

Survival Predictors of Preterm Neonates - Single Center Experience

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Abstract

Introduction: Adequate prenatal and postnatal care for preterm neonates not only affects the survival rate, but also the occurrence of chronic diseases, and in the future also affects the quality of life of that children.

Aim: To examine the influence of independent predictors (weeks of gestation, body weight, sex) on the outcome of the disease and to analyze the influence of the applied ventilatory mode on the final outcome of treatment.

Material and methods: The study included neonates (n = 248) born prematurely who were treated in the neonatal intensive care unit for a period of one year due to immaturity-related difficulties.

Results: The mean age of male neonates (n = 119) at birth was 31.13 ± 3.3 weeks of gestation (WG), and females (n = 129) 31.59 ± 3.2 WG. Weeks of gestation have a statistically significant effect on survival ($p = 0.0001$), for each more week of gestation, the chances of survival increase by 21%. There was no significant difference between birth weight and sex ($p = 0.289$), and the birth weight of the neonates had a statistically significant effect on survival ($p = 0.0001$). For every 10 grams of body weight, in our sample, the chance of survival increases by 2%. Ventilation mode showed a statistically significant effect on neonatal survival ($p < 0.05$), and intubation mode was used as an indicator. If neonates are switched from non-invasive to invasive ventilation mode, the chance of survival in our sample is reduced by 88%.

Conclusion: Weeks of gestation, birth weight, and the use of a noninvasive mode of ventilation are predictors of a positive outcome for preterm neonates.

Keywords. Preterm Birth, Neonatal, Intensive Care, born prematurely

Introduction

Prematurity is defined as the birth of a child before the 37th week of gestation (WG). The classification of preterm neonates can be performed in relation to the weeks of

pregnancy and birth weight [1]. Worldwide, the incidence of preterm birth is different and is influenced by different factors. About 15 million children are born prematurely worldwide during the year. In developed European countries, the incidence is about 5%, while in African countries this incidence is 18%. 84% of births occur in the period from 32 to 36 WG, 10% of births in the period from 28 to 32 WG, and 5% before 28 WG. According to datas from 2014 in the United States, about 9.57% of children are born prematurely. While in 2015, 8.1% of children had a lower birth weight [2. 3]. Neonatal death is defined as the death of a newborn before the 28th day of life. The definition of the preterm birth rate used is "all livebirths before 37 completed weeks, whether singleton, twin, or higher order multiples, divided by all livebirths in the population". [4]. Preterm birth rate is a direct indicator of, among other things, the quality of prenatal and postnatal medical care. There are several factors that impact on the survival rate of preterm neonates, such as: weeks of gestation (WG) at

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birth, associated congenital anomalies, the social status of the mother and the level of neonatal care. Prenatal use of steroids to prevent respiratory distress, as well as early surfactant administration, noninvasive ventilation, and other supportive therapies used in neonatal intensive care units have a significant impact on increasing the survival rate of preterm neonates [5, 6, 7]. Adequate prenatal and postnatal care for preterm neonates not only affects the survival rate, but also the occurrence of chronic diseases, and in the future also affects the quality of life of that children. Aim of this paper was to examine the influence of independent predictors (weeks of gestation, body weight, sex) on the outcome of the disease and to analyze the influence of the applied ventilatory mode on the final outcome of treatment.

Patients and Methods

Patients and study design; During the one-year period (January 1, 2019 to December 31, 2019), 402 neonates were hospitalized at the Department of Neonatal Intensive Care of the Pediatric Clinic Clinical Center University in Sarajevo. Out of the total number, 248 neonates were admitted to the Department due to preterm birth and difficulties caused by fetal immaturity. All preterm neonates with respiratory problems caused by immaturity were included in the study. We excluded from the study preterm neonates with associated congenital anomalies and other difficulties not related to the respiratory system.

Methods; The study is prospective, and analyzed the influence of gender, weeks of gestation at birth, body weight, surfactant application, ventilatory mode, and duration of ventilatory support on the disease outcome itself. Informed consent was obtained from all parents following an explanation of the purpose of the study. Ethical approval was obtained from Ethical Committee of Clinical Center University of Sarajevo.

