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Original Article

Paediatrics Section

Short Term Assessment of Growth and Neurodevelopmental Outcome in Low Birth Weight and Very Low Birth Weight Newborns Discharged from a Tertiary Care Centre- A Cohort Study

SWASTHI KABI SATPATHY[1], MANAS RANJAN UPADHYAY[2], RAJLAXMI UPADHYAY[3]

ABSTRACT

Introduction: With better healthcare facilities, despite an increase in neonatal survivor rates, the outcomes in the survivors still remains uknown to a great extent. In overburdened centres following an early discharge policy, a structured follow-up plan to evaluate growth, development and problems faced by the high-risk babies is essential.

Aim: To assess the growth, development at 52 and 64 weeks Postmentrual Age (PMA) and association of postnatal growth failure with developmental outcome in Low Birth Weight (LBW) and Very Low Birth Weight (VLBW) babies.

Materials and Methods: This was a prospective cohort study carried out amongst the newborn babies discharged from a tertiary care hospital, Sriram Chandra Bhanja Medical College and Hospital, Cuttack, Odisha, India, within 2 months period and followed-up till 64 weeks PMA. Out of 189 newborns discharged during study period, 168 met the inclusion criteria and only 114 babies could complete the follow-up till 64 weeks postmenstrual. The weight, length and head circumference were documented at discharge, 44, 52 and 64 weeks PMA and compared using INTERGROWTH 21st postnatal standards. Denver Developmental Screening Test was used for developmental screening at 52 and 64 week PMA. Descriptive analysis was performed using Statistical Package for Social Sciences (SPSS) version 20.0 and categorical data was compared using Chi-square test in trend using Epi Info software.

Results: Out of 114 patients, 51 (44.7%) were females and 63 (55.3%) were males. At birth, 72 (63.16%) of study population was below 10th centile which increased to 77 (67.54%) at 44 weeks PMA. By 64 weeks PMA, 62 (54.39%) infants showed >10th centile of weight for age. Out of total, 18 (15.79%) showed delayed developmental milestones. 11 out of 18 (61.11%) babies were with delayed development, i.e., below 3rd centile of weight for age showing that at lower postnatal weight odds of patients having developmental delay were increased.

Conclusion: Postnatal growth pattern of the study population was along the lower centiles of INTERGROWTH 21st chart. Incidence of developmental delay was higher in babies with postnatal growth failure.

Keywords: Follow-up studies, High risk newborn, Intergrowth, Postnatal growth failure

INTRODUCTION

Over the last few decades, with technological advancement, better understanding of neonatal physiology and introduction of various government schemes, there has been a substantial increase in the survival rates of high-risk newborns [1]. However, with increased survival, incidence of growth failure and developmental delay has also increased [1,2]. Improving outcomes beyond survival of high-risk newborns requires an appropriate and comprehensive follow-up programme that will aid in early detection and management of morbidity associated with perinatal events. The need for such follow-up programmes is greater in resource limited and overcrowded hospital settings practising an early discharge policy. In tertiary care setups, due to huge patient load, constraints of bed availability and poor socio-economic status of parents who are mostly daily wagers sometimes early discharge of the patients becomes essential. Hence, a discharge policy should be followed by balancing the benefits versus risks of discharging a patient. The postnatal outcome of these patients however remains largely unknown.

Few studies in past have highlighted the association of poor postnatal growth with impaired neurodevelopmental outcome [3,4]. However, there is paucity of data regarding such outcomes in low birth weight and very low birth weight neonates discharged from tertiary care hospitals in Eastern India practising an early discharge policy.

Hence, this study was conducted to assess the growth pattern and neurodevelopmental outcome in low birth weight and very low birth weight babies postdischarge from a tertiary care centre along with the developmental outcome in patients with postnatal growth failure.

MATERIALS AND METHODS

This prospective cohort study was conducted in a Neonatal Unit of Department of Paediatrics, in a tertiary care hospital of Sriram Chandra Bhanja Medical College and Hospital, Cuttack, Odisha, India, from December 2019 to October 2020. Institutional Ethical Committee Clearance was obtained (Regd. No: ECR/84/Inst/OR/2013/RR-20), and informed verbal consent was taken from the parents.

