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Analysis of hospitalization and its outcomes in extremely preterm infants

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ABSTRACT

Introduction: The aim of the study is to analyze the hospitalization course of extremely preterm infants born between 2018–2022 at the Department of Neonatal Diseases at Pomeranian Medical University in Szczecin.

Materials and methods: A single-center retrospective study included 68 extremely premature infants of both sexes. Anthropometric parameters at birth and at hospital discharge, nutrition mode, and complications of prematurity were analyzed.

Results: At the Department of Neonatal Diseases at Pomeranian Medical University in Szczecin, between 2018–2022, 68 extremely preterm infants were born. The mean gestational age was 25.8 ±1.72 weeks, and the mean birth weight was 844.89 ±213.13 g. Twenty-three infants (33.82%) died before hospital discharge; 22 deaths occurred by day 6 of life and were not included in further analysis. Most infants were born in medium condition; 35 (76.08%) preterm neonates required invasive, and 11 (23.91%) noninvasive mechanical ventilation. Thirty-four (73.91%) of all babies were born with congenital infections, and 28 (60.87%) developed acquired infections. The most common complications of prematurity were bronchopulmonary dysplasia (43.47%) and hemodynamically significant patent ductus arteriosus (52.17%). Forty (86.96%) of all extremely preterm infants were breastfed at the Department, with a mean breastfeeding duration of 71.4 ±27.51 days, and 82.05% of mothers continued breastfeeding after hospital discharge. The mean time of hospitalization was 85.5 ±26.52 days.

Conclusions: Hospitalization of extremely premature infants is associated with a high risk of complications and death. The most common complications are infections and diseases typical for this age group. Many newborns do not gain weight properly. Continuous improvement in the management, prevention, and treatment of extremely preterm infants is warranted.

Keywords: prematurity; infants; neonatology; NICU; extremely preterm birth.

INTRODUCTION

Extreme prematurity is defined as being born before completing 28 weeks of gestation. These births affect 2–5 in every 1,000 pregnancies worldwide each year, but the number may vary by region [1]. In Poland, extremely preterm births accounted for 0.41% of all births in 2021 [2]. The frequency of all preterm births (born before 37 weeks of gestation) is about 5–9% in developed countries. However, the rate of preterm birth has increased in many locations, for example, due to preterm delivery of artificially conceived multiple pregnancies. Extreme preterm births comprise 5% of all preterm births [1, 3].

Preterm labor might be spontaneous with membranes intact, caused by premature rupture of membranes (PROM), or indicated due to maternal and fetal security. The contribution of the causes of preterm birth differs by ethnicity. Spontaneous and medically indicated preterm birth are most common in Caucasian women, whereas PROM is the main cause among African-American women. The proportions among the 3 clinical subtypes of preterm birth vary, presumably due to differences in patient characteristics and the high-risk composition of patient populations.

The main gynecological risk factors are uterine overdistension (e.g., caused by multiple pregnancies), uteroplacental ischemia, hemorrhage, and greater use of assisted reproduction techniques. Additional aggravating factors include: infection, cholestasis, hypertension, diabetes, and psychiatric disorders. Also significant are genetic factors, a prior history of preterm birth, psychosocial stress, lifestyle habits such as smoking, alcohol and illicit drug use during pregnancy, the nutritional status of the mother, and race. African-American women are 3 times more likely to have a preterm birth than women from other racial or ethnic groups.

Given the drastic changes in patient demographic characteristics, including increases in the proportion of single mothers, maternal obesity, and the burden of chronic and acute illnesses during pregnancy, coupled with escalations in obstetric interventions at preterm gestations, the proportions of preterm birth clinical subtypes are likely to continue changing regarding ethnic distribution [3].

Nonetheless, it is advised that women with high-risk pregnancies supplement thyroxine, visit obstetric specialists regularly to prevent preterm delivery, and implement prenatal steroid therapy if needed.

