

Growth Pattern of Preterm Newborns under 34 Weeks of Gestation in a Tertiary Care Hospital, Tamil Nadu, India: A Retrospective Study

KIRANKUMAR HARIDAS¹, MANIKUMAR SOLAIPPAN², RAMYA SHANMUGAM³, MUTHUKUMARAN NATARAJAN⁴

ABSTRACT

Introduction: The proportion of preterm babies is increasing now a days and these babies are more prone to short and long term disabilities. Hence, growth monitoring is essential, to identify the premature infants, who are at increased risk of growth lag and poor neurodevelopmental outcomes.

Aim: To assess the growth pattern of infants, who are born ≤ 34 weeks of gestational age using the intergrowth-21st growth charts.

Materials and Methods: This retrospective study was conducted in the Department of Neonatology at Chengalpattu Medical College and Hospital, a Tertiary Care Center Chengalpattu, Tamil Nadu, India. The duration of the study was one year, from January 2020 to December 2020. A total of 118 neonates born at ≤ 34 weeks gestational age, who were admitted in the hospital and stayed for 14 days and more were included in the study. The data was collected from discharge sheets and an electronic database. Intergrowth-21st growth charts are used to assess growth. Weight, duration of hospital stay and Extrauterine Growth Restriction (EUGR) were assessed for all the newborns. At discharge, the EUGR status of the babies

was determined using a weight ≤ -1.28 Standard Deviation (SD) criterion. Continuous variables were presented as means with SD. The data was analysed using Statistical Package for Social Sciences (SPSS) version 24.0.

Results: The mean maternal and gestational age of the study participants was 24.9 ± 4.14 years and 31.6 ± 1.42 weeks and birth weight of babies were 1608.06 gm (± 275), respectively. The proportions of Appropriate for gestational age (AGA) and Small For Gestational Age (SGA) were 95 (80.5%) and 18 (15.2%), respectively. The mean time to reach full feeds was 10.4 days (± 2.7 days), and the duration of stay in the hospital was 24.8 days (± 9.6 days). The mean discharge weight and gestational age of babies were 1732 gm (± 226 gm) and 35.4 weeks (± 1.47 weeks), respectively. The common complications observed, were those requiring antibiotics (73.7%), respiratory support (61.01%), and Respiratory Distress Syndrome (RDS) (22.8%).

Conclusion: Preterm newborns are more vulnerable to EUGR. The EUGR proportion in present study was 72.8%. The issues that raise the risk of EUGR, during the hospital stay must be adequately addressed in order to ensure that, preterm neonates develops normally.

Keywords: Extrauterine growth restriction, Neonates, Nutrition, Postnatal growth

INTRODUCTION

Growth of the foetus, neonate, and child, happens continuously from conception until early childhood. Infants' growth is measured using a variety of factors, including weight, length, and head circumference. For newborns, those born under 2 kg and over this, the predicted weight increase is 15-20 g/kg/day and 20-30 g/kg/day, respectively. The predicted rate of length gain is 1 cm each week; however, these measures are only useful as a guide for brief periods of time [1]. Based on exponential statistical techniques or the average pattern of weight gain in infants between 23 and 36 weeks of gestation, these patterns of weight gain are estimated. Some newborns might not be able to follow these patterns [1].

Long term effects result from preterm neonates' growth during the first several months of life. Neurodevelopmental delay, ischaemic heart disease, poor glucose tolerance, type II diabetes mellitus, hypertension, and metabolic syndrome are only a few of the short- and long term effects of aberrant growth patterns [2,3]. The gold standard for postnatal development, the intrauterine growth status, is the foundation for the present methods for measuring growth in newborns [4]. However, there is no universal agreement on how

to track the development of preterm neonates or what the optimal pattern of growth should look like in these young children. Standard and reference charts are the two different categories of charts. Standard charts are prescriptive and outline, how a population should grow based on low risk pregnancies and ideal environmental and health conditions. Reference charts, which demonstrate the longitudinal development of a certain reference population, are descriptive in nature and are developed from both low and high risk pregnancies [5-8].