Inclusion criteria: All newborn babies with birth weight or admission weight between 1 kg-2.49 kg (measured using electronic weighing scale with a least count of 5 grams) who were discharged from the hospital during the study period.

Exclusion criteria: Babies who were lost to follow-up, had any major congenital anomaly or diagnosed cases of inborn error of metabolism, who were diagnosed as Hypoxic Ischaemic Encephalopathy (HIE) stage 3 (as per Sarnat and Sarnat staging) [5] were excluded from the study.

Procedure

All newborn babies with birth weight between 1 kg-2.49 kg, admitted to the neonatal unit were treated as per disease condition and feeding was started as per the following protocols-

1. Minimal enteral nutrition was started for all stable newborns with birth weight of 1250 grams or more on day 1 of life and after 24 hours of life for those weighing less than 1250 grams.
2. Feeding advancement was done from next day for all babies more than 29 weeks of gestation.
3. Feeding volume was increased by 10-20 ml/kg/day in neonates with birth weight <1250 grams and by 20-30 ml/kg/day in neonates with birth weight >1250 grams.
4. Mothers own milk was preferred followed by donor milk followed by formula feed for appropriate gestational age.
5. Fortification of breast milk was done once the neonate reached 100 mL/kg/day of feeds.
6. Maximum feed volume of 180-200 mL/kg/day as tolerated was provided.

Sick low birth weight neonates were discharged if the following criteria was met-

1. Minimum discharge weight of 1.2 kg
2. No signs of respiratory distress or oxygen requirement
3. Haemodynamically stable without any vasopressor support
4. Treated adequately with antibiotics as per sepsis screen/ blood culture/Cerebrospinal Fluid (CSF) analysis
5. Able to maintain body temperature in an open crib with clothing
6. Able to feed with katori and spoon or directly from mother
7. Adequate urine output (6-8 times/day)
8. Mother confident about feeding her baby/doing Kangaroo Mother Care (KMC) at home.

At the time of discharge, weight, length and head circumference were documented. Illness during hospital stay, requirement of blood products transfusion, exchange transfusion, antibiotics received were noted. Parents were explained about the risk factors for neurodevelopmental disability and the need for follow-up. A clearly written discharge summary was also provided to the parents along with exact date for follow-up visit.

For babies with birth weight between 1-1.5 kg, follow-up was done at:

- 7-14 days postdischarge
- Every fortnightly till 44 weeks PMA
- 52 weeks PMA
- 64 weeks PMA

For babies with birth weight >1.5 kg follow-up was done at:

- 7-14 days postdischarge
- 44 weeks PMA
- 52 weeks PMA
- 64 weeks PMA

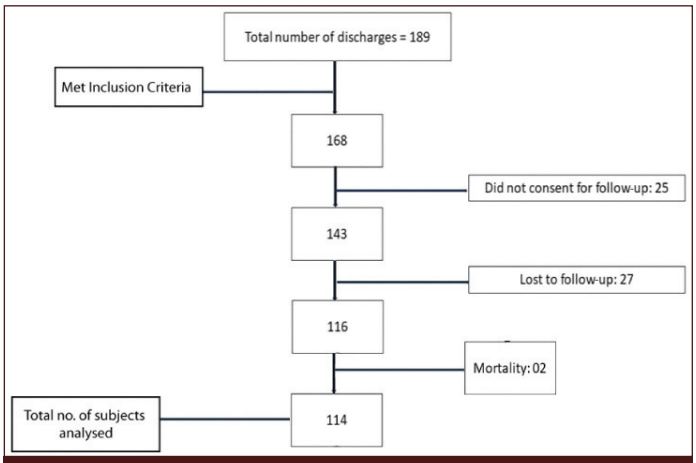
Anthropometric measurements were taken at each visit and neurodevelopmental screening was done at 52 and 64 weeks PMA. At each follow-up visit, parents were interviewed with a set of preformed questionnaire regarding health issues and feeding practices. Each newborn baby underwent anthropometry measurements and the values were plotted on growth charts. Anthropometric measurements were taken in a warm room without draught. Weight was recorded using an electronic weighing scale with a least count of 5 grams. Two readings were taken, if the difference between the two recordings was greater than 5 grams, a third measurement was taken and the average of two nearest values were recorded. Similarly, length was measured using an infantometer and head circumference with a non stretchable measuring tape. The values were plotted on INTERGROWTH 21st postnatal growth standards [6].

