ORIGINAL ARTICLE

Risk factors associated with mortality in infants weighing less than 1500 g using the CRIB II scale

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ABSTRACT

Background. Clinical Risk Index for Babies (CRIB) II score as well as other scoring systems was developed during the last decade in neonatal intensive care units in order to predict morbidity and mortality risk. Today, risk-adjusted severity of illness is frequently used in clinical research and quality assessments. The objective was to evaluate the clinical risk index in very low birth weight newborns with the CRIB II score in a tertiary hospital during 2007-2009.
Methods. We performed a case-control study in 52 patients who died (cases) and 52 survivors (controls). Descriptive statistical analysis was performed by obtaining mean and standard deviation. We also performed odds ratio with 95% confidence interval and ROC curves in order to obtain cutoff points for sensitivity and specificity.
Results. Mean gestational age was 28.5 weeks. Average weight was 865 g. Factors associated with increased risk of mortality were male gender, low Apgar score, temperature <36ºC, intraventricular hemorrhage and high frequency ventilation. The most frequent cause of mortality (90%) was extreme prematurity. Intraventricular hemorrhage was the most common direct cause (40.3%) followed by septic shock (19.2%), air leak (11.5%), hyaline membrane disease (9.6%) pulmonary hemorrhage (9.6%) and enterocolitis (3.8%).
Conclusions. The CRIB II SCALE is a useful tool for predicting neonatal mortality.
Key words: prematurity, mortality, low birth weight.

INTRODUCTION

Neonatal mortality is one of the most important health care indicators of a country. It reflects the degree of development of a nation and the health status of its population; therefore, being aware of this can pose specific health policies and strategies.[1] Since 1960, the neonatal intensive care unit (NICU) began to expand for the treatment of critically ill infants. According to the most recent data from the American Academy of Pediatrics (AAP), there were >850 NICUs and 4,300 neonatologists in the U.S. during 2008.

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There are estimates of the expenses incurred in caring for premature and low birth weight neonates: in 2001 the U.S. spent 45 billion dollars.[3] Phibbs et al. report that neonates of very low birth weight account for one third of this expenditure.[4] However, despite the high cost in the NICUs,[5] neonatal mortality rates showed a decrease of 2.6% in 1960 to 0.69% in 2007.[6]

Among the main causes of mortality in Mexico are diseases originating in the perinatal period, which include asphyxia, respiratory distress syndrome and infections followed by congenital malformations. Instituto Nacional de Perinatología "Isidro Espinosa de los Reyes" (INPer) represents a high-risk perinatal medical institution and this institution reported a mortality rate of 19.7/1,000 of live birth neonates for 2008.[1] Some specialized centers report that ~85% of newborns weighing between 1,200 and 1,550 g (29-31 weeks of gestation) and 70% of newborns in the group weighing 750-1,000 g (26-28 weeks of gestation) survive.[7-9]

During the 1990s, severity scales were developed to assess low birth weight neonates and those with a gestational age <32 weeks; however, there is no uniform application in the entire group of NICUs.[10]

In relation to the risk scales, these are tools to quantify the baseline risk of mortality and to facilitate and validate the comparison of results. This may be very useful to monitor quality and costs of the intensive care that is provided and, thus, establish an acceptable standard of performance in these units.[7,11]

Severity measurements in the NICU traditionally regarded as prognostic factors are birth weight, gestational age and Apgar score; however, correlation between mortality and these indicators is not significant when viewed in an isolated manner.[8,12] Some studies have reported significant variations in morbidity and mortality in the NICU. Establishing the source of this variation has been a difficult task due to the lack of adequate measurement of the disease severity in patients admitted to these units.[8]

The development of severity scales has several goals including the validation of the results through comparisons with the different hospital centers where they are applied.[8,13]

The objective of this study was to validate the usefulness of the CRIB II scale for mortality in neonates weighing <1,500 g at a tertiary-care pediatric health institution.

