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ORIGINAL PAPER

Assessing Mortality Risk in Very Low Birth Weight Infants

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Introduction: Preterm birth is the most important univariant risk factor of neonatal mortality. Assessment of risk factors affecting mortality in preterm infants with very low birth weight is important for the treatment of this highly vulnerable population. **Objective:** Detection of risk factors for neonatal mortality in very low birth weight premature infants. **Methods:** The current study was conducted in a tertiary research and educational hospital, NICU, Pediatric Clinic KCU Sarajevo, from January 2010 to December 2010. After admission CRIB score was determined to every hospitalized infant with birth weight <1500g, born before the full 31 weeks of gestation (30 weeks +6 days). We also gathered information about the Apgar score in 5th minute, gender, presence of respiratory distress syndrome and hemodynamic stability. 67 infants fulfilled inclusion criteria. **Results:** Mean birth weight was 1136.4 g ± 250.9, range 550-1500 g. Mean gestational age was 27.29 weeks ±1.97, range 22-30 weeks. Mean CRIB score was 3.22, range 0-18. Twenty VLBW infants out of 67 died (29.85%). There was significant difference between groups of survived and dead infants regarding gestational age, birth weight, Apgar score, Crib score, base excess, presence of respiratory distress syndrome and hemodynamic stability at the birth. **Conclusion:** CRIB score, birth weight, gestational age, base excess, Apgar score, respiratory distress syndrome and hemodynamic instability are valuable predictors for a neonatal mortality in population of preterm infants with very low birth weight. **Key words: very low birth weight preterm infant, neonatal mortality, risk factor.**

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1. INTRODUCTION

Preterm birth is the most important univariant risk factor of neonatal mortality in developed countries (1). However, advances in perinatal medicine in last decades have led to a noteworthy reduction in rates of neonatal mortality among very low birth weight infants (less then 1,500 grams). Progress in this field has brought the present limits of fetal viability into focus. Therefore, assessment for mortality risk became object of many studies (2, 3, 4).

Birth weight and gestational age were significant univariant predictors for neonatal mortality for a long time. Recently, more complete scoring systems for assessing risk of mortality have been developed. They aggregate physiological parameters that reflect initial clinical state of the newborn. Due to its simplicity and sensitivity, CRIB score (Clinical Risk Index for Babies) (5) is used in many neonatal intensive care units (NICU) worldwide. It stresses parameters which reflect the physiological conditions of the newborn soon after birth, and overcomes the disadvantages of birth weight and/or gestational age as specific predictors of neonatal mortality (6). This score may also be used in the evaluation of the performance of a single NICU throughout a period of time, or when comparing the performances of different units (7, 8, 9). 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 (10). The objective of the present study is to assess mortality predictors of very low birth weight infants.

2. PATIENTS AND METHODS

In this retrospective-prospective study undertaken during the period from January 2010 to December 2010, the CRIB score was applied to all newborns with a birth weight of <1,500 g and gestational age <31 weeks (30 weeks + 6 days), at the NICU of Pediatric Clinic, KCU Sarajevo. Gestational age was assessed on the bases of date taken from mother's last menstrual period. Besides CRIB score (Table 1), 5th minute Apgar score, gender, and signs of development of respiratory distress syndrome were also taken. As respiratory distress syndrome we considered presence of tachypnoa (respiratory rate >60 per minute), cyanosis, need for oxygen supplementation (FiO2) >40%, early "rescue" surfactant application, and need for respiratory support. We also assessed hemodynamic stability of our patients based on non-invasively measured blood pressure, and other indicators of circulatory stability (pulse moni-

toring, capillary refill time, urine output and acid base balance). Mean arterial pressure (MAP) of 30 mmHg was considered as a lower limit of normal blood pressure. We grouped infants as: 1. hemodynamicaly stabile – blood pressure within normal ranges, no need for inotropic support, nor volume expanders and 2. hemodynamicaly unstable – need for inotropic support and/or volume expanders. Criteria for exclusion from this study were: newborns that died in the first twelve hours of life, and those who presented inevitably lethal congenital malformations. As a neonatal death we define death within first 28 days. The CRIB score was calculated on the basis of an established number of points that are presented in Table 1, according to the proposal made by the International Neonatal Network (10).

