The survival rate of extremely low birth weight infants improved in Guangdong Province, China

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Research

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Abstract

Background

With the increase in extremely low birth weight (ELBW) infants, their outcomes received special attention. However, in China, studies of the outcomes of ELBW infants are rare.

Methods

The hospitalized records of ELBW infants discharged from twenty-six neonatal intensive care units were reviewed and analyzed.

Results

A total of 2575 ELBW infants were enrolled and the overall survival rate was 55.11%. From 2008 to 2017, the number of ELBW infants increased rapidly from 91 to 466, and the survival rate improved steadily from 41.76–62.02%. The survival rate rose with increasing BW, the ascending level of regional economic development and specialist hospitals. The incidence of complications was neonatal respiratory distress syndrome (85.2%), bronchopulmonary dysplasia (63.7%), retinopathy of prematurity (39.3%), intraventricular hemorrhage (29.4%), necrotizing enterocolitis (12.0%), and periventricular leukomalacia (8.0%). Among the 1156 nonsurvivors, 90.0% of infants died during the neonatal period (≤ 28 days), and the other died after the neonatal period. A total of 768 ELBW infants died after medical care withdrawal, with economic factors and expected outcome being important causes.

Conclusion

The number of ELBW infants is increasing in China, and the overall survival rate is still low but is improving steadily.

Introduction

Low birth weight premature infants have a particularly high risk for morbidity and mortality[1, 2]. In recent decades, the outcomes of preterm infants, especially extremely preterm (gestational age [GA] < 28 weeks) and extremely low birth weight (ELBW, birth weight [BW] < 1000 grams) infants, have improved worldwide due to the use of antenatal steroids, pulmonary surfactant treatment and advances in perinatal health care, such as neonatal resuscitation, mechanical ventilation and nutritional management[3-6]. However, mortality and morbidity vary widely across countries or regions. Generally, more improvements have been gained in developed countries or regions, such as the United States[2, 7], the United Kingdom[8], Japan[9, 10] and Singapore[11].

Methods

Participating centers

The membership of the collaborative study group was the same as previously described[17]. In brief, twenty-six NICUs were united as a collaborative study group before clinical data collection. These NICUs were located in three regions with different economic development levels in Guangdong Province and were representative of medical units offering neonatal intensive care in their respective areas as we described before[17]. The Third Affiliated Hospital of Guangzhou Medical University was responsible for coordinating this study. This survey was approved by the Ethics Committees of the Third Affiliated Hospital of Guangzhou Medical University. The same diagnostic criteria were applied to all enrolled NICUs.

Subjects and data collection

All ELBW infants discharged from the collaborative NICUs were studied. The study protocol was fully discussed by all members, and a standardized questionnaire for data collection, including maternal and neonatal demographics, treatments, major complications and outcomes, was designed. The study was initiated at the end of 2012 and is still ongoing. Therefore, the data from January 1, 2008, to December 31, 2012, were collected retrospectively, and data from January 1, 2013, to December 31, 2017, were collected

prospectively. The relevant records of all enrolled infants and their mothers were reviewed, and a questionnaire was completed. All sheets were sent to the Third Affiliated Hospital of Guangzhou Medical University, and the data from each questionnaire were input into the database. To minimize bias among centers and investigators, comprehensive and systematic training was provided to the staff involved in the survey. The data collected by the researchers at each collaborative NICU were supervised and checked by the director of the NICU, who was responsible for quality assurance. The records were also checked for accuracy and completeness by collaborative centers.

Definitions and classifications

In this survey, surviving infants were defined as neonates who survived to the time of discharge. GA was calculated from the date of the last menstrual period or was determined by fetal ultrasound assessment. Neonatal respiratory distress syndrome (NRDS) was diagnosed in preterm infants with the onset of respiratory distress shortly after birth and a compatible chest radiograph appearance[18]. Bronchopulmonary dysplasia (BPD) was defined as continuous oxygen dependency at 28 days of age[19]. The criteria utilized in our survey for the diagnosis of necrotizing enterocolitis (NEC) and for grading the severity of disease were based on Bell's stage[20]. Retinopathy of prematurity (ROP) and the graded standard were defined by the international classification of ROP[21]. Intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL) were diagnosed by cranial ultrasonography or magnetic resonance imaging (MRI). The Papile grading system was used to grade IVH[22], and PVL was defined as degeneration of white matter adjacent to the cerebral ventricles following cerebral hypoxia or brain ischemia[23].

