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A real-world study on the treatment of extremely preterm infants: a multi-center study in southwest area of Fujian Province in China

Liang Gao[1,2,3†], Dong-mei Chen[4†], Hui-ping Yan[4], Li-ping Xu[5†], Shu-zhen Dai[5], Rong-hua Zhong[6†], Qi-bing Chen[6], Si-min Ma[1,2,3] and Xin-zhu Lin[1,2,3*]

Abstract

Background Due to regional and cultural differences, the current status of extremely preterm infants(EPIs) treatment across different areas of mainland China remains unclear. This study investigated the survival rate and incidence of major diseases among EPIs in the southwest area of Fujian province.

Method This retrospective and multicenter study collected perinatal data from EPIs with gestational ages between 22–27^{+6}w and born in the southwest area of Fujian province. The study population was divided into 6 groups based on gestational age at delivery. The primary outcome was the survival status at ordered hospital discharge or correct gestational age of 40 weeks, and the secondary outcome was the incidence of major diseases. The study analyzed the actual survival status of EPIs in the area.

Result A total of 2004 preterm infants with gestational ages of 22–27^{+6} weeks were enrolled in this study. Among them, 1535 cases (76.6%) were born in the delivery room but did not survive, 469 cases (23.4%) were transferred to the neonatal department for treatment, 101 cases (5.0%) received partial treatment, and 368 cases (18.4%) received complete treatment. The overall all-cause mortality rate was 84.4% (1691/2004). The survival rate and survival rate without major serious disease for EPIs who received complete treatment were 85.1% (313/368) and 31.5% (116/318), respectively. The survival rates for gestational ages 22–22^{+6}w, 23–23^{+6}w, 24–24^{+6}w, 25–25^{+6}w, 26–26^{+6}w, and 27–27^{+6}w were 0%, 0%, 59.1% (13/22), 83% (39/47), 88.8% (87/98), and 89.7% (174/198), respectively. The survival rates without major serious disease were 0%, 0%, 9.1% (2/22), 19.1% (9/47), 27.6% (27/98), and 40.2% (78/194), respectively.

Conclusion The all-cause mortality of EPIs in the southwest area of Fujian Province remains high, with a significant number of infants were given up after birth in the delivery room being the main influencing factor. The survival rate

†Liang Gao, Dong-mei Chen, Li-ping Xu and Rong-hua Zhong contributed equally to this work.

*Correspondence:
Xin-zhu Lin
xinzhufj@163.com

Full list of author information is available at the end of the article

of EPIs who received complete treatment at 25–27 weeks in the NICU was similar to that in developed countries. However, the survival rate without major serious disease was significantly lower compared to high-income countries.

Keywords Extremely preterm infants, Mortality, Survival rate, Survival rate without major serious disease

Introduction

The World Health Organization (WHO) Global Report on preterm infants first introduced the concept of extremely preterm infants (EPIs) in 2012, referring to preterm infants with a gestational age < 28 weeks [1]. This accounts for 0.57% of the total number of deliveries and about 5% of all preterm infants. Due to the extremely underdeveloped state of their organs, EPIs face a high risk of death and disease after birth, requiring intensive and costly care for survival. Disparities in healthcare resources result in significant regional differences in EPIs survival rates, with a 90% chance of survival in developed countries compared to only 10% in low-income countries [2]. The Chinese Neonatal Network retrospectively analyzed data from 2010 to 2019 [3], showing that the survival rate of infants born at gestational ages 24 to 27 weeks and transferred to the NICU increased from 56.4% in 2010 to 68.0% in 2019. The survival rates for infants born at gestational ages 22, 23, 24, 25, 26, and 27 weeks were 4.8%, 18.3%, 35.3%, 48.6%, 61.0%, and 69.1%, respectively. Cao Yun et al. [4]. have analyzed data from 9552 cases EPIs from 57 neonatal centers in Chinese mainland and found that the survival rates and rates of survival without major diseases for EPIs at gestational ages < 24, 24, 25, 26, and 27 weeks were 21.7% vs. 0, 55.8% vs. 7.7%, 75.2% vs. 13%, 87.7% vs. 25.2%, 89.7% vs. 39.8%, respectively. In high-income countries, EPIs care is more advanced. A multicenter study in the United States revealed that out of 10,877 infants born at a gestational age of 22–28 weeks between 2013 and 2018 [5], the survival rate at discharge was 78.3%, and the survival rate at the discharge of preterm infants born at a gestational age of 22 weeks was 10.9%. The survival rates at discharge of preterm infants with gestational age of 22 weeks and 23 weeks who received active treatment were 30.0% and 55.8%, respectively. A 2017 multicenter survey in developed countries like Japan, Sweden, and Australia found overall EPIs survival rates ranging from 73–92% [6]. French national studies on EPIs born at gestational ages 23 to 27 weeks from 2011 to 2015 showed severe disease-free survival rates of 0%, 41.2%, 54.5%, 65.3%, and 71.9%, respectively [7]. These studies indicate positive outcomes for EPIs treatment in China, however, preterm birth is still one of the key issues in maternal and child health in China [8]. There were two issues persist when compared to developed countries: (1) While the survival rate of EPIs with gestational ages of 26–28 weeks is comparable to developed countries, the survival rate of infants with gestational ages < 25 weeks, especially those with gestational ages of 22–23^{+6} weeks, remains significantly lower. (2) The rate of survival without major disease is lower than that in developed countries. Due to regional and cultural differences, the current status of EPIs treatment across different areas of mainland China remains unclear. Therefore, this real-world study aims to explore the actual status of EPIs treatment in the four cities in the southwest of Fujian Province, offering insights into the development of treatment strategies for this special population.