The Denver Developmental Screening Test (DDST II): It was used to screen babies for developmental delay [7]. Developmental assessment was done according to corrected ages of the infants in 4 domains-gross motor, fine motor, language and personal social. The responses were rated as mentioned:

1. Pass-if child passes, fails, or refuses item on which the age line falls between the 25th and 75th percentile
2. Caution-child fails or refuses item on which the age line falls between the 75th and 90th percentile
3. Delay-child fails or refuses item that falls completely to the left of the age line

Delay in one domain or caution ratings in 2 domains were the criteria for an infant to undergo a formal developmental evaluation by a developmental Paediatrician and if found to have delay early intervention was provided.

Out of 168 newborns who met the inclusion criteria only 114 babies could complete the follow-up till 64 weeks Postmentrual Age (PMA) [Table/Fig-1].



[Table/Fig-1]: Flowchart of patients included in the study.

STATISTICAL ANALYSIS

All data was compiled and analysed using descriptive statistics in SPSS version 20.0. The mean of anthropometric data was calculated and plotted on INTERGROWTH 21st postnatal growth standards to compare the growth pattern of our population with the standard population. The Epi Info software by Centers for Disease Control was used to perform the linear analysis of Odds Ratio by Chi-square trend for intergroup comparison of categorical variables which were expressed as numbers or percentages. A p-value <0.05 was considered significant.

RESULTS

A total number of 189 newborn babies were discharged during the study period, out of which 68 were VLBW and 121 were LBW. Owing to the pandemic situation, only 114 babies could complete regular

follow-up till 64 week PMA. The number of deaths postdischarge were 2 out of 114 (1.7%), both the babies belonged to the low birth weight category. The cause of death in one patient was septicemia with acute kidney injury, and very severe pneumonia in the other baby. Both deaths occurred within one month postdischarge.

Demographic profile: Out of 114 patients, 51 (44.7%) were females and 63 (55.3%) were males. The study population included 35.1% VLBW and 64.9% LBW babies. As per modified Kuppuswamy scale [8], 67.5% of the study population was from upper lower and lower socio-economic class, while 30.7% were from lower middle class and only 1.7% were from upper middle class [Table/Fig-2].

