

The Post-Discharge Growth of Very Low Birth Weight Preterm Infants

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ABSTRACT

OBJECTIVE: In the present study, we investigate the growth characteristics of very low birth weight premature infants of up to two years corrected age, considering the factors affecting growth and catch-up growth time.

STUDY DESIGN: The demographic data, clinical features, and comorbidities of 77 preterm infants with birth weights of less than or equal to 1.500 g were examined, the infants' growth statuses in the 40th gestational week and at 6, 12, 18 and 24 months the corrected age, including their weight, height and head circumference, were evaluated.

RESULTS: The findings revealed that very low birth weight infants should be closely monitored either during their stay in the Neonatal Intensive Care Unit, or for up to 6 months corrected age, paying particular attention to growth data, and the appropriate supportive treatment should be administered. The applied support process is influential on the future somatic growth of preterm infants. It was noted in the study that bronchopulmonary dysplasia, proven sepsis, respiratory distress syndrome, steroid treatment for more than three days, patent ductus arteriosus, and ibuprofen treatment seemed to affect somatic growth negatively.

CONCLUSION: Small for gestational age newborns were found to catch up with appropriate for gestational age newborns at 2 years corrected age in terms of growth, although the percentage of catch-up growth during follow-up at the 40th gestational week, and at the 6th, 12th and 18th months was lower than that of appropriate for gestational age newborns.

Keywords: Growth, Infant, Newborn

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Introduction

With the technological development of newborn care and the increase in clinical experience, the number of premature infants that survive has also been increasing. This increase in survival rate has brought with it many problems related to growth and development in long-term follow-up programs. Neurodevelopmental and physical growth retardations are particularly important for newborns weighing less than 1500 g at

birth particularly in the 32nd gestation week (gw) (1-4). Studies examining the growth of very low birth weight (VLBW) premature infants have found that in early childhood, the VLBW infants group was weaker and shorter, and had a smaller head circumference than in the control group (5-7).

In this regard, the follow-up programs of preterm infants should be performed more frequently than term infants and, if necessary, consultations should be sought from the related departments for not only the early detection of new problems that may arise but also for a complete follow-up of pre-defined problems other than those controlled for in the routine monitoring of healthy children. Detecting growth deficiencies and providing appropriate nutrition and treatment support demands the careful monitoring of the growth data of VLBW infants.

The present study aims to investigate the growth characteristics, the catch-up growth time and the factors affecting growth up until 2 years corrected age (CA) of VLBW infants who were discharged from the Neonatal Intensive Care Unit (NICU) and were monitored in the neonatal outpatient clinic following discharge.

Material and Method

The present study included 77 preterm infants with birth weights of 1500 g and below who were discharged from the

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Neonatal Intensive Care Unit and who were monitored by the Neonatal Outpatient service between 01/01/2010 and 30/08/2012. The preterm infants' growth follow-up programs were evaluated up until they reached two years CA.

Neonatal and the maternal demographic data, obstetric history, prenatal, natal and postnatal clinical features, hospitalization period, duration of mechanical ventilation (MV) and accompanying morbidities (bronchopulmonary dysplasia, premature retinopathy, necrotizing enterocolitis (NEC), proven sepsis and patent ductus arteriosus) were garnered from the patients' files. Proven sepsis was indicated by clinical symptoms such as hypotonia, hypoactivity, restlessness, sucking, nutritional intolerance, and hypo-hyperthermia, along with a reproduction in blood, urine, and cerebrospinal fluid (CSF) cultures. Infants with patent ductus arteriosus (PDA) were divided into subgroups as those who were untreated, those treated with ibuprofen and those who underwent a surgical ligation. Infants with premature retinopathy of prematurity (ROP) were divided into stages 1-2 and 3-4, and groups with and without photocoagulation were also established. Given the lack of data concerning germinal matrix-intraventricular hemorrhage and hydrocephalus in the outpatient service, it was not possible to assess the effects of these disorders on somatic growth. Depending on the gestational age at birth, for those whose gestational age was <32 weeks in the postmenstrual (PM) 36th week and for those whose gestational age was \geq 32 weeks on the postnatal 28th day, or infants who required oxygen (\geq 21% SaO₂) at discharge, if they occurred earlier than these conditions, they were considered as bronchopulmonary dysplasia (BPD). In the present study, from which preterm infants with major congenital anomalies were excluded, as the detailed data relating to nutrition could not be obtained from the outpatient files, its effects on somatic growth could not be evaluated.

