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Original Article

A clinical analysis of very and extremely low birth weight preterm infants

Bing Wang*, Jifei Sun*, Yan Sun, Na Li, Xueying Li, Xiaozheng Song, Ping Zhang, Junting Li, Kaiyi Huang

*Department of Pediatrics, Weihai Maternity and Child Health Hospital, Weihai 264200, Shandong, China. *Equal contributors and co-first authors.*

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Abstract: Objective: To investigate the clinical characteristics, treatment strategies, and outcomes of very low birth weight (VLBW)/extremely low birth weight (ELBW) preterm infants in Weihai from January 2017 to December 2019. Methods: 107 VLBW/ELBW preterm infants admitted to our hospital were recruited as the study cohort and divided into three groups: the < 1000 g group (n = 11 cases), the ≥ 1000~1250 g group (n = 32 cases), and the ≥ 1250~1500 g group (n = 64 cases). The clinical characteristics of the VLBW/ELBW preterm infants in each group were analyzed, and the hospitalization duration times, the survival rates, the ventilator use, the main complications, and the follow-ups in each group were compared statistically. Results: There were significant differences in the occurrences of maternal anemia during pregnancy, the birth weights, the gestational ages, the births of singletons, twins, or multiples, the hospitalization duration times, the occurrences of late-onset sepsis (LOS), and the occurrences of periventricular intraventricular hemorrhages (PIVH) among the three groups (P < 0.05). Our multivariate logistic regression and ROC curve analyses showed that the lower the gestational age (OR = 12.56, 95% CI: 2.45~14.63, P = 0.01), the lower the birth weight (OR = 8.69, 95% CI: 1.95~10.34, P = 0.03), and the premature rupture of membranes (OR = 6.44, 95% CI: 1.03~9.77, P = 0.04) and LOS (OR = 9.64, 95% CI: 1.67~18.99, P = 0.02) would induce a higher death rate among premature infants. Furthermore, after one year of follow-up, the psychomotor development indexes (PDI) of the different birth weight groups were increased along with the birth weight, and the differences were statistically significant (χ^2 = 4.19, 4.99, P = 0.027, 0.01). Conclusion: Strengthening perinatal health care and actively preventing and treating various complications are of great significance in improving the survival rate and long-term quality of life of VLBW/ELBW premature infants.

Keywords: Very low birth weight (VLBW)/extremely low birth weight (ELBW) preterm infants, clinical characteristics, risk factors, complications

Introduction

With the development of perinatal medicine, the level of neonatal intensive care, the progress in assisted reproductive technology, and the strengthening of the cooperation between obstetrics and pediatrics, the survival rate of very low birth weight (VLBW)/extremely low birth weight (ELBW) preterm infants has gradually increased, but the incidence of complications has also gradually increased [1, 2]. It has been reported that the rate of very low birth weight (VLBW)/extremely low birth weight (ELBW) preterm infants in China is as high as 0.18% [3]. The rate of neonatal mortality is as high as 5.8% [4]. However, there are few comprehensive clinical analyses on VLBW/ELBW preterm infants, and there is also a lack of large sample clinical data to analyze the survival rates, mortality, diagnoses, and growth of premature infants, and to analyze the main death-related factors. In our study, we investigated the clinical characteristics, treatment strategies, and outcomes of very low birth weight (VLBW)/extremely low birth weight (ELBW) preterm infants in Weihai from January 2017 to December 2019.

Data and methods

Clinical data

A total of 107 VLBW/ELBW preterm infants admitted to our hospital from January 2017 to

December 2019 were recruited as the study cohort and divided into three groups: the < 1000 g group (n = 11 cases), the ≥ 1000~1250 g group (n = 32 cases), and the ≥ 1250~1500 g group (n = 64 cases). The study was approved by the institutional ethics committee of Weihai Maternity and Child Health Hospital and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all the patients' families before their participation.

Inclusion and exclusion standards

Inclusion standard: ① The newborn was hospitalized in the Department of Neonatology of our hospital for the first time, ② Newborns with a gestational age < 28 weeks and a birth weight < 1500 g, and ③ Newborns with complete basic information and laboratory examination data.

Exclusion standard: ① Infants who had repeated hospitalizations, ② Preterm infants born outside the hospital with a birth weight less than 1500 g but admitted to our hospital with an admission weight of more than 1500 g, and ③ Newborns with incomplete basic clinical data.