Materials and methods

Study population

From January 2018 to December 2022, preterm infants with a gestational age of 22–27^{+6} weeks were born alive in hospitals located in the southwest region of Fujian province in China, including Xiamen, Quanzhou, Zhangzhou, and Longyan. The four centers were all perinatal and neonatal treatment centers in the region, equipped with obstetric wards and neonatal intensive care units. The neonatal wards were all classified as grade IIIB [9]. The annual deliveries in each center were around 5000–13,000 cases. A meeting of researchers has been held in advance to clarify the inclusion and exclusion criteria, and conform the EpiData software 3.1 for data entry. Inclusion criteria: (1) Preterm infants with a gestational age of 22–27^{+6} weeks. (2) Live-born infants delivered in obstetrics department of the four medical centers participating in the study. (3) Preterm infants who were delivered in other primary hospitals and subsequently transferred to the four medical centers participating in the study. Exclusion criteria: Termination of labor due to medical indications (fatal malformation).

Research method

This study was retrospective and multicenter. Perinatal data of EPIs born in the southwest area of Fujian province, were collected. The data collected included: (1) Maternal pregnancy data, including demographic, pregnancy, delivery information, and antenatal corticosteroids(ACS). (2) Neonatal characteristics: gestational age, delivery mode, birth weight, Apgar score. (3) Neonatal complications: neonatal respiratory distress syndrome (nRDS), necrotizing enterocolitis (NEC), hemodynamically significant patent ductus arteriosus (hsPDA), early-onset sepsis (EOS), late-onset sepsis(LOS), neonatal NEC ≥ Bell stage 2, intraventricular hemorrhage (IVH) grade III–IV, periventricular leukomalacia(PVL), retinopathy of prematurity(ROP)

requiring intervention, metabolic bone disease of prematurity (MBDP), and parenteral nutrition-associated cholestasis (PNAC), etc., diagnosed based on criteria from "Practical Neonatology (5th edition)" [10].According to the 2018 NICHD criteria for Bronchopulmonary dysplasia (BPD) [11], preterm infants with gestational age of <32 weeks at a corrected gestational age of 36 weeks had imaging evidence of substantial lung disease, and needed different degrees of respiratory support and corresponding levels of FiO_2 to maintain arterial oxygen saturation between 0.90 and 0.95 for at least 3 consecutive days. Then according to the different respiratory support mode of FiO_2 into I, II, III level. (4) Neonatal treatments: This encompassed feeding patterns, mechanical ventilation, non-invasive positive pressure ventilation support, postnatal glucocorticoid application, laser or drug intervention for ROP, etc.

The study population was divided into 6 groups based on gestational age at delivery. The primary outcome was the survival status at ordered hospital discharge or correct gestational age of 40 weeks. The secondary outcome was the incidence of major diseases. According to the treatment received, deceased infants were divided into three subgroups: (1)EPIs gave up in the delivery room: These infants were born after induced labor with signs of life but could not be transferred to the neonatal department for treatment. Unfortunately, they eventually died. (2)EPIs received partial treatment was defined as those who were transferred to the neonatal department but were discharged against medical advice, and the hospital stay less 7 days, and eventually died. (3)Death after receiving complete treatment covers infants who were discharged from the hospital against medical advice but the length of hospital stay was 7 days or more, or later passed away due to disease-related factors after receiving active treatment within the first 7 days.

Major serious diseases in this context encompass grade 3–4 IVH, PVL, II to III level BPD, grade 2 or above NEC, LOS, and ROP requiring intervention. Severe brain injury is defined as grade 3–4 IVH or PVL.

Statistic method

Statistical analysis was conducted using SPSS 24.0(IBM, IL, USA). Quantitative data with non-normal distribution were presented as median and interquartile range (IQR), and between-group comparisons were analyzed using the Kruskal-Wallis rank-sum test. Count data were expressed as the number of cases and percentage (%). Between-group comparisons were performed using Pearson's chi-square test, continuity correction of Pearson's chi-square test, and Fisher's exact probability method. A significance level of $P<0.05$ was applied for statistical significance.

