

NEONATAL MORBIDITY AND EARLY OUTCOME OF VERY PRETERM INFANTS

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Abstract: Background: Although the mortality rate for preterm infants and the gestational age-specific mortality rate have dramatically improved over the last 3 to 4 decades, infants born preterm remain vulnerable to many complications, including respiratory distress syndrome, chronic lung disease, necrotizing enterocolitis, a compromised immune system, cardiovascular disorders, hearing and vision problems, and brain lesions.

The aim is to determine mortality and morbidity rates and selected outcome variables for preterm infant's < 30 weeks' gestation, who were admitted to the NICU.

Patients and methods: This study enrolled 102 infants with gestational age less than 30 weeks' gestation, hospitalized in Neonatal Intensive Care Unit, Pediatric Hospital, Clinical University Center Sarajevo, from Jan. 2010 to Dec. 2010. Parameters taken at admission were: birth weight, gestational age, Apgar score, excess base and CRIB score. Early outcome is considered as a survival at discharge or common preterm morbidities presented during hospitalization

Results: The mean BW of evaluated preterm infants was 1086 ± 250 g, the mean GA 27.89 ± 1.97 , Apgar score 5.41 ± 1.76 , excess base at admission 6.39 ± 1.74 and mean CRIB score 3.72 ± 3.16 . The overall survival rate was 70.5%. Selected outcomes at discharge were: RDS with 70.5% infants treated with natural surfactant, PDA treated with NSAIDS (23.5%), brain injury (\geq grade 3 IVH or PVL) 16.6%, NEC Bell stages II or III 9.8%, BPD 25/72 (33.3%) of infants who survived to 36 weeks postmenstrual age. In 38 (37.2%) infants, episodes of infections were noticed (one or more episodes in 25 infants), half of them were caused by Gram positive bacteria, most frequent coagulasa negative staphylococci. *Klebsiella pneumoniae* was the most frequent organism among Gram negative bacteria. One

patient had invasive candidiasis caused by *Candida albicans*. In 5 infants (4.9%) early onset of sepsis was documented.

Conclusion: Very preterm infants remain very vulnerable group of population, and interventions to reduce the morbidity and mortality of preterm babies include tertiary interventions such as regionalized care, transportation in uterus, and treatment with antenatal steroids.

Key words: very preterm infants, mortality rate, morbidity rate.

INTRODUCTION

Prematurity is defined as a birth that occurs before 37 completed weeks (less than 259 days) of gestation. Although the mortality rate for preterm infants and the gestational age-specific mortality rate have dramatically improved over the last 3 to 4 decades, infants born preterm remain vulnerable to many complications, including respiratory distress syndrome, chronic lung disease, injury to the intestines, a compromised immune system, cardiovascular disorders, hearing and vision problems, and neurological insult (1, 2, 3). The complications of preterm birth arise from immature organ systems that are not yet prepared to support life in the extrauterine environment. The risk of acute neonatal illness decreases with gestational age, reflecting the fragility and immaturity of the brain, lungs, immune system, kidneys, skin, eyes, and gastrointestinal system. In general, more immature preterm infants require more life support. Very preterm infants, despite being a minority in the total group of living births (about 1%), are a representative fraction of perinatal problems, accountable for nearly 50% of neonatal deaths and more than one third of infant mortality.⁴ Draper et al. have highlighted the variation across Europe in outcomes of

very preterm infants. Specifically, at 24–27 weeks' gestation, mortality as a percentage of infants alive at start of labor varied from 41.5% to 80.5%, and at <24 weeks' gestation from 0% to 9.7%.⁵ Beneficial changes have been reported to have arisen through the improved use of antenatal steroid therapy, surfactant treatment, permissive hypercapnea and increased use of non-invasive ventilation (2, 3).

Aim of this study is to determine mortality and morbidity rates and selected outcome variables for preterm infants ≤ 30 weeks' gestation, who were admitted to the NICU.