Moreover, the loss of months of fetal development leaves infants vulnerable to morbidities, many of which are unique to the preterm population. Neonatologists have raised concerns about intraventricular hemorrhage (IVH), bronchopulmonary dysplasia (BPD), hemodynamically significant patent ductus arteriosus (hsPDA), and necrotizing enterocolitis (NEC), which are the most common neonatal complications and have a significant impact on survival [4, 5].

Immaturity is associated with dysfunction of almost all organs, leading to problems with breathing, blood circulation, thermoregulation, feeding, and susceptibility to various

infections. Due to immunological immaturity, exposure to numerous invasive medical procedures, and many months of contact with hospital bacterial flora, premature babies often develop nosocomial infections such as sepsis.

Ideally, they should be born in higher-reference hospitals that are prepared to use active treatment with potentially lifesaving interventions after birth (e.g., intubation, ventilation). Research and clinical evidence suggest that interventions performed in the first minutes after birth have immense long-term consequences in addition to short-term effects on the rate and quality of survival [5, 6]. It is recommended to avoid intubation and ventilation in the first minutes of life and to opt for non-invasive respiratory support (NIV). Besides nasal continuous positive airway pressure (NCPAP), nasal intermittent positive pressure ventilation (NIPPV) and cannulas have become more popular, but the efficacy of these respiratory support methods in reducing the rates of BPD has been modest. In addition, exogenous surfactant therapy improves neonatal outcomes and reduces air leak and mortality [7].

Because of very low birth weight, nutritional support is a main component of an infant's care. Total parenteral nutrition is often initiated as soon as possible after birth to ensure a very preterm infant receives adequate supplies of protein, fat, carbohydrates, and calories despite gastrointestinal immaturity. However, this type of feeding comes with short- and long-term adverse effects such as: metabolic acidosis, electrolyte imbalance, cholestatic liver disease, and bacterial as well as fungal infections [8]. With that in mind, it is recommended to aim to shorten the time of parenteral nutrition to decrease the risk of complications. Delay in the introduction of enteral feeding increases the risk of NEC [4]. On the contrary, trophic feeding promotes intestinal maturation and decreases the time taken to reach full enteral feeding independently of parenteral nutrition. These facts shed light on how hard it is to balance gains and losses when choosing the right method of nutritional support.

The lack of a neonatal network in Poland results in a lack of reliable statistical studies on morbidities and complications occurring in extremely preterm infants at the national levels of tertiary neonatal care. In this paper, we present the effects of the care of preterm infants over the past 5 years using 1 center as an example. The data allow us to evaluate the work of our team in comparison with the results obtained by neonatologists in other countries.

MATERIALS AND METHODS

It was a single-center retrospective study that analyzed the hospitalization courses of extremely preterm infants born between 2018–2022 at the Department of Neonatology and Neonatal Intensive Care, Pomeranian Medical University in Szczecin, Poland. The only inclusion criterion was the delivery of a live baby at 22 + 0 to 27 + 7 weeks of gestation. Medical records were analyzed to collect data on anthropometric parameters at birth (centile channels according to T.R. Fenton's charts) and at hospital discharge (weight and head circumference), type of delivery (vaginal delivery or Caesarean section), obstetric history (mother's age, sequence of pregnancy, delivery, prenatal steroid therapy), postnatal status (Apgar score at 1 and 5 min), type and duration of respiratory support, type of nutrition (breast milk, donor human milk, or formula), and complications of prematurity, such as: infection, IVH, hsPDA, BPD, NEC, and death. All diseases occurred before Neonatal Intensive Care Unit (NICU) discharge or death.

