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Original Article

Predictive value of Score for Neonatal Acute Physiology and Perinatal Extension II for neonatal mortality in Sanglah Hospital, Denpasar, Indonesia

I Gede Ketut Aryana, I Made Kardana, I Nyoman Adiputra

Abstract

Background Neonatal mortality, which is largely caused by severe illness, is the biggest contributor to overall infant mortality. The World Health Organization (WHO) estimated that 4 million neonates die yearly worldwide, often due to severe infection and organ system immaturity. Neonates with severe illness require treatment in the neonatal intensive care unit (NICU), in which a reliable assessment tool for illness severity is needed to guide intensive care requirements and prognosis. Neonatal disease severity scoring systems have been developed, including *Score for Neonatal Acute Physiology and Perinatal Extension II* (SNAPPE II), but it has never been validated in our setting.

Objective To study the prognostic value of SNAPPE II as a predictor of neonatal mortality in Sanglah Hospital, Denpasar, Indonesia.

Methods This prospective cohort study was conducted in the NICU of Sanglah Hospital, Denpasar from November 2014 to February 2015. All neonates, except those with congenital anomaly, were observed during the first 12 hours of admission and their outcomes upon discharge from the NICU was recorded. We assessed the SNAPPE II cut-off point to predict neonatal mortality. The calibration of SNAPPE II was done using the Hosmer-Lemeshow goodness-of-fit test, and discrimination of SNAPPE II was determined from the receiver-operator characteristic (ROC) curve and area under the curve (AUC) value calculation.

Results During the period of study, 63 children were eligible, but 5 were excluded because of major congenital abnormalities. The SNAPPE II optimum cut-off point of 37 gave a high probability of mortality and the ROC showed an AUC of 0.92 (95%CI 0.85 to 0.99). The Hosmer-Lemeshow goodness-of-fit test showed a good calibration with P=1.0

Conclusion The SNAPPE II has a good predictive ability for neonatal mortality in Sanglah Hospital, Denpasar, Indonesia. **[Paediatr Indones. 2016;56:257-61. doi: 10.14238/pi56.4.2016.257-61]**.

Keywords: *mortality, neonates, SNAPPE II*

The WHO estimates that four million newborns die each year, and 75% of these occur in the first week of life. The most common causes of neonatal death are infection (36%), prematurity (28%), and congenital abnormalities (7%). The mortality rate from severe illness in neonates was estimated to be 16 to 30%.[1] Approximately 16% of neonates in the United States die from severe illness, and that in the UK in 1996-1997 was 10%.[2] The incidence of neonatal severe illness in developing countries is quite high, at 1.8 to 18 per 1000. In Cipto Mangunkusumo Hospital, neonatal mortality rates from severe illness reached 14%.[3] The Neonatology Department of Sanglah Hospital, Denpasar reported in 2009 that of 159 neonatal deaths, 42.7% of deaths were due to respiratory distress, 17.6% due to sepsis, and 9.4% due to low birth weight and other causes.[4]

The initial handling of neonatal emergencies (resuscitation) and the availability of the NICU are critical to the prognosis and the likelihood of death

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in neonates.[5] Some health centers have developed a scoring system to determine severity of illness in neonates. The Score for Neonatal Acute Physiology and Perinatal Extension II (SNAPPE II) is a scoring system developed for suspected neonatal mortality.[6] Some studies suggest that SNAPPE II is very good for predicting death in neonates. Several studies found that SNAPPE II could be used to effectively predict neonatal mortality.[7-10] However, the performance of SNAPPE II may differ between various NICU settings and, therefore, the optimal cut-off points such as those reported by Mia *et al*. in Surabaya (score of 30) and Thimoty *et al*. in Bandung (score of 51).[9,10]

There has been no study to evaluate the performance of SNAPPE II in NICU of the Sanglah Hospital, Denpasar, Bali. Therefore we aimed to obtain the study the performance and optimum cut off point of SNAPPE II to predict neonatal death in Sanglah Hospital, Denpasar, Bali.

