

Can the Score for Neonatal Acute Physiology II (SNAPII) Predict Morbidity and Mortality in Neonates with Sepsis?

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Abstract

Objective: We investigated whether Score For Neonatal Acute Physiology II (SNAP II) score can predict mortality and or Organ Dysfunction (OD) in neonatal sepsis.

Methods: Eighty Egyptian newborns hospitalized for neonatal sepsis were investigated through a multicenter observational prospective study to determine whether SNAP II applied in the 1st 12 hours of admission would predict mortality and or OD.

Results: The median SNAP II was significantly higher in babies who died or developed OD versus those who survived and improved (P=0.003 and P=0.001 respectively). Individual parameters of the SNAP II didn't contribute equally to the risk of death, low mean arterial blood pressure and lowest blood pH were significantly associated with OD and death (P=0.002). ROC curves for the SNAP II score ≥ 40 showed moderate predictive accuracy and 90.4% and 88.9% sensitivity for OD and death, respectively.

Conclusion: SNAP II score can predict mortality and OD in neonatal sepsis.

Keywords: SNAP II; Neonate; Sepsis; Organ dysfunction; Mortality

Introduction

Neonatal sepsis is a worldwide public health issue in which marked variations concerning its risk and prognostic factors have been reported [1]. Neonatal sepsis is a common life threatening disease with an incidence of 3.5 to 8 cases per 1,000 live births and mortality rate of 16 to 30% [2], causing about 1.6 million deaths annually in developing countries [3]. Neonatal illness severity scoring systems assess the severity of illness in terms of degree of derangement from normal physiology across a number of physical examination findings and laboratory test results.

The SNAP score (developed and mainly used in the United States and Canada) is used for describing populations, stratifying risk in epidemiologic and clinical trials and projecting resource utilization. It is based on 28 variables obtained during the first 24 hours after admission with each parameter weighted according to expert opinion, with a score of 0, 1, 3 or 5 assigned to each variable [4].

In 2001, Richardson et al. [5] developed and validated SNAP II score reducing the number of evaluated items to six (mean blood pressure, lowest temperature, PO_2/FiO_2 ratio, serum pH, multiple seizures, and urine output), in order to facilitate utilization of the system and the period of data collection to 12 hours.

Previous studies have applied SNAP II as a measure of illness severity in mechanically ventilated term babies and to predict short term adverse respiratory outcomes in newborns 34 weeks gestation admitted to the neonatal intensive care unit (NICU) [6-8]. Many babies may not be very sick at admission to NICU and may develop severe sickness later in the course of NICU stay. Hence, we applied SNAP II to the diagnosis of septicemia in babies already admitted in the NICU and we observed them for 14 days for their outcomes.

A recent Indian study [9] has attempted to use SNAP II parameters as prognostic markers among neonates after the onset of sickness in the NICU. This study is a novel Egyptian work that aimed to investigate whether SNAP II score applied in the 1st 12 hours of admission can predict mortality and or Organ Dysfunction (OD) in neonates with septicemia and to determine the contribution of the individual parameters of SNAP II score to the risk of OD and death.

Methods

This was an observational prospective study which included 80 newly admitted neonates with neonatal sepsis at the NICUs of Fayoum University Hospital (Fayoum Governorate), El Mounira Cairo University Children Hospital and Al-Kasr Al-Aini hospital (Cairo Governorate) over a period of 6 months starting from June 2012 to November 2012. Approval of Research Committee of Pediatric Units was obtained. Data confidentiality was preserved according to the Revised Helsinki Declaration of Bioethics [10].

Our inclusion criteria were preterm and term neonates of both gender with clinical and/or laboratory signs consistent with neonatal sepsis. Gestational age was confirmed by new Ballard score [11]. Neonates with major congenital anomalies, those with genetic disorders and neonates with surgical conditions were excluded from the study. Babies were observed till day 14 of admission.

We termed sepsis as a suspected or confirmed infection in the presence of Systemic Inflammatory Response Syndrome (SIRS). This meant a newborn must have a positive blood culture and fulfill at least 2 of the 4 SIRS criteria (in reference to the study Sundaram et al. [9]).

• Core temperature >38.5 or <36.0°C.

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Pge 2 of 5

 \bullet Tachycardia, defined as a mean heart rate >2 SD above normal for age, and bradycardia, defined as a mean heart rate $<\!10^{\rm th}$ percentile for age.

• Mean respiratory rate >2 SD above normal for age.

 \bullet Leukocyte count elevated or depressed for age or >10% immature neutrophils.

And or those with at least one organ dysfunction [12].

