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Postnatal growth failure of very low-birth-weight infants in Southwest Iran: A descriptive analytical study

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Abstract

Background and Aims: Preterm infants are more prone to poor growth and neurodevelopment. The first few weeks of life play an important role in the growth and neurodevelopment of very-low-birth-weight (VLBW) infants. The Vermont Oxford Network, evaluating the postnatal growth of preterm newborns, considers growth failure as body weight <10th percentile for postmenstrual age. This study aims to assess the frequency of postnatal growth failure in VLBW infants in Southwest Iran.

Methods: This descriptive analytical study was performed on VLBW infants in the neonatal intensive care unit (NICU) of Imam Khomeini Hospital (Ahvaz, Iran) from September 2019 to August 2020. Growth failure was confirmed when a newborn's weight at discharge was smaller than the 10th percentile corrected age (≤−1.28 *Z*-score), based on the Fenton growth chart as a standard. This study was performed on 353 infants. Intrauterine growth retardation was detected in 29% of female and 10.6% of male newborns, who were born at a gestational age of 32 and 31 weeks or higher respectively. Upon hospital discharge, postnatal growth failure was detected in all newborn girls, except for those born at 32 weeks of gestation, and all newborn boys, except for those born at a gestational age of 33–34 weeks.

Conclusion: Postnatal growth retardation in VLBW infants born in our NICU was much higher than that of other centers. Overcrowding, short length of hospitalization, low nurse-to-patient ratio, and untrained nurses were among the reasons for poor postnatal growth in our center.

KEYWORDS

hospitalization; intrauterine growth retardation, mortality rate; postnatal growth failure, very low birth weight

1 | INTRODUCTION

Preterm infants are generally more prone to poor growth and neurodevelopment.[1] The survival of very-low-birth-weight (VLBW) infants has increased with improved care for VLBW infants. Currently, despite improvement in the survival of VLBW infants, they are generally more prone to poor growth and neurodevelopment.[1] As stated by the American Academy of Pediatrics Committee on Nutrition (CON), the nutrition of preterm infants should lead to postnatal growth comparable to normally growing fetuses at the same gestational age.[2] However, this rarely occurs in reality, and postnatal growth restriction is regarded as a global concern among VLBW newborns.[3] The first few weeks of life play an important role in the growth and neurodevelopment of VLBW infants. The nutritional needs for optimal growth during this period are greater than in any other life stage. Although the consequences of undernutrition in this period remain unclear, the neonatal research network of the National Institute of Child and Human Development (NICHD) demonstrated that at birth 16% of VLBW infants were intrauterine growth retarded (IUGR); however, at 36 weeks of corrected age, 89% of them had postnatal growth failure (PGF).[4]

Significant evidence suggests that growth failure during the first few weeks of life negatively affects the growth and neurodevelopment of children, which can persist into adult life.[5] Early life growth failure is related to ischemic heart disease, neurodevelopmental delay, disrupted glucose tolerance, diabetes mellitus type 2, hypertension, and metabolic syndrome in the adult period.[6]

Birth body weight, hospitalization length, gestational age, respiratory distress, chronic lung disease, and sepsis are related to the postnatal growth and neurodevelopment of VLBW infants.[7] The Vermont Oxford Network, evaluating the postnatal growth of preterm newborns, considers growth failure as body weight smaller than the 10th percentile for postmenstrual age. The growth failure prevalence among neonates registered in this network was estimated at 50.3%.[7]

In Iran, in recent years, the survival of VLBW increased with the improvement of care for VLBW infants. However, information on the rate of PGF in my country is scarce. Since the postnatal growth of very low-birth infants has a very important effect on their future neurodevelopment and physical growth, we evaluated the frequency of PGF in VLBW infants at the time of hospital discharge as the main aim in the biggest neonatal intensive care in Southwest Iran.

2 | METHODS AND MATERIALS

This descriptive analytical study assessed VLBW infants admitted to the neonatal intensive care unit of Imam Khomeini Hospital (Ahvaz, Iran) between September 2019 and August 2020. The neonatal intensive care unit of this hospital is the main referral center for women with a high-risk pregnancy in Southwest Iran, with 32 beds and an overall bed occupancy rate above 122%. The nutrition of admitted infants consisted of partial parenteral nutrition (amino acid and dextrose) and breast milk or formula. The inclusion criterion in this study was a VLBW (<1500 g), while the exclusion criteria were death before discharge and major congenital anomalies, or referral of patients to other centers. Census sampling was performed to select the participants.