PATIENTS AND METHODS

This study enrolled 102 infants with gestational age less than 30 weeks' gestation, hospitalized in Neonatal Intensive Care Unit, Pediatric Hospital, Clinical University Center Sarajevo, during 2010y. Parameters taken at admission were: birth weight, gestational age, Apgar score, excess base and CRIB score. Gestational age (GA) was defined as the best estimate based on early prenatal ultrasound, obstetric examination and obstetric history, followed by pediatric estimate unless the postnatal pediatric estimate of gestation differed from the obstetric estimate by more than 2 weeks. In that case, the pediatric estimate was used instead. CRIB score uses six different variables obtained routinely during the first 12 hours of life: birth weight, gestational age, presence of congenital malformations excluding inevitably lethal congenital malformations, minimum and maximum appropriate inspired oxygen concentration and maximum base excess (6). Early outcome is considered as a survival at discharge or common preterm morbidities presented during hospitalization. Neonates were considered to have received a complete course of antenatal steroid if two doses were given to the mother between 2 and 7 days prior to birth. Bronchopulmonary dysplasia (BPD) was defined as the need for any form of respiratory support (oxygen or positive pressure support) at 36 weeks post-menstrual age or at the time of discharge to level two centers (7). Intraventricular hemorrhage (IVH) was defined according to the criteria of Papile et al. from the most severe findings on head ultrasound during the infant's stay (8). Periventricular echogenicity or leukomalacia were reported based on ultrasound findings (9). Necrotizing enterocolitis (NEC) was defined according to Bell's criteria (stage 2 or higher), and was classified as medical NEC (clinical symptoms and signs plus evidence of pneumatosis on abdominal X-ray in patients who were treated medically) or surgical NEC (laparotomy in addition to medical treatment) (10). Patent ductus arteriosus (PDA) was diagnosed

clinically, with or without echocardiography (11). The survey also included microbiological findings needed for documentation of systemic infection. Standard statistical analyses were performed for the study populations characteristics and clinical outcomes.

RESULTS

	Mean ± SD	Range
BW (g)	1086 ± 250.9	550–1480
GA (weeks)	27.89 ± 1.97	23–30
APGAR score	5.41 ± 1.76	1–9
BE	6.39 ± 1.74	–2(–25)
CRIB score	3.72 ± 3.16	0–18

Table 1. Clinical parameters at admission

The mean BW of evaluated preterm infants was 1086 ± 250 g, the mean gestational age 27.89 ± 1.97, Apgar score 5.41 ± 1.76, excess base at admission 6.39 ± 1.74 and mean CRIB score 3.72 ± 3.16.

	n	%
Surfactant	72	70.5
1 dose	44	43.1
2 or more	28	27.4
MV > 3 days	57	55.8
BPD	25/72*	33.3
PDA-NSAIDS	24	23.5
IVH/PVH gr. III/IV or/and cystic PVL	17	16.6
NEC	10	9.8
Sepsis, 1 or more episodes	38	37.2
Survivors	72	70.5

*BPD — infants survived to 36GW of postmenstrual age

Table 2. Clinical course and early outcome of very preterm infants (n = 102)

The overall survival rate was 70.5%. Approximately two thirds of patients (70.5%) were treated with at least one dose of natural surfactant (Survanta), 28 (27.4%) of them with two or more doses. About half of patients were conventionally ventilated longer than 3 days, others were ventilated shortly or using NCPAP with early surfactant replacement (INSURE strategy). Selected outcomes of very low birth weight infants VLBW infants were: PDA treated with NSAIDS (23.5%), brain injury (≥ grade 3 IVH or PVL) (16.6%), infection (37.2%), necrotizing enterocolitis Bell stages II or III

(9.8%), BPD (33.3%) of infants who survived to 36 weeks postmenstrual age.