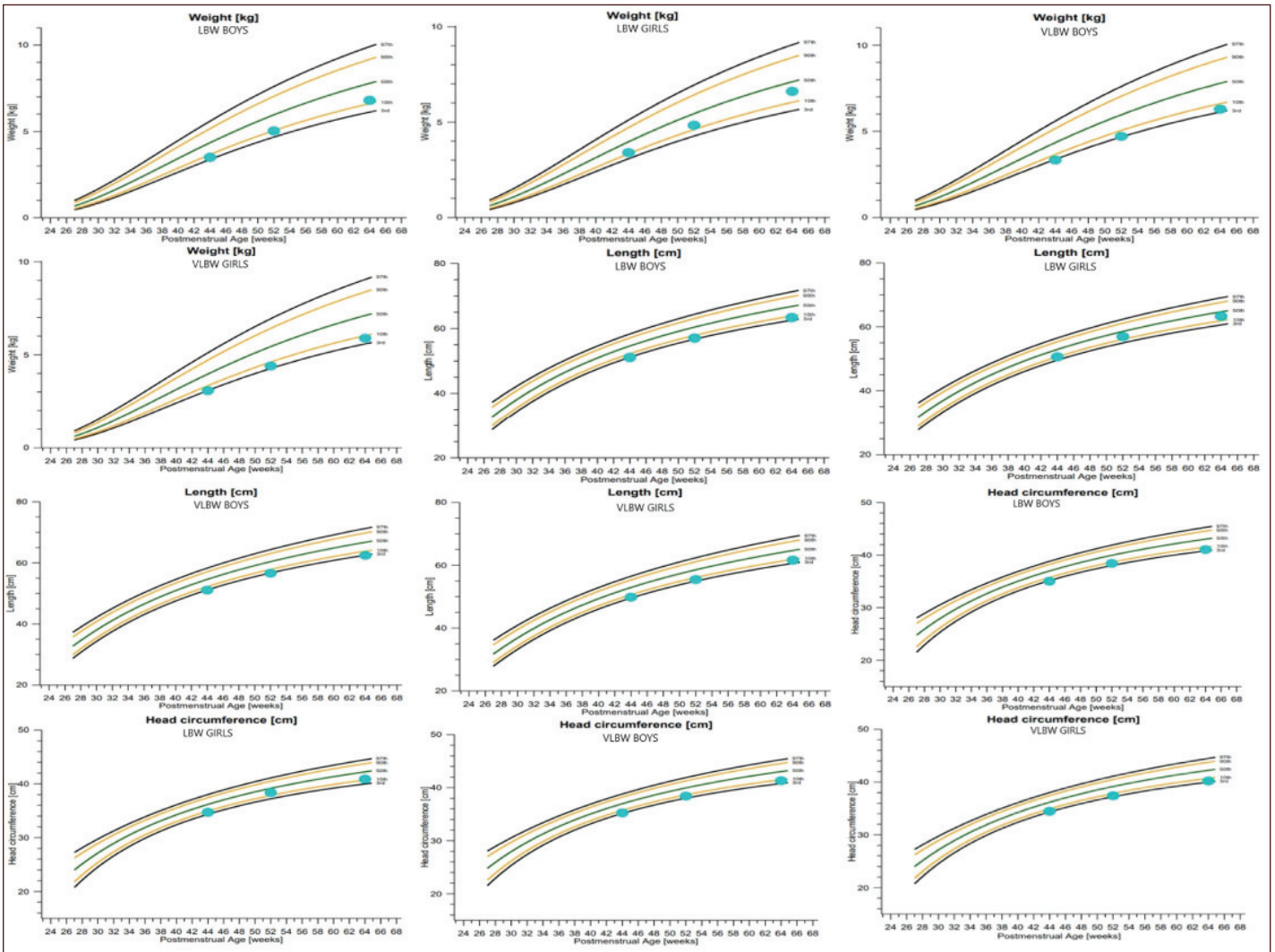
Demographic variables	n (%)
Birth weight	
VLBW*	40 (35.1%)
LBW**	74 (64.9%)
Gender	
Males	63 (55.3%)
Females	51 (44.7%)
Socio-economic status	
Upper class	0
Upper middle class	2 (1.7%)
Lower middle class	35 (30.7%)
Lower class	77 (67.5%)

[Table/Fig-2]: Demographic profile (N=114).
*VLBW: Very low birth weight; **LBW: Low birth weight; SES: Socioeconomic class as per modified kuppuswamy scale [8]

Growth outcome: In the LBW group, the rate of weight gain {23.56 grams/day with an Inter-Quartile Range (IQR) of 3.11} was slightly higher than in the VLBW group (21.43 grams/day with an IQR of 2.88). The rate of increment of head circumference and length in both groups was 0.7 cm/week. The incidence of growth failure (number of babies below 10th centile as per INTERGROWTH 21st charts) was 63.16%, 67.54%, 60.52% and 45.61% at birth, 44 weeks, 52 weeks and 64 weeks PMA respectively [Table/Fig-3]. The number of infants below 3rd centile decreased from 20.2% at 44 weeks PMA, 13.15% at 52 weeks PMA to 11.4% at 64 weeks PMA.

The median z-score value for weight in VLBW infants at birth, 44, 52 and 64 weeks PMA was -0.73 (IQR 0.96), -1.64 (IQR 0.55), -1.62 (IQR 0.42), -1.47 (IQR 0.7) respectively. The median z score value for weight in LBW infants at birth, 44, 52 and 64 weeks was -1.45 (IQR 1.1), -1.5 (IQR 0.82), -1.35 (IQR 0.99), -1.06 (IQR 1.05) respectively. This shows that there was increased incidence of growth failure in the postnatal period usually in the 1st month with increasing catch up growth observed towards completed 6 months. But, a significant percent of infants (45.61%) were still below 10th centile by 64 weeks PMA. The percentage of underweight babies were higher amongst VLBW babies as compared to LBW babies, however the incidence of stunting and microcephaly was more in the LBW group [Table/Fig-4].