Intergrowth-21st curve is a prescriptive growth patterns, which means they describe, how newborns without risk factors or congenital malformations should grow under ideal nutritional conditions. The data were collected longitudinally from selected healthy pregnant women with no complications of any specific gender and of multiple ethnicities. They used eight geographically defined urban population cohorts, that were similar enough in terms of health status, nutritional needs of mothers, and adequate antenatal care to allow for analytical and statistical grouping [8-10]. The intergrowth-21st consortium published the growth standards for birth weight and gender of neonates in the gestational age range of 33-42 weeks of gestation, and only reference charts for preterm infants below

33 weeks of gestation. Therefore, the intergrowth-21st prescriptive curves are considered robust for preterm infants with gestational ages >33 weeks [11].

Monitoring is essential to identify any deviations from the normal pattern. Although, the majority of studies focused on extremely preterm infants, or Very Low Birth Weight (VLBW) infants [12-14], because infants, as young as, 32 weeks of gestation are at risk of growth lag and poor neurodevelopmental outcomes [15,16]. The risk of adverse developmental outcomes is increased by premature birth and Small for Gestational Age (SGA) [17,18]. The extrauterine growth of preterm infants has been reported to fall behind when compared to their term counterparts [19]. In earlier studies, conducted to assess the growth of preterms [20-23]. The intergrowth-21st chart has not been used in any other studies to define growth in preterm newborns, especially. The aim of present study was to evaluate the growth pattern of preterm infants at birth and also, to assess the extent of EUGR.

MATERIALS AND METHODS

This retrospective study was conducted in the Department of Neonatology at Chengalpattu Medical College and Hospital, a Tertiary Care Centre, Chengalpattu, Tamil Nadu, India. The duration of the study was one year, from January 2020 to December 2020. Annual admission rate was, over 3000 infants. The study was approved by the Institutional Ethics Committee (IEC number of ECR/774/INST/TN/2015). As this was a retrospective descriptive study, consent from parents was not taken.

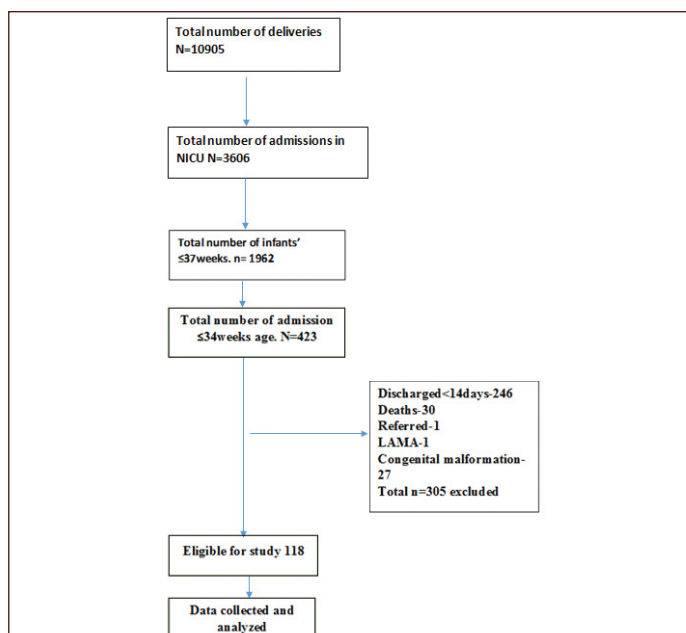
Inclusion criteria: The infants delivered at ≤ 34 weeks, who stayed in the hospital for at least 14 days or more and anthropometric measurements were available in medical records at birth and at the time of discharge, were included in the study.

Exclusion criteria: Newborns discharged within 14 days were excluded since, they were still in their physiologic weight loss stage, which cannot be considered EUGR because catch-up weight gain is still feasible in these infants. Any newborn with a serious congenital defect or probable chromosomal abnormalities or syndrome and infants, who were transferred to different hospitals or those who passed away, while receiving medical attention were also excluded from the study.

Sample size calculation: In the present study, total 423 infants overall were born at or before 34 weeks of gestation, and were admitted during the study period. Among them, 118 infants, who were required to stay beyond two weeks in the hospital, were enrolled in the study and their details have been collected for analysis [Table/Fig-1].

Study Procedure

Data was collected from case sheets and discharge summaries of infants, who were admitted to the Neonatal Intensive Care Unit (NICU), which were present in hospital medical records and an electronic database. In NICU, birth weight and daily measurements of body weight were done using electronic scales with an accuracy of ± 10 gm. The size at birth and at discharge was documented in the form of percentiles and z-scores. These measurements were done by computer software provided by the intergrowth-21st consortium study group, which was accessed via the link <https://intergrowth21.tghn.org>, [9] which has intergrowth-21st preterm size at birth and postnatal follow-up growth reference charts.



