

Determination of Predictive Power of CRIB-II and SNAPPE-II in Mortality Risk of Neonates with Low Gestational Age or Birth Weight Admitted to the Neonatal Intensive Care Unit

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ABSTRACT

Background: Risk scoring systems evaluate neonatal outcomes using perinatal and neonatal status. The present study aimed to predict the mortality risk of preterm or low birth weight infants using the Clinical Risk Index for Babies (CRIB-II) and Score for Neonatal Acute Physiology Perinatal Extension (SNAPPE-II) scoring systems.

Methods: This prospective cohort study investigated the preterm neonates admitted to the Neonatal Intensive Care Unit (NICU) of Vali-e-Asr Hospital, Tehran, Iran, with the birth weight of <1500g or a gestational age <32 weeks using the CRIB-II and SNAPPE-II scoring systems within the first 12 h after birth. The area under the curve, sensitivity, specificity, positive and negative predictive values of the scoring systems, as well as the association between neonate factors and neonatal death were calculated in this study.

Results: Out of 344 neonates under study, 253 cases survived after 24 h of birth and 91 newborns died. The total CRIB-II scores in survived and deceased infants were 6.12 and 10.28, respectively. The area under the receiver operating characteristic (ROC) curve with a cut-off point of 8.5 was obtained at 0.838. Moreover, the sensitivity, specificity, positive predictive value, and negative predictive value were estimated at 74.4%, 78.65%, 55.37%, and 89.68%, respectively, for the CRIB-II system. Total scores of SNAPPE-II in survived and deceased infants were 16.9 and 51.6, respectively. The area under the ROC curve with a cut-off point of 27.5 was determined at 0.887. Sensitivity (84.44%) and specificity (79.05%) were calculated for the SNAPPE-II. Furthermore, positive and negative predictive values were 58.91% and 93.46%, respectively.

Conclusion: This study demonstrated that the CRIB-II and SNAPPE-II scoring systems can be useful mortality predictors for at-risk neonates.

Keywords: CRIB-II, Neonatal intensive care unit, NICU, Mortality risk prediction, Preterm infants, SNAPPE-II

Introduction

The neonates are at risk during, even before, or immediately after birth as they are transitioning from intrauterine to extrauterine life. Mortality rates are high due to the sensitivity and fragility of neonates in this period of life such that two-thirds of deaths in the first year of life occur during the neonatal period. Since the intrauterine life of preterm and low weight infants is shorter than the

physiological norm, they are susceptible to numerous complications regarding function, maturity, and development of various organs.

Therefore, they require meticulous care and special measures in the Neonatal Intensive Care Units (NICUs). The structural and functional immaturity of organs exposes these neonates to the risk of death. Utmost care must be exercised

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when dealing with these infants due to their sensitivity and fragility; moreover, their every cell is premature and sensitive requiring special care (1, 2). This has led physicians and researchers to determine risk levels, probability of death, and special complications for these neonates based on their clinical circumstances. The tools that can identify critically-ill neonates during the first h after birth can help evaluate a medical team's performance. These tools can also be an effective means for periodic performance reviews and reassessment of the NICUs as necessary (3, 4).

Traditionally, gestational age and birth weight were used to predict the probability of neonate survival as they were considered to be important predictors of the necessary level of intervention as well as patient outcome (5). Nowadays, however, in order to evaluate the effects and success rate of neonatal intensive care, databases have been created which include demographic characteristics of the infants during gestational and neonatal periods, as well as the results of laboratory tests (6).

It is now believed that in addition to gestational age and birth weight, other perinatal factors and physiological conditions unique to each infant influence the severity of their illnesses. Therefore, the use of tools to identify critically-ill neonates immediately after admission can play an important role in the evaluation of the medical team's performance (3, 7).

Numerous scoring systems have been developed including the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), Clinical Risk Index for Babies (CRIB and CRIB-II), Agency for Healthcare Research and Quality, NICHD2008, Score for Neonatal Acute Physiology (SNAP and SNAP-II), Score for Neonatal Acute Physiology with Perinatal Extension (SNAPPE and SNAPPE-II), and Vermont Oxford Network-Risk Adjustment (8, 9). The scoring systems used for the evaluation of neonatal status and mortality prognosis in the NICUs differ concerning type and number of variables, as well as the manner of scoring.