In order to compare the number of patients showing improved growth (crossing over 10th centile) at 44 week PMA, increased with increasing birth weight, Chi-square test was used in trend. Linear analysis of odds ratio by Chi-square trend test showed a downward



[Table/Fig-3]: Comparison of growth of study population as per INTERGROWTH 21st postnatal growth standards.

decreasing trend in odds ratio, which confirmed that those with higher birth weight category had better growth as compared to those with lower birth weight. This difference was statistically significant with a p-value <0.001. A similar trend was observed at 52 and 64 weeks PMA [Table/Fig-5].

Outcomes	44 weeks PMA (N=114)		52 weeks PMA (n=114)		64 weeks PMA (n=114)	
	VLBW n=40	LBW N=74	VLBW n=40	LBW N=74	VLBW n=40	LBW N=74
Weight for age z-score (Median)	-1.64 IQR 0.55	-1.5 IQR 0.82	-1.62 IQR 0.42	-1.35 IQR 0.99	-1.47 IQR 0.7	-1.06 IQR 1.05
Underweight (weight for age <2 SD)	11 (27.5%)	12 (16%)	7 (17.5%)	8 (10.8%)	6 (15%)	7 (9.45%)
Stunting (length for age <2 SD)	9 (22.5%)	15 (20.27%)	8 (20%)	13 (17.6%)	4 (10%)	11 (14.86%)
Microcephaly (head circumference for age <3 SD)	5 (12.5%)	11 (14.86%)	3 (7.5%)	9 (12.16%)	3 (7.5%)	7 (9.45%)

[Table/Fig-4]: Growth outcomes of study population (N=114).

Weight for age	Centile		Odds ratio
	≤10th	>10th	
44 weeks			
1 kg-1.249 kg	23	1	1
1.25 kg-1.49 kg	10	6	0.072
1.5 kg-1.749 kg	19	5	0.165
1.75 kg-1.99 kg	12	5	0.104
2 kg-2.49 kg	13	20	0.028
Chi-square value	16.672	p-value	0.0000456
52 weeks			
1 kg-1.249 kg	22	2	1
1.25 kg-1.49 kg	7	9	0.444
1.5 kg-1.749 kg	16	8	0.615
1.75kg-1.99 kg	10	7	1.143
2kg-2.49 kg	14	19	0.444
Chi-square value	9.659	p-value	0.0018858
64 weeks			
1 kg-1.249 kg	20	4	1
1.25 kg-1.49 kg	7	9	0.156
1.5 kg-1.749 kg	11	13	0.169
1.75 kg-1.99 kg	8	9	0.178
2 kg-2.49 kg	6	27	0.044
Chi-square value	19.714	p-value	0.0000102

[Table/Fig-5]: Linear analysis of weight for age centile by Chi-square trend at 44, 52 and 64 week PMA.
A p-value <0.05 was considered significant

Developmental outcome: At 52 weeks PMA, number of infants having impaired neurodevelopmental outcome was 12 (10.53%). At 64 weeks PMA, number of infants having impaired neurodevelopmental outcome was 18 (15.79%) [Table/Fig-6]. The difference in LBW and VLBW group was not statistically significant.

The causes or associations that were attributable to developmental delay were Hypoxic-Ischaemic Encephalopathy (HIE) stage 2 present in 10 (55.56%) subjects, postnatal growth failure 11 (61.11%), hypoglycaemia 3 (16.67%), prematurity 4 (22.22%). Multiple risk factors were present in 6 (33.33%) of patients with abnormal developmental screening results [Table/Fig-7].

