Challenges in Early Postnatal Care and Growth in Extremely Low Birth Weight Infants: A Multi-Center Study

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Abstract

Background

Postnatal care and growth in extremely low birth weight (ELBW) infants are being increasingly focused on worldwide. However, few data from China have been reported, especially multicenters. This multicenter study was designed to investigate the problems existing in postnatal care, weight gain and the related risk factors in in-patient ELBW infants.

Methods

Eligible ELBW infants admitted to involved neonatal intensive care units (NICUs) in 2017 in Beijing were studied retrospectively. Except for general early outcomes, Weight Z score and feeding practice related information was calculated, and collected. Growth retardation (GR) was diagnosed if body weight Z score at discharge dropped more than one standard deviation (SD) compared with birth.

Results

Of our cohort of 137 ELBW infants, 92 infants discharged with medical advice were analyzed. Full enteral feeding reached at 37.0 (27.0, 51.8)days. Exclusive breast milk feeding rate was 30.4% at discharge. All infants had decreased weight Z score, and its change was similar in different weight subgroups. The incidence of GR was 66.3%. Multiple-factor analysis showed the risk factors for GR were small for gestational age(OR 34.768, 95%CI 1.652-731.728), average weight gain rate < 15 g/(kg.d)(OR 249.062, 95%CI 11.211-5532.889), and non-invasive and/or mechanical ventilation duration > 28days(OR 6.867, 95%CI 1.211–38.957), $P=0.05$. Keeping ELBW infants staying in hospital longer was beneficial to their weight gain (OR = 0.950, 95% CI 0.909–0.993, $P<0.05$).

Conclusion

Maintaining appropriate weight gain in early age is still a great challenge in ELBW infants. Fetal growth, early nutrition and sickness are critical influencing factors.

Background

In recent decades, great improvement in perinatal and neonatal health care has been made in China. Neonatal mortality decreased dramatically, from 25‰ in 1990 to 8‰ in 2013⁽¹⁾. Preterm birth (delivered before 37 weeks gestation) complications are major results in neonatal death, accounting for 35% neonatal death rate⁽²⁾ and are also leading causes of mortality under 5 globally⁽³⁾. Not only high demise rate, but preterm infants are also highly risky to cognition, movement and behavior problems⁽⁴⁾. Early

nutrition strategy underlies the basis for treatment of preterm infants, and guarantees their physical growth, disease recovery, and good long-term outcome⁽⁵⁾. The early growth of preterm infants is affected by a variety of factors, and early nutritional management played an important role in it. The preterm infants admitted to neonatal intensive care unit (NICU) are especially high risk infants for early growth failure that was defined as extrauterine growth retardation (EUGR) or growth retardation (GR)^(6,7). Extremely low birth weight (ELBW) infants are ones whose birth weight less than 1000 g. Generally, they are low in birth weight, small in gestational age, and suffer from intrauterine growth troubles and maternal-fetal complications. ELBW infants are the highest risky infants for high mortality and disability rate. In Japan, the mortality of ELBW infants from 2003 to 2008 was 17.7%~25.6%, while in Hungary, such a mortality rate from 2011 to 2015 was 30%^(8,9). A follow up study on ELBW infants with gestational age (GA) 22-26wk in Finland showed that the incidence of cerebral palsy was 11%~14%⁽¹⁰⁾.

As shown by the data of multi-center studies conducted in 2011 and from 2008 to 2012 in China, the mortality rates of ELBW infants were 50.0% and 50.3%, respectively^(11,12), indicating a significant difference from the developed countries. Previous studies found that the growth of ELBW infants in NICU would have an important influence on the growth and development at 18 ~ 22 months' corrected age⁽¹³⁾. Dueing to the relatively developed economy, medicine and well established citizen medical insurance system, Beijing is one of the lowest neonatal mortality cities in China, 1.52‰ in 2015⁽¹⁴⁾. The majority of general hospitals, children's hospitals and maternal and child health hospitals in Beijing have their own NICUs, and most of NICUs are well equipped. But the fact is that most NICUs have limited bed number, so ELBW infants management is distributed. Under the circumstance, We conducted this multicenter study in Beijing area to summarize and analyze the challenges in ELBW infants treatment, and provided some improvement suggestions. This paper focuses on ELBW infants early in-patient care, weight gain, and its influencing factors.

