in our unit are preterm and about two third of them are more than 32 weeks gestation we went ahead to study the growth of all preterm neonates and not just those who were VLBW. Our aims were to determine the incidence of EUGR, mean Z scores and growth velocities for weight, length and head circumference (HC) during hospital stay and after discharge till term PMA.

2. Methods

This prospective observational study was conducted at the level 3 neonatal unit of a tertiary care teaching hospital after seeking approval from Institutional Ethics Committee over a period of 1 year. An informed consent was taken before enrollment from the parents of the neonate.

Consecutive preterm neonates admitted within 24 h of birth were enrolled and studied from admission till discharge and then till term PMA in the OPD with the intention to analyze the growth of those who stayed in the unit for more than 7 days and acquired term gestation at least one week after discharge. Preterm neonates with major congenital malformations, not giving consent and those admitted after 24 h of birth were excluded.

Baseline characteristics of neonates such as birth weight, length, head circumference, gestational age (GA), gender, and diagnosis at admission were noted. Patients were managed according to the unit consultants. Neonates were fed according to the protocol of the unit. Clinical status, anthropometry and medical and nutritional interventions of the neonates were monitored. During hospital stay daily weight, weekly length and HC were measured. Weight, length and HC were also measured at discharge. Feeding details such as age at initiation of feeds, type of feed i.e. breast/dairy/formula milk and days to attain full enteral feed were also noted. Infants were discharged when they were clinically stable, euthermic at room temperature, gaining weight and mother was confident of caring for the baby at home. They were then followed up in the OPD till term PMA when weight, length and HC were again measured.

Body weight (BW) was measured using electronic weighing scale accurate to 10 g. Length (L) was measured by using

infantometer with an accuracy of 0.1 cm. Head circumference (HC) was measured using a non-stretchable measuring tape with accuracy of 0.1 cm. All measurements were taken twice and an average of the two readings was taken.

The Z scores for weight, length and HC were calculated using Fenton's reference data.^{13,14} Neonates with weight less than minus two Z score at discharge were designated as having EUGR. Growth velocities were calculated for the period of hospitalization and then from discharge to term PMA.

2.1. Feeding protocol of our unit

Fluid intake: VLBW infants are started at 80 mL/kg/d of fluid on first day of life. Total fluid is increased by 15 mL/kg daily till 150–200 mL/kg/day is reached. For neonates weighing >1500 g at birth fluids are started at 60 mL/kg/day and increments of 15 mL/kg are made daily reaching 150 mL/kg/day by 7-day.

Neonates of GA between 28 and 31 weeks are kept on oro-gastric (OG) tube feeding with occasional spoon-feeding. Neonates of GA between 32 and 34 weeks are fed by spoon and those more than 34 weeks are breastfed. All stable LBW infants, irrespective of their initial feeding method are put on their mother's breast (non-nutritive sucking). Neonates with GA less than 28 weeks are kept on intravenous fluids initially. Minimal enteral nutrition (MEN) is initiated once the infant is hemodynamically stable (10 mL/kg of expressed breast milk divided 6 hourly) and then increments of 20–30 mL/kg/day are made as tolerated. For healthy preterm infants enteral feeding is initiated immediately after birth with the appropriate feeding method determined by their gestation and oral feeding skills.

Sick preterm infants are usually started on intravenous (IV) fluids. Enteral feeds are initiated as soon as they are hemodynamically stable. Effort is made that all infants receive breast milk. If it is not available dairy milk (single toned) provided by the hospital is used. Formula milk for preterm neonates (Lactodex LBW) is also used (but mostly after discharge).

Supplementation for infants with BW of 1500–2500 g: vitamin D 400 IU per day from 2 weeks of age and iron 2 mg/kg/day from 2 months of age.