The CRIB, initially implemented in the NICUs in 1988-90, is one of the most common methods for detecting the risk of death. It is used as an indicator of mortality risk in infants with very low birth weights determining the illness severity in neonates with a gestational age of fewer than 31 weeks, as well as those with birth weights lower than 1,500 g (10). This scoring system was later updated to CRIB-II by Parry et al. in 2003(10). In this method, clinical data including birth weight,

gestational age, minimum and maximum values of base excess required to maintain normal oxygen saturation (SpO₂), serum alkaline phosphatase deficiency, and congenital anomalies in the first 12 h of life are gathered and rated culminating in a final score(11).

The SNAP was first developed by Richardson et al. in 1993(8, 11). Contrary to CRIB, the SNAP can be used for neonates of all gestational ages and birth weights (12, 13). It includes 26 clinical and vital variables. Later on, birth weight, Apgar scores, and small for gestational age (SGA) were added as perinatal extensions (SNAP-PE). Since gathering the data for these scoring systems was time-consuming, SNAP-II and SNAPPE-II were developed using only 6 and 9 variables, respectively, in 2001. The SNAP-II questionnaire included physiological variables, such as lowest blood pressure, temperature, serum pH, partial pressure of oxygen (PaO₂)/ fraction of inspired oxygen (FiO₂) ratio, urine output, and seizures in the first 12 h after admission (8, 9, 12, 14).

In recent years, significant measures have been taken in Iran to reduce neonatal mortality. One such measure was the remarkable increase in the number of NICUs in the country. To the best of our knowledge, the significant number of preterm and low-birth-weight infants admitted to the NICUs, as well as the clinical risks have not been seriously and accurately evaluated. Therefore, it is of utmost importance to classify infants with low gestational age and birth weight immediately after admission, plan clinical measures and follow-ups accordingly, and estimate the need to increase clinical care over time.

With this background in mind, this study aimed to determine the predictive power of the CRIB-II and SNAPPE-II questionnaires in terms of risk of death among neonates with low gestational age or birth weight admitted to the NICUs. With the approval of instruments' validity and reliability, it will be possible to identify high-risk infants with minimal time and cost

Methods

Population Sampling and Design

A prospective cohort study was carried out on 344 preterm infants admitted to the NICU of Vali-e ASR Hospital from the winter of 2016 to the spring of 2017. The sample size was calculated with a precision (corresponding to effect size) level of 8%, the prevalence of death in premature neonates of 25%, 85% sensitivity of SNAPPE-II as a diagnostic test by a previous study (15), confidence interval of 95%, and 80% test power.

The community-based clinical trial protocol was approved by the Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran (IR.TUMS.REC.1394.1203).

Variables Measurement

The CRIB II scoring is an indicator of five factors including the birth weight, gestational age, gender, base excess, as well as the temperature at the time of admission. Moreover, in the first 12 h after birth, the point value of each item has been set out.

The SNAPPE-II scoring system includes 9 variables, such as the lowest blood pressure, temperature, serum pH, PaO₂/FiO₂ ratio, urine output, seizures, weight, gestational age, as well as five-minute Apgar score after birth within the first 12 h after birth (7). The overall score here is calculated by the assigned point value of the responses to each particular question.

Clinical data and perinatal factors of preterm infants with gestational ages below 32 weeks or birth weights below 1,500 g were recorded upon admission after obtaining parental consent. Initially, infant demographic characteristics, as well as possible underlying causes in infant death, including maternal and neonatal factors were recorded in a checklist. Subsequently, the gestational age of eligible infants was determined using the Ballard Scale based on the last menstrual period date and previous ultrasound reports. Infants with a gestational age of fewer than 23 weeks or birth weight of less than 500 g, as well as those who were discharged from the hospital before the completion of data gathering, were excluded from the study.

Data including Apgar score and SGA history were recorded in this study. Infant weight was determined using digital Seca scales. The temperature upon admission was measured using a digital thermometer in the axillary area. Serum alkaline phosphatase levels were determined using a blood gas test. The FiO₂ required to maintain normal SpO₂ was determined by trained nurses using oxygen analyzers (in infants receiving oxygen through a hood), ventilators (in intubated infants), or a Continuous Positive Airway Pressure machine. The presence of congenital anomalies was determined through examination by neonatal physicians in the first 12 h after birth.