Methods

1. Subjects

This was a retrospective multicenter study in Beijing area, with cooperation of regional neonatal specialist association. All units having ELBW infants (birth weight <1000g) admission and therapy were invited to participate in this study. ELBW infants ,including outborn infants transferred to included centers, admitted within 48h after birth in 2017 were included. Exclusion criteria: The infants had any severe congenital malformations, hereditary or metabolic disorders, and no available medical records.

2. Data collection and Grouping

2.1 Data collection: Data collected was put into the designed Epidata database designed for this study and was collected, stored and anlyed in Department of Pediatrics, Peking University First Hospital, which coordinated this study. Data collected from all eligible ELBW infants included: demographics, major

complications, therapy: outcomes, weight gain calculated and weight Z score change calculated during hospitalization.

2.2 Grouping: According to discharge conditions and birth weight, they were divided into discharge with medical advice group and without medical advice group, and birth weight <750g, 750–<900g and 900–<1000g group.

3. Diagnostic criteria

3.1 Definitions and diagnostic criteria: (1) SGA: birth weight was lower than the 10th percentile (P10) for a specific GA by gender, evaluated by Fenton growth chart ; (2) Weight Z score=(the measured value - the average value at the same gestational age)/the standard deviation at the same gestational age; (3) GR: defined as reduction in weight Z score between birth and discharge ≥ 1 standard deviation (SD); (4) cholestasis: Total bilirubin ≤ 5 mg/dl, while direct bilirubin ≥ 1 mg/dl; total bilirubin >5mg/dl, while direct bilirubin >20% total bilirubin; (5) Breast milk feeding at discharge: Breast milk volume >0ml or total breast milk feeding within 72 hours before discharge; (6) Non-invasive ventilation (NIV) and mechanical ventilation (MV): the assisted ventilation without or with endotracheal intubation. (7) Complications, respiratory distress syndrome(RDS)⁽¹⁶⁾, BPD defined as oxygen usage at 36 weeks' corrected gestational age⁽¹⁷⁾, more than and equal ($\geq$) Stage II necrotizing enterocolitis (NEC)⁽¹⁸⁾, intraventricular hemorrhage(IVH) and classification⁽¹⁹⁾, and late-onset sepsis (LOS)⁽²⁰⁾ were diagnosed and managed according to the relevant references.

3.2 Outcome criteria: (1) discharge with medical advice: Infant with stable vital signs, full enteral feeding, body weight >1800g, discharge order was given by physician; (2) discharge without medical advice: including death due to invalid rescue; terminating therapy in critical conditions, or request earlier discharge without fully stabilized or enteral feeding; transfer to other centers for surgical treatment.

3.3 Growth evaluation: Body weight worked as growth index for its accuracy. Body weight obtained daily with infant's scale. Body weight percentile and Z score were evaluated by Fenton growth chart (2013)⁽¹⁴⁾ or WHO growth standard in infants GA ≤ 42 wk or GA >42wk respectively. Weight gain rate was calculated with equation, [g/(kg·d)]=[1000×ln (discharge weight/birth weight)]/length of stay⁽²¹⁾.

4. Nutrition scheme

The guideline for clinical practice of nutrition support in Chinese neonates (2013)⁽²²⁾ was followed. Full enteral feeding was determined based on adequate intestinal feeding, no need for parenteral nutrition support, and stopping amino acids intravenous administration.

5. Ethics

The study was evaluated and approved by "Biomedicine Ethics committee of Peking University First Hospital" .