Supplementation for VLBW infants: Supplementation is ensured by one of the following methods once the neonate is on full enteral feeds. (a) 400 IU/day of vitamin D, calcium 120–140 mg/kg/day and phosphorus 60–90 mg/kg/day, folate (about 50 mcg/kg/day). (b) Fortification of expressed breast milk with human milk fortifiers (HMF). It is started once they reach 150 mL/kg/day of enteral feeds in the dose recommended by the manufacturer (Lactodex HMF; Raptakos, Brett and Co. Ltd.; 4 g/100 mL of milk). Iron is started at 4–6 weeks in the dose of 2 mg/kg/day. Fortification is continued till the infant reaches 40 weeks PMA or attains 2 kg weight (whichever is later). VLBW neonates are provided kangaroo mother care as a routine.

2.2. Statistical analysis

The statistical analysis was done on SPSS statistical analysis software version 11. The values were represented in mean $\pm$ SD for continuous variables. Differences of means

were tested by Mann–Whitney *U* test for continuous variables. Growth velocities for weight, length, HC were compared using “*t*” test. Sample size assuming a prevalence of EUGR of 50%, confidence interval of 10 & confidence level of 95% was calculated to be 500.

3. Results

During the study period, a total of 488 preterms were admitted in the neonatal unit. Of these, 108 were excluded because 60 were more than 24 h at admission and 48 had major congenital anomalies. All the remaining 380 were closely monitored. Of these, 269 were excluded as 100 expired, 123 left against medical advice, 6 absconded and 40 were discharged before 7 days of admission or became term before discharge or within 6 days of discharge. Finally 111 neonates formed the study population and were followed up in the OPD till term PMA. At term gestation, 108 of these were available for growth monitoring (Two had expired and 1 was lost to follow-up) (Fig. 1).

Gestational age and birth weight varied between 28 and 36 weeks (median 33) and 880–2460 g (median 1580 g) in the 111 neonates enrolled. Seventy-two (64.8%) had EUGR at discharge. Baseline characteristics of neonates with and without EUGR are given in Table 1. Both groups were similar in all characteristics except that SGA were significantly more in the EUGR group.

For weight, the mean Z scores for neonates with EUGR and without EUGR, at birth, discharge and term were -1.36 ± 0.80 and -0.40 ± 0.63 ($p = 0.000$), -2.84 ± 0.60 and -1.38 ± 0.79 ($p = 0.000$), -2.84 ± 1.18 and -2.44 ± 1.16 ($p = 0.102$) respectively. For length, the mean Z scores for neonates with EUGR and without EUGR, at birth, discharge and term were -1.21 ± 1.27 and -0.38 ± 0.90 ($p = 0.000$), -1.92 ± 1.26 and -0.85 ± 0.88

Table 1 – Baseline characteristics of the study neonates.

Neonatal variables	EUGR (72)	No EUGR (39)	P value
	No (%)	No (%)	
Male sex	41 (56.9%)	24 (61.5%)	0.40
SGA	36 (50%)	2 (5.13%)	0.001
Gestational age <32 wks	13 (18.1%)	14 (35.9%)	0.033
Birth weight <1500 g	36 (50%)	9 (23.1%)	0.005
Sepsis	22 (30.6%)	10 (25.6%)	0.38
Jaundice	45 (62.5%)	27 (69.2%)	0.31
Mechanical ventilation	18 (25%)	8 (20.5%)	0.38
Vasopressors	7 (9.7%)	3 (7.7%)	0.51
HMD	5 (6.9%)	1 (2.5%)	0.31
Asphyxia	10 (13.9%)	7 (18%)	0.38
BPD	2 (2.8%)	0 (0%)	0.42
PDA	3 (4.17%)	0 (0%)	0.25
NEC	2 (2.8%)	0 (0%)	0.42
Exclusive breast feeding	40 (55.7%)	28 (71.8%)	0.11

SGA – Small for gestational age, HMD – Hyaline membrane disease, BPD – Bronchopulmonary dysplasia, PDA – Patent ductus arteriosus, NEC – Necrotizing enterocolitis.

($p = 0.000$), -2.44 ± 1.33 and -1.95 ± 1.29 ($p = 0.071$) respectively. For HC the mean Z scores for neonates with EUGR and without EUGR, at birth, discharge and term were -1.35 ± 1.04 and -0.44 ± 1.02 ($p = 0.000$), -1.85 ± 1.10 and -0.88 ± 1.11 ($p = 0.000$), -2.03 ± 1.14 and -1.28 ± 1.61 ($p = 0.005$) respectively (Table 2).