Statistical analysis; The results of statistical analyzes are presented in absolute (n) and real values (%), arithmetic mean and standard deviation, and comparisons between

them with the appropriate test (t-test). The independent influence of individual factors on the binary dependent variable change (survived / did not survive), in a function of time, was compared with the help of univariate and multivariate Cox regression analysis. The analysis data are presented in a table. Statistical level of 95% ($p < 0.05$) was taken as significant for all performed tests.

Results

Out of the total number, 129 (52.0%) subjects were female and 119 (48.0%) male. The mean age of male neonates at birth was 31.13 ± 3.3 WG, and females 31.59 ± 3.2 WG, with no significant statistical difference between weeks of gestation at birth and sex ($p = 0.259$). Weeks of gestation have a statistically significant effect on survival in our study ($p = 0.0001$). In our study, for each more week of gestation, the chances of survival increase by 21%, while in the population of such subjects the chance ranges between 29-12%. The average birth weight of male neonates was 1791.6 ± 630.6 grams and females 1709.8 ± 580.6 grams, in our study we found that there was no significant statistical differences between birth weight and sex ($p = 0.289$). The birth weight of the neonates has a statistically significant effect on survival ($p = 0.0001$). (Tab. 1)

For every 10 grams of birth weight, in our study, the chance of survival increases by 2%, while in the population the chance of survival increases by 3-1%. We administered the surfactant in 117 (47.2%) cases, while 131 (52.8%) did not receive the surfactant. The reason for not administering surfactant in 131 subjects or 52.8% of cases was the higher gestational age of the neonates, good general condition - during initial care, satisfactory radiological findings of the respiratory system as well as a good response to initial treatment and care. Out of the 117 neonates, 87 (74.3%) received a single dose of surfactant. Univariate Cox regression analysis examined the influence of independent predictors in a function of time on the dependent variable, disease outcome (survived / did not survive). In our study,

Table 1. Individual influence of independent predictors in a function of time on the dependent variable, disease outcome (survived / did not survive)

	B	SE	Wald	df	p.	Exp(B)	95,0% CI for Exp(B)	
							Lower	Upper
Sex (m/f)	,029	,309	,009	1	0,924	1,030	,562	1,885
Weeks of gestation	-,235	,055	18,055	1	,0001	,790	,709	,881
Birth weight (x10 grams)	-,021	,004	21,784	1	,0001	,980	,971	,988
Received surfactant (yes/no)	,675	,462	2,130	1	0,144	1,964	,793	4,860
Surfactant dose (0/1/2/3)	,296	,163	3,306	1	0,066	1,347	,980	1,851
MV modus			19,008	2	,000			
MV modus(1) Nasal CPAP	11,020	125,830	,008	1	,930	61053,434	,000	7,809E+111
MV modus(2) Invasive ventilation	-2,120	,486	19,000	1	,0001	,120	,046	,311

B- standardized regression coefficient, Wald - nonstandardized regression coefficient, df- degrees of freedom, p- significance of the statistical test,

EXP(B) - odds ratio with 95% confidence interval (CI) (lower, upper)

Table 2. Common influence of independent predictors in a function of time on the dependent variable, disease outcome (survived / did not survive).

Model 1	B	SE	Wald	df	Sig.	Exp(B)	95,0% CI for Exp(B)	
							Lower	Upper
Weeks of gestation	,078	,090	,759	1	,384	1,081	,907	1,290
Birth wight (x10 grams)	-,021	,007	9,678	1	,002	,979	,966	,992
MV modus			12,508	2	,002			
MV modus ⁽¹⁾	12,111	124,003	,010	1	,922	181831,70	,000	6,47E+11
MV modus ⁽²⁾	-1,742	,493	12,498	1	,000	,175	,067	,460

B- standardized regression coefficient, Wald - nonstandardized regression coefficient, df - degrees of freedom, p - significance of the statistical test, EXP(B) - odds ratio with 95% confidence interval (CI) (lower, upper)

the sex of the subjects, as well as the administration of surfactant (compared to non-administration of the same) did not show a statistically significant effect on survival ($p > 0.05$). Multivariate Cox regression analysis examined the influence of independent predictors (weeks of gestation, birth weight and mode of ventilation) in a function of time on the dependent variable, disease outcome (survived / did not survive). Lower weeks of gestation as well as lower values of birth weight statistically significant affect the survival rate. Ventilation mode also showed a univariate statistically significant effect on neonatal survival $p < 0.05$, and intubation mode was used as an indicator. If neonates are transferred from the mode of non-invasive to the mode of invasive ventilation, the chance of survival in our study is reduced by 88%, while in the newborn population it ranges between 95-69%. (tab. 2)