Observation indexes

① Collection of the clinical data: The infants' general data, such as their birth weights, gestational ages, and gender, were collected. We also recorded the high risk factors of the pregnant females: mode of delivery, pregnancy induced hypertension, gestational diabetes mellitus, premature rupture of the membranes, and the related risk factors of the infants such as the times of administration of surfactants, the durations of the mechanical ventilation, the neonatal sepsis, IVH, NEC, the lengths of their hospital stays, their survival rates, their periventricular-intraventricular hemorrhages (PIVH), and their early-onset sepsis (EOS), late-onset sepsis (LOS) etc.

② Outcome assessment: 1) Survival: *Cured* indicates that the vital signs were stable at the time of hospitalization, the weight was more than or equal to 1800 g, and the newborn could be fed normally. *Improved* indicates that although the above discharge standards were not met, the newborn was discharged without its life being in danger as determined by the clinical evaluation, or that the family members strongly requested the newborn be discharged and was alive at the follow-up. 2) *Died*: The infant died after finishing the treatment because of ineffective treatment, unstable vital signs, or mechanical ventilation. 3) *Abandoned treatment*: There were no life-threatening complications, and the vital signs were still stable. The parents voluntarily asked to abandon the treatment because of their economic situation and because they were worried about the poor prognosis.

Survival rate = survival cases/(survival cases + death cases) × 100%.

③ The surviving VLBW/ELBW premature infants were followed up and given health care. The Bailey infant development scale was used to evaluate the intelligence development index (MDI) and the motor development index (PDI) at 6 and 12 months of corrected gestational ages.

Statistical analysis

All the data were analyzed using SPSS 25.0. Among them (n, %) refers to the calculated data. The comparisons of the relevant data between groups and within groups were performed using chi square tests, and the measurement data were analyzed using ($\overline{X}$ ± SD). The comparisons between groups were analyzed using t tests, and $P < 0.05$ indicated a statistically significant difference.

Results

The infants' clinical data

The study involved 107 VLBW/ELBW preterm infants, including 11 infants in the < 1000 g group with a mean gestational age of (28.35 ± 0.91) weeks, and a mean birth weight of (902.65 ± 52.3) g, and 32 infants in the ≥ 1000~1250 g group, with a mean gestational age of (28.15 ± 1.19) weeks, and a mean birth weight of (1105.4 ± 71.6) g, and 64 infants in the ≥ 1250~1500 g group, with a mean gestational age of (30.8 + 4.2) weeks, and a mean birth weight of (1381.95 ± 63.9) g, and the differences among the three groups were statistically significant ($P < 0.05$). The singleton and twin or multiple births cases in the < 1000 g group were 9 (81.8%) and 2 (18.2%), and in the ≥ 1000~1250 g group they were 27

Table 1. A comparison of the clinical data in the three groups

	Weight < 1000 g group (n = 11 cases)	Weight ≥ 1000~1250 g group (n = 32 cases)	Weight ≥ 1250~1500 g group (n = 64 cases)	t/χ^2	*P*
Gestational age (weeks)	28.35 ± 0.91	28.15 ± 1.19	30.8 + 4.2	6.15	0.000
Sex				2.68	0.062
Male (n %)	6 (54.5%)	17 (53.1%)	28 (43.8%)		
Female (n %)	5 (45.5%)	15 (46.9%)	36 (56.2%)		
Birth weight (g)	902.65 ± 52.3	1105.4 ± 71.6	1381.95 ± 63.9	7.29	0.002
Delivery modes				5.52	0.067
Cesarean section	7 (63.6%)	19 (59.4%)	44 (68.8%)		
Natural labor	4 (36.4%)	13 (40.6%)	20 (31.2%)		
Singleton (n %)	9 (81.8%)	27 (84.4%)	58 (90.6%)	8.65	0.023
Twins or multiple (n %)	2 (18.2%)	5 (15.6%)	6 (9.4%)	7.29	0.034
Stay in hospital (d)	41 ± 16.9	40 ± 17.4	39.2 ± 6.5	9.95	0.000

Note: a significant difference is P < 0.05.