Statistical analysis

All statistical analyses were performed using SPSS 18.0 for Windows (IBM, Armonk, NY, USA). Continuous variables were presented as the means ± standard deviation (*SD*) when their distributions were highly skewed or as medians (*P*25, *P*75) when their distributions were not skewed and were analyzed using *t-tests* or *Mann-Whitney tests*. Categorical variables were presented as rates and odds ratios with 95% confidence intervals (*CIs*), which were analyzed using chi-square tests. $P < 0.05$ was considered statistically significant.

Results

Demographics of ELBW infants and mothers

From 2008 to 2017, 2575 ELBW infants were enrolled in this survey. The overall survival rate at discharge was 55.11% (1419 of 2575). The lowest BW in the survivors was 480 grams. In total, the median BW was 900 (800, 950) grams, and the distribution ranged from 22 (0.85%) for less than 500 grams, 52 (2.02%) for 500 – 599 grams, 150 (5.83%) for 600 – 699 grams, 372 (14.45%) for 700 – 799 grams, 685 (26.60%) for 800 – 899 grams to 1294 (50.25%) for 900 – 999 grams. The mean GA was 27.96 ± 2.06 weeks, and the distribution ranged from 26 (1.01%) for less than 24 weeks, 102 (3.96%) for 24 weeks, 246 (9.55%) for 25 weeks, 420 (16.31%) for 26 weeks, 515 (20.00%) for 27 weeks, 521 (20.23%) for 28 weeks, 315 (12.23%) for 29 weeks to 430 (16.70%) for equal to or above 30 weeks.

To clarify the current treatment and outcome of ELBW infants, we specifically grouped the ELBW infants based on whether they survived, as presented in Table 1. Both the BW and GA in the survivor group were greater than those in the nonsurvivor group ($p < 0.001$). In the survivor group, there were fewer infants with Apgar scores ≤ 3 at 1 min and ≤ 3 or 4□7 at 5 min (all $p < 0.001$). The survivor group had a longer hospital stay and a higher rate of receiving surfactant therapy ($p < 0.001$), but there was no significant difference between those who required two or more doses of surfactant therapy. No significant difference in sex was found between the survivor and nonsurvivor groups.

Table 1
Demographics of extremely low birth weight (ELBW) infants and the mothers in outcome categories

Characteristics	Survivors (N=1419)	Non-survivors (N=1156)	*OR* (*95%CI*)	*p*-value
Characteristics of infants				
Gender (male), n (%)	745 (52.50)	623 (53.89)	0.946 (0.809-1.105)	NS
GA (weeks), mean ± SD	28.37 ± 1.95	27.45 ± 2.08	/	<0.001
BW (grams), median (P25, P75)	910 (840, 960)	850 (750, 930)	/	<0.001
Apgar score, n (%)				
≤ 3 at 1 min	125 (8.81)	209 (18.08)	0.438 (0.345-0.555)	<0.001
4~7 at 1 min	479 (33.76)	431 (37.28)	0.857 (0.729-1.008)	NS
≤ 3 at 5 min	14 (0.99)	48 (4.15)	0.230 (0.126-0.498)	<0.001
4~7 at 5 min	148 (10.23)	251 (21.71)	0.420 (0.337-0.523)	<0.001
Surfactant therapy (any dose), n (%)	1150 (81.04)	801 (69.29)	1.895 (1.579-2.274)	<0.001
Surfactant therapy (two doses or more), n (%)	166 (11.70)	164 (14.19)	0.801 (0.636-1.010)	NS
Length of hospital stay (days), median (P25, P75)	69 (53, 85)	3 (1, 11)	/	<0.001
Characteristics of mothers				
History of bad motherhood[a], n (%)	589 (41.51)	452 (39.10)	1.105 (0.943-1.295)	NS
Age ≥35 years, n (%)	310 (21.85)	221 (19.12)	1.183 (0.975-1.435)	NS
Cesarean section, n (%)	691 (48.70)	399 (34.52)	1.801 (1.535-2.113)	<0.001
Twin/multiple pregnancy, n (%)	530 (37.35)	466 (40.31)	0.883 (0.753-1.035)	NS
Antenatal corticosteroid, n (%)	800 (56.38)	467 (40.40)	1.907 (1.629-2.232)	<0.001
Premature rupture of membranes, n (%)	342 (24.10)	203 (17.56)	1.491 (1.228-1.810)	<0.001
Infection in perinatal period, n (%)	78 (5.50)	62 (5.36)	1.026 (0.728-1.446)	NS
Gestational diabetes mellitus, n (%)	123 (8.67)	84 (7.27)	1.211 (0.907-1.617)	NS
Pregnancy induced hypertension syndrome, n (%)	398 (28.05)	240 (20.76)	1.488 (1.239-1.787)	<0.001

[a]History of bad motherhood refers to that the mother had at least one of the histories as follow: spontaneous abortion, induced abortion, stillbirth, preterm birth, ectopic pregnancy, or baby died during neonatal period. GA: Gestational age; BW: Birth weight; SD: Standard deviation; P25: The 25th percentile; P75: The 75th percentile; OR: Odds ratio; CI: Confidence intervals; NS: No significant difference.