6. Statistics

The data of normal distribution were expressed by $\bar{x} \pm s$, and the comparison among groups was performed through independent t -test. The data of skewed distribution were expressed by $M(Q_1, Q_3)$, and the comparison among groups was performed through rank-sum test. The categorical variables were compared with Person χ^2 or Fisher's exact test; a multiple-factor analysis was performed with the binary logistic regression analysis (Enter method). The statistical analysis was performed with SPSS version 22.0 software (IBM Corporation, NY). $P < 0.05$ was considered statistically significant.

Results

1. General characteristics of subjects

Sixteen NICUs participated in this study. All city-level and district-level neonatal care centers and transfer centers were involved. Of the 16 NICUs, there were 12 general hospitals, 2 children's hospitals, and 2 maternal and children's hospitals. In 2017, there were 139 ELBW infants admitted in centers. Excluding 2 infants without medical records, 137 ELBW infants were eligible for study.

The median admitting age of ELBW infants was 0.50 (0.25, 1.25)h (h means hours), 46 (33.6%) were transferred from other hospitals; the mean maternal age was (33.2 ± 4.0) years, 38 (27.7%) accepted assisted reproduction, 72 (52.6%) had gestational complications (chronic hypertension, gestational hypertension, diabetes/gestational diabetes), and 28 (20.4%) subjected to natural premature rupture of membrane.

Of our cohort of 137 ELBW infants, 92 (67.2%) and 45 (32.8%) discharged with and without medical advice, respectively. Among the latter 45 ELBW infants, 33 (24.1%) were discharged within 14d after birth (median hospital stay was 4 days, d means days); 34 (24.8%) withdrew therapy, 5 (3.6%) failed therapy, and 6 (4.4%) transferred for operation dueing to retinopathy of preterm infants (ROP), patent ductus arteriosus (PDA), or NEC. (Fig. 1 and Table 1).

Table 1
General characteristics of ELBW infants discharged with and without medical advice

Variable	Total cases	Discharge with medical advice	Discharge without medical advice		χ^2 value	P value
			LOHs < 14d	LOHs $\geq$ 14d		
n(%)	137	92(67.2)	33(24.1)	12(8.8)		
GA (wk)	27.6 (26.4, 28.9)	27.8 (27.0,28.9)	26.4 (25.9,28.0) ^a	27.2 (26.0,30.0)	9.344	0.009
Birth weight (g)	900(820, 950)	900 (832,960)	850 (785,925)	890 (810,942)	5.785	0.055
Male, n(%)	61(44.5)	37(40.2)	19(57.6)	5(41.7)	3.006	0.222
SGA, n(%)	33(24.1)	22(23.9)	7(21.2)	4(33.3)	0.712	0.701
Multiple birth, n(%)	59(43.1)	28(30.4)	14(42.4)	7(58.3)	4.435	0.109
1-min Apgar $\leq$ 3, n(%)	19(13.9)	3(3.3)	10(30.3) ^a	2(16.7)	17.060	< 0.001
IV $\geq$ degree $\boxtimes$, n (%)	26(19.0)	10(10.9)	12(36.4) ^a	4(33.3)	12.029	0.002
RDS, n (%)	110 (80.3)	76(82.6)	26(78.8)	8(66.7)	1.767	0.413
MV, n (%)	112 (81.8)	72(78.3)	30(90.9)	10(83.3)	2.627	0.269
LOHs (d)	60.0(14.0,82.5)	75.5 (58.5,91.0)	4.0 (2.0,8.0) ^a	21.0 (14.8,47.0) ^a	90.418	< 0.001
a: Compared with the group of infants discharged with medical advice, $P < 0.01$. LOHs: Length of hospital stay, RDS: respiratory distress syndrome. IVH: Intraventricular hemorrhage. MV: mechanical ventilation						

80.3% of ELBW infants suffered from RDS and most of them had been mechanically ventilated. Compared with infants discharged with medical advice, the infants discharged without medical advice were more immature and had more severe early complications, ie. lower Apgar score and more severe

IVH. ($P < 0.01$). No statistical difference in birth weight, multiple birth, and SGA proportion existed. See Table 1.