Newborns who did not require respiratory support and gasometrical control received scores equal to zero in the FiO_2 factors (maximum and minimum), and maximum base excess. Quantitative variables were evaluated regarding to mean value and standard deviation. While comparing survivors with children who died we applied Student t test in evaluation of gestational age, birth weight, 5th minute Apgar score, base excess (BE) and CRIB score, and Chi square test for variables: gender, respiratory distress syndrome and hemodynamic stability. Statistics tests were carried out at the 5% significance level.

Factor	Score
Birth weight (g)	
>1350	0
851-1350	1
701-850	4
≤700	7
Gestational age (weeks)	
>24	0
≤24	1
Congenital malformations*	
None	0
Not acutely life threatening	1
Acutely life threatening	3
Maximum base excess in first 12h	
>-7.0	0
-7 do -9.9	1
-10 do -14.9	2
≤-15.0	4
Minimum appropriate FiO2 in first 12h	
<0.40	0
0.41-0.80	2
0.81-0.90	3
0.91-1.00	4
Maximum appropriate FiO2 in first 12h	
<0.40	0
0.41-0.80	1
0.81-0.90	3
0.91-1.00	5

Table 1. CRIB score *Excluding inevitable lethal malformations

3. RESULTS

Including criteria fulfilled 67 prematurely born infants. Mean birth weight is 1136.4 g ± 250.9 ranges 550-1500g. Mean gestational age is 27.29 weeks ± 1.97 ranges 22-30 weeks. Mean CRIB score is 3.22 ranges 0-18. 20 infants (29.85%) died.

Mortality rate in VLBW infants with BW between 750 and 999g was 46%, but in infants with BW <750g mortality was 100% (all 4 babies died). Survival rate of infants BW between 1000 and 1500g was 81%. Children born within or < 28 gestational weeks have survival rate of 61%; in infants born after 28 gestational weeks survival rate is 87%.

We found statistically significant difference between two groups (survivors and deaths) in relation to variables: gestational age (p=0.01058), birth weight (p=0.022192), Apgar score (p=0.03316), base excess (p=0.03776), CRIB score (p=0.00166), respiratory distress syndrome (p=0.013) and hemodynamic stability (p=0.000002).

Variable	Survivors N (%)	Deaths N (%)	Total N
BW (g)			
<750	0	4 (100%)	4
750-999	8 (53%)	7 (46%)	15
1000-1500	39 (81%)	9 (19%)	48
GW			
≤ 28	27 (61%)	17 (39%)	44
>28	20 (87%)	3 (13%)	23

Table 2. Mortality rate related to BW and GA. BW= birth weight, GW= Gestational weeks

We did not find statistically significant difference between these two groups in relation to variable gender (p=0.8959).

4. DISCUSSION

Despite enormous efforts done in order to reduce neonatal mortality, mortality rate in prematurely born infants with very low birth weight (VLBW, <1,500g) and low gestational age (VLGA, <32weeks) especially in countries with reduced resources is still relatively high. The survival is more questionable in population of premature infants with extremely low gestational age and birth weight (ELGA/BW, <28 weeks and <1,000g) (11). Interpretation of mortality rate generally should be considered related to quality of perinatal care and transport system, number of referrals, as well as level of accessible resources which vary widely between countries, and also between different neonatal intensive care units.

In studied period, the overall mortality rate of VLBW admissions was 29.85% with variations between groups: BW<750g (100%), BW 750-999g (53%) and BW 1,000-1,500 g (81%). VLBW infants at our center had similar survival rates compared with reports from other developing countries,. Survival rate is lower, especially for extremely low birth weight infants compared to developed countries (12, 13, 14, 15, 16).

There is interaction between gestational age and mortality rate. In our study, mortality of VLBW infants <29 GW was 63%, compared to 10% of VLBW infants >29GW.