Characteristics	Survivors (N=1419)	Non-survivors (N=1156)	*OR* (*95%CI*)	*p*-value
Placental abruption/Placenta previa, n (%)	115 (8.10)	101 (8.74)	0.921 (0.697-1.218)	NS
Cervical incompetence, n (%)	20 (1.41)	35 (3.03)	0.458 (0.263-0.798)	0.01
Fetal distress, n (%)	108 (7.61)	64 (5.54)	1.406 (1.021-1.935)	0.05

[a]History of bad motherhood refers to that the mother had at least one of the histories as follow: spontaneous abortion, induced abortion, stillbirth, preterm birth, ectopic pregnancy, or baby died during neonatal period. GA: Gestational age; BW: Birth weight; SD: Standard deviation; P25: The 25th percentile; P75: The 75th percentile; OR: Odds ratio; CI: Confidence intervals; NS: No significant difference.

The mothers in the survivor group had a higher proportion of antenatal steroid therapy and cesarean section (both $p < 0.001$) but a lower incidence of cervical incompetence ($p < 0.01$). Interestingly, the mothers in the survivor group even had higher incidences of premature rupture of membranes ($p < 0.001$), fetal distress ($p < 0.05$) and pregnancy-induced hypertension syndrome ($p < 0.001$). Between the survivor and nonsurvivor groups, there was a similar incidence in the history of pregnancy problems, as in mother's age (≥ 35 years), multiple pregnancy (twins/triplets), infection in the perinatal period, gestational diabetes mellitus, or placental disease (placental abruption/placenta previa).

Both the number and survival rates of ELBW infants increased from 2008 to 2017. The number of ELBW infants discharged from the involved NICUs increased rapidly from 91 cases in 2008 to 466 cases in 2017, as shown in Table 2. Moreover, the proportion of ELBW infants among all discharged preterm infants rose annually from 1.09% in 2008 to 2.62% in 2017 ($p < 0.001$), and the proportion of ELBW infants among all discharged infants increased annually from 0.27% in 2008 to 0.77% in 2017 ($p < 0.001$, Fig. 1). It was encouraging that the survival rate of ELBW infants improved steadily from 41.76% in 2008 to 62.02% in 2017 ($p < 0.001$, Table 2).

Table 2
The survival rate of extremely low birth weight (ELBW) infants at discharge from 2008 to 2017

Discharged year	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	*p*-value
ELBW infants, n	91	102	114	237	210	244	308	340	463	466	/
Survived, n (%)	38 (41.76)	48 (47.06)	56 (49.12)	110 (46.41)	110 (52.38)	136 (55.74)	164 (53.25)	195 (57.35)	273 (58.96)	289 (62.02)	0.001
Died despite active treatment, n (%)	13 (14.29)	14 (13.73)	17 (14.91)	39 (16.45)	23 (10.95)	27 (11.07)	57 (18.51)	61 (17.94)	77 (16.63)	60 (12.88)	/
Died after medical care withdrawal, n (%)	40 (43.96)	40 (39.22)	41 (35.96)	88 (37.13)	77 (36.67)	81 (33.20)	87 (28.25)	84 (24.71)	113 (24.41)	117 (25.11)	/

R×2 Chi-square test (linear-by-linear association) showed that the annual survival rate of ELBW infants improved from 2008 to 2017 (*P* 0.001). ELBW: Extremely low birth weight.

Survival rates of ELBW infants improved with increasing BW

With the increase in BW, the number of ELBW infants increased sharply from 22 in the group with BW < 500 grams to 1294 in the group with BW 900 – 999 grams, as demonstrated in Table 3. Only one infant survived with BW < 500 grams. However, the survival

rate rose dramatically from 30.77% in the group with BW 500 – 599 grams to 65.53% in the group with BW 900 – 999 grams (p < 0.001). Of course, the survival rate of infants weighing 500 – 749 grams was lower than that of infants weighing 750 – 999 grams (35.15% (129 of 367) *vs.* 58.97% (1289 of 2186), OR = 0.377, 95% CI: 0.300 – 0.475, p < 0.001).