[Table/Fig-1]: Flowchart depicting the study.
LAMA: Left against medical advice

The feeding protocol authors used in NICU, included starting feeds at 30 mL/kg/day on day 1 in infants under 1500 gm and 60 mL/kg/day in infants over 1500 gm. The feeds were increased at a rate of 30 mL/kg/day if the baby had no intolerance to the initial feeds. The authors used Mother's Own Milk (MOM), and if, it was not available, then Pasteurised Donor Human Milk (PDHM) was used for the period, until MOM was available. The authors did not use any kind of infant formula in the unit. The authors did not aspirate the gastric residuals routinely, unless there was an increase in abdominal girth of ≥ 2 cm from the baseline. Abdominal girth was monitored before every feed. The infants, who required Total Parenteral Nutrition (TPN) were started on proteins at 2 gm/kg/day and lipids at 1 gm/kg/day on day one, keeping the protein:calorie ratio of 25-40 by adjusting the Glucose Infusion Rate (GIR). The authors added human milk fortifier in case, the infant did not gain weight of > 15 gm/kg/day at a feed volume of ≥ 180 mL/kg/day. During the period of illness, the feeds were restricted to trophic feeds only. The infant was discharged, on feeds of 150 mL/kg/day, when they gained adequate weight for three consecutive days and were haemodynamically stable [24].

The SGA defined as weight ≤ -1.28 SD (10th percentile) [25]. The EUGR status of infants was assessed at discharge, using a weight criteria of ≤ -1.28 SD (10th percentile) [26], and a difference of more than 2SD score, i.e., the difference between the birth and discharge weight score of > 2 SD, was also calculated [27].

STATISTICAL ANALYSIS

The data was collected in a Microsoft Excel spreadsheet. Continuous variables are represented as means with standard deviations. SPSS version 24.0 was used to analyse the data.

RESULTS

In present study, the mean maternal age was 24.9 ± 4.14 years and mean gestational age was 31.6 ± 1.42 weeks. The most common reasons for preterm delivery were spontaneous onset of labour pain in 56 (47.4%) and preterm premature rupture of membranes in 29 (24.5%). There was almost an equal distribution of male and female infants in the study. The average weight at birth was 1608.06 ± 275 gm. Babies required around 8.4 days ± 2.77 days to reach 150 mL/kg/day of feeds, and the mean

duration of hospital stay was 24.8 days ±9.6 days. The mean gestational age at discharge was 35.4 weeks ±1.47 weeks and the mean weight at discharge was 1732±226 gm. The most common Co-morbidities identified in admitted neonates were respiratory distress in 27 (22.8%), need for respiratory support in 72 (61%), need for antibiotics either for clinically or culture-proven sepsis 87 (73.7%) [Table/Fig-2].

Variables	n (%)	
Age (Mean±SD)	24.9±4.14 years	
Obstetric index	Primigravida	71 (60.17)
	Multigravida	47 (39.8)
GA (Mean±SD)	31.6±1.42 weeks	
GA assessed by	Early scan 109 (92.3)	
	LMP 5 (4.20)	
	15-20 weeks 2 (1.68)	
	21-28 weeks 1 (0.84)	
New Ballard score 1(0.84)		
GHT	36 (30.5)	
GDM	02 (1.69)	
PPROM	29 (24.5)	
Hypothyroidism	07 (5.9)	
Oligohydramnios	12 (10.1)	
Polyhydramnios	01 (0.85)	
ANS	104 (88.1)	
MOD	Vaginal	73 (61.8)
	LSCS	45 (38.1)
Preterm phenotype	Spontaneous 56 (47.4)	
	PPROM 29 (24.5)	
	Indicated 33 (28.2)	
Risk of EOS	24 (20.3)	
Maternal weight (Mean±SD)	58.6±12.3 kg	
Neonatal sex distribution	Male	60 (50.8)
	Female	58 (49.1)
Gestational age at birth (Mean±SD)	31.6±1.42 weeks	
Birth weight (Mean±SD)	1608.06±275 grams	
Singleton	93 (78.9)	
TTR (150 mL/kg/day) (Mean±SD)	8.4±2.77 days	
Duration of stay (Mean±SD)	24.8±9.6 days	
Gestation at discharge (Mean±SD)	35.4±1.47 weeks	
Weight at discharge (Mean±SD)	1732±226.3 gm	
RDS	27 (22.8)	
Respiratory support	72 (61.01)	
Antibiotics (sepsis)	87 (73.7)	
Inotropes	25 (21.1)	