Since 1952 when, thanks to Virginia Apgar, assessment of newborn's vitality became routine in nurseries worldwide, lots of studies have confirmed its practical value. Regardless the major lack of this way of evaluation which refers to the highly subjective moment by the assessor, the score was undisputed place in the assessment of vitality of infant at birth, but also in terms of the outcome. Considering its positive and also questionable characteristics, we must conclude that Apgar score still holds its place in prediction of morbidity and mortality in term and preterm

	SURVIVAL	DEATH	p
GW	27.74 ±1.74 (X±SD)	26.25±2.17(X ± SD)	0.0105
BW (g)	1189.57±206.93 (X±SD)	1011.5 ± 298.32 (X±SD)	0.0219
APGAR score	5.96±1.74 (X±SD)	4.9 ±1.8 (X±SD)	0.0331
Base excess	-5.39±3.52 (X±SD)	-9 ±6.94 (X±SD)	0.0377
CRIB score	2.0±2.16 (X±SD)	6.1 ±4.92 (X±SD)	0.0016
Gender	M 29 (61.7%) N(%) F 18 (38.2%) N(%)	M 12 (60%) N(%) F 8 (40%) N(%)	0.8959
Respiratory distress syndrome	25 (53.19%) N(%)	16 (85%) N(%)	0.0137
Hemodynamic instability	15 (31.91%) N(%)	19 (95%) N(%)	0.0002

Table 3. Mortality risk factors for VLBW infants

infants. This statement is confirmed by American authors who emphasize that "Low Apgar score was associated with increased mortality in premature neonates, including those at 24-28 weeks gestational age, and may be a useful tool for clinicians in assessing prognosis and for researchers as a risk prediction variable." (17). In this study we also found statistically significant difference between survivors and group of infants who died considering Apgar score ($p<0.05$).

Respiratory distress syndrome (RDS) is the most common cause of respiratory insufficiency in preterm infants, especially those born at <30 weeks of gestation (18). In our study ,62% had signs of developing RDS, requiring surfactant or respiratory support, which is comparable with other similar studies (19). The significant difference in outcome, depending of signs of RDS between study groups, confirms the fact that RDS still persists as a problem, regardless of big benefits that were given by the praxis of prenatal corticosteroid use, prophylactic and therapeutic use of surfactant, and rising praxis of non invasive techniques of mechanical ventilation by nasal CPAP (continuous positive airway pressure). RDS is associated with an increased risk in the incidence of retinopathy of prematurity, presence of persistent arterial duct, late onset sepsis, severe intraventricular bleeding and oxygen requirement at 36 weeks of corrected gestational age (19). RDS also increases the use of resources (19).

We used CRIB score in prediction of mortality and verified that it was easily applied, since it uses variables that are part of the routine care of preterm newborns.

This score is practical, easy to calculate using physiological variables, and it does not take additional time. Initial clinical state of infant is product of previous obstetric events, those that occur during labor and available perinatal and health care within first 12 hours. CRIB score can be easily reproduced, avoiding interpretation errors due to individual subjectivity. The median CRIB score for infants who survived was 2.0 and 6.1 for those who did not survive ($p<0.005$), and this result is similar to other studies (5).

We also assessed base excess BE as possible predictor of unfavorable outcome. We found the significant difference between group of survivors and group of infants who died $p<0.05$ and conclude that base excess can be considered as mortality predictor. Canadian colleagues emphasize that "umbilical cord pH and BE are related to subsequent adverse outcome events for infants delivered preterm. Worsening acidosis is associated with progressively greater increases in these outcomes with no discriminatory value within or between umbilical artery and umbilical vein pH and BE. "(20).

Hemodynamic instability is a risk factor for mortality as well. It is well known fact that organ damage from circulatory compromise occurs when tissue oxygen demand exceeds delivery (21). Hypoperfusion and ischemia lead to cascade of events that result in metabolic disorder (acidosis), and their final result is development of different substrates of organs and systems like: intraventricular bleeding, necrotizing enterocolitis, renal failure, etc. Statistically, we found significant difference in hemodynamic stability between survivors and death, and conclude that hemodynamic instability can be recognized as a mortality predictor.

We didn't prove previously published results (22) of female gender as a protective, ($p>0.05$).

Recognition of mortality risk factors for VLBW infants may help us in early identification of high risk infants to give maximum efforts for their survival. CRIB score is a useful tool in comparing different neonatal intensive care units, and work evaluation of one unit during different periods of time as well. CRIB score can also help us to evaluate level of perinatal care and quality of neonatal transport.

5. CONCLUSION

CRIB score, birth weight, gestational age, base excess, Apgar score, respiratory distress syndrome and hemodynamic instability are valuable predictors of mortality in population of prematurely born infants with very low birth weight.

The authors declare no conflict of interest.

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