Table 3
The survival rate of extremely low birth weight (ELBW) infants in relation to birth weight

Birth weight (grams)	≤500	500～599	600～699	700～799	800～899	900～999	*p*-value
ELBW infants, n	22	52	150	372	685	1294	/
Survived, n (%)	1 (4.55)	16 (30.77)	46 (30.67)	145 (38.98)	363 (52.99)	848 (65.53)	＜0.001
Died despite active treatment, n (%)	2 (9.09)	15 (28.85)	43 (28.67)	63 (16.94)	110 (16.06)	155 (11.98)	/
Died after medical care withdrawal, n (%)	19 (86.36)	21 (40.38)	61 (40.67)	164 (44.09)	212 (30.95)	291 (22.49)	/

R×2 Chi-square test (linear-by-linear association) showed that the survival rate of ELBW infants improved with increasing birth weight (*P*＜0.001). ELBW: Extremely low birth weight.

Variations in survival rates among different regions

According to the level of economic development where the NICUs were located, the collaborative NICUs could be divided into three categories. Specifically, Guangzhou and Shenzhen (including eleven NICUs) had a high level, the other cities in the Pearl Delta (including ten NICUs) had a medium level, and the cities outside the Pearl Delta (including five NICUs) had a low level of development. From the low to the high level, the mean GA of ELBW infants was 28.26 ± 2.04 weeks, 28.13 ± 2.01 weeks and 27.80 ± 2.08 weeks, which showed a mild deceasing tendency (r=0.090, p < 0.001), while no significant difference was found in BW (the median BW was 885 (800, 950) grams, 900 (813, 960) grams and 890 (790, 950) grams, respectively). However, the overall survival rates increased with the ascending level of regional economic development (p < 0.05). This is shown in Table 4.

Table 4
Differences of survival rate among regions or between hospitals

	Economic development levels of region				Types of hospital		
	Low-level	Middle-level	High-level	p-value	Specialist hospitals	General hospitals	p-value
NICUs, n	5	10	11	/	7	19	/
ELBW infants, n	352	728	1495	/	1068	1507	/
Survived, n (%)	175 (49.72)	400 (54.95)	844 (56.45)	＜0.05	642 (60.11)	777 (51.56)	＜0.001
Died despite active treatment, n (%)	69 (19.60)	93 (12.77)	226 (15.12)	/	133 (12.45)	255 (16.92)	/
Died after medical care withdrawal, n (%)	108 (30.68)	235 (32.28)	425 (28.43)	/	293 (27.43)	475 (31.52)	/

R×2 Chi-square test (linear-by-linear association) showed that the overall survival rate of ELBW infants discharged from different regions improved with the ascending level of economic development (*P*＜0.05). And 2×2 Chi-square test showed that the survival rate of ELBW infants discharged from specialist hospitals was higher than those from general hospitals (*P*＜0.001). NICUs: Neonatal intensive care units; ELBW: Extremely low birth weight.

Variations in survival rates between general hospitals and specialist hospitals

Among the twenty-six NICUs involved, seven were in specialist hospitals (maternal and children's hospitals), and the others were in general hospitals. The median BW and mean GA of ELBW infants discharged from specialist hospitals (880 (790, 950) grams and 27.59 ± 2.03 weeks, respectively) were both smaller than those of infants discharged from general hospitals (900 (800, 950) grams and 28.22 ± 2.05 weeks, respectively, both $p < 0.001$). However, the overall survival rate of ELBW infants discharged from specialist hospitals was higher than that of infants discharged from general hospitals (OR = 1.416, 95% CI: 1.208 – 1.660, $p < 0.001$) (Table 4).

Complications of ELBW infants during hospitalization

The incidence of complications was high in ELBW infants: 85.2% for NRDS, 63.7% for BPD at 28 days of age, 39.3% for ROP, 29.4% for IVH, 12.0% for NEC and 8.0% for PVL in total. The calculated incidence of complications in each BW group is listed in Table 5. To identify the difference relative to BW, comparisons were made between groups with BW 500-749 grams and 750-999 grams. The group with BW 500-749 grams had higher incidence than the group with BW 750-999 grams in NRDS (91.3% *vs.* 84.0%, OR=1.989, 95% CI:1.360-2.909, $p < 0.001$), BPD (83.3% *vs.* 61.4%, OR=3.144, 95% CI: 1.981-4.989, $p < 0.001$), ROP (49.4% *vs.* 38.2%, OR=1.580, 95% CI: 1.139-2.191, $p < 0.01$) or ROP above stage III (19.8% *vs.* 9.0%, OR=2.498, 95% CI: 1.626-3.838, $p < 0.001$), IVH (37.7% *vs.* 27.9%, OR=1.564, 95% CI: 1.178-2.078, $p < 0.01$) or severe IVH (15.5% *vs.* 6.3%, OR=2.708, 95% CI: 1.807-4.057, $p < 0.001$), and NEC (17.2% *vs.* 11.4%, OR=1.615, 95% CI: 1.118-2.333, $p < 0.05$). There was no significant difference in the incidence of NEC above stage IIb (2.9% *vs.* 1.7%, OR=1.705, 95% CI: 0.740-3.925) or PVL (5.4% *vs.* 8.5%, OR=0.622, 95% CI: 0.346-1.117) between the two groups (Fig. 2).