Growth data, including the weight, height and head circumference of the infants up to two years CA, was evaluated. The growth data at birth and discharge were evaluated with Fenton growth curves taken as a reference, and growth rates were assessed taking into account the corrected age of the infants. The growth data at the 40thgw, and the 6th, 12th, 18th and 24th months were evaluated from corrected growth percentile curves and the Z-scoring system for Turkish children. Catch-up growth was considered as the month in which weight per age, height, and head circumference began to continue at -2 standard deviation scores (-2SDS) and above.

The study was approved by the local Ethics Committee (Protocol No: 2014/452) and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the parents of each infant.

Statistical Analysis

The statistical analysis was performed using SPSS 22 software (IBM statistics for Windows version 22, IBM Corporation, Armonk, New York, United States). An evalua-

tion of the normal distribution of the data was made with a Shapiro-Wilk test and a Mardia (Dornikand Hansen omnibus) test, a Levene test was used to measure variance homogeneity, paired-samples T-test, General Linear Model-Repeated analysis of variance (ANOVA) (Bonferroni for post-hoc analysis), Pearson Correlation and Spearman's rho tests. Quantitative data were expressed as mean \pm standard deviation (SD) and the median value (minimum-maximum), as seen in table I, while categorical data were expressed as numbers (N) and percentages (%). A p-value of <0.05 was considered statistically significant.

Results

The demographic data of the infants and neonatal morbidities of infants are presented in table I and table II. A total of 28.6 percent of infants' birth weights was below 1000 g, while 71.4 percent of them were between 1001 and 1500 g. No significant difference between the two groups was noted in terms of the compared SDS values of weight, height and head circumference by months ($p>0.005$). When the SDS values of weight, height and head circumference were evaluated, it was noted that the loss of SDS increased between the 40thgw and the 6th month, decreased to the lowest value in the 6th month and was then followed by an increase in SDS. At 2 years CA 98.7 percent of the VLBW infants had caught up in terms of weight, height, and head circumference, and the SD values of all three growth parameters were detected to be low (Figure 1,2,3).

Bronchopulmonary dysplasia, proven sepsis, RDS, and corticosteroid treatment for more than three days were determined as having an effect on somatic growth, and it was also noted that PDA and ibuprofen treatment had a borderline significant effect on the growth of head circumference. The rates of those who were unable to achieve catch-up growth regarding weight for infants with RDS in the 24th month were significantly higher ($p=0.041$, OR 5.357, 95% CI [3.34-8.59]).

The rates of the infants who were unable to achieve catch-up growth regarding weight for infants with BPD at the 40thgw were significantly higher ($p=0.026$, OR 0.109, 95% CI [0.018-0.649]). The rates of those who were unable to achieve catch-up growth in terms of height for infants with BPD at the 6th month were significantly higher ($p=0.002$, OR 0.041, 95% CI [0.004-0.380]). No statistically significant correlation was identified between the NEC and growth data of the follow-up program, and statistical analysis was not possible given that the number of patients with NEC at stage 3 was lower in the study group.

The rates of those who were unable to achieve catch-up growth regarding weight for infants with sepsis at the 12th and 18th months were significantly higher ($p=0.039$, OR 0.188, 95% CI [0.036-0.975], $p=0.034$, OR 2.433, 95% CI [1.849-3.202], respectively). The rates of those who were unable to

achieve catch-up growth regarding weight for infants with sepsis in the 6th, 12th, and 18th month were significantly higher ($p=0.034$, OR 0.297, 95%CI [0.098-0.905], $p=0.005$, OR 0.166, 95% CI [0.048-0.572], $p=0.014$, OR 2.483, 95% CI [1.874-3.289], respectively).

The rates of those who were unable to achieve catch-up growth regarding weight for infants who received steroid treatment for more than three days at the 40thgw were significantly higher ($p=0.043$, OR 0.148, 95% CI [0.027-0.802]).

The rates of those who were unable to achieve catch-up growth in terms of height for infants who received steroid treatment for more than three days at the 6th month were significantly higher ($p=0.005$, OR 0.083 95% CI [0.014-0.478]). The rates of those who were unable to achieve catch-up growth regarding the head circumference for infants diagnosed with PDA and receiving ibuprofen treatment in the 12th month were significantly higher at the borderline (for both $p=0.033$, OR 0.5, 95% CI [0.077-3.234]).