[Table/Fig-2]: Maternal and neonatal characteristics.
 GA: Gestational age; LMP: Last menstrual period; GHT: Gestational hypertension; GDM: Gestational diabetes mellitus; PPROM: Preterm premature rupture of membrane; ANS: Antenatal steroids; MOD: Mode of delivery; LSCS: Lower segment cesarian section; EOS: Early onset sepsis; TTR: Time to reach; RDS: Respiratory distress syndrome N=118

In present study, out of 118 preterms, majority 95 (80.5%) were AGA, least 5 (4.2%) were Large for Gestational Age (LGA) and SGA at birth was 18 (15.2%) using intergrowth-21st growth charts. According to intergrowth-21st growth charts, out of 95 infants born AGA at birth, 80 (84.2%) remained AGA and 15 (15.8%) were EUGR at discharge, while 17 (95%) of infants born SGA at birth remained EUGR [Table/Fig-3].

Weight classification	IG 21 st at birth n (%)	EUGR at discharge n (%)
AGA	95 (80.5%)	15 (15.8%)
SGA	18 (15.2%)	17 (95%)
LGA	5 (4.2%)	-

[Table/Fig-3]: Distribution of infants' growth at birth and EUGR rate at discharge N=118.
 IG: Intergrowth-21st

The mean percentile weight at birth was 42.7; at discharge, it was 10.2 percentile. The mean weight percentile in SGA infants was 4.3 percentile, and at discharge it was 0.92 percentile. In present study, the authors tried to represent EUGR using two different criteria. The first was a discharge weight of ≤-1.28 SD, and the second was a z-score difference of 2SD between birth and discharge. The EUGR component using ≤-1.28 SD was present in 86 (72.8%). The EUGR proportions using the 2SD difference from birth to discharge were 20 (16.9%) [Table/Fig-4,5].

EUGR at discharge	n (%)
EUGR ≤-1.28SD	86 (72.8)
EUGR >2SD difference	20 (16.9)

[Table/Fig-4]: Distribution of infants' EUGR rate at discharge.
 EUGR: Extrauterine growth restriction

Weight classification	IG-21 st n (%)	EUGR ≤-1.28SD n (%)	EUGR >2SD n (%)	p-value
AGA	95 (80.5)	69 (58.4)	15 (12.7)	<0.001
SGA	18 (15.2)	17 (94.4)	5 (27.7)	0.0041
LGA	5 (4.2)	0	0	-

[Table/Fig-5]: Comparing the two definition of EUGR.

The mean percentile weight loss for infants with and without co-morbidities was RDS 32 vs 29.2 percentile, respiratory support 35 vs 23 percentile, use of antibiotics 29.8 vs 25.7 percentile, and inotropes 35.2 vs 29.2 percentile, respectively [Table/Fig-6].

Co-morbidity	EUGR (%)	No EUGR (%)
RS	35	23
RDS	32	29.2
Antibiotic	29.8	25.7
Inotrope	35.2	29.2

[Table/Fig-6]: Comparison of co-morbidities and mean percentile weight loss at discharge among infants with EUGR and no EUGR.

DISCUSSION

The growth of preterm infants is always a matter of debate and controversy. There are numerous standards for defining growth in preterms, but none of them holds well for all sets of preterm babies. It is a well-known fact that, EUGR is very common among preterm infants, even when, they do not have any co-morbidity compared to those of infants with certain co-morbidities [28]. In the present study, authors tried to define the growth pattern of preterm infants, who were admitted to NICU. There are various studies, that describe the postnatal growth of preterm infants [20,21-23,29]. Belfort MB et al., used the Fenton growth curves, to estimate the incidence of Postnatal Growth Failure (PGF), which they characterised as a discharge weight below the 10th percentile, at 32.6% amongst surviving infants of 31 weeks gestation [20]. The Vermont Oxford Network (VON) reported that, 50.3% of VLBW infants were discharged with weights, that were below the 10th percentile in 2013. The mean gestational age of the cohort at birth was 28.7 weeks and the weight was 1.11 kg, and

at discharge, the gestational age was 37.99 weeks and the weight was 2.57 kg [21]. Based on a definition of EUGR as a z-score of ≤ -1.28 SD (10th percentile) using the intergrowth-21st growth charts, the present study found an incidence of EUGR of 72.8% among preterm infants ≤ 34 weeks.