Growth indices, including head circumference, weight, and height, were evaluated at admission and upon discharge for all the participants. Neonatal length was assessed using a standard length board, head circumference was measured with a standard tape measure (SECA) with an accuracy of ±2 mm, and weight was calculated using a standard scale (SECA) with an accuracy of ±20 g. Based on the Vermont Oxford Network, PGF is considered as a body weight smaller than the 10th percentile for postmenstrual age.[8]

According to our review, the PGF measures for evaluating preterm infants vary among studies, and there are no universal criteria to define this phenomenon. In general, growth failure refers to a newborn's weight below the 10th percentile (≤−1.28 *Z*-score). Nevertheless, there are many reference charts and variable postnatal periods. We defined PGF as weight below 10% of intrauterine growth expected at the corrected age for hospital discharge, with the Fenton growth chart as a standard.[8]

2.1 | Statistical analysis

Statistical analysis was performed by SPSS25 using descriptive statistics, such as standard deviation (SD), mean, frequency, and frequency percentage. The *t*-test (or nonparametric Mann–Whitney test), and the Chi-square test (or Fisher's exact test) and Pearson's correlation.

A coefficient test (or Spearman's test) was used for data analysis.

2.2 | Ethical consideration

The parents provided informed consent in this study. In all stages of the research, all ethical standards of the Declaration of Helsinki as well as the principles of patient information confidentiality were observed. An ethics code (IR.AJUMS.REC.1399.258) was obtained from the Research Council and Ethics Committee of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

3 | RESULTS

From September 2019 to August 2020, 1813 neonates were hospitalized in our NICU, 366 of whom weighed less than 1500 g. Thirteen neonates were excluded from the study because of a referral to another hospital. Finally, this study was performed on a total of 353 neonates. The overall mortality rate was estimated at 28.32% (100/353). It was 73.33% (22/30) in neonates with a birth weight of <750 g, 54.27% (36/81) in newborns with a birth weight of 750–999 g, 25.68% (28/109) in newborns with a birth weight of

1000–1249 g, and 10.52% (14/133) in newborns with a birth weight of 1250–1499 g. Among the neonates evaluated in this study, 122 (48.23%) were male, and 131 (51.77%) were female. For male and female infants' the mean birth body weight was 1228 ± 140 g and 1274 ± 141 g, respectively ($p = 0.50$). Also, the differences in the length of male and female babies at birth were not significant (male 39 ± 1.85, female 38 ± 1.50, $p = 0.11$). The mean head circumference of males and females at birth was 28 ± 1.6 and 27 ± 1.9 with no significant differences ($p = 0.31$).

IUGR was detected at birth in 29% of girls born at 32 weeks and 34.4% of boys at 31 weeks gestation or higher. The demographic characteristics of female and male newborns at birth are shown in Tables 1 and 2.

Postnatal growth failure was detected in all female and male newborns upon discharge, except for 32 weeks of gestation for females and 33–34 for male infants (Tables 3 and 4).

At discharge, the weight of 91.6% of girls and 75.4% of boys was under the percentile 10. The differences between them were significant (male 1764 ± 215, female 1482 ± 175, $p = 0.007$). Also, the length of boys was 42 ± 1.2 and females 41 ± 0.79 without significant differences($p = 0.08$). In order, the head circumference of boys and girls at discharge was 30 ± 0.58 and 29 ± 1.2 cm ($p = 0.09$). The mean duration of hospitalization for boys was 26 ± 12.7 and females 26 ± 12.9 ($p > 0.99$).

Flowchart showing the rate of PGF of VLBW neonates in our study.

4 | DISCUSSION

In our research, the survival rate of VLBW infants was 71.68%. The 1-month survival of VLBW infants was estimated at 68% in Tehran, Iran, in 2018.[9] Besides, in a study conducted in Tabriz, Iran, the survival rate was estimated at 71.3%.[10] The survival rate of VLBW infants was 78.5% in a referral hospital in Tehran, Iran, during 2004–2005.[11] In another study conducted at Mahdieh Hospital of Tehran, the survival rate of VLBW infants was estimated at 70.9%.[12] Additionally, the overall survival rate of VLBW infants was estimated at 56.70% in Iran.[13]

The survival rate of VLBW infants in our research was higher than the average survival rate in Iran, except for a study by Khodapanahandeh et al.,[11] where the mortality rate was lower than that of the present study. To explain this difference, it should be noted that their study was performed in a referral hospital and that patients with more stable conditions were admitted and evaluated. Moreover, the overall survival rate of VLBW infants was estimated at 32% in South Africa,[14] 74.1% in Brazil in 2015,[15] 92% in Japan in 2008,[16] and 92.6% in the United States in 2006.[17] In recent years, the survival of VLBW infants has shown a significant increase around the world and in Iran. However, our infant mortality rate was much higher than that of developed countries.