Organism	EONS*	LONS*
Gram positive bacteria-total	3	16
Streptococcus beta haemolyticus	1	
Other streptococci		1
Coagulasa negative staphylococcus	1	10
MSSA	1	2
MRSA		2
Enterococcus species		1
Gram negative bacteria-total	2	17
Klebsiella pneumoniae	1	9
E.coli	1	2
Stenotrophomonas		3
Acinetobacter baumani		2
Serratia marcescens		1
Fungi — total		1
Candida albicans		1

EONS* Early Onset of Neonatal Sepsis

LONS* Late Onset of Neonatal Sepsis

Table 3. Organisms associated with bloodstream infections in < 30 GW neonates

38 (37.2%) episodes of infections were noticed (one or more episodes in 25 infants), half of them were caused by Gram positive bacteria, most frequent coagulasa negative staphylococci (CoNS). Klebsiella pneumoniae was the most frequent organism among Gram negative bacteria. One patient had invasive candidiasis caused by *Candida albicans*. In 5 infants (4.9%) early onset of sepsis was documented.

DISCUSSION

There are wide variations in the survival rates to discharge from neonatal intensive care for very preterm deliveries and in the timing of death. The overall survival rate of enrolled preterm infants in our study was 70.5%. This rate generally depends of organization of healthcare centers with creation of network for perinatal referral centers, policy of transportation in-uterus for all high risk pregnancies and Neonatal transport system (12). Survival rate of 70.5% for infants less than 30 weeks is comparable to data from literature (4), but it can be improved by significant restructuration of healthcare services and improving special training in neonatology (12).

The most frequent disease was respiratory distress syndrome. Only 38 (37%) of admitted preterm infants

were antenatally treated with steroids, so frequency and severity of RDS could be associated with the low rate of antenatal prevention. Antenatal steroids are recommended for all women between 25 and 34 weeks of pregnancy if preterm delivery is expected (13). As a result, the profile of RDS incidence and severity in high-income countries has altered allowing wider use of non-invasive ventilation and continuous airway pressure ventilation, reducing damage to the lungs (14). The picture of RDS has been changing using a new, less aggressive strategy for the treatment, including INSURE strategy (15). Approximately two thirds of patients (70.5%) were treated with at least one dose of natural surfactant (Survanta), 28 (27.4%) of them with two or more doses. About half of patients were conventionally ventilated longer than 3 days, others were ventilated shortly or using NCPAP with early surfactant replacement (INSURE strategy). PDA was documented in almost forth of all cases (23.5%), conservatively treated with single course of ibuprofen (11).

Brain injury (major hemorrhage or PVL) was documented in 16.6% cases. Occurrence of IVH-PVH is multifactorial (16, 17), but generally related to severity of RDS and hemodynamic instability (18, 19, 20) 25 very preterm babies developed BPD, making 33.3% of infants who survived to 36 weeks postmenstrual age. This percentage is similar to other studies (21).

Neonatal sepsis contributes to great mortality and morbidity among very-low-birth-weight (VLBW) infants. Prevalence and pathogen distribution of sepsis in the neonatal intensive care units vary with time and geographic location (22). In our study we had early onset sepsis prevalence of 5/102 (4.9%), with slightly more Gram positive than Gram negative bacteria. Late onset sepsis prevalence is much higher 33/102 (32.3%), half of which caused by Gram positive bacteria, and CoNS as a leading pathogen (comparable to other studies) (22).

Necrotizing enterocolitis (NEC) is a leading cause of infant mortality, and the most common reason for emergent surgery in very low birth weight infants (23). During their stay in NICU there were 37 (37.2%) episodes of infection or necrotizing enterocolitis, 10 patients (9.8%) developed NEC of Bell stages II or III. This rate is comparable with rate wide world (24), but is significantly higher than in high developed industrialized countries.

Since systemic infection is the first cause of death outcome in intensive care units, every effort should be made to reduce this rate in the future.

CONCLUSION

Very preterm infants remain very vulnerable group of population. Interventions to reduce the morbidity and mortality rate of preterm babies include tertiary in-

terventions such as regionalised care, transportation in uterus, and treatment with antenatal steroids.