Weight gain velocity during hospitalization for neonates with EUGR and without EUGR was 7.98 ± 4.63 and 10.85 ± 5.53 respectively ($p = 0.120$); after discharge it was 12.99 ± 8.54 and 12.70 ± 7.58 g per day respectively ($p = 0.924$). Velocity for length during hospitalization for neonates with EUGR and without EUGR was 0.65 ± 0.24 and 0.72 ± 0.37 ($p = 0.222$) and after discharge was 0.72 ± 0.35 and 0.62 ± 0.22 cm per week respectively ($p = 0.145$). Velocity for HC during hospitalization for neonates with EUGR and without EUGR was 0.43 ± 0.14 and

Fig. 1 – Flow chart of the study.

Table 2 – Comparison of Z scores of weight, length and head circumference in preterm neonates with and without EUGR.

Z scores	EUGR			No EUGR			P
	n	Range	Mean $\pm$ SD	n	Range	Mean $\pm$ SD	
Weight							
At birth	72	0.9 to 3.3	-1.36 ± 0.80	39	1.45 to -1.61	-0.40 ± 0.63	0.000
At discharge	72	-2.02 to -4.41	-2.84 ± 0.60	39	-1.99 to 2.54	-1.38 ± 0.79	0.000
At term	71	-0.63 to -6.86	-2.84 ± 1.18	37	1.11 to -4.18	-2.44 ± 1.16	0.102
Length							
At birth	72	2.1 to -6	-1.21 ± 1.27	39	2.3 to -2.21	-0.38 ± 0.90	0.000
At discharge	72	0.4 to -6.1	-1.92 ± 1.26	39	0.8 to -3.2	-0.85 ± 0.88	0.000
At term	71	0.6 to -5.9	-2.44 ± 1.33	37	1.4 to -3.9	-1.95 ± 1.29	0.071
Head circumference							
At birth	72	0.7 to -5.1	-1.35 ± 1.04	39	2 to -3.7	-0.44 ± 1.02	0.000
At discharge	72	1.4 to -5.8	-1.85 ± 1.10	39	1.9 to -4.3	-0.88 ± 1.11	0.000
At term	71	0.5 to -5.8	-2.03 ± 1.14	37	2.5 to -6.1	-1.28 ± 1.61	0.005

0.41 ± 0.15 respectively ($p = 0.439$) and after discharge was 0.49 ± 0.16 and 0.43 ± 0.14 cm per week respectively ($p = 0.048$) (Table 3). Exclusive breast milk was given to 40 (55.7%) of neonates with EUGR and 28 (71.8%) of with no EUGR.

4. Discussion

Data of postnatal growth of preterm neonates is presented in a number of ways. Most studies are on VLBW, some on ELBW and fewer on LBW preterm neonates. Some report growth restriction in terms of <10 th centile and a few as less than minus 2 Z score. Some assess postnatal growth at discharge and others at term PMA. We chose to include all preterm neonates and use weight less than minus two Z scores at discharge as cut off for EUGR.

Our study included 111 neonates the GA of 65 of whom was between 28 and 33 weeks and the rest between 34 and 36 weeks. Seventy-two (64.8%) had EUGR at discharge and an even greater proportion: 83 out of 108 (76.8%) had EUGR at term. Many neonates who did not have Z scores below minus two at discharge dropped centiles to become less than minus 2 Z score by term. This observation may be due to the fact that 36 (50.0%) of these premature neonates were both SGA and VLBW.