Outcome	Number	VLBW	LBW	p-value (Chi-square)
52 weeks PMA	12 (10.53%)	4 (33.33%)	8 (66.67%)	0.8929
64 weeks PMA	18 (15.79%)	5 (27.77%)	13 (72.22%)	0.4788

[Table/Fig-6]: Neurodevelopmental delay (N=114).
Developmental outcome at 52 weeks and 64 weeks PMA as per DDST II screening

Causes	n (%)
Hypoxic-ischaemic encephalopathy Stage 2	10 (55.56%)
Postnatal growth failure (<3rd centile)	11 (61.11%)
Hypoglycaemia	3 (16.67%)
Preterms <32 weeks (Very Preterm Babies)	4 (22.22%)
Multiple risk factors	6 (33.33%)

[Table/Fig-7]: Causes attributable to developmental delay (n=18).

Association of postnatal growth failure with developmental outcome: Out of 12 patients who had developmental delay, at 52 weeks PMA, 8 (66.67%) were below 3rd centile and 3 (25%) were between 3rd-10th centile. Similarly, at 64 weeks PMA, out of 18 patients who had developmental delay, 16 were below 10th centile out of which 11 (61.11%) were below 3rd centile. On performing a linear trend analysis of odds ratio for patients with developmental delay versus no delay with increasing weight centiles, a decreasing trend was observed which indicated that patients with postnatal growth failure were at higher risk of abnormal neurodevelopmental outcome [Table/Fig-8].

Weight for age centile	Delay	No delay	Odds ratio
52 weeks PMA			
<3rd Centile	8	6	1
3rd-10th Centile	3	52	0.043
>10th Centile	1	44	0.017
Chi-square	21.921	p-value	0.000004
64 weeks PMA			
<3rd Centile	11	2	1
3rd-10th Centile	5	34	0.027
>10th Centile	2	60	0.006
Chi-square	38.716	p-value	0.000001

[Table/Fig-8]: Linear analysis of risk of developmental delay with postnatal weight for age.
p-value <0.05 considered significant

DISCUSSION

In the study population, the number of infants below 10th centile decreased from 67.54% at 44 weeks PMA (out of which 20.2% were below 3rd centile), 60.5% (13.15% below 3rd centile) at 52 weeks PMA to 45.61% at 64 weeks PMA (out of which 11.4% were below 3rd centile). The incidence of stunting and microcephaly by 64 weeks PMA was 13.15% and 8.7%, respectively.

The LBW group of infants showed improvement in weight gain, however, they had higher incidence of stunting and microcephaly as compared to VLBW babies at all three follow-up visits, though the difference was statistically insignificant. In VLBW babies, the incidence of growth failure at 3 months postnatal age as reported by Sharma PK et al., [more than 50%] was much higher compared to current population, and similar improvement of anthropometric

parameters over period of time was seen. However, one third of their cohort was still undernourished, half were stunted and one fourth had microcephaly at 18 months Corrected Age (CA) [9]. A similar observation was made by Westerberg AC et al., with growth failure (<10th centile) in 60% babies at 0 months CA and 40% babies at 12 months CA with more catch up growth between 3 months to 6 months [10]. Mukhopadhyay K et al., also observed a similar trend of increase in mean z-score for weight and length from 40 weeks to 1 year with maximum growth between 3 months to 6 months [11]. However, the mean z score for head circumference showed an initial decline by 3 months CA followed by a gradual increase. In a study conducted in Uganda by Abdallah Y et al., they used the INTERGROWTH 21st charts to assess the postnatal growth of VLBW babies at 12 weeks postdischarge. Growth failure was evident in 38.7% of the VLBW babies by 12 weeks postdischarge. However, a similar trend in catch up growth was observed between 4 weeks postdischarge to 12 weeks postdischarge [12].

The lower incidence of underweight, stunting and microcephaly in the present study population as compared to the one by Sharma PK et al., could be due to improved feeding practices and use of separate growth charts [9]. Sharma PK et al., used World Health Organisation Multisite Growth Reference Study (WHO MGRS) charts, whereas it was the INTERGROWTH 21st postnatal growth standards for assessment of anthropometric parameters in this study.

The rate of weight gain of the VLBW babies are comparable to the observation made by Saluja S et al., and Rathore AS et al., (17.6 grams/kg/day versus 17.7±7.8 g-/kg/day and 15.18±1.7 g/kg/day). However, the growth rate of head circumference (0.39 cm/week) and length (0.52 cm/week) was lower in both studies [13,14].