Table I: Demographic data of the very low birth weight infants

	Mean \pm SD (Minimum-Maximum)	The number of cases (%)
Gestational age (week)	29.09 \pm 2.2 (26-35)	
Gender	Female	38 (49)
	Male	39 (51)
Birth weight (g)	1136 \pm 210 (670-1500)	
Birth height (cm)	36.9 \pm 2.60 (30-42)	
Head circumference at birth (cm)	26.7 \pm 1.80 (23-31)	
Mode of delivery	Caesarean	61 (79)
	Vaginal Birth	9 (12)
Size in terms of birth age	SGA	9 (12)
	AGA	64 (83)
	LGA	4 (5)
Apgar Score		
	1 st minute	6.05 \pm 1.83(1-9)
	5 th minute	7.98 \pm 1.14 (5-10)

SGA: Small for gestational age, AGA: Appropriate for gestational age, LGA: Large for gestational age

Table II: Neonatal morbidities of very low birth weight infants

Neonatal Morbidities	The Number of Cases (%)
RDS	61 (79)
BPD	6 (8)
NEC (Stage \geq 2)	4 (5)
Sepsis	34 (44)
ROP	34(44)
Stage 1-2	25 (32)
Stage 3-4	9 (12)
Photocoagulation	8 (10)
PDA	20 (26)
Ibuprofen	17 (22)
Surgical ligation	1 (1)
Steroid treatment (more than 3 days)	7 (9)
Duration of staying in the intensive care unit (days), mean \pm SD	41.5 \pm 19.94

RDS: Respiratory distress syndrome, BPD: Bronchopulmonary dysplasia, NEC: Necrotising enterocolitis, ROP: Retinopathy of prematurity, PDA: Patent ductus arteriosus