SUBJECTS AND METHODS

We included all neonates weighing <1,500 g who were admitted to the NICU and who died during the period between 2007 and 2009. The study design was case/control.

The CRIB II (*Clinical Risk Index for Babies II*) is a risk index for newborns weighing <1,500 g that includes the following variables: birth weight, gestational age, congenital malformations, base deficit and temperature in the first 12 h of life. The scale is divided according to gender, and weights are compared with gestational age. The range of scores for weight compared with gestational age in males is 0-15 and in females is 0-14. For temperature range the score is 0 to 5 and for base excess is 0 to 7. At the end, the scores are totalled.[14,15]

Inclusion criteria were newborns with birth weight <1,500 g and who died in the NICU. Exclusion criteria included the following: 1) newborns who died prior to 12 h of life, or 2) major congenital malformation. Criteria for elimination included if the patient was transferred to another hospital unit.

Statistical analysis was performed by obtaining averages, odds ratios with confidence interval 95%, and ROC curves for cohort points of sensitivity and specificity.

RESULTS

We analyzed 104 cases of newborns, of whom 52 died (cases) and 52 survived (controls). In terms of associated maternal risk factors, we found only a decreased risk of mortality due to the use of prenatal steroids 0.18 (95% CI, 0.07-0.44) (Table 1). The four main maternal risk conditions were severe preeclampsia in 12 cases (37.5%), chorioamnionitis in five cases (15.6%), recurrent pregnancy loss in three cases (9.3%) and gestational diabetes in three cases (9.3%) (Figure 1).

In relation to maternal pathologies and the CRIB II score, we found that the average score of deaths for preeclampsia was 9.1 and for controls was 7.6. The average for deaths due to chorioamnionitis was 10.4 (for controls, chorioamnionitis was not diagnosed).

For deaths according to maternal pathology, there were 32 cases (62%) corresponding to mothers with an underlying disease and 20 cases (38%) corresponding to healthy mothers. Regarding the newborns, the average deaths per year was 11.53% in 2007, 20% in 2008 and 16.77% in 2009.

The average age of the study group was 28.5 weeks of gestation (WG) (range: 24-36 WG) and the control group had an average of 29.4 WG (range 27-33 WG). The average weight (g) for the study group was 865.1 g (range: 516-1,315 g) and in the control group was 881 g (540-1,466 g). In relation to newborns who died, we found that the lower the weight, the greater the number of cases. Of the 52 deaths, 34.6% corresponded to neonates between 500 and 749 g, 40.4% between 750 and 999 g and 17.3% between 1,000 and 1,249 g (Figure 2).

According to the study of nine neonatal variables, seven showed significant differences in increased risk: male gender, low Apgar score at 1 min, low Apgar score at 5 min, temperature <36°C, intraventricular hemorrhage (IVH), and high-frequency ventilation (Table 2).

Extreme prematurity represented the most common underlying cause of death (90%) followed by intrauterine pneumonia and sepsis with 4%; asphyxia accounted for 2%. IVH was the most common direct cause in 21 cases (40.3%) followed by septic shock in 10 cases (19.2%), air

Table 1. Maternal risk factors associated with mortality in newborns weighing <1500 g

Maternal risk factors	*Cases (died) n = 52*	*Controls (survivors) n = 52*	*OR*	*95% CI*
Reside in the Federal District	32 (61.5%)	34 (65.3%)	0.85	0.38-1.88
Teenage mother	7 (13.5%)	7 (13.5%)	1	0.32-3.08
Age ≥35 years	10 (19.2%)	16 (30.8%)	0.53	0.21-1.32
Primary, secondary or preparatory education	41 (78.8%)	43 (82.7%)	0.78	0.29-2.08
Married	21 (40.4%)	20 (38.5%)	1.08	0.49-2.38
First pregnancy	20 (38.5%)	18 (34.6%)	1.18	0.53-2.62
Prenatal care	15 (28.8%)	17 (32.7%)	0.83	0.36-1.92
Multiple pregnancy	16 (30.8%)	15 (28.8%)	1.09	0.43-2.54
Pathology associated with pregnancy	32 (61.5%)	37 (71.2%)	0.64	0.28-1.47
Cesarean	44 (84.6%)	46 (88.5%)	0.71	0.23-2.23
Premature rupture of membranes	17 (32.7%)	13 (25%)	1.45	0.62-3.42
Prenatal steroids (complete scheme)	20 (38.5%)	40 (77%)	0.18	0.07-0.44