Table 2. A comparison of the clinical features of the mothers of the infants in the two groups [n (%)]

	Weight < 1000 g group (n = 11 cases)	Weight ≥ 1000~1250 g group (n = 32 cases)	Weight ≥ 1250~1500 g group (n = 64 cases)	t/χ^2	*P*
Delivery modes				5.52	0.067
Cesarean section	7 (63.6%)	19 (59.4%)	44 (68.8%)		
Natural labor	4 (36.4%)	13 (40.6%)	20 (31.2%)		
Premature rupture of membranes	7 (63.6%)	21 (65.6%)	29 (45.3%)	3.37	0.214
Pregnancy-induced hypertension	5 (45.5%)	14 (43.75%)	21 (32.8%)	7.29	0.098
Gestational diabetes	3 (27.3%)	10 (31.25%)	12 (18.75%)	5.52	0.066
Infection in the second and third trimester of pregnancy	1 (9.1%)	2 (3.1%)	2 (3.125%)	4.52	0.334
Placental abruption	2 (18.2%)	4 (12.5%)	6 (9.4%)	8.61	0.253
Placenta previa	0 (0)	1 (3.125%)	2 (3.125%)	13.25	0.313

Note: A significant difference is P < 0.05.

(84.4%) and 5 (15.6%), and in the ≥ 1250~1500 g group they were 58 (90.6%) and 6 (9.4%), but there were no statistically significant differences between the three groups (P > 0.05). The mean hospital stay duration in the < 1000 g group was (41 ± 16.9) d, and in the ≥ 1000~1250 g group it was (40 ± 17.4) d, and in the ≥ 1250~1500 g group it was (39.2 ± 6.5) d, and there were statistically significant differences between the three groups (P < 0.05) (**Table 1**).

Clinical features of the mothers of the infants

The number of pregnant women who suffered a premature rupture of the membranes in the < 1000 g group was 7 (63.6%) cases, in the ≥ 1000~1250 g group, it was 21 (65.6%) cases, and in the ≥ 1250~1500 g group it was 29 (45.3%) cases, and there was no statistically significant differences among the three groups (P > 0.05). The infection rate in the second and third trimesters of pregnancy in the < 1000 g group was 9.1% (1/11), and in the ≥ 1000~1250 g group it was 3.1% (2/32), and in the ≥ 1250~1500 g group, it was 3.125% (2/64). The number of pregnant women who had pregnancy-induced hypertension in the < 1000 g group was 5 (45.5%) cases, and in the ≥ 1000~1250 g group it was 14 (43.75%) cases, and in the ≥ 1250~1500 g group it was 21 (32.8%) cases. The number of pregnant women who had gestational diabetes in the < 1000 g group was 3 (27.3%) cases, and in the ≥ 1000~1250 g group it was 10 (31.25%) cases, and in the ≥ 1250~1500 g group it was 12 (18.75%) cases. The rates of placental abruption and placenta previa in the < 1000 g group were 18.2% (2/11) and 0, and in the ≥ 1000~1250 g group the rates were 12.5% (4/32) and 3.125% (1/32), and in the ≥ 1250~1500 g group the rates were 9.4% (6/64) and 3.125% (2/64). There were no statistically significant differences between the three groups (P > 0.05) (**Table 2**).

Table 3. A comparison of the outcomes of the infants among the three groups [n (%)]

group	Number of cases	Survival	Death	Give up treatment	Survival rate
weight < 1000 g group	11	7	2 (22.22%)	2 (18.18%)	77.78
Weight ≥ 1000~1250 g group	32	24	4 (14.29%)	4 (12.5%)	85.71
Weight ≥ 1250~1500 g group	64	58	3 (4.92%)	3 (4.69%)	95.08
t	-	-	9.737	4.261	5.378
P	-	-	0.032	0.047	0.006

Note: A significant difference is P < 0.05.

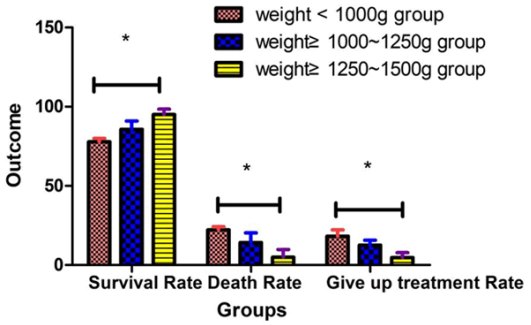

Figure 1. A comparison of the infants' outcomes in the three groups. *P < 0.05.