Result

General condition

A total of 2004 cases EPIs with a gestational age of $22–27^{+6}$ weeks were enrolled in the study. Among them, 1121 (55.9%) were male, and 98 (4.9%) were delivered by cesarean section. The number of cases in the gestational age groups $22–22^{+6}$w, $23–23^{+6}$w, $24–24^{+6}$w, $25–25^{+6}$w, $26–26^{+6}$w, and $27–27^{+6}$w were 189, 223, 407, 428, 357, and 400 cases, respectively. 1535 cases EPIs were abandoned in the delivery room (76.6%), 469 cases (23.4%) were transferred to the neonatal department for treatment, 101 cases (5.0%) received partial treatment, and 368 cases (18.4%) received complete treatment, as shown in Fig. 1. Among the infants who received complete treatment, 235 cases (63.9%) were male, 58 cases (15.8%) had mothers who underwent assisted reproductive techniques, 98 cases (26.6%) had multiple pregnancies, and 247 cases (67.1%) received more than one dose of glucocorticoids. Significant differences existed in the rates of reproductive assistance, multiple pregnancies, and ACS among different gestational age subgroups ($P<0.05$), as shown in Table 1.

We have found that EPIs receiving complete care were associated with an older maternal age, a lower incidence of placental abruption, a higher incidence of premature rupture of membranes, and a higher rate of ACS, as well as a higher gestational age and a lower incidence of SGA. There were no significant differences between gender, mode of delivery, ART, GDM, HDCP, and multiplets, as shown in supplemental Table 1.

Care practice

A total of 368 EPIs cases received complete care, and the proportion of EPIs with complete care in each gestational age group was as follows: 0%, 3.1% (7/223), 5.4% (22/407), 11% (47/428), 27.5% (98/357), and 48.5% (194/400). This proportion increased with gestational age ($P<0.05$). Out of the 101 patients who were transferred to the NICU but eventually abandoned treatment, 90 (89.1%) were abandoned due to social factors. Among the 368 patients who received complete care, 354 (94%) received pulmonary surfactant (PS), 283 (79.4%) received mechanical ventilation, 146 (39.7%) received postnatal glucocorticoids, and 41 (13.1%) received interventions for retinopathy of prematurity (ROP). Additionally, 327 (88.9%) received breastfeeding, and 230 (62.5%) received human milk fortifier. Significant differences existed in the rates of mechanical ventilation, postnatal glucocorticoid use, breastfeeding, and ROP requiring intervention among different gestational age groups ($P<0.05$). There were no significant differences in the use of PS and human milk fortifier among different gestational age groups ($P>0.05$), as shown in Table 3.