Methods

We conducted a prospective cohort study in the NICU at Sanglah Hospital from November 2014 to February 2015. All neonates were observed during the first 12 hours of admission and outcomes were assessed at the time of discharge from the NICU.

The minimum required sample size was estimated to be 58 subjects. Inclusion criteria were neonates admitted to the NICU whose parents provided informed consent. We excluded neonates >48 hours of age, those who were discharged against medical advice, and those with major congenital abnormalities such as anencephaly, pulmonary atresia, or omphalocele. This study was approved by the Medical Research and Hospital Ethics Committee of Sanglah Hospital, Denpasar, Indonesia.

The dependent variable in this study was the outcome at the time of discharge from the NICU, i.e., survived or died. History-taking, physical examination, and the worst score within the first 12 hours after NICU admission were analyzed. The SNAPPE II value was calculated as the sum of the points assigned to each variable (**Table 1**). Descriptive analyses of the study variables were calculated to determine the characteristics of subjects. Probability of mortality was examined by logistic regression analysis, and used to find the SNAPPE II score cut-off point. The ROC and Hosmer-Lemeshow goodness-of-fit analyses were used to to validate the SNAPPE II. The probability of outcomes was calculated using the following formula:[11]

$$P = \frac{1}{1 + e^{-y}}$$

P = probability

e = exponent

y = logistic equation = $a+b_1x_1+b_2x_2+.....+b_1x_1$.

a = constant

b = coefficient

x = prognostic variable

Results

During the study period, 63 neonates were admitted to the NICU. However, five infants were excluded because of major congenital abnormalities: three with

Table 1. SNAPPE II variables: categories and scores[6]

Variables	Measurements	Points
Lowest mean blood pressure	>29 mmHg	0
	20-29 mmHg	9
	<20 mmHg	19
Lowest temperature	>35.6 °C	0
	35-35.5 °C	8
	<35 °C	15
PaO_2/FiO_2 ratio	>2.49	0
	1.0-2.49	5
	0.3-0.99	16
	<0.3	28
Lowest serum pH	>7.19	0
	7.10-7.19	7
	<7.10	16
Seizures	No	0
	Multiple	5
Urine output	>0.9 ml/BW/hour	0
	0.1-0.9 ml/BW/hour	5
	<0.1 ml/BW/hour	18
Birth weight	>999 g	0
	750-999 g	10
	<750 g	17
Small for gestational age	≥3rd percentile	0
	<3rd percentile	12
Apgar score at 5 min	≥7	0
	<7	18

gastroschizis, one with omphalocele, and one with pulmonary atresia. Of the 58 subjects, 34 (59%) were male, and mortality occurred in 21 (36%) subjects. The characteristics of study subjects are presented in **Table 2**.

The SNAPPE II had a significant correlation with mortality. **Table 3** shows that mortality increased with higher SNAPPE II values. The SNAPPE II prognostic value was determined by calculating the probability of the subject experiencing a poor outcome (death). Logistic regression analysis revealed a SNAPPE II regression coefficient of 0.255, with constant -8.255 ($P<0.001$). For probability calculations, we used the formula for SNAPPE II values from all subjects (**Figure 1**). The SNAPPE II cut-off points were determined by the intersection of a probability of 0.5 or more for poor prognosis, and found to be 37. Calibration of SNAPPE II tested with Hosmer-Lemeshow goodness-of-fit showed that the observed value and the expected value were similar between subjects who survived and died ($P=1.0$). The value of SNAPPE II discrimination in this study was obtained by ROC analysis, and the AUC was 0.92 (95%CI 0.85 to 0.99) (**Figure 2**).