Outcomes

As shown in **Table 3** and **Figure 1**, among a total of 107 very and extremely low-birth-weight preterm infants and premature infants, 89 survived, 9 died, and 9 abandoned treatment. The survival rate in the < 1000 g group was 77.78% (7/9), and the rate in the ≥ 1000~1250 g group was 85.71% (24/28), and the rate in the ≥ 1250~1500 g group was 95.08 (58/61). Overall, the survival rate increased, but there were no significant differences among the groups (χ^2 survival = 5.378, P > 0.05). The death rate in the < 1000 g group was 22.22% (2/9), and in the ≥ 1250~1500 g group it was 14.29% (4/28), and in the ≥ 1250~1500 g group it was 4.92% (3/61). Overall, the death rate decreased, but there were no significant differences among the groups (χ^2 death = 9.737, P > 0.05).

Clinical complications in infants

The incidence of complications in the preterm infants included 70 cases of RDS (65.42%), 42 cases of neonatal sepsis (39.25%), and 24 cases of LOS (22.42%), 18 cases of EOS (16.82%), 26 cases of PIVH (24.30%), 20 cases of PDA (18.69%), 7 cases of PPHN (6.54%), and 4 cases of BPD (3.74%). The LOS and PIVH incidence rates decreased with an increase in the body weight (the difference was statistically significant) (the χ^2 values respectively were 9.10 and 7.09, P < 0.05) (**Table 4**).

Treatment in infants

86 cases (80.37%) were treated with respiratory support, including 60 cases (56.07%) using noninvasive ventilation and 26 cases (24.29%) using invasive ventilation. 55 cases (51.40%) were treated with PS, 43 cases (40.18%) were treated with PS once, 12 cases (11.21%) were treated with PS twice or more, and 11 cases (10.28%) were comorbid with EOS. 47 cases (43.93%) were treated with blood transfusions. 40 cases (37.38%) were treated with meropenem. The blood transfusion and meropenem treatment rates in the premature infants with birth weight ≥ 1000 g-1250 g group were higher than they were in the birth weight < 1000 g and birth weight ≥ 1250 g-1500 g groups (P < 0.05) (**Table 5**).

A univariate analysis of the death factors of prognoses of the premature infants

Our univariate analysis showed that the proportions of gestational ages and birth weights in the death group was lower than it was in the survival group. The proportion of maternal age and premature rupture of membranes in the death group was higher than it was in the survival group (P < 0.05) (**Table 6**).

Multivariate logistic analysis of the death risk of premature infants

Our multivariate logistic regression and ROC curve analyses showed that the lower the gestational age (OR = 12.56, 95% CI: 2.45~14.63, P = 0.01), the lower the birth weight (OR = 8.69, 95% CI: 1.95~10.34, P = 0.03), and the

Table 4. A comparison of the clinical complications of the infants among the three groups [n (%)]

	Weight < 1000 g group (n = 11 cases)	Weight ≥ 1000~1250 g group (n = 32 cases)	Weight ≥ 1250~1500 g group (n = 64 cases)	t/χ^2	*P*
Asphyxia	4 (36.36)	6 (18.75)	10 (15.63)	2.66	0.24
RDS	8 (72.73)	20 (62.5)	42 (65.63)	0.38	0.82
LOS	4 (44.44)	11 (42.31)	9 (15)	9.10	0.01
EOS	1 (9.09)	5 (15.63)	12 (18.75)	0.67	0.73
PIVH	6 (60.0)	6 (19.35)	14 (22.95)	7.09	0.03
PDA	2 (20.0)	6 (19.35)	12 (19.67)	2.39	0.21
PPHN	0	5 (16.13)	2 (3.28)	15.23	0.14
BPD	0	4 (14.29)	0	5.58	0.24

Note: A significant difference is P < 0.05. RDS: Respiratory distress syndrome; LOS: Late-onset sepsis; EOS: Early-onset sepsis; PIVH: Periventricular intraventricular hemorrhage; PDA: Arterial catheter opening; PPHN: Persistent pulmonary hypertension; BPD: Bronchopulmonary dysplasia.