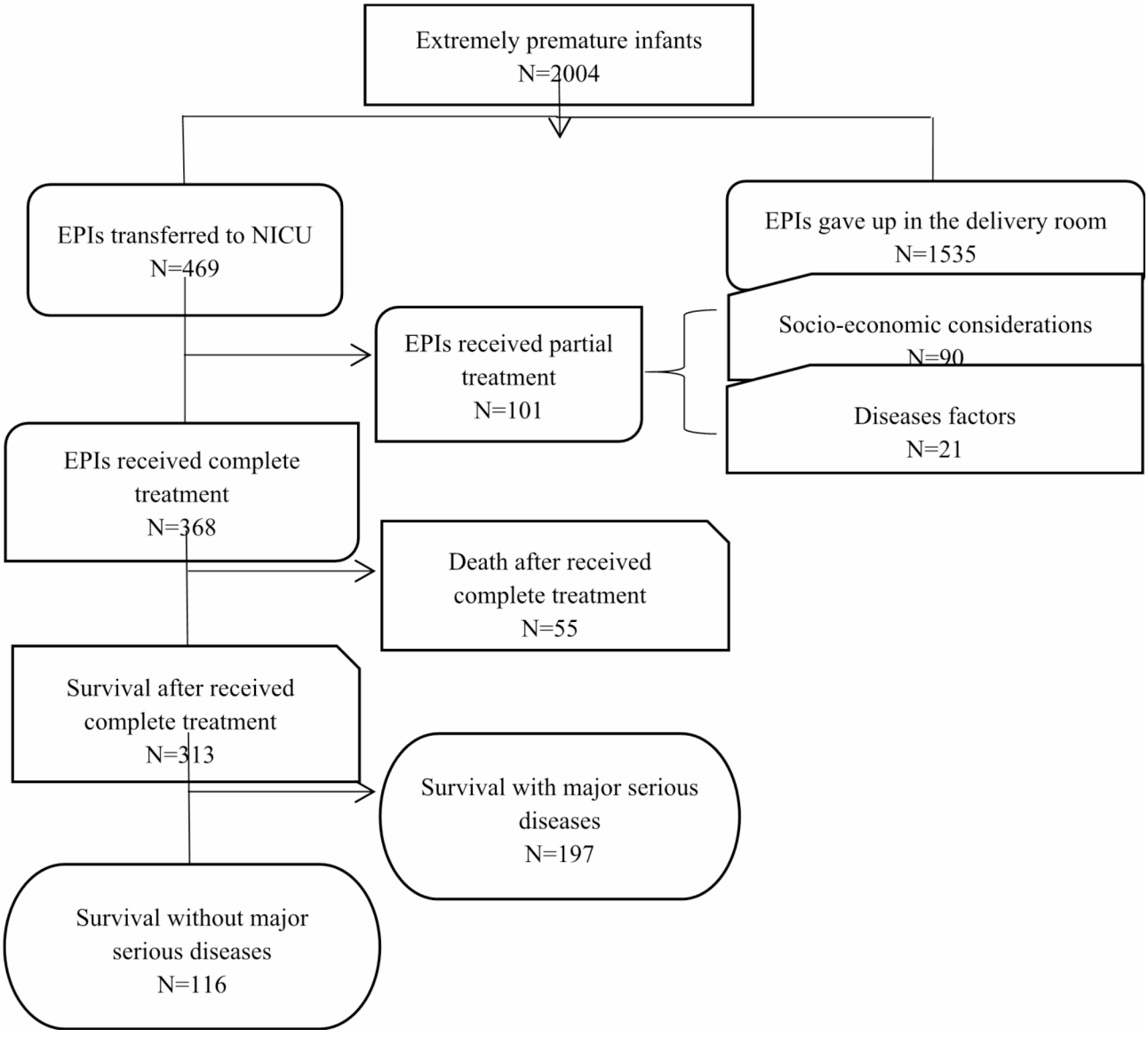

Fig. 1 Flow chart. Note: EPIs: Extremely premature infants

Morbidities

Among the 368 EPIs who received complete treatment, 118 cases had grade 3–4 RDS (32.1%), 132 cases had hsPDA (35.9%), 40 cases had grade 3–4 IVH (10.9%), 255 cases had ROP (69.8%), and 148 cases had II to III level BPD (40.2%). For EPIs with a gestational age between 25 and 27 weeks, the incidence of these diseases decreased with gestational age. Significant differences were observed in the incidence of major serious diseases among different gestational age groups, including grade 3–4 RDS, hsPDA, grade 3–4 IVH, and ROP ($P<0.05$). No significant differences were found in the incidences of II to III level BPD, grade≥2 NEC, MBDP, PNAC, VAP, EOS, and LOS among the different gestational age groups ($P>0.05$), as shown in Table 2.

Survival rate and survival rate without major serious diseases

EPIs had a high risk of postnatal mortality, with an all-cause mortality rate of 84.4% (1691/2004) observed in the overall study cohort. Among the 368 EPIs transferred to the NICU after birth and provided with comprehensive treatment, 313 (85.1%) survived. However, these surviving EPIs were at high risk for disease, and only 116 EPIs (31.5%) managed to remain free from major serious diseases throughout their hospitalization. In addition, the survival rate and the survival rate without major severe diseases increased with gestational age, and the differences between gestational age subgroups were statistically significant ($P<0.05$), as shown in Fig. 2.

Table 1 Characteristics of EPIs with gestation age < 28w receiving complete care

		N = 368	22–22^{+6}w *n* = 0	23–23^{+6}w *n* = 7	24–24^{+6}w *n* = 22	25–25^{+6} *n* = 47	26–26^{+6}w *n* = 98	27–27^{+6}w *n* = 194	Z/χ^2	*P*
Cesarean delivery		78(21.2)	-	1(14.3)	1(4.5)	1(2.1)	20(20.4)	55(28.4)	23.027	< 0.001
Birth weight		938(830,1058)	-	520(490,605)	655(600,700)	800(750,850)	900(830,993)	1020(933,1100)	170.525	< 0.001
SGA		52(14.2)	-	3(42.9)	5(22.7)	12(25.5)	16(16.3)	16(8.2)	16.835	0.001
Male		235(63.9)	-	6(85.7)	16(72.7)	34(72.3)	54(55.1)	125(64.4)	6.528	0.157
Transferred from another hospital		84(22.8)	-	2(28.6)	4(14.2)	8(17)	27(27.6)	43(22.2)	2.607	0.653
Maternal age		31(27,34)	-	28(28,34)	30(26,33.5)	30(28,36)	30(27,33)	32(27,34)	2.210	0.697
Assisted reproductive technology		58(15.8)	-	3(42.9)	6(28.6)	12(25.5)	16(16.3)	21(10.9)	13.094	0.008
ACS	no	121(32.9)	-	5(71.4)	9(40.9)	19(40.4)	32(32.7)	56(28.9)	22.223	0.005
	Imcomplete treatment	133(36.1)	-	2(28.6)	8(36.4)	23(48.9)	32(32.7)	68(35.1)		
	Complete treatment	114(31.0)	-	0	5(22.7)	5(10.6)	34(34.7)	70(36.1)		
GDM		49(13.3)	-	0	0	6(12.8)	11(11.2)	32(16.5)	5.931	0.177
HDCP		12(3.3)	-	0	0	2(4.3)	6(6.1)	4(2.1)	3.854	0.359
Multiplets		98(26.6)	-	3(42.9)	8(36.4)	20(42.6)	23(23.5)	44(22.7)	10.055	0.034
PROM		122(33.2)	-	2(28.6)	6(27.3)	13(27.7)	33(33.7)	68(35.1)	1.291	0.878
Placental abruption		22(6.0)	-	0	1(4.5)	3(6.4)	8(8.2)	10(5.2)	1.254	0.850

Data are presented as median(inter quartile range) or n (%); χ^2 is the statistic value of the Pearson's chi-square test or continuity correction of Pearson's chi-square test, and Z is the statistic value of the Kruskal-Wallis rank-sum test

Note: EPIs: extremely preterm infants; GDM: Gestational diabetes mellitus; HDCP: Hypertensive disease during pregnancy; ACS: antenatal corticosteroids; SGA: small for gestational age; PROM: premature rupture of membranes.