Abbreviations

BW — Birth weight
 GA — Gestational age
 RDS — Respiratory distress syndrome
 PDA — Patent Ductus Arteriosus
 IVH-PVH — Intraventricular-Periventricular Hemorrhage

PVL — Periventricular leucomalacia
 NSAIDS — Nesteroid Anti Inflammatory Drugs
 BPD — Bronchopulmonary Dysplasia
 NEC — Necrotizing enterocolitis
 CoNS — coagulosa a negative staphylococci
 VLBW — very low birth weight infants

DECLARATION OF INTEREST

The authors declare no conflict of interest.

Sažetak

NEONATALNI MORBITET I RANI ISHOD VEOMA PREMATURNE NOVOROĐENČADI

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Premda su stope mortaliteta prevremeno rođene dece (i ukupna i dobno specifična), jako redukovane tokom poslednje 3–4 decenije, pretermimska deca ostaju vulnerabilna i predisponirana za razvoj mnogih komplikacija, uključujući respiratorni distres sindrom, hroničnu plućnu bolest, nekrotizirajući enterocolitis, kompromitovan imunološki sistem, kardiovaskularne poremećaje, probleme vida i sluha, oštećenja mozga.

Cilj rada je odrediti stopu mortaliteta i stope morbiditeta izabranih varijabli ishoda pretermimske dece < 30 nedelja gestacije, primljenih u Jedinicu neonatalnog intenzivnog lečenja.

Pacijenti i metode: Studija je uključila 102 dece gestacijske dobi < 30 gestacijskih nedelja, primljenih u Jedinicu neonatalnog intenzivnog lečenja Pedijatrijske klinike Kliničkog centra Univerziteta u Sarajevu u toku 2010. godine. Parametri uzeti kod prijema bili su: porođajna težina, gestacijska dob, Apgar score, bazni eksces (BE) i CRIB score. Ranim ishodom smatralo se preživljavanje kod otpusta iz bolnice te selektovane varijante ishoda koje predstavljaju najčešće komplikacije u toku hospitalizacije.

Rezultati: Prosečna porođajna težina ispitivane pretermimske dece bila je 1086 ± 250 gr, prosečna gestacijska dob $27,89 \pm 1,97$, Apgar score $5,41 \pm 1,76$, bazni eksces (BE) kod prijema $6,39 \pm 1,74$ i srednji CRIB score $3,72 \pm 3,16$. Ukupna stopa preživljavanja

bila je 70,5%. Izabrane varijable morbiditeta kod otpusta bile su: RDS sa 70,5% dece tretirane barem jednom dozom surfaktanta, perzistentni ductus arteriosus (PDA) tretiran nesteroidnim antireumaticima (NSAIDS) (23,5%), povrede mozga (\geq stepen 3 IVH ili PVL) (16,6%), nekrotizirajući enterokolitis II ili III stepena po Bell-u (9,8%), bronhopulmonalna displazija (BPD) kod 25/72 (33,3%) dece koja su preživela do 36 sedmica postmenstrualne dobi. U celoj grupi notirano je ukupno 38 (37,2%) epizoda sistemske infekcije (jedna ili više kod 25 dece), u polovini slučajeva uzrokovane gram pozitivnim bakterijama, najčešće koagulaza negativnim stafilokokom. Klebsiella pneumoniae je bila najčešće zastupljen mikroorganizam među gram negativnim bakterijama. Invazivna kandidijaza uzrokovana gljivicom Candida albicans nađena je kod jednog pacijenta. Kod 5 pacijenta (4,9%) dokumentovan je rani početak bolesti (unutar 48h), dok se kod ostalih radilo o infekciji sa kasnim početkom.

Zaključak: Prevremeno rođena deca ostaju veoma vulnerabilna populacijska skupina a postupci koji će redukovati stopu mortaliteta i morbiditeta uključuju intervencije tercijarne razine, kao što su regionalizacija, transport in utero, te široka antenatalna primena steroida.

Ključne reči: veoma prematurna novorođenčad, stopa mortaliteta, stopa morbiditeta.

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