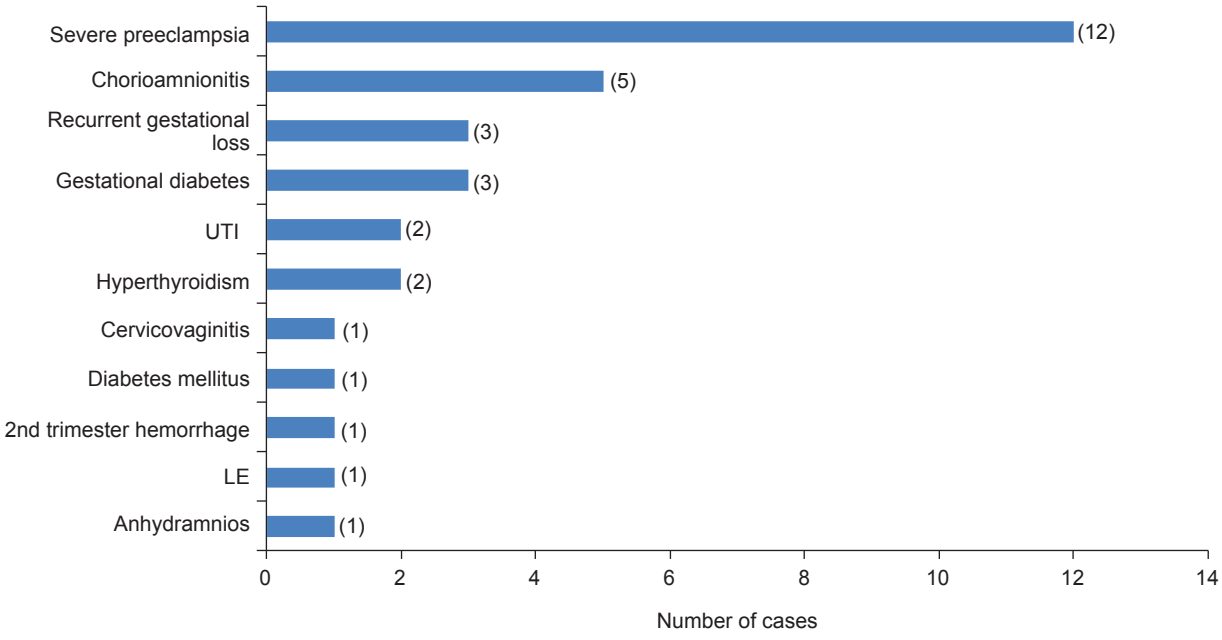

Figure 1. Neonates <1500 g who died according to maternal pathology, 2007-2009.

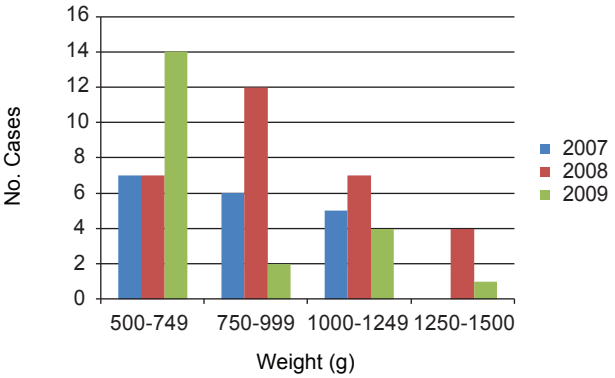

Figure 2. Mortality in neonates weighing <1500 g, 2007-2009.

leak in six cases (11.5%), and hyaline membrane disease and pulmonary hemorrhage in five cases (9.6%) (Figure 3).