Discussion

Discrepancies in the definition of the perinatal period exist across regions. Presently, China's definition of the perinatal period adheres to the 1976 WHO standard, which designates it as gestational age ≥ 28 weeks up to 7 days postpartum, a notable departure from the definitions in developed nations [12]. The current guidelines from the Chinese Society of Obstetricians and Gynecologists, Chinese Medical Association, classify preterm infants as those born with a gestational age of 28–36^{+6} weeks [13]. Notably, the guidelines exclude preterm infants with a gestational age < 28 weeks, which is defined as a viable age after 24 weeks [14]. Infants born at 22–24 weeks of gestation are regarded as peri-survival infants. Consequently, due to this considerable discrepancy in China's perinatal period definition, these infant deaths aren't categorized as neonatal deaths but rather classified as miscarriages, escaping discussion within maternal and child health institutions at all levels. This situation has fostered a negative disposition among obstetricians toward the treatment of EPIs. Based on a 2021 cross-sectional survey on obstetricians' attitudes toward preterm infant care [15], a mere 27.2% of obstetricians advocated for lowering the gestational age threshold for preterm infant care. Neonatologists, on the other hand, exhibited a relatively higher willingness to treat EPIs. A study by Li Qiuping et al. [16]. revealed that 63.0% of surveyed pediatricians believed that the lower limit for actively resuscitating EPIs should be set at 25 weeks or lower. They endorsed a reduction in the lower gestational age threshold for preterm infant care. The overall willingness within this group to treat EPIs was markedly higher than that of obstetricians, yet still lower than that of pediatricians in developed countries [17]. The existing cognitive bias among obstetricians and pediatricians toward EPIs care is undoubtedly exerting a detrimental influence on the care of extremely preterm infants at younger gestational ages. The national perinatal academic community has acknowledged this reality, prompting the Society of Perinatal Medicine to propose that active care be provided to EPIs over 24 weeks of age, while EPIs between 22 and 23 weeks of age are not eligible for active care. This decision should involve comprehensive consultation with parents [18].

The willingness of obstetricians and family members plays a pivotal role in determining whether EPIs are admitted to the neonatal intensive care unit for treatment. The elevated risk of adverse outcomes and concerns about substantial financial burden constitute significant factors influencing treatment decisions for these preterm infants [19, 20], both from the perspective of parents and medical staff. Our study revealed that merely 23.4% of EPIs in the region were transferred to the NICU, and a strikingly high 76.6% abandonment rate was

Table 2 Morbidites and survival in EPIs with gestation age < 28w receiving complete care

		N **= 368**	**22–22^{+6}w *n* = 0**	**23–23^{+6}w *n* = 7**	**24–24^{+6}w *n* = 22**	**25–25^{+6} *n* = 47**	**26–26^{+6}w *n* = 98**	**27–27^{+6}w *n* = 194**	**Z/χ^2**	***P***
RDS	0	46(12.5)	-	2(28.6)	4(18.2)	4(8.5)	15(15.3)	21(10.8)	25.796	< 0.001
	1	204(55.4)	-	1(14.3)	9(40.9)	18(38.3)	49(50)	127(65.5)		
	2	118(32.1)	-	4(57.1)	9(40.9)	25(53.2)	34(34.7)	46(23.7)		
II to III level BPD		148(40.2)	-	2(28.6)	10(45.5)	24(51.1)	47(48)	65(33.5)	9/030	0.056
VAP		22(6.0)	-	1(14.3)	1(4.5)	4(8.5)	7(7.1)	9(4.6)	3.265	0.443
hsPDA		132(35.9)	-	0	9(40.9)	24(51.1)	35(35.7)	64(33)	9.500	0.045
ROP		255(69.8)	-	1(14.3)	11(50)	39(83)	76(77.6)	130(67)	20.380	< 0.001
ROP requiring intervention		41(13.1)	-	1(14.3)	4(18.2)	8(17.0)	16(16.3)	13(6.7)	10.209	0.027
NEC ≥ 2		29(7.9)	-	0	1(4.5)	4(8.5)	12(12.2)	12(6.2)	3.410	0.445
BI		84(22.8)	-	2(28.6)	7(31.8)	16(34)	21(21.4)	38(19.6)	5.418	0.247
IVH ≥ 3		40(10.9)	-	2(28.6)	6(27.3)	6(12.8)	10(10.2)	16(8.2)	9.355	0.040
PVL		63(17.1)	-	1(14.3)	3(13.6)	15(31.9)	17(17.3)	29(14.9)	3.710	0.576
MBDP		21(5.7)	-	1(14.3)	1(4.5)	5(10.6)	2(2)	12(6.2)	6.468	0.126
PNAC		68(18.5)	-	1(14.3)	1(4.5)	4(8.5)	21(21.4)	41(21.1)	7.350	0.096
EOS		34(9.2)	-	2(28.6)	2(9.1)	5(10.6)	8(8.2)	17(8.8)	3.396	0.439
LOS		52(14.1)	-	1(14.3)	2(9.1)	4(8.5)	18(18.4)	27(13.9)	2.949	0.542
Morbidities of major serious disease		221(60.1)	-	3(42.9)	16(72.7)	32(68.1)	64(65.3)	106(54.6)	11.743	0.008
All-cause mortality		1691/2004(84.4)	189/189(100)	223/223(100)	394/407(96.8)	389/428(90.9)	270/357(75.6)	226/400(56.5)	394.360	< 0.001
Survival rate of EPIs transfered to NICU		313/469(66.7)	0	0	13/38(34.2)	39/75(52)	87/124(70.2)	174/216(80.6)	75.708	< 0.001
Survival rate of EPIs received complete care		313(85.1)	-	0	13(59.1)	39(83.0)	87(88.8)	174(89.7)	38.718	< 0.001
Survival rate of EPIs without major serious diseases		116(31.5)	-	0	2(9.1)	9(19.1)	27(27.6)	78(40.2)	19.142	0.001