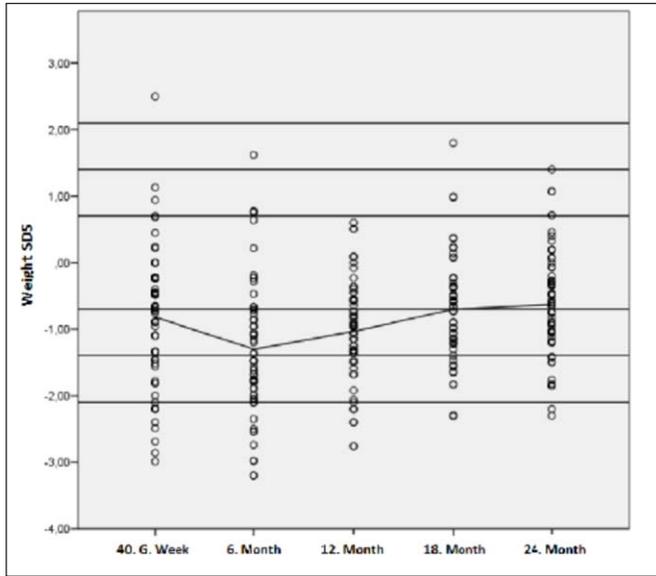


Figure 1: Standard deviation scores of weight distribution by months

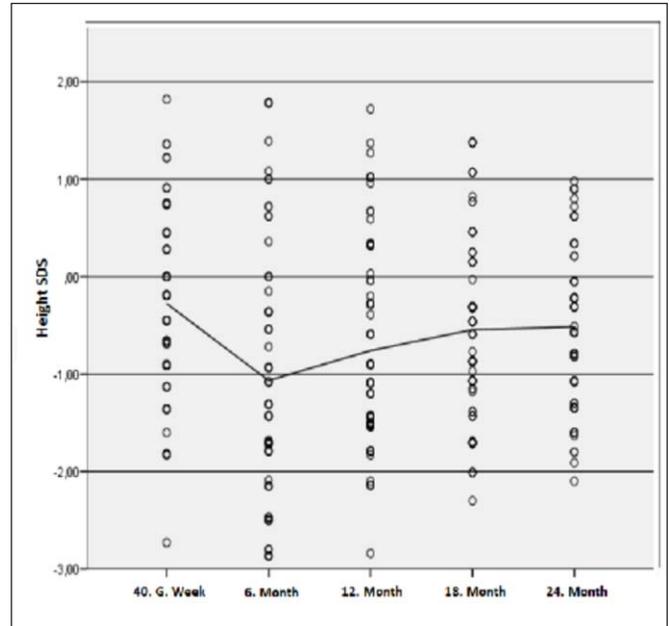


Figure 2: Standard deviation scores of height distribution by months

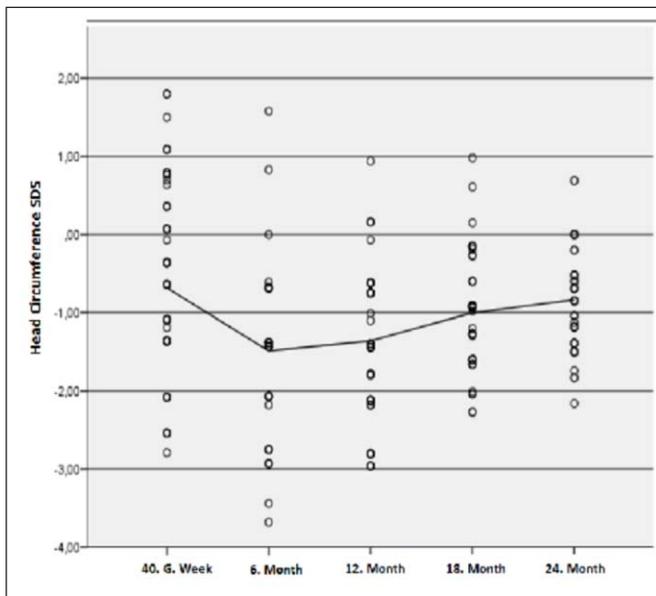


Figure 3: Standard deviation scores of head circumference distribution by months

Discussion

Given the increase in the survival of preterm infants, the growth, metabolic status and neurocognitive development of such infants are today even more important than ever (4). In many studies examining the growth of VLBW infants following discharge from the hospital, findings have shown that growth in early childhood was retarded (5-7). Wang et al (5) showed that the values of VLBW infants' weight, height, and head circumference in the 6th, 12th, 24th and 60th months were lower than those of a healthy control group. The EPICure study group, in an evaluation of children born with extremely low birth weight (ELBW) at the age of 6, found that the children were detected to be weaker, shorter and had a lower head

circumference than those in the control group (6). In another single-center study, the mean SD values of preterm infants' weight and height in the second and fifth years of age were found to be lower than those in the normal population (7). Dusick et al. (8) reported that although the majority of ELBW infants in the 8th and 18th months caught up in terms of growth, for 40 percent of their sample, the infant weights were lower than the 10 percentile. In the present study, VLBW infants in the 6th, 12th and 24th month recorded values of -1.3/-1.0/-0.8 SD for the average weight, -1.1/-0.8/-0.5 SD for the height and -1.5/-1.4/-0.8 SD for the head circumference, in accordance with the literature. When findings for different months were evaluated for the present study, the SDS loss of weight, height and head circumference variables increased between the 40th gw and the 6th month and reached their lowest values in the 6th month, and the SDS values finally increased after the 6th month.

In the most long-term follow-up studies of VLBW and low birth weight (LBW) infants, they caught up on growth in terms of their weight in childhood (5-10). In a study investigating the growth of VLBW premature infants, it was reported that they were late in catching up on physical growth, but that all of the premature infants had caught up with growth by the end of their second year of life 5. McCowan et al. (10) found that 82 percent of the preterm infants in their study had caught up on growth by the 6th month. In the EPICure study group, it was observed that for extremely preterm infants, the postnatal growth insufficiency observed after birth and in the third year continued until school age and it was found that the growth deficit decreased during the catch-up period, but was at a minimum level for head growth (6). When the present study was evaluated in terms of month, catch-up growth times were found to differ for the head circumference, weight and height

variables. Also in the present study, the catch-up growth rate for the weight, height, and head circumference values of the VLBW infants at the age of 2 years was found to be 98.7 percent, whereas the catch-up growth rate of head circumference was found to be lower than that rates of weight and height in the 40thgw, 6th, 12th and 18th months.