Table 5
The incidence of complications during hospitalization in ELBW infants

	≤500g (n=22)	500-599g (n=52)	600-699g (n=150)	700-799g (n=372)	800-899g (n=685)	900-999g (n=1294)	Total (n=2575)
NRDS							
Assessed, n	22	52	150	372	685	1294	2575
Diagnosed, n (%)	21(95.5)	46(88.5)	141(94.0)	331(89.0)	579(84.5)	1075(83.1)	2193(85.2)
BPD at 28 days of age							
Assessed, n	5	18	58	140	360	821	1402
Diagnosed, n (%)	5(100.0)	16(88.9)	46(79.3)	111(79.3)	249(69.2)	466(56.8)	893(63.7)
ROP							
Assessed, n	5	22	71	187	412	819	1516
Diagnosed (any grade), n (%)	1(20.0)	10(45.5)	32(45.1)	77(41.2)	155(37.6)	321(39.2)	596(39.3)
Diagnosed (≥ grade 3), n (%)	0	8(36.4)	10(14.1)	29(15.5)	44(10.7)	62(7.6)	153(10.1)
NEC							
Assessed, n	12	38	102	242	508	1074	1976
Diagnosed (any stage), n (%)	0	6(15.8)	19(18.6)	32(13.2)	52(10.2)	128(11.9)	237(12.0)
Diagnosed (≥ stage ≥b), n (%)	0	1(2.6)	5(4.9)	5(2.1)	15(3.0)	21(2.0)	37(1.9)
IVH							
Assessed, n	12	38	92	252	493	958	1845
Diagnosed (any grade), n (%)	8(66.7)	15(39.5)	38(41.3)	95(37.7)	140(28.4)	246(25.7)	542(29.4)
Diagnosed (≥ grade ≥), n (%)	6(50.0)	6(15.8)	16(17.4)	32(12.7)	33(6.7)	51(5.3)	144(7.8)
PVL							
Assessed, n	12	38	92	252	493	958	1845
Diagnosed, n (%)	0(0)	1(2.6)	5(5.4)	20(7.9)	45(9.1)	77(8.0)	148(8.0)

BPD was assessed in infants who survived more than 28 days. ROP was assessed in infants who had undergone fundus examination. NEC was assessed in infants who survived more than 48 hours. IVH and PVL were assessed in infants who had undergone transcranial ultrasound or MRI examination. NRDS: Neonatal respiratory distress syndrome; BPD: Bronchopulmonary dysplasia; ROP: Retinopathy of prematurity; NEC: Necrotizing enterocolitis; IVH: Intraventricular hemorrhage; PVL: Periventricular leukomalacia.

Survival days of the nonsurvivors and the causes for care withdrawal

Among the 1156 nonsurvivors, 90.0% (1040 of 1156) of infants died during the neonatal period (≤ 28 days), and the other 10.0% (116 of 1156) died after the neonatal period (> 28 days). Specifically, 27.2% (314 of 1156) of infants died during the first 24 hours, 16.4% (190 of 1156) on the second day, 9.4% (109 of 1156) on the third day, 15.2% (176 of 1156) during the fourth to seven days, 9.7% (112 of 1156) in the second week, 7.4% (85 of 1156) in the third week and 4.7% (54 of 1156) in the fourth week. The survival

days (or hours) of nonsurvivors under active treatment or after medical care withdrawal are shown in Table 6. The chi-square test showed that there was a significant difference in the distribution of survival days between the two groups ($p < 0.001$).

Table 6
Survival days (or hours) of the non-survivors

Age of death	ENP				LNP			ANP
	≤24 h	2 d	3 d	7 d	14 d	21 d	28 d	28 d
Died despite active treatment, n (%)	80(20.6)	58(14.9)	33(8.5)	57(14.7)	43(11.1)	26(6.7)	25(6.4)	66(17.0)
Died after medical care withdrawal, n (%)	234(30.5)	132(17.2)	76(9.9)	119(15.5)	69(9.0)	59(7.7)	29(3.8)	50(6.5)
Total, n (%)	314(27.2)	190(16.4)	109(9.4)	176(15.2)	112(9.7)	85(7.4)	54(4.7)	116(10.0)
ENP: early neonatal period; LNP: late neonatal period; ANP: after neonatal period								

In this study, 768 ELBW infants died after medical care withdrawal. The causes were summarized and analyzed. Economic and outcome factors were both important. More specifically, for 35.9% (276 of 768) of infants, there were concerns about the economic burden together with the fear of poor or uncertain outcomes; for 29.6% (227 of 768) of infants, there were only fears of poor or uncertain outcomes; and for 14.7% (113 of 768) of infants, there were concerns only about the economic burden. For 1.6% (12 of 768) of infants, medical care was withdrawn due to other factors, such as gender preference, but for 18.2% (140 of 768) of infants, the exact reasons were not mentioned.