Data are presented as median(inter quartile range) or n (%); χ^2 is the statistic value of the Pearson's chi-square test or continuity correction of Pearson's chi-square test, and Z is the statistic value of the Kruskal-Wallis rank-sum test.

Note: EPIs: extremely preterm infants; RDS: neonatal respiratory distress syndrome, 2 refers to the grade 3–4 RDS; EOS: early onset sepsis; LOS later onset sepsis; NEC: necrotizing enterocolitis; hsPDA: hemodynamically significant patent ductus arteriosus; BPD: bronchopulmonary dysplasia; BI: brain injury. ROP: retinopathy of prematurity; MBDP: metabolic bone disease of prematurity; PNAC: parenteral nutrition-associated cholestasis.

Table 3 Care practices in preterm infants with gestation age < 28w receiving complete care

	N **= 368**	**22–22^{+6}w *n* = 0**	**23–23^{+6}w *n* = 7**	**24–24^{+6}w *n* = 22**	**25–25^{+6} *n* = 47**	**26–26^{+6}w *n* = 98**	**27–27^{+6}w *n* = 194**	**χ^2**	***P***
EPIs transfered to NICU	469/2004(23.4)	2/189(1)	14/223(6.3)	38/407(9.3)	75/428(17.5)	124/357(34.7)	216/400(54)	375.212	< 0.001
EPIs received complete care	368/2004(18.4)	0	7/223(3.1)	22/407(5.4)	47/428(11.0)	98/357(27.5)	194/400(48.5)	400.137	< 0.001
EPIs abandoned for Socio-economic considerations	90/101(89.1)	2/2(100)	7/7(100)	14/16(87.5)	25/28(89.3)	23/26(88.5)	19/22(86.4)	1.225	0.990
The time of initiating feeding, h	29(20,43.3)	-	37	31(21,62)	34(17,54)	27.5(28,41.3)	29(20,44)	2.912	0.573
Breast-feeding	327(88.9)	-	2(28.6)	16(72.7)	39(83)	86(87.8)	184(94.8)	29.832	< 0.001
Human milk fortifier	230(62.5)	-	1(14.3)	9(40.9)	30(63.8)	64(65.3)	126(64.9)	11.545	0.018
PS	345(94)	-	7(100)	22(100)	45(95.7)	90(91.8)	175(90.2)	2.985	0.516
IMV	283(79.4)	-	7(100)	22(100)	43(91.5)	73(74.5)	138(71.1)	25.945	< 0.001
Postnatal corticosteroids	146(39.7)	-	1(14.3)	11(50)	31(66)	40(40.8)	63(32.5)	31.969	< 0.001

Data are presented as n (%); χ^2 is the statistic value of the Pearson's chi-square test or continuity correction of Pearson's chi-square test.

Note: EPIs: extremely preterm infants; IMV: Invasive mechanical ventilation; PS: pulmonary surfactant; NICU: neonatal intensive care unit.