ROC curves were performed and we calculated the following results: for newborns who died, in those who scored 9 or greater for the CRIB II, the OR for dying was 4.07 (95% CI, 1.76-9.37), sensitivity was 73% and specificity was 60% (Figure 4).

The relationship between weight and CRIB II score was inversely proportional to the deaths. The average hospital stay in the case group was 6.25 days (range: 1-21 days) and for the controls was 37.2 days (range: 2-175 days).

DISCUSSION

Neonatal assessment scales began to be used in the UK with the intention of identifying populations at risk of mortality with the implementation of the CRIB scale. In the U.S., the SNAP scale was used.[7] Currently, both have >10 years of use in Europe, U.S. and Canada. In Mexico, there are few reports of investigation of the systematic use of neonatal severity scales.[16]

The neonatal CRIB II severity scale can be used as a predictive factor of mortality in addition to the following factors not included in severity scales: no prenatal care, prematurity, prolonged rupture of membranes with associated chorioamnionitis, among others affecting the premature neonate with low birth weight.[16] Regarding the applicability of the neonatal severity scales, these are practical and are quickly completed because they have only five variables.[16]

A study of extremely low birth weight neonates reports that 85% were born before 28 WG.[17] However, when comparing our results with those of Osorio et al., we found that the average gestational age coincides with their study (28-32.6 WG).[18] Of the maternal risk factors associated with mortality, the only one that showed a significant difference was use of prenatal steroids. Different authors have observed a decrease in mortality with a scheme of steroids.[19-21]

Severe preeclampsia was the most important disease to cause premature delivery. The frequency in the InPer is similar to that reported elsewhere in Mexico (38%). According to the U.S. Secretary of Health, the rate of preeclampsia increased to 40% during the period between 1990 and 1999 and was comprised of up to 40% of iatrogenic premature deliveries.[22] The second most important condition that caused death was chorioamnionitis. It is possible that this pathology is associated with the increased infections in newborns and development of septic shock. Production of immunoglobulins initiates at

Table 2. Neonatal risk factors associated with mortality in newborns weighing <1500 g

Neonatal risk factors	*Cases (died) n = 52*	*Controls (survivors) n = 52*	*OR*	*95% CI*
Male	33 (63.5%)	16 (30.8%)	3.9	1.72-8.83
Low Apgar at 1 min (≤3)	29 (55.8%)	17 (32.7%)	2.59	1.16-5.76
Low Apgar at 5 min (≤3)	9 (17.3%)	1 (1.92%)	10.67	1.29-87.6
Temperature <36ºC	19 (36.5%)	1 (1.92%)	29.36	3.74-229.9
Base deficit -10	28 (53.8%)	2 (3.84%)	29.16	6.41-132.6
Prophylactic surfactant	45 (86.5%)	49 (94.2%)	0.39	0.09-1.61
Reapplication of surfactant	9 (17.3%)	11(21.2%)	0.78	0.29-2.07
Intraventricular hemorrhage	22 (42.3%)	5 (9.6%)	6.89	2.35-20.17
High-frequency ventilation	17 (32.7%)	1 (1.92%)	24.77	3.15-194.7