Congenital infections were diagnosed within the first 72 h of life by severe general medical conditions implying sepsis (cardiorespiratory instability, apnea, thermal dysregulation, neurological deterioration, or ill appearance) and/or confirmed by blood culture and high inflammatory parameters (2 of the following biochemical criteria present: C-reactive protein – CRP >5 mg/L, procalcitonin – PCT – on the second day of life >20 ng/mL, interleukin-6 – IL-6 >100 pg/mL; hematological criteria: white blood cells – WBC <5 G/L or >30 G/L, leukocyte index >0.2; platelet count – PLT <100 G/L). Acquired sepsis was diagnosed after 72 h of life if the same criteria were met, except for PCT >2 ng/mL.

The diagnosis of IVH and its severity were defined by transcranial ultrasound examination. The degree of hemorrhage was established using the modified Papile classification. Grade III (IVH with ventricular dilatation occupying >50% of the ventricle) and grade IV (IVH with intraparenchymal hemorrhage) were defined as severe [9].

Hemodynamically significant patent ductus arteriosus was diagnosed based on clinical symptoms such as continuous or systolic murmur, low diastolic blood pressure, hypotension, tachycardia, tachypnea, oliguria, hepatomegaly (3 of these), and echocardiographic criteria: a growing pattern left-to-right by ductus arteriosus (DA) or a pulsating left-right flow by DA, ductus diameter >1.4 mm/kg, left atrium to aortic ratio >1.8, end-diastolic flow velocity in the left pulmonary artery ≥0.2 m/s, or no flow/ retrograde flow in the descending aorta below the PDA (3 of these) [10].

The current definitions of BPD from 2019, suggested after the workshops organized by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), include the use of supplemental oxygen treatment, or oxygen plus NIV, or plus respiratory support (severe form) at 36 weeks postmenstrual age (PMA) [11].

Necrotizing enterocolitis was defined as at least 1 clinical symptom (bilious gastric aspirate or emesis, abdominal distension, positive fecal occult blood test, or fresh blood in the stool) and at least 1 radiographic finding (pneumatosis intestinalis, hepatobiliary gas, or pneumoperitoneum) [12].

RESULTS

At the Department of Neonatal Diseases at Pomeranian Medical University in Szczecin, between the years 2018–2022, 68 infants were born extremely premature. Twenty-three infants died before hospital discharge, giving a mortality rate of 33.82%, with 10 deaths occurring on the first day of life. Six deaths were due to lethal congenital malformations – the percentage of deaths without lethal defects was 25%. Twenty-two deaths occurred within the first 6 days of life, and these infants were not included in further analysis due to information shortage. One premature baby died at 147 days of life (as a result of severe BPD), so the

complications that occurred during hospitalization were also included in the statistical analysis. Ultimately, the study comprised 46 infants of both sexes born before 28 weeks of gestation. There were 5 pairs of twins, 1 set of triplets, and 39 mothers in total (Tab. 1). Most of the mothers gave birth via Caesarean section, and only 56.4% received prophylactic antenatal corticosteroid administration (betamethasone or dexamethasone). The mean maternal age at delivery was 31.5 ±5.7 years, and most were primiparas.

Most of the children were born with weight appropriate for gestational age and in average general condition.

TABLE 1. Characteristics of the study group

Variables	Number of patients	%
Mothers		
VD/CS	6/33	15.38/84.62
Primiparas/pluriparas	21/18	53.85/46.15
Antenatal course of corticosteroids	22	56.41
Mean gestational age (weeks)	25.81 (22 + 6 – 27 + 6)	±SD 1.72
Newborns		
Male/female	28/18	60.97/39.1
Mean birthweight	844.89 g (450–1390)	±SD 213.13
Birthweight <3 centile	1	2.17
Birthweight 3–9 centile	1	2.17
Birthweight >90 centile	6	13.04
Symmetrical hypotrophy	1	2.17
Mean head circumference at birth	24.02 cm	±SD 2.05
Head circumference at birth <3 centile	0	0.0
Head circumference at birth 3–9 centile	1	2.17
Head circumference at birth >90 centile	8	17.39
Apgar score at 1 min		
0–3 points	13	28.26
4–7 points	32	69.56
8–10 points	1	2.17
Apgar score at 5 min		
0–3 points	5	10.86
4–7 points	26	56.52
8–10 points	15	32.6
Type of infection		
Congenital sepsis	9	19.57
Congenital meningitis	5	10.86
Congenital other infections	20	43.48