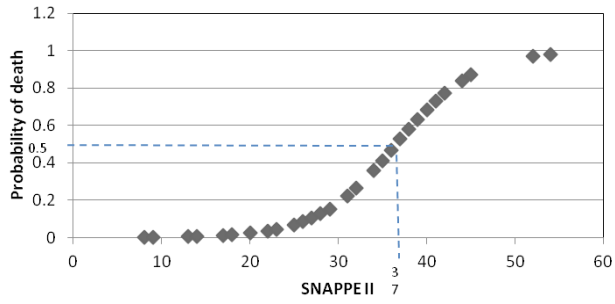

Figure 1. Correlation between SNAPPE II and probability of death

Table 2. Characteristics of the study subjects

Characteristics	Discharged from NICU	
	Died (n=21)	Survived (n=37)
Gender, male, n	17	17
Type of delivery, n		
Vaginal	14	16
Caesarean section, maternal indication	1	18
Caesarean section, fetal indication	6	3
Median gestational age, weeks (minimum-maximum)	31 (21-39)	33 (29-42)
Median birth weight, g (minimum-maximum)	1,470 (500-3,100)	1,750 (1,050-3,190)
Median APGAR score at 5 min, (minimum-maximum)	7 (3-9)	7 (3-9)
Small-for-gestational age, n	4	5
Diagnosis, n		
Sepsis	1	4
Sepsis + pneumonia	6	22
Sepsis + hyaline membrane disease	9	5
Sepsis + others	5	6
Lowest mean blood pressure, mmHg (SD)	27.1 (6.1)	35.0 (6.8)
Lowest median temperature, °C (minimum-maximum)	35.4 (34.8-36.8)	35.8 (34.4-36.5)
Mean urine output, mL/BW/hour (SD)	1.68 (0.99)	1.76 (0.92)
Multiple seizures, n	3	5
Lowest median serum pH (minimum-maximum)	7.32 (7.00-7.54)	7.31 (6.97-7.50)
Median PaO2/FiO2 ratio (minimum-maximum)	3.21 (1.3-4.98)	3.75 (1.14-8.85)
Median length of stay, days (minimum-maximum)	10 (1-52)	8 (2-27)
Cause of death, n		
Sepsis	10	
Prematurity	9	
Other	2	
Median SNAPPE II score (minimum-maximum)	37 (22-54)	23 (8-39)

Table 3. SNAPPE II in all neonates and those who died

SNAPPE II values, n	All neonates (n=58)	Died (n=21)
0-9	3	0
10-19	14	0
20-29	18	3
30-39	14	9
40-49	7	7
≥50	2	2

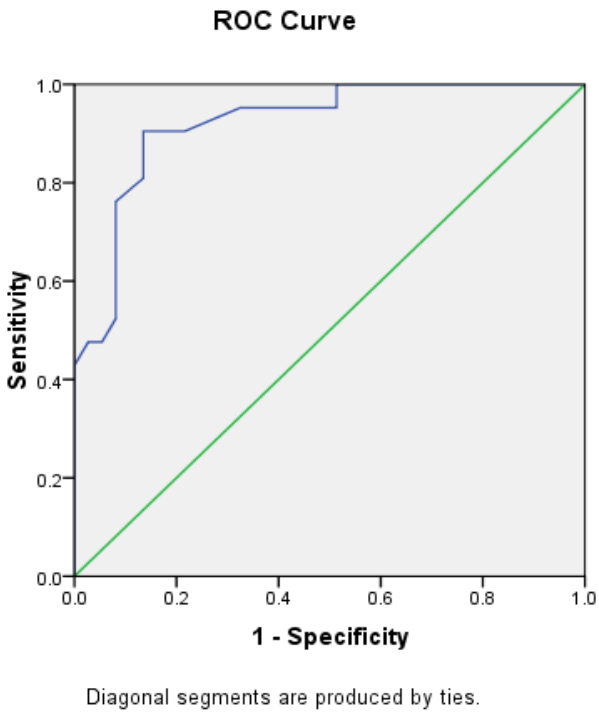

Figure 2. Receiver operating characteristic (ROC) curve for SNAPPE II

Discussion

Our study showed that the SNAPPE cut off point of 37 were associated with more than 50% probability of death among neonates admitted to the Sanglah Hospital NICU. Of 58 neonates in the NICU, 21 (36%) died. The median SNAPPE II value of subjects who died was higher than that of the survivors. Subjects with SNAPPE II <30 had lower probability of death (3/35), while SNAPPE II ≥30 were suggestive of poor outcomes with high probabilities of death (18/23).