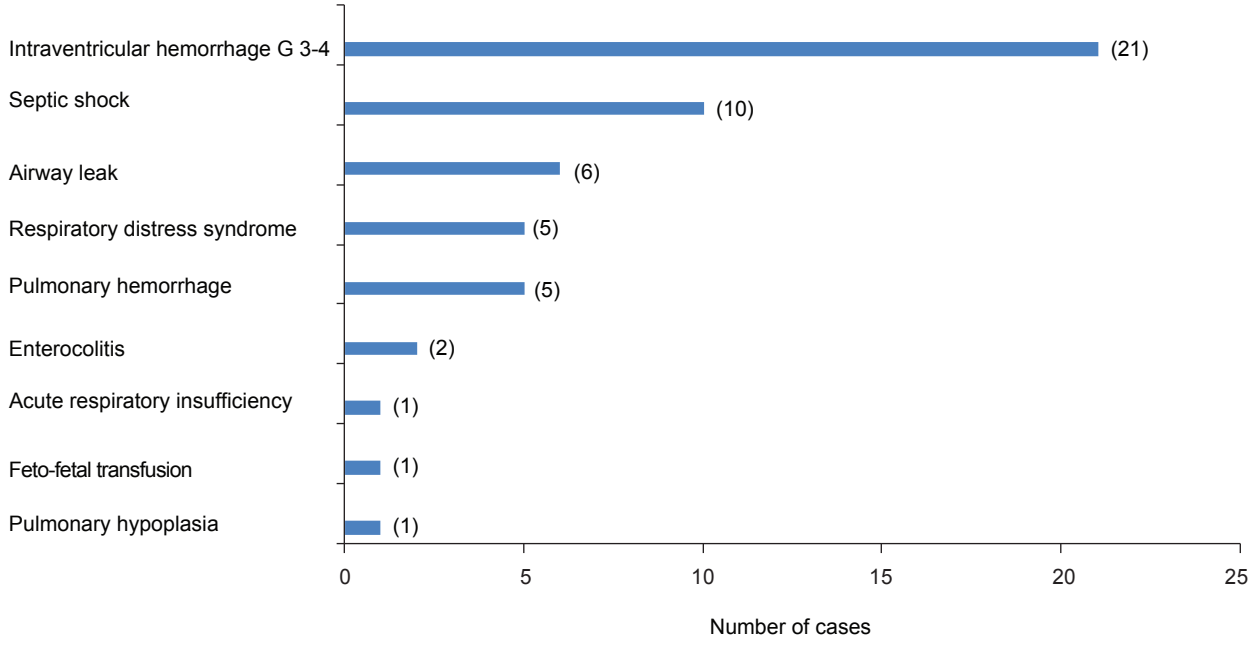

Figure 3. Direct case of death, 2007-2009.