VD – vaginal delivery; CS – Caesarean section; SD – standard deviation

The mean duration of respiratory support was 55.8 ±29.38 days. Most preterm neonates required invasive mechanical ventilation, while 23.91% needed only noninvasive mechanical ventilation such as continuous positive airway pressure (CPAP), bilevel positive airway pressure (BPAP), or synchronized nasal intermittent positive pressure ventilation (SNIPPV) – Table 2.

TABLE 2. Respiratory support

Respiratory support	Number of patients	%
Invasive mechanical ventilation	35	76.08
Only noninvasive mechanical ventilation	11	23.91
The mean duration of respiratory support (days)	55.8	±SD 29.38

SD – standard deviation

Thirty-four (73.91%) of all studied patients were born with congenital infections, including 5 cases of meningitis (10.86%) and 9 cases of sepsis (19.57%) – Table 1.

Twenty-eight (60.87%) infants acquired infections during hospitalization, such as: sepsis (16 cases; 34.78%), meningitis (13 cases; 28.26%), and other infections (20 cases; 43.48%) – Table 3. Most infections were caused by *Staphylococcus* spp., *Escherichia coli*, and *Klebsiella* spp.

All patients experienced complications of prematurity (Tab. 3). The most common complications were BPD (20 cases; 43.47%) and hsPDA (24 cases; 52.17%). Infants with BPD received systemic steroids (hydrocortisone) for 7–10 days, followed by inhaled steroids (budesonide) during the period of oxygen dependence.

Twenty-four newborns were diagnosed with hsPDA. It was initially treated conservatively with paracetamol for 5–7 days. Due to paracetamol ineffectiveness, 7 (26.92%) required ibuprofen. Surgical intervention was necessary in only 2 (7.69%) cases. There were 5 (10.87%) cases of NEC, 2 of which required surgery. Five (10.87%) neonates had severe IVH.

TABLE 3. Complications of prematurity

Complications	Number of patients	%
hsPDA	24	52.17
BPD	20	43.47
NEC	5	10.87
Acquired sepsis	16	34.78
Acquired meningitis	13	28.26
Acquired other infections	20	43.47
Severe IVH	5	10.87
Death	23	33.82
Deaths without lethal defects	17	25.00

hsPDA – hemodynamically significant patent ductus arteriosus; BPD – bronchopulmonary dysplasia; NEC – necrotizing enterocolitis; IVH – intraventricular haemorrhage

The distribution of complications of prematurity over time is shown in Table 4. There was a trend toward lower rates of death, sepsis, meningitis, BPD, NEC, and IVH. Hemodynamically significant patent ductus arteriosus occurred with similar frequency over time.

Forty (86.96%) of all extremely preterm infants were fed with maternal breast milk during hospitalization, with a mean breastfeeding duration of 71.4 ±27.51 days, and 32 mothers out of 39 (82.05%) continued breastfeeding at hospital discharge (Tab. 5).

The median time to the introduction of full enteral nutrition was 14.5 days (range 7–39).

Regarding weight centile channels at birth and hospital discharge, most patients (56.52%) had no centile crossing. Twelve (26.08%) babies had weight at hospital discharge below the 10th percentile, compared to only 2 neonates born with weight below the 10th percentile.

The mean time of hospitalization was 85.5 ±26.52 days. The mean weight at hospital discharge was 2836.28 ±601.07 g.