A positive correlation was found between the percentile of weight and head circumference at birth and the SDS value of the weight and head circumference at discharge in the present study, and we also noted a negative correlation between the variables related to gestation week at discharge reported above. In our study, a significant difference was seen in the growth of follow-up programs and catch-up growth rates of male and female infants.

Saigal et al. (9) reported that birth weights lower than the 10th percentile coexisted with insufficient growth, developmental retardation, and language problems during the 56th month follow-up program. Kavuncuoğlu et al. (11) reported that all of the appropriate for gestational age (AGA) and small for gestational age (SGA) premature infants in their study caught up on growth, irrespective of the gestational week. In a longitudinal long-term study, Tenovuo et al. (12) reported that SGA premature infants also caught up on growth as AGA infants at two years of age. Yeşinel et al. (13) found that gestational age, AGA, SGA, and gender did not cause a significant difference in VLBW premature infants in terms of reaching the target height. Likewise, in the present study, no difference was seen between the catch-up growth of SGA and AGA infants in their 2nd year of age; although the catch-up rate of SGA infants was detected to be lower than that of AGA infants during their follow-up, until their 2nd year of age.

In a study evaluating the growth of infants with mild and severe RDS, no significant difference was found between the two groups and growth problems were found to be associated with the degree of prematurity, BPD rather than RDS complications (14). Studies have also shown that the SDS values of preterm infants with BPD are lower than those in healthy controls (15-17). In a study of infants with BPD who underwent dexamethasone treatment, retardation was noted in both growth and development, and particularly in weight (18). Furthermore, in a study by Sonntag et al. (19), in which NEC-diagnosed VLBW infants were compared with those without NEC, it was reported that there no difference existed between the two groups in terms of somatic growth. In a study by Yeşinel et al. (13), it was reported that the presence of RDS, BPD, ROP, NEC, hypoglycemia, sepsis, and meningitis was not a risk factor in catching up with the target height, whereas advanced stage intracranial hemorrhage (ICH), hydrocephalus and the receiving of mechanical ventilator support were considered as risk factors. In the present study, the effects of ROP, photocoagulation therapy and the duration of ventilatory support on growth were not identified, although BPD, proven sep-

sis, RDS and corticosteroid treatment for more than three days were found to affect somatic growth. The presence of PDA and ibuprofen treatment was determined to be significant only at the borderline for the SDS values of head circumference in the 12th month. When the SDS values of head circumference were investigated, it was found that the head growth of infants diagnosed with sepsis in the 6th, 12th and 18th months was more retarded.

Our study has shown that the SDS values of all three growth parameters were low, and at 2 years CA, 98.7 percent of VLBW infants had caught up on growth in terms of weight, height and head circumference. The detection of decreases in SD values up to 6 months CA indicates that the growth rates of VLBW infants should be closely monitored and there should be no delay in providing proper nutrition and treatment support in this period. It can be concluded that follow-up on the head circumference is an important parameter in the follow-up of somatic growth, as well as in neuromotor development. The continuous monitoring of growth parameters, particularly the head circumference, during the hospitalization in the NICU, as well as the administration of the necessary support treatment, have been shown to be influential in the future somatic growth of preterm infants. BPD, proven sepsis, RDS, steroid treatment for more than three days, PDA and ibuprofen treatment have been determined as having an effect on somatic growth. Furthermore, it has also been established that SGA infants caught up on growth at 2 years CA, although the catch-up growth percentages of the SGA infants at the 40thgw and the 6th, 12th and 18th months CA were lower than those of the AGA infants.

Study Limitations

We should highlight that the study was conducted with 77 preterm infants, which is one of the limitations of the present research, however, future research with larger cohorts could provide valuable insights.

Conclusion

Small for gestational age (SGA) newborns were found to catch up with appropriate for gestational age (AGA) newborns at 2 years CA in terms of growth, although the percentage of catch-up growth during follow-up at the 40th gw, and at the 6th, 12th and 18th months was lower than that of AGA newborns.

Conflict of interest: The authors have no conflicts of interest relevant to this article. No funding source. The study was approved by the local Ethics Committee (Protocol No: 2014/452) and was conducted in accordance with the principles of the Declaration of Helsinki.

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Author contribution: TO:, ABA:, MKT:, Proposed the study and wrote the first draft. All authors contributed to the design, writing, and interpretation of the study and to further drafts. TO:, ABA:, MKT:, are the guarantors.

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