Table 5. A comparison of the infants' treatment in the three groups [n (%)]

	Weight < 1000 g group (n = 11 cases)	Weight ≥ 1000~1250 g group (n = 32 cases)	Weight ≥ 1250~1500 g group (n = 64 cases)	t/χ^2	*P*
Noninvasive ventilation	5 (45.45)	18 (56.25)	37 (57.81)	0.58	0.75
Noninvasive ventilation + Invasive ventilation	3 (27.27)	4 (12.5)	11 (17.18)	1.29	0.46
Invasive ventilation	2 (18.18)	4 (12.5)	2 (3.13)	4.74	0.09
PS for one time	5 (45.45)	17 (50.13)	21 (32.81)	3.80	0.17
PS for twice or more	2 (18.18)	2 (6.25)	8 (12.5)	1.43	0.58
Blood transfusion	5 (45.45)	20 (62.5)	22 (34.36)	6.86	0.03
Meropenem treatment	4 (36.36)	18 (56.25)	18 (28.13)	7.21	0.02

Note: A significant difference is P < 0.05.

Table 6. A univariate analysis of the prognoses of the premature infants

group	Number of cases	Gestational age	Birth weight	Singleton	Cesarean section
Survival group	89	30.5 + 4.2	1271 (800, 1490)	81 (91.01)	70 (78.65)
Death group	9	29.2 + 2.1	1158 (960, 1400)	7 (77.78)	6 (66.67)
t	-	2.36	-2.78	1.56	0.67
P	-	0.005	0.01	0.19	0.43
group	Number of cases	Elderly puerpera (age ≥ 35 years)	Placental abruption	Placenta previa	Pregnancy-induced hypertension
Survival group	89	15 (16.85)	8 (8.99)	3 (3.37)	36 (40.45)
Death group	9	4 (44.44)	2 (22.22)	0	3 (33.33)
t	-	3.98	1.56	-	0.17
P	-	0.04	0.19	0.53	0.7
group	Number of cases	Gestational diabetes	Infection in the second and third trimester of pregnancy		Premature rupture of membranes
Survival group	89	20 (22.47)	4 (4.49)		44 (49.43)
Death group	9	3 (33.33)	0		8 (88.89)
t	-	0.54	-		5.11
P	-	0.48	0.46		0.02

Note: A significant difference is P < 0.05.

premature rupture of membranes (OR = 6.44, 95% CI: 1.03~9.77, P = 0.04) and LOS (OR = 9.64, 95% CI: 1.67~18.99, P = 0.02) would induce a higher death rate of premature in-

Table 7. A multivariate logistic analysis of the death risk of the premature infants

Factors	B	Wald	*P*	OR	95% CI
Gestational age < 1000 g	3.98	11.48	0.01	12.56	2.45~14.63
Birth weight < 28 weeks	2.59	8.93	0.03	8.69	1.95~10.34
Elderly puerpera (age > 35 years)	0.85	0.74	1.72	0.38	0.29~0.84
Premature rupture of membranes	1.63	5.57	0.04	6.44	1.03~9.77
LOS	2.49	8.12	0.02	9.64	1.67~18.99
PDA	0.17	1.22	0.99	0.33	0.02~0.69
BPD	0.44	0.83	0.67	0.42	0.62~2.33

Note: A significant difference is P < 0.05.

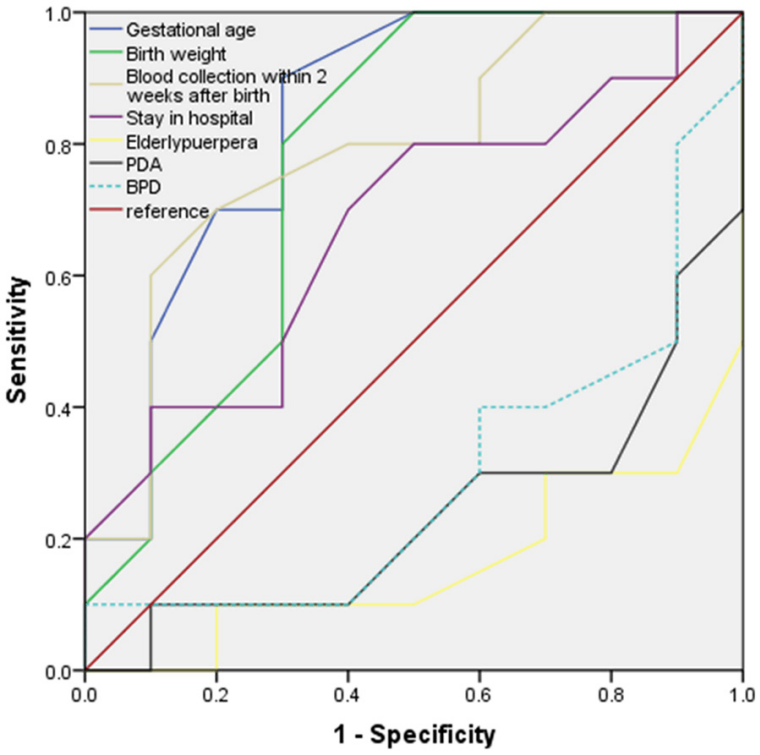

Figure 2. An ROC curve of the preterm infants' related risk factors.

fants. Therefore, the gestational age, the premature rupture of membranes, the birth weight, and LOS were independent predictors (**Table 7** and **Figure 2**).