2. Nutritional practice in ELBW infants discharged with medical advice

2.1 Basic characteristics of ELBW infants discharged with medical advice

92(67.2%) of this cohort of 137 ELBW infants discharged with medical advice. Infants discharged with medical advice were grouped by birth weight: <750 g, $750-900$ g and $900-1000$ g. SGA infants accounted for 23.9%(22/92). The smaller the birth weight was, the lower the birth weight Z score would be ($P < 0.001$). There was no statistical difference in GA (median 27.4wk, 27.5wk and 28.0wk for three groups above, respectively, $P = 0.540$), SGA proportion (25.0%, 34.4% and 17.3% for three groups above, respectively, $P = 0.204$), respiratory support duration (median 45.0d, 38.3d and 35.8d for three groups above, respectively, $P = 0.137$), chronic respiratory complications (75.0%, 53.1% and 51.9% for three groups above, respectively, $P = 0.489$). Although infants < 750 g seem stayed longer in hospital, but the difference had no statistic significance ($P = 0.107$). See Table 2.

Table 2
Basic characteristics of ELBW infants discharged with medical advice

variable	Total cases	< 750 g	750- <900 g	900- <1000 g	χ^2 value	<i>P</i> value
n(%)	92	8(8.7)	32(34.8)	52(56.5)		
GA (wk)	27.8 (27.0,28.9)	27.4 (26.4, 28.2)	27.5 (26.8, 29.7)	28.0 (27.0, 28.9)	1.233	0.540
Birth weight (g)	900 (832, 960)	710 (652, 720) ^a	840 (800, 870) ^a	955 (912, 978)	70.956	< 0.001
SGA, n (%)	22(23.9)	2(25.0)	11(34.4)	9(17.3)	3.177	0.204
Birth weight Z score	-0.6 (-1.2, 0.0)	-1.2 (-1.6, -1.1) ^b	-0.8 (-1.5, -0.4) ^c	-0.4 (-0.9, -0.2)	13.655	0.001
oxygen therapy at CGA 36wk, n(%)	50(54.3)	6(75.0)	17(53.1)	27(51.9)	1.438	0.489*
NIV and/or MV duration (d)	37.6 (22.2, 56.6)	45.0 (37.0, 75.5)	38.3 (26.0, 70.0)	35.8 (18.6,52.2)	3.969	0.137
Postnatal steroids, n(%)	44(47.8)	7(87.5)	13(40.6)	23(44.2)	5.819	0.057*
LOHs (d)	75.5 (58.5,91.0)	88.5 (70.8, 98.0)	75.5 (62.2, 93.0)	71.0 (56.0, 86.8)	4.446	0.107
Compared with the group of 900-<1000 g, a : $P < 0.001$, b : $P < 0.01$, c : $P < 0.05$. *: Fisher's exact test. LOHs: Length of hospital stay. NIV: Non-invasive ventilation. MV: mechanical ventilation.						

2.2 Nutritional practice

The feeding strategy based on initiation of enteral feeding was implemented actively after birth. The ratio of first feeding with breastmilk was 20.7%(19/92), and the ratio in infants < 750 g was zero(0/92). By the time of discharge, 57.6%(53/92) of the ELBW infants were breast milk feeding, and the ratio of exclusive breast milk feeding reached 30.4%(28/92). Full enteral feeding was achieved in all weight groups, at median 37.0d (27.0, 51.8). There was no statistical difference among groups in the incidence of NEC $\geq$ stage II($P = 0.064$) and cholestasis($P = 0.485$). See Table 3.