Mean blood pressure in normal neonates depends on gestational age (GA). At GA ≤28 weeks, the mean arterial pressure normally ranges from 29-35 mmHg, while that of GA 33-43 weeks is 29-32 mmHg, GA 39-47 weeks is 33-36 mmHg, and GA ≥37 weeks is 44-52 mmHg.[12] We found that the lowest mean blood pressure as a SNAPPE II variable of subjects who died was 27.1 mmHg, while that of survivors was 35.0 mmHg. Similarly, Sundaram *et al.* found that 76% of neonates admitted to the NICU with a mean arterial pressure <29 mmHg died. Optimal blood pressure is needed to ensure optimal metabolism. In neonates with shock, the blood pressure drops or is not measurable, decreasing perfusion to tissues and to vital organs, and increasing risk of death. Blood pressure is also associated with urine production.[13,14]

We also found that median lowest temperature in subjects who died was lower than that of survivors, 35.4°C vs. 35.8°C, respectively. Neonates' lack of ability to maintain a balance between heat production and heat loss may lead to hypothermia. Heat regulation failure is, in general, due to a malfunction of the hypothalamus. The neonatal neurological response for maintaining temperature is influenced by a hypoxic state, neurological disorders, exposure to analgesic drugs, sepsis, or severe illness with the possibility of the death.[15]

Multiple seizures within the first 12 hours of admission were observed in 14% of subjects who died. However, a limitation of this study was that subtle seizures in neonates could not be observed. Richardson *et al.* found that multiple seizures were a risk factor for mortality in neonates with an odds ratio of 6.50 (95%CI 4.01 to 10.53).[6] Multiple seizures may be caused by primary disorders of the central nervous system because of intracranial processes (meningitis, encephalitis, intracranial hemorrhage, or tumor), or secondary systemic problems such as hypoxic ischemic encephalopathy, hypoglycemia, or hyponatremia. Multiple seizures can lead to hypoxia of the brain which increases the possibility of the death.[16]

Blood gas analysis is an indicator of lung function and metabolic impairment. Impaired pulmonary function in neonates is often due to infection and immaturity, as in acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). During ALI and ARDS lung compliance decreases, causing the failure in gaseous exchange and increases in anaerobic metabolism. This condition decreases serum pH and the PaO2/FiO2 ratio, increasing the risk of death.[17] Richardson *et al.* reported that serum pH and decreased PaO2/FiO2 ratio increased the risk of neonatal mortality.[6] In our study, the median serum pHs were similar in the died and survived groups, perhaps because the incidences of pulmonary problems were identical in both groups.

We observed that subjects with higher SNAPPE II scores were more likely to experience death. Calibration and discrimination are good techniques

to determine the effectiveness of a scoring system.[11] We found the SNAPPE II cut-off point to be ≥37, with good calibration using the Hosmer-Lemeshow goodness-of-fit test (P=1.0). The discrimination value of SNAPPE II was excellent with AUC 0.92. As such, we found SNAPPE II to be very good as predictor of neonatal mortality in Sanglah Hospital NICU. The cut off point and performance were different compared to those of previous studies in different settings in Indonesia,[9,10] In contrast, our study was more similar to studies conducted in developed countries. Richardson *et al*. reported a SNAPPE II cut-off point of 40 with AUC 0.91,[6] and Zardo *et al*. reported a cut-off point of 40 with AUC 0.94.[18]

In conclusion, the *Score for Neonatal Acute Physiology Perinatal Extension II* (SNAPPE II) is a good instrument for predicting neonatal mortality in Sanglah, Hospital Denpasar with the optimum cut off point of 37. Future research must be done in other health centers to obtain the ideal SNAPPE II cut-off point for different settings.

Conflict of interest

None declared.

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