One year follow-up of the premature infants

As shown in the **Table 8** and **Figure 3**, 89 preterm infants survived, and 81 cases were followed up for 12 months, including 7 cases in the < 1000 g group, 21 cases in the ≥ 1000 g-1250 g group, and 53 cases in the ≥ 1250 g-1500 g group. The follow-up results showed that with an increase in the birth weight, the psychomotor development index (PDI) and MDI were higher than they were in the low birth weight group, the PDI differences were statistically significant (P < 0.05), and the MDI differences were not statistically significant (P > 0.05).

Discussion

Currently, the birth rate of premature infants in China is increasing. One multicenter study showed that the incidence of premature infants was 7.8% among newborns born in China from 2002 to 2003 [5]. In 2005, the incidence of premature infants was 8.1%, and 27.5% of the hospitalized infants were in neonatal departments [6]. The VLBW/ELBW treatment success rate was significantly higher than before. The VLBWI and ELBWI survival rates in the United States were 92.6% and 85.5% respectively in 2006, and the VLBW/ELBW infant survival rates in South Korea from 2008 to 2009 were 92.0% and 85.5%, respectively [7]. Some studies found that the mortality of very low birth weight infants with a birth weight < 1200 g was 41.3%, which is significantly higher than the rate of premature infants with a birth weight of 1200-1500 g (7.0%) [8-10]. As shown in our study, from a total of 107 VLBW/ELBW preterm infants, 89 survived, 9 died, and 9 abandoned treatment. The survival rate in the < 1000 g group was 77.78% (7/9), and in the ≥ 1000~1250 g group it was 85.71% (24/28), and in the ≥ 1250~1500 g group it was 95.08

Table 8. One year follow-up of the premature infants

group	Number of cases	MDI		PDI	
		6 months	12 months	6 months	12 months
weight < 1000g group	11	85.47 + 6.12	90.32 + 5.82	81.45 + 5.49	84.45 + 5.98
Weight ≥ 1000~1250 g group	32	90.56 + 5.89	95.43 + 4.29	87.92 + 4.78	90.67 + 6.12
weight ≥ 1250~1500 g group	64	94.78 + 5.34	102.44 + 4.12	93.55 + 5.23	97.43 + 5.26
t	-	1.31	2.34	4.19	4.99
P	-	0.09	0.12	0.027	0.01

Note: A significant difference is P < 0.05.