TABLE 4. Percentage distribution of prematurity complications over the years

Variables	Year					All
	2022	2021	2020	2019	2018	
Quantity of infants studied (born extremely prematurely overall)	8 (11)	9 (12)	10 (14)	8 (14)	11 (17)	46 (68)
			n (%)			
Deaths	3 (27.0)	4 (33.3)	4 (28.6)	6 (42.9)	6 (35.0)	23/68 (33.82%)
Acquired infections	7 (87.5)	4 (44.4)	5 (50.0)	6 (75.0)	6 (54.5)	28/46 (60.90%)
Sepsis	2 (25.0)	4 (44.4)	3 (30.0)	3 (37.5)	4 (36.4)	16/46 (34.78%)
Meningitis	1 (12.5)	3 (33.3)	3 (30.0)	3 (37.5)	3 (36.4)	13/46 (28.26%)
Other	7 (87.5)	2 (22.2)	4 (40.0)	4 (50.0)	3 (27.3)	20/46 (43.47%)
NEC	0 (0.0)	2 (22.2)	2 (20.0)	0 (0.0)	1 (9.0)	5/46 (10.87%)
Operation	0	1	1	0	0	
hsPDA	4 (50.0)	4 (44.4)	5 (50.0)	4 (50.0)	7 (63.6)	24/46 (52.17%)
Paracetamol	4	4	5	4	7	
Ibuprofen	1	0	3	1	2	
Operation	1	0	0	0	1	
BPD	2 (25.0)	2 (22.0)	8 (80.0)	4 (50.0)	4 (36.0)	20/46 (43.47%)
Mild	1	1	6	1	3	
Moderate	1	0	1	0	0	
Severe	0	1	1	3	1	
IVH	3 (38.0)	7 (77.0)	3 (30.0)	4 (50.0)	8 (73.0)	25/46 (54.35%)
Stage I–II	3	5	3	2	7	
Stage III–IV	0	2	0	2	1	5/46 (10.90%)

NEC – necrotizing enterocolitis; hsPDA – hemodynamically significant pendant ductus arteriosus; BPD – bronchopulmonary dysplasia; IVH – intraventricular haemorrhage

TABLE 5. Nutrition of the patients

Type of nutrition	Number of patients	%
Exclusive breastfeeding	14	30.43
Mixed (maternal milk + formula)	5	10.87
Mixed (donor human milk + formula)	4	8.70
Mixed (maternal milk + donor human milk)	8	17.39
Mixed (maternal milk + donor human milk + formula)	16	34.78
Exclusive formula feeding	0	0.00

DISCUSSION

There is a lack of recent publications available on the course of hospitalization of extremely premature newborns around the world, especially in Poland. The purpose of this paper is to summarize the results of the treatment of extremely preterm infants born between 2018–2022 and to analyze the course of hospitalization and complications associated with prematurity. Despite significant advancements in neonatal medical care over the years, infants born before 28 weeks of gestation remain in the group with the highest risk of severe illnesses and death.

An analysis of hospitalization outcomes for 10,000 extremely preterm infants born in the USA between 2013–2018 demonstrated

that 21.7% did not survive until hospital discharge [13]. Yang et al. studied data of infants born before 32 weeks of gestation from 57 hospitals in China, where the survival rate from birth to discharge was 87.6%. However, survival without serious morbidities was 51.8% [14]. On the contrary, in the study by da Cunha Durães et al. including neonates born before 26 weeks of gestation, the survival rate was only 25%, and survival to discharge for newborns in the USA born before 27 weeks of gestation was 78.3% [13, 15].

The mortality rate for this population of patients in Poland in 2021 was 32.21% [2]. In comparison, the mortality rate of the same population in our department from 2018–2022 was 33.82%.

It is believed that variations in mortality rates are partly attributable to the current restrictive abortion laws in Poland – 6 deceased neonates had lethal congenital anomalies. Another unfavorable prognostic factor is the low percentage of neonates whose mothers received prenatal steroid therapy, which was only 56.41%. Additionally, congenital infection was identified in 66.7% of deceased preterm infants.