Various factors affect postnatal growth of infants including biological factors like birth weight, gestational age, sex and intrauterine growth. Here authors compared the postnatal growth trends in various birth weight cohorts. In order to analyse if there was a relation of postnatal weight to the birth weight of babies, a linear analysis of the odds ratio by using Chi-square trend was performed comparing the number of infants below and above 10th centile amongst different weight bands at 44, 52 and 64 weeks PMA. It was observed that the odds of postnatal weight being below 10th centile decreased as the birth weight increased.

The growth parameters observed in study population which included sick babies from a tertiary care centre, lay between 3rd-10th centile of INTERGROWTH 21st postnatal charts which was similar to the growth pattern observed by Abdallah Y et al., [12]. This could be because, the INTERGROWTH 21st prescriptive standard was developed using healthy urban population and included booked pregnancies with adequate antenatal check-ups, adequate intrauterine growth on antenatal ultrasound with institutional deliveries who largely followed recommended feeding practices [15-17]. To our knowledge, this is the first study in a tertiary care hospital in India to use INTERGROWTH 21st postnatal charts.

At 64 weeks PMA ,15.79% babies showed delayed developmental milestones. The greater incidence of delayed developmental milestones in LBW babies i.e. 17.56% compared to 12.5% in VLBW group in our study correlates with increased number of LBW babies with microcephaly.

The common underlying causes that could be attributable for delayed development included perinatal asphyxia (HIE Stage 2 as per Sarnat and Sarnat staging), hypoglycaemia/hypoglycaemic convulsions, prematurity (gestational age <31 week 6/7 days) and postnatal growth failure. It was observed that as the postnatal weight z-score/centile increased, the odds of patients having developmental delay decreased, which suggested that infants with postnatal growth failure were also lagging behind in achieving developmental milestones as per age. However, this does not establish the causality of postnatal growth failure in relation to delayed development. Results similar to this study were reported by Latal-Hajnal B et al., where, incidence of developmental delay (diagnosed using Bayley developmental scale), was more in both Appropriate for Gestational Age (AGA) and Small for Gestational Age (SGA) group of infants having growth failure (<10th centile) at 2 years. They inferred that the course of postnatal growth, rather than the appropriateness of weight for gestational age at birth, determines later neurodevelopmental outcome [18]. Similar results were seen in studies by Ross G et al., and Scharf RJ et al., [19,20]. In a study by Das S et al., high risk babies were followed-up till 1 year and DDST was used to assess the developmental outcome [21]. It was observed that patients with weight <3rd centile, 71.42% patients had delayed developmental milestones. In comparison, we observed that at 64 weeks PMA, 84.67% patients with weight below 3rd centile had developmental delay.

Limitation(s)

This study had limitations in its sample size, which was considerably less owing to the COVID-19 pandemic situation, however its strength lies in it being a prospective study.

CONCLUSION(S)

The incidence of postnatal growth failure in this study was inversely proportional to the birth weight of the baby. Babies with postnatal growth failure at 52 and 64 weeks PMA also had higher incidence of developmental delay. As a result of inevitable early discharge in some cases, it is mandatory to observe the postnatal growth and development of all patients discharged from our hospital so as to allow us to intervene early and hence improve the quality of lives. Since the study population comprised of sick outborn patients in a tertiary care referral hospital, the findings of this study cannot be extrapolated to the general population. The International postnatal growth charts being prescriptive standards, we need more such hospital-based studies to compare the growth failure rates and developmental delay in such high risk newborns who were discharged early.

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PARTICULARS OF CONTRIBUTORS:

1. Resident, Department of Paediatrics, Sriram Chandra Bhanja Medical College and Hospital, Cuttack, Odisha, India.
2. Associate Professor, Department of Paediatrics, Fakir Mohan Medical College and Hospital, Balasore, Odisha, India.
3. Associate Professor, Department of Pharmacology, Shree Jagannath Medical College and Hospital, Puri, Odisha, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Rajlaxmi Upadhyay,
Plot Number D54, CDA Sector 7, Cuttack, Odisha, India.
E-mail: drrajlaxmi@yahoo.co.in

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