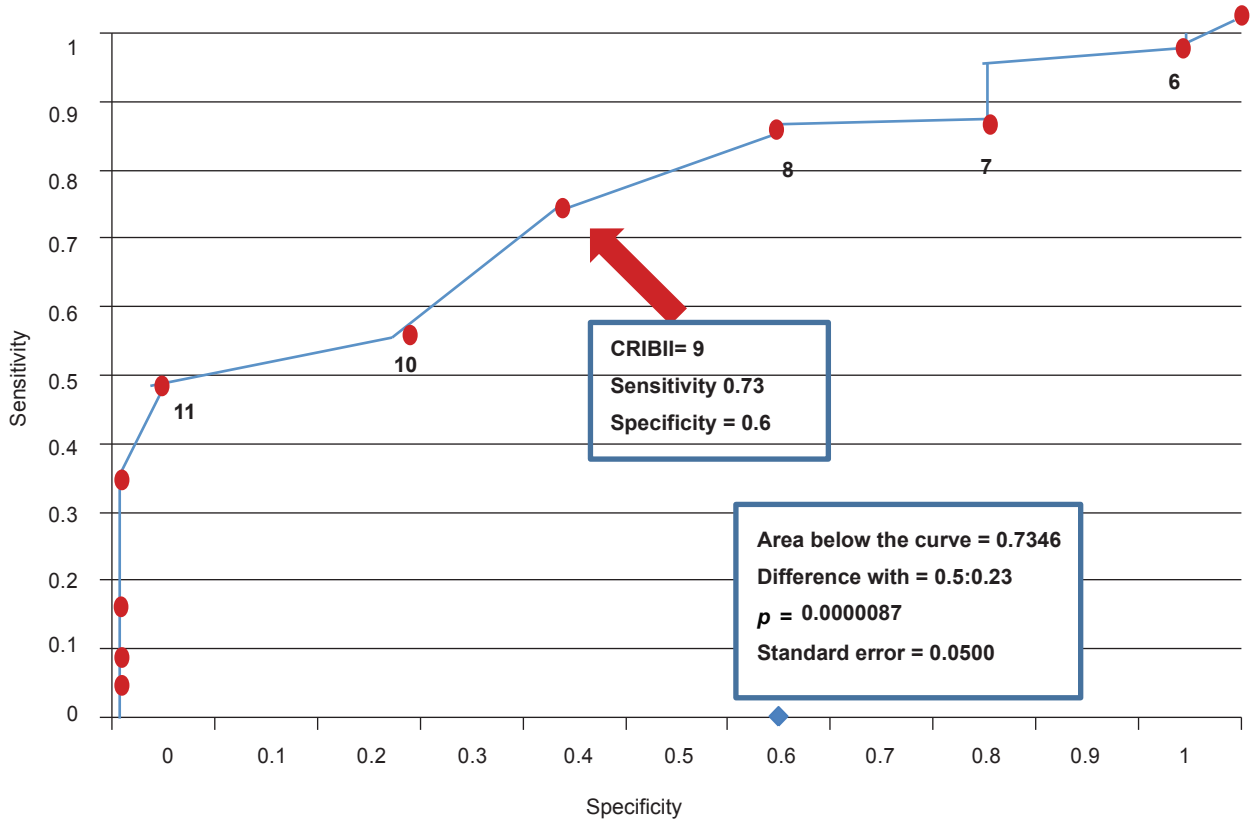

Figure 4. ROC curve with CRIB II score in the first 12 h of life as a predictor of death in the neonatal intensive care unit (NICU), 2007-2009.

between 32 and 34 WG and the average age of neonates who died was 28 WG.[23] Likewise, there was a relationship between the first two maternal diseases (preeclampsia and chorioamnionitis) and the mean CRIB II score between cases and controls. Cases had averages above the cut-off values for these two diseases. Of the risk factors associated with neonatal mortality, we consider that these variables (gender, weight, gestational age, bicarbonate deficiency and temperature) play a central role in the risk of neonatal mortality because of measured physiological aspects of neonatal homeostasis.[24]

The most important direct cause of death was grade III IVH. This is in agreement with the study by Volpe who reported that 60% of the neonates with this condition perish.[25] We found no relationship between minor heart diseases such as persistence of patent ductus arteriosus (PDA) without impact (five cases for each group) and IVH.

With regard to Apgar, a close relationship exists (increased risk) between low scores both at the first minute as well as at after 5 min and the death of the neonate, as demonstrated in this study where the low Apgar score at 5 min increased the risk of mortality more than 10 times. Casey et al. found, in neonates between 26 to 36 WG, increased mortality with Apgar scores of 0-3 in 315 × 1,000 births (RR 59, 95% CI 40-87 and Apgar 4-6 in 72 × 1,000 births (RR of 13, 95% CI 9-20).[26]

ROC curve shows sensitivity and specificity of the CRIB II scale as predictive of mortality; the cohort score was 9. When the score was 11, mortality was 96%, 12 or more points had 100% mortality. Sensitivity was 73%, which predicts mortality in a little over 7/10 cases; nevertheless, specificity was low (60%).

The relationship between weight and CRIB II score was inversely related to those who died. The importance of birth weight in the prediction of neonatal morbidity and mortality is indisputable. In fact, many studies refer to it as the main predictor.[27-30] The average hospital stay of the deceased patients was 6 days. It is important to recognize this period as the period with the highest probability of neonatal mortality because most die during the first 7 days of life.[31]

Based on the results of this study, we can conclude the following:

CRIB II scale of mortality presented a sensitivity of 73% and specificity of 60%.

Cut-off point for mortality was 9 points; with a score of 11 the mortality was 96% and 12 or more was 100%.

Weight and gestational age are determinant for mortality.

Variables that resulted with a higher risk for mortality were male gender, low Apgar score at 1 min, low Apgar score at 5 min, temperature <36°C, IVH, and high-frequency ventilation.

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