Disussion

The outcome of ELBW infants has become a hot topic in recent decades worldwide. In this study, we confirmed that the number of ELBW infants increased rapidly from 2008 to 2017 in Guangdong Province, China. At the same time, the survival rate improved steadily year by year. These data from China provide helpful information to complement the understanding of ELBW infants from developing countries.

Similar to reports from other countries, our study has suggested an increase in ELBW infants. From the 1990s or 2000s, the number of ELBW infants began to increase in many developed countries[24-26]. In our study, we also see a significant increase in ELBW infants over the ten years, from 1.09 per 1000 discharged infants in 2008 to 2.62 per 1000 discharged infants in 2017. A 2.4-fold increase is noted. Although this is not a national population-based survey, it can partly reflect the situation of ELBW infants in China.

The improvement in the outcome of ELBW infants depends on the development of the economy and the advancement of medicine. During the past decades, the mortality rate of ELBW infants has decreased in many developed countries or regions. In Japan, the neonatal mortality rate and the mortality rate of ELBW infants during NICU stays were 13.0% and 17.0% in 2005[9]. In the United States, the standardized mortality rates for infants weighing 501-750 grams and 751-1000 grams in 2009 were 36.6% and 11.7%, respectively[27]. In Korea, the survival rate of ELBW infants increased dramatically from 14.0% in 1985-1989 to 69.6% in 2010-2014[28]. However, in China, it was reported that just half of ELBW infants survived in 2011[29]. In our survey, the overall survival rate of ELBW infants at discharge was 55.11%, while it was 46.41% in 2011. An encouragingly improving tendency was found, from 41.76% in 2008 to 62.02% in 2017. This reflects the great progress gained.

The achievement of economic development can promote advancements in medicine. We found that the survival rate of ELBW infants in different regions was positively correlated with the level of economic development. Hong Kong, a developed modern city neighboring Guangdong Province but not involved in this study, reports a higher survival rate[30]. In China, specialist hospitals, such as children's hospitals or maternal and children's hospitals, have more and better facilities in neonatal care than general hospitals. As a result, a higher survival rate was noted in the specialist hospitals in our study. A similar phenomenon was found in another multicenter study from China[30].

Perinatal management is essential for the outcomes of ELBW infants. Many studies have shown that antenatal corticosteroids effectively decrease the mortality of preterm infants and even reduce various complications, such as NRDS, NEC, IVH and ROP[31, 32]. Although there is still some controversy regarding the side effects[33], there is a consensus that the advantages of prenatal corticosteroids outweigh the disadvantages[4, 34]. Unfortunately, only 49.2% of infants' mothers received antenatal corticosteroids in this study, but this figure was 80%-90% in developed countries[12, 35, 36]. Therefore, this situation should be changed as soon as possible.

Interestingly, many studies have shown that the premature rupture of membranes (PROM) and pregnancy-induced hypertension (PIH) syndrome are high-risk factors for premature delivery and infant death[37, 38], but our study showed that the incidence of PROM and PIH syndrome in the survivor group was higher than that in the nonsurvivor group. Moreover, cesarean section was more common in the survivor group. A possible explanation is that PROM or PIH syndrome could have been an early warning that attracted the attention of pregnant women and led them go to the hospital for help in a timely manner. When they were admitted to the hospital, more active medical care, such as antenatal corticosteroids, cesarean section, neonatal resuscitation and pulmonary surfactant, was given. Nevertheless, the other potential reasons still need to be further studied and analyzed.

ELBW infants are unstable and tend to suffer various complications due to their prematurity. Without active life support, many infants die during the neonatal period, especially in the first 7 days of age, and some die due to critical illnesses despite receiving active treatments. In our study, 90.0% of nonsurviving infants died during the neonatal period, while nearly 68.3% died in the first 7 days, and the majority died after medical care withdrawal (Table 6). Although active treatment withdrawal in these infants is a controversial issue, it truly exists in developing countries because of the high hospital costs in addition to the high risk for later complications[39]. We can reasonably believe that the outcomes of ELBW infants will continue to improve with the continued economic development and advancement of medicine in China.