Reliability

Internal consistency of the CRIB-II and SNAP-II scores was evaluated by Cronbach's alpha.

However, external consistency evaluation was not possible due to the death of a significant number of infants, and the fact that the test was unrepeatable. Moreover, inter-rater reliability was analyzed by the kappa in a pilot study on 10 people.

Validity

The CRIB II and SNAPPE II questionnaires were translated into Persian based on an international quality of life assessment (IQOLA) that included the stages of translation, assessment of quality, backward-translation, and finally the comparison between backward-translation and the original version (16, 17). Furthermore, a panel of five specialists in neonatology checked the validity of the translated questionnaires in the target language. The translation, face, and content validity were evaluated qualitatively based on the IQOLA protocol. The criterion validity of the CRIB-II and SNAP-II scores based on the outcome of the infants during follow-up (until discharge or death) was determined by accuracy tests.

Analysis

Descriptive statistics were used to measure the mean \pm SD and median. Moreover, Cronbach's alpha and Cohen's Kappa were utilized to calculate internal and inter-observer reliability, respectively. It should be noted that the area under the ROC curve (AUC) analysis, Youden's statistic, predictive values, and multiple logistic regressions were performed for the examination of Criterion validity.

Variables with the probability value ≤ 0.2 in univariate logistic regression analysis were investigated in multiple logistic regressions. Multiple logistic regression was utilized to evaluate the criterion validity (from the aspect of predictive validity), as well as AUC analysis. The Exp (B) [anti-natural logarithm of coefficient B (estimated Odds Ratio)] or Odds ratio (CI 95%) was used for reporting output of categorical independent variables and B (SE) [coefficient B (Standard Error)], for continuous independent variables.

Results

Descriptive data

This study included 344 preterm infants with very low birth weight, 180 (52.3%) of which were male. Out of these 344 neonates, 253 cases survived past the 24h mark (death rate of 26.4%, n=91). Table 1 tabulates the descriptive data of each group.

Reliability

In order to evaluate the internal consistency of the SNAPPE-II using 344 completed questionnaires and after omitting one of the questions, Cronbach's alpha was obtained at an acceptable limit ($\alpha=0.659$). External consistency was not determined due to the death of a significant number of infants, and the fact that the test was unrepeatable. Equivalence (reproducibility) was calculated at 0.77 by coherence Kappa. The internal consistency of the CRIB using 344 cases was calculated to be 0.79 using Cronbach's alpha. Furthermore, inter-rater reliability (reproducibility) was estimated at a good level (Cohen's Kappa=0.79).

Validity

Criterion Validity

Receiver Operating Characteristic Analysis

The Receiver Operating Characteristic (ROC) analysis was performed to evaluate the criterion validity of the SNAPPE-II. According to the results, the accuracy of this tool was 0.887 (CI 95%: 0.847-0.927) ($P<0.05$). Moreover, the results of Youden's statistic showed the cut-off point and Youden's

index of 27.5-29.5 and 0.64, respectively. Based on the SNAPPE-II, prognosis sensitivity and specificity at a cut-off point of 27.5 were 84.44% (CI 95%: 84.443-84.445) and 79.05% (CI 95%: 79.051-79.052) respectively. In addition, these corresponding values were 82.22% (CI 95%: 82.222- 82.223) and 81.42 % (CI 95%: 81.422-8.423) at the cut-off point of 29.5.

Regarding the validity analysis of CRIB using ROC analysis, its accuracy was determined at 0.838 (CI 95%: 0.790-0.886) (appropriate). This indicator was statistically significant ($P<0.001$). The results of the Youden's statistic revealed the cut-off point of 8.5 based upon which the prognosis sensitivity, specificity, and the Youden's index were 74.4 %, (CI 95%: 74.444-74.445), 78.65% (CI 95%: 78.655-78.656), and 0.53, respectively (Table 2).

The positive predictive value of SNAPPE-II was 58.91% (CI 95%: 58.914-58.915), and the negative predictive value was obtained at 93.46 % (CI 95%: 93.458-93.461). Additionally, the positive and negative predictive values of CRIB-II were 55.37 % (CI 95%: 55.370-55.372) and 89.64% (CI 95%: 89.643-89.644), respectively.