Table 3 Nutritional practice and complications in different birth weight groups,

cases (%)

Variable	Total cases	<750g	750-<900g	900-<1000g	X ² value	P value
n(%)	92	8(8.7)	32(34.8)	52(56.5)		
Initiating enteral feeding (d)	2.0 (1.0,3.8)	1.5 (1.0, 8.8)	2.0 (1.0, 3.8)	2.0 (1.0, 3.8)	0.143	0.931
First feeding with breast milk, n(%)	19(20.7)	0	7(21.9)	12(23.1)	2.298	0.317
Reaching full enteral feeding (d)	37.0 (27.0,51.8)	38.5 (26.8, 65.0)	39.0 (28.0, 52.0)	37.0 (25.5, 51.0)	1.044	0.593
Breast milk feeding at discharge, n(%)	53(57.6)	4(50.0)	20(62.5)	29(55.8)	0.575	0.750
Exclusive breast milk feeding at discharge, n(%)	28(30.4)	2(25.0)	10(31.3)	16(30.8)	0.124	0.940
NEC≥stage II, n(%)	4(4.3)	2(25.0)	1(3.1)	1(1.9)	5.897	0.064*
Cholestasis, n(%)	14(15.2)	2(25.0)	6(18.8)	6(11.5)	1.448	0.485

*: Fisher's exact test.

3. Nutritional outcomes of ELBW infants at discharge

By the time of medical discharge, all ELBW infants reached full-term GA, and their weight Z scores were lower than those at birth, the median decline was more than one, -1.20(-1.88, -0.80). 66.3%(61/92) of ELBW infants were diagnosed as GR at discharge. Mean velocity of weight gain was 14.7 ± 2.4 g/(kg.d), 13.4 ± 2.0 g/(kg.d), 12.7 ± 2.2 g/(kg.d), respectively ($P < 0.037$). There were no statistical differences in weight, weight Z score, weight ΔZ during hospitalization, rate of GR and LOHs ($P > 0.05$) See Table 4.

Table 4
Nutrition outcomes of ELBW infants in different birth weights at discharge

variable	Total cases	< 750 g	750<900 g	900-<1000 g	χ^2 value	P value
n(%)	92	8(8.7)	32(34.8)	52(56.5)		
Discharge weight(g), median(IQR)	2325 (2060,2660)	2485 (2302,2742)	2295 (1980,2800)	2282 (2060,2645)	1.139	0.566
Discharge GA (wk), median(IQR)	38.7 (37.3, 41.1)	40.0 (38.1,41.8)	39.0 (37.6,41.5)	38.0 (37.0,40.6)	3.796	0.150
Weight gain rate, g/(kg·d),mean (SD)	13.1 ± 2.2	14.7 ± 2.4 ^a	13.4 ± 2.0	12.7 ± 2.2	3.429	0.037
Discharge weight Z score, mean(SD)	-1.96 ± 1.16	-2.2 ± 0.5	-2.2 ± 1.2	-1.8 ± 1.1	0.607	0.547
weight Z score change (ΔZ),median (IQR)	-1.20 (-1.88, -0.80)	-1.05 (-1.28, -0.50)	-1.10 (-1.90, -0.90)	-1.30 (-1.20, -0.80)	2.505	0.286
GR, n (%)	61(66.3)	5(62.5)	20(62.5)	36(69.2)	0.458	0.795
LOHs(d), median (IQR)	75.5 (58.5,91.0)	88.5 (70.8,98.0)	75.5 (62.3,93.0)	71.0 (56.0,86.8)	4.466	0.107
a: Compared with the group of 900- <1000 g, $P < 0.05$. IQR:interquartile arrange.SD:standard deviation.						

4. Risk factors of growth retardation during in-patient period

We conducted a multiple-factor analysis, and assumed independent variables below were the risk factors causing GR, male infant, birth weight (g), GA (wk) at birth, SGA at birth, LOS, NEC $\geq$ stage II, PDA, oxygen usage at CGA36wk, cholestasis, total fluid intake < 150 ml/kg/d at 28d postnatally, time to full enteral feeding (d), postnatal steroid, LOHs (d), NIV and/or MV duration > 28d, average weight gain rate < 15 g/(kg.d). Results showed that SGA at birth, average weight gain rate < 15 g/(kg.d), NIV and/or MV duration > 28d were risk factors posing GR ($P < 0.05$), and the LOHs (d) was a protective factor ($P < 0.05$). See Table 5.