Conclusion

In conclusion, this survey presents an overall outcome of ELBW infants in China. Both the number and the survival rate of ELBW infants increased annually from 2008 to 2017. To the best of our knowledge, this study covers the largest population sample and the longest time span addressed by such studies on ELBW infants in China to date. It can provide helpful information for family consultation, clinical practice and further research. However, there are some limitations in this study. First, it is not a population-based or nationwide study. Second, the long-term outcomes of ELBW infants are not addressed, and further studies are needed.

Abbreviations

ELBW: extremely low birth weight; GA: gestational age; BW: birth weight; NICUs: neonatal intensive care units; NRDS: neonatal respiratory distress syndrome; BPD: bronchopulmonary dysplasia; NEC: necrotizing enterocolitis; ROP: Retinopathy of prematurity; IVH: Intraventricular hemorrhage; PVL: periventricular leukomalacia; MRI: magnetic resonance imaging; CIs: confidence intervals

Declarations

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Authors' contributions

FW conceptualized and designed the study, carried out the initial analyses, drafted the initial manuscript, and completed its final submitted version. CHJ, ZSF, SSH, CZY, YHD, XZY, LD, HXC, ZZ, WMH, BYY, LYH, HPR, YY, DL, SGD, CMY, BW, YGH, WZL, YLC, ZFC, XYL, NYL, ZHW, BB, YXY collected data, carried out the initial analyses, interpreted data and and critically revised the manuscript. XJL, QLC, YJ, GSL, XTY, WYL, JM, BQW, CWL, XR, WS, JFL, HWH, WKY, XJR, FFW, XYL, QM, LJZ, DA, JLC, WL, YQD, YFH, YFC, YB and GHL managed data collection instruments, collected data. All authors approved the final manuscript as submitted.

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Availability of data and materials

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

Ethics approval and consent to participate

Data collection was approved by the Institutional Review Board of the Third Affiliated Hospital of Guangzhou Medical University. Written consent was obtained from the parents at the time of admission.

Consent for publication

Not applicable.

Competing interests

The authors have no conflicts of interest to declare.