Table 1. Descriptive data of survived and dead infants in the first 24 h after birth

		Mean	SD	Median	IQR
CRIB ^a score	Living	6.12	2.66	6.00	4.00
	Dead	10.28	3.14	10.00	4.00
SNAPPE-II ^b score	Living	16.94	16.46	12.00	20.00
	Dead	61.60	22.98	51.00	34.00
Weight (gr)	Living	1213.73	281.90	1210.00	412.50
	Dead	912.67	334.08	867.50	293.75
Ventilator duration (days)	Living	2.36	6.55	.000	2.00
	Dead	6.10	8.30	3.00	6.25
Head circumference (cm)	Living	27.44	2.35	27.50	3.00
	Dead	25.34	2.90	25.00	4.00
Height (cm)	Living	39.09	3.83	39.00	5.25
	Dead	34.77	4.64	35.00	6.25
Length of hospitalization (days)	Living	40.46	18.57	38.00	26.25
	Dead	11.15	12.32	7.00	15.25

a: Clinical Risk Index for Babies

b: Score for Neonatal Acute Physiology Perinatal Extension

Table 2. Area under the Receiver Operating Characteristic curve (confidence interval), cut-off point, sensitivity (confidence interval), specificity (confidence interval), and Youden's index of SNAPPE-II and CRIB in preterm infants admitted to the neonatal intensive care unit

Indicators	Area Under The Curve (CI 9%)	Cut-Off Point	Sensitivity; % (CI 95%)	Specificity; % (CI 95%)	Youden Index
SNAPPE-II	.887 (0.847-0.927)	27.5 29.5	84.44 (84.44-84.45) 82.22 (82.222 – 82.223)	79.05 (79.05-79.0) 81.42 (81.422-8.423)	0.64
CRIB	0.838 (0.790-0.886)	8.5	74.4 (74.444-74.445)	78.65 (78.655-78.656)	0.53

Table 3. Association between SNAPPE-II score and some neonatal variables with death probability in infants

	P. Value	OR	95% C.I	
			Lower	Upper
SNAPPE	0.005	1.059	1.018	1.102
Weight (gr)	0.542	0.999	0.996	1.002
IVH ^a	0.061	0.175	0.028	1.085
Length (cm)	0.105	0.843	0.685	1.037
Head (cm)	0.791	0.960	0.707	1.302
Hosp. Duration ^b (day)	<0.0001	0.853	0.803	0.905
Ventilation (day)	0.042	1.161	1.005	1.341

a:Intra-ventricular hemorrhage, b:Hospitalization Duration

Table 4. Association between CRIB II score and some neonatal variables with death odds in infants

	P. Value	OR	95% C.I	
			Lower	Upper
CRIB	0.001	2.696	1.516	4.792
Weight (gr)	0.184	1.003	0.999	1.008
IVH*	0.284	0.333	0.045	2.488
Length (cm)	0.671	0.955	0.772	1.182
Head (cm)	0.620	0.898	0.585	1.377
Hosp. Duration ^b (day)	<0.0001	0.827	0.769	0.890
Ventilation (day)	0.021	1.167	1.024	1.329

a:Intra-ventricular hemorrhage, b:Hospitalization Duration

Logistic Regression

Logistic regression analysis was used following the confirmation of the required assumptions. For a one-unit increase in SNAPPE-II, the odds of the neonatal death increased by 1.05 (CI 95%: 1.02-1.102) (Table 3), and for a one-unit increase in CRIB-II, the odds of the neonatal death increased by 2.696 (CI 95%: 1.59-4.72) (Table 4). These results were obtained using the variables, such as weight, height, head circumference, duration of hospitalization, ventilation duration, and IVH. The CRIB-II and SNAPPE-II remained significant (Tables 3 and 4).

Discussion

The survival rate of neonates is not only related to birth weight and gestational age, but also other pathological factors, especially illness severity in the first few h immediately after birth. These factors can be determined using the scoring tools. The CRIB is utilized only for neonates with birth weights below 1,500 g; however, the SNAP may be used with all gestational ages and birth weights (12). Richardson et al. proposed SNAP as a scoring system for the prediction of mortality risk in the NICU hospitalized neonates, and it has been used in its various versions over a decade (18).