The incidence of EUGR at discharge for <37 weeks GA LBW neonates has been reported as 56.8% (<10 th centile) by Hong Mei Shan et al; for <34 weeks GA, <1800 g birth weight neonates as 30.4% by Firouzeh Nili and 28% by Reese H. Clark.^{1,15,16} The incidence reported for VLBW neonates was 57% by Motoichiro Sakurai et al, 97% (at 36 weeks PMA) by Lemons et al and 75% (at 28 days) by Camilia et al.^{17–19} The

prevalence of malnutrition at discharge in ELBW neonates has been reported as 89% by Steward DK and 59% by Paula et al.²⁰

Jaiswal et al¹¹ reported that 43% of their VLBW babies were malnourished at term. This is less than our figures. This could be because only 7.5% of their subjects were SGA as compared to a third of ours. Their population comprised of only inborn babies while ours included mostly out born babies. They used parenteral nutrition for 15.5% of their neonates while we did not use it at all. Moreover they used the intrauterine growth charts by Singh et al²¹ for Indian infants for weight and those by Ghosh et al²² for length and head circumference the anthropometric values of which are lower than those in Fenton's charts used by us.

In our study the fall of Z scores from birth to term gestation is most for weight (1.48) and least for HC (0.68) in EUGR babies. For babies with no EUGR also the fall in Z scores is most for weight (2.04) and least for HC (0.84). This indicates a brain sparing effect of malnutrition. This finding is similar to the findings of Saluja et al¹² who reported the mean Z score for weight, length and HC at birth as -1.17 , -1.09 and -0.54 , respectively and -2.16 , -2.24 and -1.35 , respectively by discharge. In our study growth velocity for weight and length was less in neonates with EUGR. For HC it was significantly more in neonates with EUGR by term gestation indicating a brain sparing effect. One major weakness of our study is small sample size. We could not do anything about this as we enrolled as many neonates who fulfilled the inclusion criteria over a period of one year.

Postnatal malnutrition is high in our unit despite early initiation of enteral feeds and adequate use of HMF. Strongly motivating the hospital administration to provide preterm formula in place of toned dairy milk in our unit will be our immediate endeavor.

Table 3 – Comparison of growth velocities of weight, length and head circumference at discharge and term gestation.

Growth velocity	EUGR			No EUGR			'p'
	N	Range	Mean $\pm$ SD	N	Range	Mean $\pm$ SD	
Weight gain velocity at discharge (g/kg/day)	27	1.92–16.60	7.98 ± 4.63	10	2.80–20.00	10.85 ± 5.53	0.120
Weight gain velocity at term (g/kg/day)	28	0.99–32.29	12.99 ± 8.54	10	3.24–21.51	12.70 ± 7.58	0.924
Length velocity at discharge (cm/week)	72	0.02–1.5	0.65 ± 0.24	39	0.35–2.5	0.72 ± 0.37	0.222
Length velocity at term (cm/week)	70	0.02–2.58	0.72 ± 0.35	38	0.14–1.0	0.62 ± 0.22	0.145
Head circumference velocity at discharge (cm/week)	72	0.02–0.83	0.43 ± 0.14	39	0.10–0.75	0.41 ± 0.15	0.439
Head circumference velocity at term (cm/week)	70	0.02–1.00	0.49 ± 0.16	38	0.09–0.78	0.43 ± 0.14	0.048

5. Conclusions

Prevalence of EUGR is high in our NICU (64.8%) at discharge. Growth Z scores continue to drop even after discharge. Growth velocities for weight and length are lower in neonates with EUGR but for HC they are significantly higher indicating a brain sparing effect. The strengths of our study are that we included all preterm neonates not only those less than 32 weeks. We used the well made Fenton's growth chart rather than the local ones. Our weakness was a small sample size. We will strive to get in-house preterm formula to supplement mother's milk to decrease EUGR.

Enhancing enteral and parenteral nutrition is essential to combat EUGR.

Contributors list

MK designed the study, supervised patient management, analyzed the data and edited the manuscript.

ST analyzed the data, helped in writing the manuscript.

NA collected the data, analyzed it and helped in writing the manuscript.

SNS supervised the patient management.

Conflicts of interest

All authors have none to declare.