The present findings revealed that 29% of newborn girls and 34.4% of infant boys had IUGR upon admission to the NICU. At

TABLE 1 The demographic characteristics of newborn girls upon hospital admission.

Variables											
Gestational age (weeks)	<28	28	29	30	31	32	33	34	35		
Number	20	34	11	20	8	23	6	3	6		
Weight (g) ±SD	975 ± 112.50	1242.91 ± 149.39	1153.75 ± 266	1287.85 ± 164.4	1306.66 ± 188.23	1288.12 ± 176.16	1440	1400 ± 50	1375 ± 35.35		
Percentile	>10	>10	>10	>10	>10	>3	<3	<3	<3		
Length (cm)	34.87 ± 1.24	37.41 ± 2.60	38.62 ± 3.59	39.14 ± 2.41	40 ± 2.64	39.37 ± 2.29	38.75 ± 4.59	39 ± 1	38.75 ± 1.06		
Percentile	>10	>10	>10	>10	>10	>10	<3	3	<3		
Head circumference (cm)	24.25 ± 1.55	26.04 ± 0.78	25.87 ± 0.62	28.07 ± 1.05	27	27.68 ± 0.92	29	30.33 ± 0.57	29.50 ± 2.12		
Percentile	>10	>10	>10	>10	>10	10	>10	>10	>3		

TABLE 2 The demographic characteristics of newborn boys upon hospital admission.

Variables										
Gestational age (weeks)	< 28	28	29	30	31	32	33	34	35	
Number	18	32	11	19	8	21	5	3	5	
Weight (g) ±SD	963.1 ± 21.2	1081 ± 19.2	1152 ± 18.3	1212.5 ± 24	1263.3 ± 23.3	1310 ± 18.6	1345 ± 16.8	1385 ± 20.2	1345 ± 23.2	
Percentile	> 10	> 10	> 10	> 10	> 3	< 3	< 3	< 3	< 3	
Length (cm)	36.24 ± 1.32	37.82 ± 1.16	39.16 ± 1.33	41.12 ± 1.23	41.11 ± 1.16	39.11 ± 1.19	41.12 ± 1.33	40.11 ± 0.83	42.12 ± 1.02	
Percentile	> 10	> 10	> 10	> 10	> 10	> 10	< 10	< 3	< 3	
Head circumference (cm)	25.12 ± 1.42	26.72 ± 0.93	27.30 ± 1.02	29.11 ± 1.16	29.17 ± 1.42	29.45 ± 1.18	29.17 ± 1.18	29.82 ± 1.02	29.57 ± 0.86	
Percentile	> 10	> 10	> 10	> 10	> 10	> 10	3	10	> 3	

discharge, 91.6% of newborn girls and 75.4% of infant boys demonstrated PGF. In this regard, Lima et al., 33% of VLBW newborns were small for gestational age (SGA) at admission; PGF was demonstrated in 26% of these newborns upon discharge.[7] In another study by Park et al., 21% of VLBW infants were SGA at admission, and PGF was detected in 58% of them upon discharge.[18] Additionally, in a study conducted in Uganda, 54% of VLBW infants were SGA upon admission, and PGF was detected in 88% of them at discharge.[19] In another study from Tanzania, 86.8% of VLBW infants showed IUGR at discharge.[19] Moreover, a study by Vidal et al., in Spain showed that the rate of PGF was 70% in VLBW infants.[20] In developed countries, the rate of PGF was reported to be 50.3% upon discharge.[21] The overcrowding of patients, nurse-to-patient ratio of 1:8–10, untrained midwives accompanying nurses (80%), unsuitable conditions for the attendance of mothers, and nonuse of total parenteral nutrition were the main reasons for PGF in our NICU.

A direct relationship has been observed between growth before 40 weeks of gestation and neurodevelopmental outcomes. Additionally, according to long-term follow-up studies, hospitalization length, preterm gestational age, respiratory distress syndrome, sepsis, and bronchopulmonary dysplasia affect development and growth. Regarding the burden of neurodevelopmental disorders on societies and families, it is necessary to decrease the risk of PGF during hospitalization. Following adjustment for potential confounding factors, a longer time to achieve full enteral feeding can be an important risk factor for PGF in appropriate-for-gestational-age (AGA) and SGA infants, which is consistent with other reports suggesting that aggressive nutrition is needed to prevent PGF.[18,19,22]

In this regard, according to Wilson et al., an aggressive nutritional regimen (enteral feeding parenteral feeding), starting from postnatal day one, reduces the PGF incidence (59% vs. 82% in preterm infants with no nutritional intervention).[1820] Moreover, an aggressive nutritional diet decreased the prevalence of adverse metabolic or clinical squeal. The ESPGHAN Committee recommends enteral nutritional supplementation for preterm VLBW newborns, including using fortified human milk and formulae developed for premature newborns, offering an appropriate range of energy intake (110–135 kcal/kg/day).[23]