Similarly, Clark RH et al., in their study on premature infants < 34 weeks of gestational age, which included infants with a mean gestational age of 31 weeks and a birth weight of 1.3 kg, found that, the EUGR, defined as being below the 10th percentile at the time of discharge according to an intrauterine growth chart, was reported to be 28% and 34%, respectively, among preterm infants born at 23-34 weeks GA [22]. A study reported from Israel found that, from their national VLBW database, the EUGR rate was 8.1% and 35.5% had a decrease in z-scores of $> 2SD$ and $1-2SD$, respectively, using a Canadian reference [23]. Venkat Reddy K et al., conducted a prospective study on preterm infants ≤ 32 weeks of gestational age and found that the incidence of EUGR, defined as the discharge weight of the $< 10^{\text{th}}$ percentile for weight, length, and head circumference, was 56.9%, 35.5%, and 33.3%, respectively [29]. Infants born SGA had poor growth outcomes [30,31]. Similar to these studies, the authors also had infants, whose growth percentile was lower due to their SGA status at birth. These SGA infants remained at lower percentile scores even at discharge. In the present study, almost all the SGA infants were EUGR at discharge. This emphasises that, these SGA infants need more aggressive nutrition right from birth to achieve a good weight gain pattern.

The proportion of difference in identifying the EUGR in different studies [20,21-23,29] may be due to differences in inclusion criteria, growth charts used, and criteria used to define the EUGR. The proportion of EUGR in the present study was higher compared to other studies, which could be because of the restriction of feeding policies, especially, during periods of illness. The mean percentile weight loss in infants, also suggested that, those with co-morbidities at birth grew less than those, who did not have any co-morbidities. The results of the present study were similar to the previous studies conducted on preterm infants [21,32-34]. This indicates that, there is a need for these infants to be fed aggressively during their illness and recovery period, which is supposed to prevent, to some extent, the long term complications. Due to the low survival rate of extreme preterm infants in the unit, co-morbidities including Necrotising Enterocolitis (NEC) and Bronchopulmonary Dysplasia (BPD), which are often associated with extreme preterm newborns, are not evident in the present study.

The EUGR identified by all growth charts, despite variations in their application, has remained a serious issue, explaining why postnatal growth is hindered in preterm infants and highlighting the significance of nutrition and growth monitoring in preterm children. In the present study, co-morbidities that made it difficult for their nutritional needs to be addressed during their sickness to be met resulted in newborns born with AGA, having poor growth during their hospital stay. Thus, even with these AGA infants, there will be EUGR.

Limitation(s)

The length and head circumference was not used in identifying the EUGR rate, which could have given a robust insight into the growth of these infants.

CONCLUSION(S)

In the present study, proportion of Intrauterine Growth Restriction (IUGR) was lower. Infants born prematurely had a higher incidence

of EUGR. Morbidities at birth, increased the likelihood of EUGR. Almost all of the SGA infants remained SGA upon discharge. Based on the present research, the authors strongly believe that, active nutrition should be practiced during both, the birth hospitalisation and the newborn illness period in order to avoid EUGR and long term consequences. Future research should concentrate on an aggressive nutrition policy, during illness in order to prevent EUGR and identify the complications associated with aggressive nutrition.

Author contribution: Protocol development was done by all the authors, literature search and assessing for eligibility done by KH and NM, data extraction by KH, analysis done by KH, SR and SM, critical review and approval of the manuscript was done by all the authors.

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PARTICULARS OF CONTRIBUTORS:

1. Resident, Department of Neonatology, Chengalpattu Medical College and Hospital, Chengalpattu, Tamil Nadu, India.
2. Assistant Professor, Department of Neonatology, Chengalpattu Medical College and Hospital, Chengalpattu, Tamil Nadu, India.
3. Associate Professor, Department of Neonatology, Chengalpattu Medical College and Hospital, Chengalpattu, Tamil Nadu, India.
4. Professor, Department of Neonatology, Chengalpattu Medical College and Hospital, Chengalpattu, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Kirankumar Haridas,
Plot No. 100, Prashant Nagar (A), Rajapur, Gulbarga-585105, Karnataka, India.
E-mail: kiranharidas@gmail.com

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