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Figures

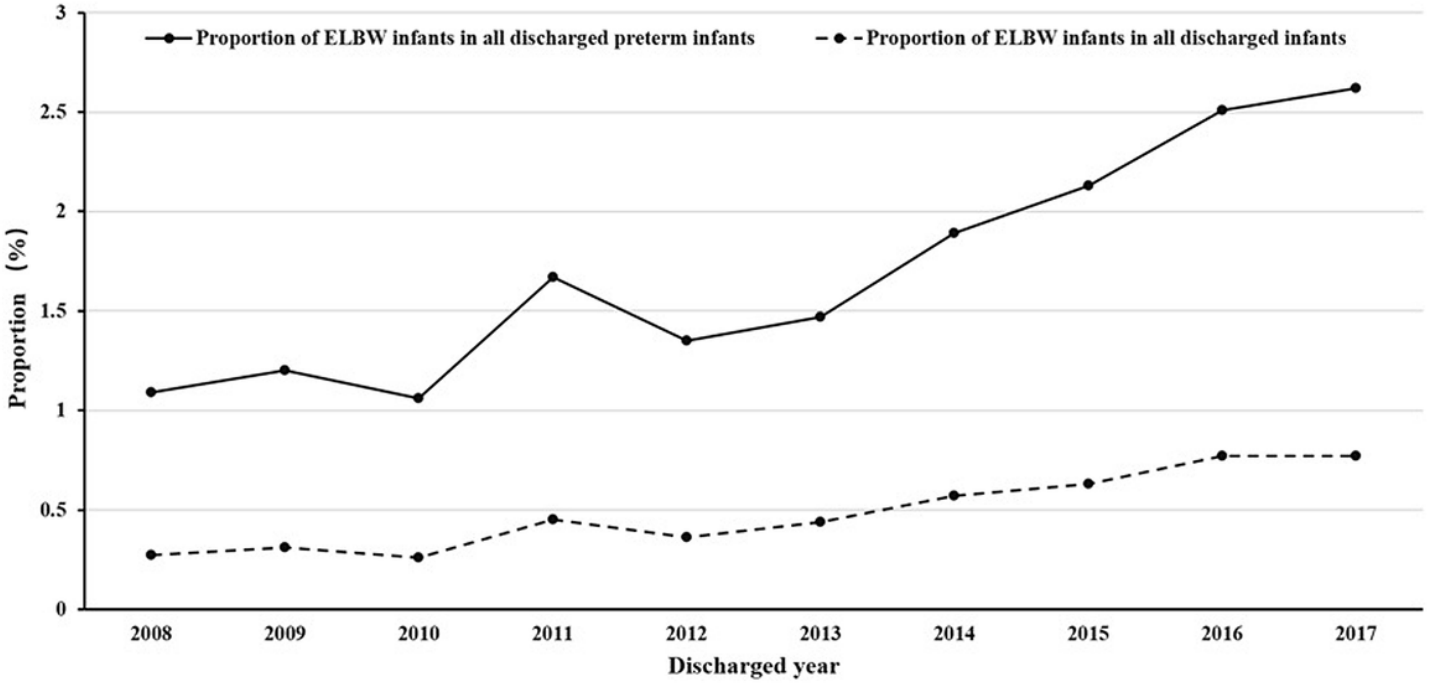

Figure 1

The proportion of ELBW infants in all discharged preterm infants or in all discharged infants from 2008 to 2017. R×2 Chi-square test (linear-by-linear association) showed that the proportions of ELBW infants in all discharged preterm infants or in all discharged infants increased annually (both P□0.001).

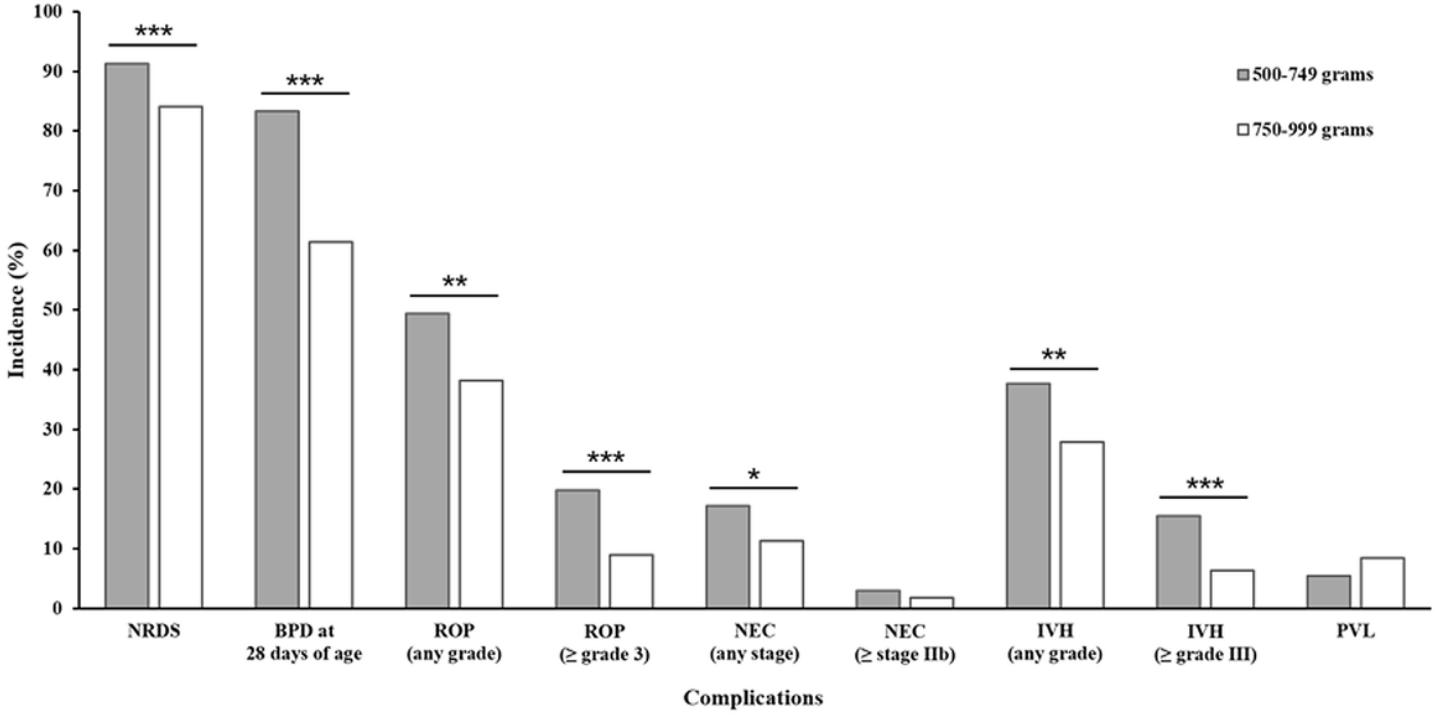

Figure 2

The incidence of complications between groups with a birth weight of 500-749 grams and 750-999 grams. NRDS: Neonatal respiratory distress syndrome; BPD: Bronchopulmonary dysplasia; ROP: Retinopathy of prematurity; NEC: Necrotizing enterocolitis; IVH: Intraventricular hemorrhage; PVL: Periventricular leukomalacia. ***: P□0.001; **: P□0.01; *: P□0.05