The average hospitalization length was 34.85 days in our neonates (weight <1000 g, 44.66 days; weight of 1000–1500 g, 25.05 days). In an Armenian study conducted in Isfahan, Iran, in 2015, the average length of infants' hospital stay was estimated at 22 days.[24] In European countries, the hospitalization rate of VLBW neonates was 60.5 days during 2006–2009 in Finland, 55.6 days in Hungary, 46.2 days in Italy, 53.4 days in the Netherlands, 53.2 days in Norway, 50.7 days in Scotland, and 61 days in Sweden.[25] Also, in Saudi Arabia, the average hospitalization length was 73.6 days from 2011 to 2018.[26] Overall, the duration of hospitalization in developed countries is much longer than the average length of hospitalization in our study and the study conducted in Isfahan, Iran.

TABLE 3 The demographic characteristics of newborn girls upon hospital discharge.

Variables									
Mean post-conceptual age (weeks)	35	34	32	34	34	35	36	37	37
Number	20	34	11	20	8	23	6	3	6
Weight (g) ±SD	1618 ± 180	1583 ± 196	1435 ± 93	1583 ± 169	1496 ± 87	1531 ± 151	1640 ± 14	1496 ± 15	1487 ± 17
Percentile	< 3	< 3	> 10	> 3	3	< 3	< 3	< 3	< 3
Length (cm)	40.87 ± 1	42.16 ± 1.5	41 ± 3.16	41.85 ± 1.95	42 ± 1.52	41 ± 1.64	40 ± 4.94	41 ± 1.15	40 ± 1.41
Percentile	10	>10	50	>10	>10	>3	<3	3	<3
Head circumference (cm)	28 ± 1	29 ± 1.52	28 ± 0.75	30 ± 0.99	27 ± 50	29 ± 0.62	30 ± 0.35	31 ± 0.86	30 ± 1.76
Percentile	3	>10	>10	>50	<3	>3	>3	10	3
Hospitalization duration (days)	55 ± 19.6	39 ± 1.5	24 ± 6.2	25 ± 11.0	18 ± 10.0	20 ± 6.9	24 ± 4.2	18 ± 5.8	13 ± 2.1

TABLE 4 The demographic characteristics of newborn boys upon hospital discharge.

Variables									
Mean postconceptual age (weeks)	34	34	33	34	34	35	36	37	37
Number	18	32	11	19	8	21	5	3	5
Weight (g) ±SD	1680 ± 142	1702 ± 122	1722 ± 116	1902 ± 104	1702 ± 119	1305 ± 101	1902 ± 131	2010 ± 116	1982 ± 121
Percentile	>3	>3	>10	>10	>3	>3	<3	<3	<3
Length (cm)	42 ± 1.16	41 ± 1.13	40 ± 1.09	42 ± 1.15	41 ± 0.99	41 ± 1.09	44 ± 1.08	42 ± 1.14	43 ± 1.15
Percentile	10	>3	10	>10	>3	>3	<10	<3	<3
Head circumference (cm)	30 ± 1.36	30 ± 1.18	29 ± 1.16	31 ± 1.11	30 ± 1.13	30 ± 1.32	30 ± 0.35	31 ± 0.83	31 ± 0.69
Percentile	>10	>10	>10	>10	<10	>3	3	3	3
Hospitalization duration (days)	51 ± 16.23	40 ± 3.41	27 ± 4.17	23 ± 9.72	15 ± 12.4	22 ± 5.14	25 ± 3.16	16 ± 4.15	11 ± 1.05

5 | CONCLUSION

The rate of PGF was much higher in VLBW infants born in our NICU compared to other centers.

Factors such as a bed occupancy rate of nearly 120%, patient-to-nurse ratio of about 8–10:1, nonuse of full intravenous feeding due to lack of access to clean rooms and equipment, poor conditions for the attendance of mothers, and the short duration of hospitalization may be the reasons for the PGF of VLBW infants in our center. The main limitation of this research was a no follow-up of discharged infants in terms of postdischarge mortality rate and possible developmental disorders.

AUTHOR CONTRIBUTIONS

Masoud Dehdashtian: Conceptualization; data curation; formal analysis. **Mohammad-Reza Aramesh**: Conceptualization; data curation; formal analysis. **Arash Malakian**: Conceptualization; data curation; formal analysis. **Seyyed Mohammad Hassan Aletayeb**: Conceptualization; data curation; formal analysis. **Amene Rasti**: Data curation; resources.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

TRANSPARENCY STATEMENT

The lead author Seyyed Mohammad Hassan Aletayeb affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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SUPPORTING INFORMATION

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