Table 5
Logistic analysis on risk factors of growth retardation

Variable	β	S.E.	Wald	df	P value	OR value	95% CI	
							Lower limit	Upper limit
SGA	3.549	1.554	5.212	1	.022	34.768	1.652	731.728
Weight gain rate < 15 g/kg·d	5.518	1.582	12.164	1	.000	249.062	11.211	5532.889
NIV and/or MV duration > 28d	1.927	.886	4.734	1	.030	6.867	1.211	38.957
LOHs(d)	-.051	.023	5.114	1	.024	.950	.909	.993

Discussion

In our study, 67.2%(92/137) of ELBW infants finished their in-patient therapy and discharged by physicians, other 32.8%(45/137) transferred, discharged without medical advice or died. The lower birth weight infants had lower birth weight Z score. Median LOHs was 75.0d, 66.3%(61/92) of them was diagnosed with GR. SGA, average weight gain < 15 g/kg.d, respiratory support (NIV and/or MC) were risk factors for GR. Staying longer in NICU was helpful to early growth.

Generally, ELBW infants are those with GA < 28wk, just like our infants. It was reported in 2019 that preterm infants with GA < 28wk accounted for 4.1% of preterm population globally in 2014⁽²³⁾. Although the proportion of ELBW infants is not high, they have higher mortality, morbidity and disability rate⁽²⁴⁾. As some infants transferred for operation, the actual survival rate of ELBW infants in Beijing was higher than 67.2%. This was higher than that reported in other studies from China^(11, 12), but lower than the developed countries^(24, 25). There is a report that Parental economical condition influences the outcomes of ELBW infants in other areas of China⁽¹¹⁾. This paper focuses on the ELBW infants in Beijing area. Developed medicine, economy, and insurance system in Beijing underlie the steady foundation for ELBW infants' therapy, and contribute to the lower mortality. Most of infants with birth weight more than 900 g and higher proportion of SGA infants in our study may have a positive effect on lower mortality. ELBW infants' rescue dispersed in many centers may not be beneficial to experience accumulation in each NICU, and may have adverse effects on therapy and outcomes.

First 7 days is a fragile period for newborn infant and the death rate in this period accounts for more than 2/3 of neonatal death⁽²⁶⁾. Generally, ELBW infants discharged within 14d after birth will succumb. Our ELBW infants all received intensive care in NICU, so we prolonged our early intervention and observation window to 14 days. We don't have information about the prognosis of the ones who discharged without medical advice 2 weeks later. Long-term follow-up information is not available in this study.

Weight gain is associated with the growth and neurological outcome of preterm infants^(27, 28). SGA and GR affect the health of infants, increase the society and family burden and the mortality rate of infants⁽²⁹⁾. Researches showed that, dueing to EUGR, ELBW infants had a higher risk of multiple complications, including hindered growth at corrected 18–22 months, cerebral palsy, mental developmental index (MDI) < 70 and neurodysplasia^(30–32). In our study, a high proportion of ELBW infants subjected to intrauterine growth restriction, reaching 24.1%, which exposed our infants to relatively high risks of GR. That some more immature infants discharged before 14 days lightened our later growth care challange, and may have influence on our results. As some infants discharge after CGA 42 weeks, our study used GR instead of EUGR, but EUGR was included in GR. Currently, EUGR is still a serious problem for ≤ 34 w preterm infants, and the risk factors leading to EUGR include gestational age, birth weight, BPD, and SGA^(7, 33). Previous studies reported that the EUGR incidence of preterm infants with gestational age ≤ 32 w was 57%-71%^(33–36), and Chinese studies reported that the incidence of EUGR in preterm infants with birth weight ≤ 1200 g was 83.8%⁽³⁷⁾. In this literature, the overall survival rate of ELBW infants was higher than the domestic level, but approximately 2/3 of ELBW infants suffered from GR, defined as the decline of Z score more than one. Instead of weight percentile less than tenth in growth charts⁽³⁷⁾, the definition we used can exclude the influence of intrauterine growth retardation or SGA at birth, and the duration of hospitalization. International growth chart/standard used to evaluation renders our results comparable to other studies. Head circumference and length are very important indexes for physical growth, but their accuracy can't be guaranteed. We selected systemic and accurate body weight as our growth index⁽³⁷⁾.