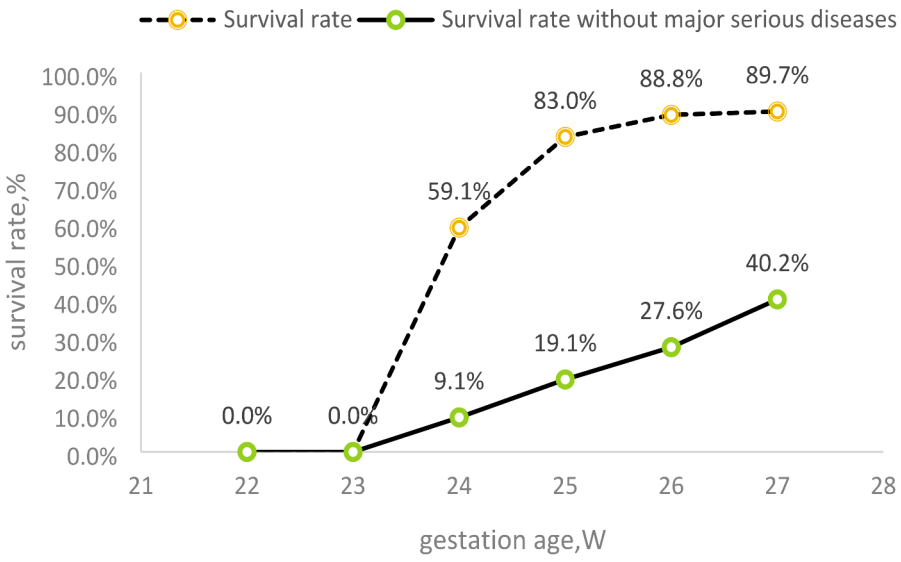

Fig. 2 Survival rate of extremely preterm infants receiving complete care

recorded in the delivery room. This finding closely aligns with Zhang et al.'s observations [21], who reported data from a single center indicating that 73% of EPIs were not admitted to the NICU for treatment. Most of these cases arose from non-medical inductions, and in theory, the risk of mortality could be substantially reduced if these infants received comprehensive care. Even among those transferred to the NICU, a portion was eventually discontinued from treatment due to non-medical reasons, and merely 18.4% of the cases ultimately underwent complete treatment. Notably, the proportions of receiving complete treatment within the 22–24w group were 0%, 3.1%, and 5.4%, respectively. This indicates a considerable shortfall in providing complete medical treatment to a large number of infants at the fringes of viability, contrasting starkly with high-income countries. A Japanese study unveiled that approximately 50% of EPIs with a gestational age of 22–23 weeks received active care [22]. The United States has witnessed a notable upsurge in active treatment for live births occurring between 22 weeks and 25 weeks of gestation, with around 52% of infants in this gestational age bracket benefiting from active care [23]. Moreover, our study uncovered that gender also emerged as a decisive factor influencing the active provision of treatment. In our study, male infants constituted 55.9% (1121/2004) of the cohort, yet the proportion of male infants transferred to the NICU and receiving comprehensive treatment was significantly higher (63.9%). Considering the distinct cultural norms within our region, differing parental preferences for male infants led to a greater willingness to shoulder the costs of hospitalization, and had a higher tolerance for their long-term poor prognosis.

Therefore, it is necessary to enhance the awareness of obstetricians and pediatricians regarding the treatment of EPIs and promote equal access to medical care for female infants. The age of these EPIs mothers was 31 (27, 34) years old, and 15.8% of them conceived through assisted reproductive technology. This suggests that these mothers were older, with nearly one-sixth of them conceived through assisted reproductive technology. Therefore, treating these infants is of practical significance for these older mothers with pregnancy difficulties.

EPIs were at an extremely high risk of death after birth. The overall survival rate of EPIs in this study was only 15.6%, but the survival rate of EPIs transferred to the NICU after birth and receiving complete treatment was 85.1%. Hence, a large number of EPIs were abandoned in the delivery room, significantly affecting the survival rate of EPIs. The study indicated that the survival rate of EPIs and the survival rate free from major diseases increased significantly with gestational age in this region. National data from 2019 indicated that the survival rates of EPIs with gestational ages < 24 weeks, 24 weeks, 25 weeks, 26 weeks, and 27 weeks were 21.7%, 55.8%, 75.2%, 87.7%, and 89.7%, respectively [4]. Data from 233 cases EPIs with gestational ages of 22–25 weeks at Shenzhen Maternal and Child Health Hospital from 2015 to 2021 showed an overall survival rate of 61.8% [24]. According to a study by the Child Health and Human Development Neonatal Research Network, from 2006 to 2011, 4987 EPIs were born at 26 and 24 weeks, with survival rates of 81.55% and 76%, respectively, without severe sequelae. The survival rates without mild and severe sequelae were 59% and 30%, respectively [25]. In a study of preterm infants born at gestational ages of 22–28 weeks in the UK

region of Wales, the overall survival rate of infants after live birth was approximately 71.8% [26]. Accordingly, we found that the survival rate of EPIs with gestational ages over 25 weeks in southwest Fujian Province was more than 83%, which was close to the average level of China and the level of developed countries. However, there still exists a significant gap in the survival rate without serious diseases compared to developed countries. Furthermore, the survival rate of EPIs at gestational ages of 22–24 weeks was still significantly low. Even with active treatment, their survival status could not be improved. Therefore, improving the survival rate without major serious diseases and the success rate of peri-survival infants is the direction of future efforts.

EPIs were at risk of many diseases after birth [27]. Our studies have found that the lower the gestational age, the higher the incidence of early-life diseases, such as grade 3–4 RDS, where gestational age follows a similar dose-response relationship. However, for diseases that frequently occur later in hospitalization, like II to III level BPD, ROP, NEC, BI, LOS, hsPDA, MBDP, PNAC, etc., the incidence did not decrease with increasing gestational age. This appears to contradict medical common knowledge. Considering potential causes, most of the peri-survival marginal infants died shortly after birth, before reaching the corrected gestational age or the high-incidence age of these diseases. Consequently, the incidence of these diseases in this population is relatively low compared to the actual situation. We found that in EPIs born at gestational ages of 25–27 weeks, with higher survival rates, the incidence of major severe diseases decreased with gestational age. This reduction in risk led to a decrease in the risk of death during hospitalization, as evidenced by a progressive increase in the survival rate of EPIs without major serious diseases with increasing gestational age.