The present study demonstrated that neonates with higher risk levels were kept alive in our research environment. The total SNAPPE-II score in survived infants was 16.94, and it was obtained at 51.60 in those who died. For CRIB-II, these numbers were 6.1 and 10.28 respectively. In a

study conducted in Brazil, the mean total SNAPPE-II scores for survived and deceased neonates were 12.6 and 30.5, respectively (19). Furthermore, a study performed in Indonesia showed the same scores of 15 and 46.6, respectively (20). Mohkam et al. estimated survived and deceased CRIB-II scores to be 4.5 and 6.8, respectively (21). However, Babaei et al. obtained 5.8 and 9.8, respectively (15).

In the present study, the sensitivity of the SNAPPE-II was obtained at 84.44%. Moreover, the specificity was estimated at 79.05% with a cut-off point of 27.5. Furthermore, the sensitivity of the CRIB-II was 74.4%, and the specificity was 78.65% with a cut-off point of 8.5. In one study using SNAP-II, the sensitivity and specificity were reported at 94% and 83%, respectively (12). Another study reported a sensitivity of 60% for SNAPPE-II (22). In a study carried out by Khosravi et al., a cut-off point of 13 was calculated for CRIB-II with a sensitivity of 82% and specificity of 50% (23). In the same vein, Gagliardi et al. reported a sensitivity of 76% for CRIB-II which was in line with the results of our study (22).

In the present study, the AUCs of the SNAPPE-II and CRIB-II were 88.7% and 83.8%, respectively. Other studies reported the AUCs of 83.5% (23) and 91 % (9, 24) for SNAPPE-II. Babaei et al. reported an AUC of 85% for CRIB-II which was in line with our results (15). Similar studies reported the AUCs of 91%, 92%, and 96% (10, 22, 25).

Mortality rates for premature neonates may be evaluated using SNAPPE-II and CRIB-II. According

to our results, the SNAPPE-II had a positive predictive value of 58.91% and a negative predictive value of 93.46%. For SNAP-II, a score over 40 had a positive predictive value of 88% in terms of death and dysfunction (26). Our results demonstrated that CRIB-II can predict mortality and survival in 55% and 89.6% of the cases, respectively. Moreover, Khosravi et al. reported positive and negative predictive values of 65% and 72% for CRIB-II, respectively (23).

In our study, it was observed that the CRIB-II indicator had a high predictive value concerning the mortality rate in neonates with low birth weight (less than 1,500 g). In other words, CRIB-II scores predicted death in preterm infants with an accuracy of 85%, which demonstrated the great utility of this indicator.

Limitations

In this study, there were a small number of premature infants and incomplete medical records of the patient files which resulted in the loss of several samples. The base excess in the first 24 h after birth could not be recorded for some newborns. This limitation was either due to a lack of arterial gas analysis or lack of time and date identification. Moreover, the temperature was not recorded for some newborns within the first 12 h. Therefore, the case studies should be conducted to reach the number of samples selected in the sample size.

Suggestions for Further Studies

It seems crucial to perform further studies in different hospitals with various levels of care provisional across Iran in order to determine the accuracy and precision of the tools and identify a more accurate score limit for prediction of the mortality outcome in neonates.

Conclusion

In our study, the final scores for SNAPPE-II and CRIB-II in deceased neonates were higher than those in other studies carried out within Iran using the same scoring systems. This demonstrates the higher tendency of the medical care team in our research environment such that neonates with comparatively worse conditions were able to survive. Considering that, according to the present study and similar studies, the sensitivity and specificity of these two scoring systems, as well as their cut-off points were acceptable along with the fact that a better cut-off point was achieved in our study, compared to other Iranian studies. These tools are useful for

the prediction of mortality for at-risk neonates.

Our study demonstrated that the sensitivity and specificity of these two tools were very similar. Therefore, considering that CRIB-II utilizes variables that are part of the routine examination of low birth weight neonates, and that their measurement is quick, easy, and not subject to human error, it is recommended that only CRIB-II be utilized for neonates with a birth weight of less than 1500 g.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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