REFERENCES

- Clark RH, Thomas P, Peabody J. Extrauterine growth restriction remains a serious problem in prematurely born neonates. *Pediatrics*. 2003;111:986–990.
- Cooke RJ, Ainsworth SB, Fenton AC. Postnatal growth retardation: a universal problem in preterm infants. *Arch Dis Child Fetal Neonatal Ed*. 2004;89:F428–F430.
- Astbury J, Orgill AA, Bajuk B, Yu VY. Sequelae of growth failure in appropriate for gestational age, very low-birthweight infants. *Dev Med Child Neurol*. 1986;28:472–479.
- Jefferis BJ, Power C, Hertzman C. Birth weight, childhood socioeconomic environment, and cognitive development in the 1958 British birth cohort study. *BMJ*. 2002;325(7359):305. [Article|PubMed].
- Richards M, Hardy R, Kuh D, Wadsworth ME. Birth weight and cognitive function in the British 1946 birth cohort: longitudinal population based study. *BMJ*. 2001;322(7280):199–203. [Article|PubMed|ChemPort].
- Richards M, Hardy R, Kuh D, Wadsworth ME. Birthweight, postnatal growth and cognitive function in a national UK birth cohort. *Int J Epidemiol*. 2002;31(2):342–348. [Article|PubMed].
- Hack M, Schluchter M, Cartar L, Rahman M, Cuttler L, Borawski E. Growth of very low birth weight infants to age 20 years. *Pediatrics*. 2003;112:e30–e38.
- Sridhar K, Bhat BV, Srinivasan S. Growth pattern of low birth weight babies in the first year of life. *Indian J Pediatr*. 2002;69:485–488.
- Kalra SK, Sarkar P, Vatwani V, De NC. A longitudinal study of low birth weight babies. *Indian J Pediatr*. 1983;50:279–283.
- Hack M, Weissman B, Borawski-Clark E. Catch-up growth during childhood among very low-birth-weight children. *Arch Pediatr Adolesc Med*. 1996;150:1122–1129.
- Jaiswal A, Reddy A, Gaddam P, Murki S. Growth and nutritional status at corrected term gestational age in very low birth weight infants. *J Pediatr*. 2011;78(6):673–678.
- Saluja S, Modi M, Kaur A, Batra A, Soni A, Garg P. Growth of very low birth-weight Indian infants during hospital stay. *Indian Pediatr*. Oct 17 2010;47:851–856.
- Fenton TR. A new growth chart for preterm babies: Babson and Benda's chart updated with recent data and a new format. *BMC Pediatr*. 2003;3:13–22.
- Fenton TR. Preterm Growth Chart 2003 Calculations. Available from: <http://members.shaw.ca/growthchart/FentonGrowthChartcalculations.xls>.
- Shan HM, Cai W, Cao Y, Fang BH, Feng Y. Extrauterine growth retardation in premature infants in Shanghai, a multicenter retrospective review. *Eur J Pediatr*. 2009;168:1055–1059.
- Nili F, Ebadi A. Nutritional status of preterm infants at discharge: a study at Tehran Valie-e-asr hospital. *Med J Islam Repub Iran*. 2006;20(1):33–36.
- Sakurai M, Itabashi K, Sato Y, Hibino S, Mizuno K. Extrauterine growth restriction in preterm infants of gestational age ≤ 32 weeks. *Pediatr Int*. 2008 Feb;50(1):70–75.
- Lemons JA, Bauer CR, Oh W, et al. Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through December 1996. NICHD Neonatal Research Network. *Pediatrics*. 2001 Jan;107(1):E1.
- Martin CR, Brown YF, Ehrenkranz RA, et al. Nutritional practices and growth velocity in the first month of life in extremely premature infants. *Pediatrics*. 2009 August;124(2):649–657.
- Radmacher PG, Looney SW, Rafail ST, Adamkin DH. Prediction of Extrauterine growth retardation (EUGR) in VVLBW infants. *J Perinatology*. 2003;23:392–395.
- Singh M, Paul VK, Deorari AK, Singhal PK. Changing trends in intrauterine growth curves. *Indian Pediatr*. 1991;28:281–283.
- Ghosh S, Bhargava SK, Madhavan S, Taskar AD, Bhargava V, Nigam SK. Intrauterine growth of north Indian babies. *Pediatrics*. 1971;47:826–832.