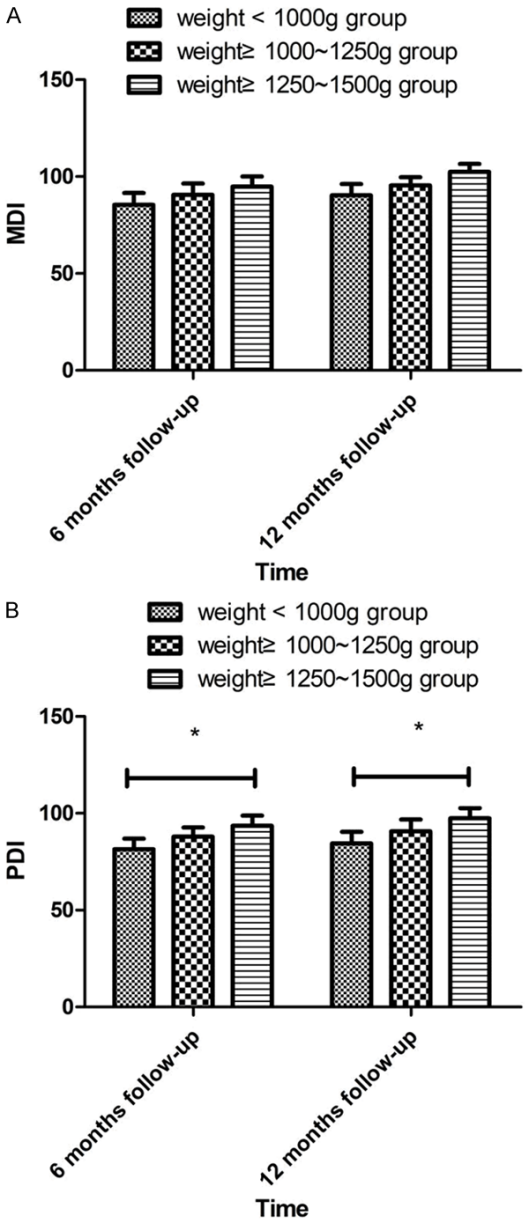

Figure 3. One year follow-up of the premature infants. *P < 0.05. A: One year follow-up of MDI. B: One year follow-up of PDI.

(58/61), but there was a significant difference between the < 1000 g group and the ≥ 1250~1500 g group.

Studies have shown that the incidence rate of RDS in preterm infants is higher than 10%, so it is an important cause of neonatal death [11]. In our study, the top 3 VLBW/ELBW complications in preterm infants were RDS, septicemia, and PIVH. The lower the birth weight, the higher the rates of PIVH and LOS, and those incidence rates were 24.30% and 22.42%.

Premature brain injuries include intraventricular hemorrhages, periventricular leukomalacia, brain tissue and sensory center, motor center, nerve conduction pathway damage, leading to cognitive, motor, and sensory dysfunctions in children, and ultimately neurodevelopmental damage [12, 13]. Premature infants are vulnerable to mechanical or hypoxic, acidosis and other physical and chemical adverse factors, resulting in brain injury [14]. The results showed that the PDI of the 81 VLBW/ELBW infants with high birth weights was higher than it was in the VLBW/ELBW infants with low birth weights. This suggests that the VLBW/ELBW infants with lower birth weights are at a higher risk of developing psychomotor disorders in the later stage.

Our study showed that birth weight, gestational age, premature rupture of membranes, and LOS are the risk factors for VLBW/ELBW premature infant deaths, and they are also the main causes of early deaths. Most premature infants suffer prenatal infections, and the smaller the body weights and the longer the hospital stays, the higher the incidences of infection. When very low and very low birth weight infants are comorbid with respiratory distress syndrome, tracheal intubation, mechanical ventilation, invasive catheterization,

and other operations are more likely to lead to various infections, especially pneumonia, respiratory failure, and metabolic acidosis, which can further aggravate the brain injuries in premature infants [15-17]. At present, the main causes of early deaths are NRDS and severe asphyxia, accounting for 48.9% [18], and the main causes of the later deaths are infection (sepsis, severe pneumonia), accounting for 45.0% [19]. Therefore, it is important to improve the treatment levels of these three diseases to reduce the mortality of ELWB infants. There are a lot of data show that pregnant women use glucocorticoids prophylactically. Pulmonary surfactants can effectively reduce the incidence of NRDS [20].

Moreover, in our study, the patients in the ≥ 1000-1250 g group had the highest rate of blood transfusions and meropenem treatments during their hospitalization. It may be related to the infections and iatrogenic blood loss occurring in a high proportion of these children, the long hospital stays, the various invasive procedures, and long duration of the mechanical ventilation [21]. Therefore, it is necessary to strengthen the management of these children during their hospitalization to reduce the incidence of nosocomial infections and iatrogenic blood loss.

The following limitations deserve comment. First, the cohort was small, and this was a single-central trial. Second, residual confounding is plausible due to the complicated medical backgrounds of the participants. Last but not least, the study covered a limited time period, and we didn't observe the long-term efficacy or the recurrence among the patients. Therefore, further studies of very low birth weight (VLBW)/extremely low birth weight (ELBW) preterm infants are still needed.

In conclusion, with the development of neonatal medicine, the VLBW/ELBW premature infant survival rate will continue to improve. Strengthening perinatal health care and actively preventing and treating various complications are of great significance for shortening the hospitalization durations and improving the long-term quality of life of VLBW/ELBW infants.

Disclosure of conflict of interest

None.

Address correspondence to: Bing Wang, Department of Pediatrics, Weihai Maternity and Child Health Hospital, No. 51 Guangming Road, Huancui District, Weihai 264200, Shandong, China. Tel: +86-0631-5271326; E-mail: 13001635845@163.com

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