Chinese and international nutritional guidelines for newborns are used widely in China, including enteral and parenteral nutrition. Our ELBW infants initiated enteral feeding at relatively early age, but the progress delayed compared to the guideline of Canada⁽³⁸⁾. Although some studies identified the safety and efficacy of early aggressive infant's feeding^(39, 40), restrictive feeding practice, ie. prolonged parenteral nutrition and late achieved full enteral feeding, still exists in Chinese NICUs⁽⁴¹⁾. Our study demonstrated the same problem. Delayed reaching full enteral feeding contributes to the individual feeding policy in NICU, individual physician' opinion and experience, infants' health conditions, and feeding milk property. Breast milk feeding and fortified breast milk feeding are increasingly emphasized and used in NICU in China^(42, 43). In Beijing, the any and exclusive breastfeeding rate at discharge for ELBW infants reached 57.6% and 30.4%, similar to that reported by Battersby C et al⁽⁴⁴⁾ after breastfeeding improvement action in 2016 in England. Limited by lack of human milk bank, maternal health conditions and promotion efforts, only 20.7% of ELBW infants started feeding with breast milk. Our ELBW infants had lower NEC incidence than that previously reported in China⁽¹¹⁾, this assigned to better ELBW infants management. But the lower NEC incidence was also influenced by early withdrawing therapy in very high risk infants and several severe NEC infants transferred to other hospitals.

This multicenter study with cooperation with local neonatologic association, almost all NICUs in local area are involved. Study conducted in an economy and medicine-developed area in China, and detailed

information regarding early therapy and growth pattern of ELBW infants was investigated systematically. The therapy of ELBW infants can partly represent the development of neonatology in China. Study results illuminate the problems and the related risk factors, and that would be conducive to improve clinical management. The insufficiency of the study is that the number of ELBW infants is small in 1 year, only body weight as the physical growth index, and no follow-up information.

In conclusion, ELBW infants are highly risky of mortality and morbidity, whose treatment and comprehensive management are subjected to various challenges. Although relatively good therapeutic experience and ability in developed area in China, there is still a long way to go for better short and long-term outcome of ELBW infants.

Declarations

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Author Contributions

Shuai-Jun Li and Qi Feng designed the study and prepared the manuscript. Qi Feng, Xiao-Mei Tong, Qiu-Ping Li, Jun-Yi Wang, Ya-Juan Wang, Wei-Peng Liu, Chao-Mei Zeng, Dan-Hua Wang, Wen-Li Zhao, Li-Hua Li, Hong Cui, Ming-Yan Hei, Li Li, Xue-Feng Zhang, Jing Liu, Ming Yang participated in the study protocol design and confirmation. They were responsible in guiding and instructing the protocol proceeding in each unit. Shuai-jun Li and Qi Feng had full access to all of the data in the study and took responsibility for the review, integrity of the data and statistical analysis. supervised the data collection and implemented the study. Shuai-jun Li and Qi Feng finalized the manuscript. Qi Feng: acts as the guarantor of the paper.

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Availability of data and materials

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was evaluated and approved by “Biomedicine Ethics committee of Peking University First Hospital” . All methods were carried out in accordance with relevant guidelines and regulations. Written Informed consent was obtained from all the study subjects’ parents before enrollment.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no conflict of interest.

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Figures

Figure 1

Study flowchart. *LOHs: Length of hospital stay