Antenatal steroids are a key factor in increasing the survival rate of premature newborns, with a significant impact on the reduction of respiratory distress syndrome (RDS) incidence. In addition to increasing survival, steroid therapy reduces the need for surfactant use and mechanical ventilation after birth, which is supported by numerous studies [11, 16]. Some studies also show that corticosteroids reduce the risk of developmental disorders [17, 18].

However, the administration of antenatal steroids varies widely among centers worldwide. In a prospective cohort study in NICUs, including premature infants born before 32 weeks of gestation, Dong et al. found that 51.4% of newborns received a complete course of antenatal steroid therapy within 48 h to 7 days before birth, while 14.1% did not receive any dose of steroids prenatally [16]. In a study by Cao et al., antenatal corticosteroids were used in 76.5% of neonates born before 32 weeks of gestation [17]. In contrast, in a study by da Cunha Durães et al., only 18.1% of neonates born between 23–25 + 6 weeks of gestation received a full course of prenatal steroid therapy [15].

A surprising finding from the study was the very high frequency of acquired infections diagnosed in the analyzed group of neonates, with sepsis occurring in over 34%. A similar rate of acquired sepsis was noted in the USA 24 years ago [19]. Although continuous training in anti- and aseptic principles has reduced the rate of bloodstream infections from 43.4% in 2021 to 25% in 2022, it remains very high. According to hospitalization data at the Department of Neonatology and Neonatal Intensive Care, Pomeranian Medical University in Szczecin, the incidence of early-onset sepsis (EOS) occurred in 9 patients (19.57%), while late-onset sepsis (LOS) occurred in 16 patients (34.78%). According to a study by Perez et al., in a group of 936 newborns, the incidence of confirmed EOS was 6% and confirmed LOS was 20% [19].

It is supposed that the higher rate of sepsis in the clinic in Szczecin may be due to the inclusion of neonates born at 22–28 weeks of gestation in the statistical sample, compared to the study group of neonates born at 24–28 weeks of gestation in the aforementioned publication. Such a high rate of acquired infections may also be partly due to the dire conditions in which the neonates were located – the last renovation of the department was 30 years ago, there was insufficient space, and the hospital's communication flow within the NICU was inadequate. Fortunately, in mid-2023, the clinic was moved to a newly built facility.

Delayed closure of the DA primarily occurs in preterm infants, remaining open at 7 days in 64% of infants born at 27–28 weeks of gestation and in 87% of those born at 24 weeks [20]. Therefore, the earlier the infant is born, the higher the risk of the ductus remaining patent at 7 days after birth. The clinical problem is not the presence of an open ductus but the significant hemodynamic shunt through the ductus, impairing blood flow and thus the function of the intestines, kidneys, and ultimately the brain. Therefore, early diagnosis and treatment of hsPDA are crucial for the health of preterm infants.

In the analyzed group of extremely premature infants, more than half required treatment for hsPDA, a percentage that has remained consistent over recent years. Paracetamol was used as the first-line medication, which proved ineffective in 26.92% of patients, necessitating the use of ibuprofen. Two preterm infants (7.69%) did not respond to conservative treatment and required surgical ligation.

The incidence of hsPDA among infants born between 24–28 weeks of gestation and with a birth weight less than 1500 g varies between 65–90%, depending on the time of birth. Some of these infants may experience spontaneous closure during the neonatal period. However, the rates of spontaneous ductal closure among extremely preterm infants with RDS are not known [21]. In Korea, between 2011–2014, the overall incidence of hsPDA was 57% at the end of the first postnatal week [22].

Bronchopulmonary dysplasia is a chronic, life-threatening lung disease predominantly affecting preterm infants. It is an iatrogenic condition resulting from medical procedures such as long-term mechanical ventilation and high oxygen concentrations. The incidence of BPD is inversely proportional to gestational age and birth weight. Infants born before 28 weeks of gestation and with an extremely low birth weight (ELBW; <1000 g) have the highest risk of developing BPD. Other risk factors include caloric deficiency, infections, and prolonged mechanical ventilation.