Reasonable perinatal interventions could enhance the short-term and long-term prognosis of EPIs [18]. ACS were effective prenatal interventions to improve perinatal outcomes in EPIs. This study revealed that 67.1% (247/368) of pregnant women received at least one dose of corticosteroids before delivery, and the rate of ACS usage gradually increased with gestational age. This rate was similar to the 71.1% rate of ACS use in EPIs reported by the Chinese Neonatal Network in 2021 [4]. In developed countries, this proportion has risen from 64% in the 1990s to stabilize at over 70%. Moreover, in some high-resource countries, more than 85% of pregnant women with a gestational age of 24–28 weeks received ACS [7, 28, 29]. For pregnant women facing inevitable premature delivery before 34 weeks' gestation, glucocorticoid usage has been recommended [14, 30]. However, for EPIs with a very low gestational age, obstetric guidelines do not recommend routine ACS use for mothers with a gestational age of <23 weeks. Consequently, there is a low rate of ACS use in infants with a gestational age of <24 weeks. However, other studies have shown that the smaller the gestational age, the greater the benefit of preterm infants, suggesting that EPIs may be the group with the greatest benefit from ACS use. Moreover, ACS use at "any" time could help improve long-term quality of life for EPIs [31]. The low rate of cesarean delivery (4.9%) in the study population was considered to be related to the high rate of abandonment among EPIs with a gestational age less 26 weeks, during the delivery of these women cesarean delivery was a secondary option for obstetricians. Among EPIs received complete care, 79.4% had received invasive mechanical ventilation, and 94% had received PS. The breastfeeding rate increased with gestational age. Given that parents possess a strong desire to treat preterm infants with a higher gestational age, they exhibit greater compliance and provide ample breast milk. An increase in breastfeeding rates would be beneficial to improve the prognosis of EPIs.

In short, the mortality risk of peri-survival infants in the southwest region of Fujian Province was markedly high. It is crucial to enhance the perinatal management of EPI, facilitate communication between obstetricians and pediatricians, and involve neonatologists actively in pre-delivery consultations. This will furnish parents and obstetricians with more comprehensive and accurate information about the success rate and prognosis of EPIs treatment in their region, thereby reducing the abandonment rate in delivery rooms and offering more medical treatment opportunities. ACS should be promptly administered when unavoidable delivery approaches to expedite fetal maturation. Upon admission of premature infants to the NICU, referring to the best neonatal management strategy [32], providing respiratory support, and utilizing exogenous pulmonary surfactant should be pursued vigorously to develop personalized nursing and assessment plans for EPIs. This will enhance both short-term and long-term prognoses.

Inevitably, this study was retrospective and encompassed data from all pregnant women and infants undergoing obstetric induction and obstetric delivery. Detailed analysis of pregnancy complications for some women undergoing obstetric induction was not feasible, possibly affecting accuracy of the results.

Conclusion

The all-cause mortality rate of EPIs in the southwest area of Fujian Province remained high, with a significant proportion being abandoned in the delivery room. The survival rate of EPIs born at 25–27 weeks and receiving complete NICU care is comparable to that of developed countries. However, the rates of survival without major severe diseases and the survival rate of peri-survival

infants were markedly lower than those in high-income countries.

Supplementary Information

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Supplementary Material 1

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Author contributions
XZL conceptualized and designed the study, reviewed and revised the manuscript, and approved the final manuscript. LG, DMC, LPX and RHZ collected data and performed the data analysis, drafted the initial manuscript, and approved the final manuscript. SMM, HPY, SZD, and QBC coordinated and supervised data collection at their own sites and approved the final manuscript.

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Data availability
The datasets used during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The research protocol was approved by the Ethics Committee of Women and Children's Hospital affiliated to Xiamen University/Xiamen Maternal and Child Health Hospital (Batch number kY-2023-089-K01). Consent to participate and for publication all participants gave written informed consent. The informed consent was obtained from the families of the children.

Competing interests
The authors declare no competing interests.

Consent to participate and for publication
All data published here received consent for publication.

Conflict of interest
The authors declare that there is no conflict of interest.

Author details
[1]Department of Neonatology, Women and Children's Hospital, School of Medicine, Xiamen university, Xiamen 361003, China
[2]Xiamen key laboratory of perinatal-neonatal infection, Xiamen 361003, China
[3]Xiamen Clinical Research Center for Perinatal Medicine, Xiamen 361003, China
[4]Department of Neonatology, Quanzhou Maternity and Children's Hospital, Quanzhou 362000, China
[5]Department of Neonatology, Zhangzhou Affiliated Hospital of Fujian Medical University, Zhangzhou 363000, China
[6]Department of Neonatology, Longyan First Hospital Affiliated to Fujian Medical University, Longyan 364000, China

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