Discussion

According to the World Health Organisation (WHO), globally, the number of preterm births is 11%. This percentage varies in the range of 5% in European countries and 18% in some parts of Africa [2, 3]. In the United States, approximately 550,000 preterm neonates are born annually [2, 3]. The rate of preterm birth in Bosnia and Herzegovina in 2012 was 7.9% according to the data stated in the EMBARGO study - WHO [11]. In our study in the period January 1, 2019 to December 31, 2019, a total of 3,213 neonates were born at the Clinic for Gynecology and Obstetrics. In the same period, a total of 402 neonates were admitted to the Department of Neonatal Intensive Care, and of the total number, 248 (61.6%) were admitted due to preterm birth and difficulties caused by immaturity.

According to Blencowe H *et al.* of the total number of preterm births, 84% occurs in the period of 32-36 weeks of gestation (WG), 10% in the period of 28-32 WG and 5% at the age of less than 28 WG. [4]. In our study, there was no statistically significant difference between the sex of preterm neonates treated at the Department of Neonatal Intensive Care, nor were there differences in their birth weight [9, 10, 12, 13, 14, 15]. It should be noted that neonates born as late prematures and who were in good general condition were

not hospitalized at the Department of Neonatal Intensive Care. As Watkins WJ *et al.* states the mortality rate of preterm neonates correlates with birth weight and weeks of gestation [10].

In our study, we concluded that for each week of gestation more, the chances of survival increase by 21%. The results obtained coincide with data from 2017 which state that the mortality rate in the United States per 1000 live births increases with lower gestational age [8]. The birth weight of the neonates has a statistically significant effect on survival. [15, 16, 17, 18, 19, 20, 21]. In our study, for every 10 grams of body weight of the neonate, the chance of survival increased by 2%, while in the population this chance ranges between 3-1%. Advances in the approach to the treatment of preterm neonates in intensive care units, which include, among other things, early use of surfactant, non-invasive ventilation and other supportive therapy, have resulted in a reduced neonate mortality rate.

The situation in Bosnia and Herzegovina has changed significantly with the establishment of neonatal intensive care. In 1986, the infant mortality rate was 26.1 per 1,000 live births, and in 2019, 5.1 per 1,000 live births (World Bank – World Development indicators) [11]. In a large prospective study, Patel RM *et al.* and Norman M *et al.* have shown that adequate access and initially adequate care of preterm neonates significantly increases the survival rate of preterm neonates [12, 13]. In our study, due to clinical and radiological signs of respiratory distress syndrome (RDS), surfactant was administered to 117 (47.2%) preterm neonates, while due to good general condition and good response to initial care, 131 of them did not receive surfactant. In the presented model, the greatest influence on survival had the ventilation mode, then the birth weight and at the end the weeks of gestation. In our study, if preterm neonate for any reason was translated from non-invasive to invasive ventilatory mode, the chance of survival was reduced by 88%, while in the population this value ranges between 95-69%. Although there are studies that state that male preterm neonates have a higher mortality rate than females [15, 16], in our study, the sex of the subjects did not show a statistically significant impact on survival. Simultaneously, initial adequate care involving early surfactant administration as well as

noninvasive ventilation showed a better outcome compared to repeated surfactant doses that did not prove statistically significant for the survival of treated subjects. The study limits are a short study period (12 months), lack of data on the obstetric measures (prenatal use of corticosteroids), as well as insight into other factors that contribute to mortality such as infections, bleeding, necrotic enterocolitis of the neonates.

Conclusion

Weeks of gestation, birth weight, and the use of a noninvasive mode of ventilation are predictors of a positive outcome for preterm neonates. Each week of pregnancy increases the chance of survival by one-fifth, which can be an important indicator for gynecologists to try to influence on the duration of pregnancy as much as possible (in the case of pathological and risky pregnancies). The result of prolonged gestation is a higher birth weight and a higher chance of survival (2% for each 10 grams of body weight)

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