In a retrospective cohort study of premature infants 22–29 weeks of gestation in the USA, BPD occurred with a frequency of 40.6%, with only 3.7% developing grade 3 BPD [23]. According to a systematic literature review by Siffel et al., the incidence of BPD in Europe ranged 10–73%, in North America 18–89%, in Asia 18–82%, and in Oceania 30–62%. The wide range of reported global BPD incidence reflects differences in gestational ages and birth weights, diagnostic criteria, treatment protocols, and survival rates across study populations and institutions [24].

In our unit, based on the NICHD definition from 2019, the incidence of BPD was estimated at 43.47%, with a trend toward a decrease to 22–25% in the last 2 analyzed years. The development and widespread adoption of NIV methods and the reduction of acquired infections undoubtedly influenced this reduction.

Another significant health problem in extremely preterm infants is IVH, a catastrophic neurological consequence usually occurring within 72 h after birth, affecting mortality and long-term neurological development, and often leading to cognitive impairment. In a study by Pande and Vagha, the overall

incidence of IVH in extremely preterm infants born at 22–28 weeks of gestation was 32% [25]. At the Department of Neonatology and Neonatal Intensive Care, Pomeranian Medical University in Szczecin, the incidence of severe IVH was 10.9%. These serious hemorrhagic complications are closely related to hemodynamic changes caused by a hsPDA [10].

Necrotizing enterocolitis is a catastrophic disease with an unclear pathogenesis. Necrotizing enterocolitis occurs in nearly 10% of infants born with a birth weight below 1500 g and is associated with high mortality and long-term neurodevelopmental morbidity [26]. Overall, the incidence of NEC is highest among the most preterm infants. In infants born before 28 weeks of gestation, the lowest reported incidence of NEC was in Japan (2%) and the highest in Australia, Canada, and Italy (7–9%) [27]. Diagnosing NEC can be challenging, especially in the early stages, due to the lack of a definitive case definition. The incidence of NEC at the Department of Neonatology and Neonatal Intensive Care, Pomeranian Medical University in Szczecin, was 10.86%. The higher incidence compared to other countries is difficult to explain given our standards of neonatal nutrition in the first days of life, exclusively with breast milk or donor human milk, and the relatively short time required to achieve full enteral feeding. It may be related to the high rate of congenital infections and the necessity for antibiotic therapy.

It is worth noting that 86.96% of all extremely preterm infants were breastfed during hospitalization, with a mean duration of breastfeeding of 71.4 ±27.51 days, and 82.5% of mothers continued to breastfeed at hospital discharge. In South Africa, by comparison, 59.5% of mothers breastfed ELBW infants at hospital discharge [28]. In a study by Kulkarni et al., only 36.7% of newborns <34 weeks of gestation were breastfed at discharge [29]. In cases of temporary unavailability of maternal milk, infants were fed with donor human milk. When maternal milk was permanently unavailable, formula supplementation was introduced.

Despite the emphasis on breastfeeding, the use of milk fortifiers, and additional protein supplementation, nearly 40% of the infants' weight fell within the lower centile range upon discharge from the hospital. This is consistent with reports from Sweden. In the Swedish EXPRESS cohort of ELBW infants, 44% had a Z-score below –2 standard deviations at discharge [30]. Researchers in France reduced the number of ELBW infants with body weights <10th percentile to 27.1% and to 8.4% with a Z-score for body weight below the third percentile at discharge through the introduction of individually adjusted fortified human milk [31].

CONCLUSIONS

In conclusion, conducting comprehensive analyses of hospitalization outcomes for extremely preterm infants is essential for identifying critical areas of improvement and implementing evidence-based interventions. Such studies not only highlight variations in neonatal care practices and outcomes across the world but also guide policy changes and clinical protocols to enhance the survival and health of these vulnerable patients. Continued research and data collection are imperative to address the ongoing challenges and optimize care strategies for premature newborns worldwide.

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