Confirmatory tests were done using the practical sepsis screen [13] .The screen is considered positive if any two or more of these tests were abnormal: Total leukocyte count is <5000 or >20000/mm³, low absolute neutrophil counts as per Manroe chart [14] for term and Mouzinho's chart [15] for very low birth weight infants, immature/total neutrophil >0.2, Micro-ESR >15 mm in 1st hour and C reactive protein (CRP)>10 mg/L.

We diagnosed OD according to the criteria of Goldstein et al. [12].

Coagulation profile was done in patients suspected with disseminated intravascular coagulation (DIC) including International Normalized Ratio (INR), activated partial thromboplastin time (APTT) and platelet count.

Blood chemistry included: Na⁺, K⁺, Ca⁺² (total and ionized), kidney function tests, liver function tests , arterial blood gases and others as required to detect OD.

SNAP II [9] was applied on all our septic neonates in the $1^{\rm st}$ 12 hours of admission.

Variables of SNAP II score are shown in table 1.

Interpretation of SNAP II score

Severity of the illness was arbitrarily graded according to the SNAP II score as follows: mild: 1-20, moderate: 21- 40, severe: >40.

All subjects were followed up to a maximum of 14 days to detect their outcome (improvement, OD or death).

Statistical analysis

Data management and analysis were performed using Statistical

VARIABLES	VALUES	POINTS
	≥ 30 mmHg	0
Mean blood pressure 20-29 mmHg <20 mmHg	20-29 mmHg	9
	19	
	>35.6°C	0
Temperature	35 - 35.6°C	8
	<35°C	15
PO ₂ (mmHg) / FiO ₂ (%)	>2.49	0
	1.0-2.49	5
	0.3-0.99	16
	<0.3	28
	≥ 7.2	0
Lowest serum pH	7.1-7.19	7
	<7.1	16
Multiple esizuree	No	0
Multiple seizures	Yes	19
	≥ 1	0
Urine output(ml/kg/h)	0.1-0.9	5
	<0.1	18

 Table 1: Variables of SNAP-II:

 (FiO₂): Fraction of inspired Oxygen.

Initial diagnoses	Number of patients	Percentage (%)
Respiratory distress syndrome (RDS)	24	30.0
Pneumonia	10	12.5
Preterm neonates (PT)	10	12.5
Hypoxic ischemic encephalopathy (HIE)	6	7.5
Jaundice	4	5.0
Neonatal convulsions	4	5.0
Non specific manifistations	4	5.0
Cholestasis	3	3.8
Acute bilirubin encephalopathy	2	2.5
Hemorrhagic disease of newborn	2	2.5
Intracranial hemorrhage (ICH)	2	2.5
Inborn error of metabolism	2	2.5
Meconium aspiration syndrome (MAS)	2	2.5
CNS infection	1	1.3
Congenital heart disease	1	1.3
Necrotizing enterocolitis (NEC)	1	1.3
Neck abscess	1	1.3
Transient tachypnea of newborn (TTN)	1	1.3
Total	80	100.0

Table 2: Initial diagnoses of enrolled neonates.

Organism	Number (%)		
coagulase–ve Staphylococci	8 (10)		
Pseudomonas	6 (7.50)		
Acinetobacter	5 (6.25)		
Klebsiella	2 (2.50)		
Enterobacter	1 (1.25)		
E.coli	1 (1.25)		

Table 3: Distribution of organisms in blood culture.

Analysis Systems. The graphs were done using Microsoft Word.

Numerical data were summarized using means and standard deviations or median and ranges. Categorical data were summarized as percentages. Comparisons between two groups with respect to numeric variables were done by Mann-Whitney test, a nonparametric test equivalent to the Student's t test. The Kruskal-Wallis test, a nonparametric test equivalent to analysis of variance was used to compare more than 2 groups. Comparisons between categorical data were done using the chi-square test or the Fisher's exact test for small sample size. The Receiver-Operator Characteristic (ROC) curve was used to display the relationship between sensitivity and specificity [16]. All *P*-values were two-sided. *P*-values <0.05 were considered significant.

Results

The initial diagnoses associated with neonatal sepsis were as following: 24 (30%) neonates presented with respiratory distress syndrome, 10 (12.5%) patients with confirmed pneumonia, and 10 (12.5%) newborns were admitted because of prematurity. (The other diagnoses are listed in table 2).

Neonates were as follow: number of neonates with early onset sepsis (EOS) was 33 (41.3%) and in those with late onset sepsis (LOS) was 47 (58.8%). Forty three (53.8%) neonates were boys and 37 (46.3%) were girls. The mean gestational age of the enrolled neonates was 34.95 weeks (28-40 weeks). The mean weight on admission was 2.32 Kg (1-3.5 Kg). The median of day of onset of illness was 3.5 days (1-28 days).

Blood culture was positive in 23 (28.75%) neonates and sepsis screen was positive in 73 (91.3%) neonates. All culture negative subjects

Pge 3 of 5

had a positive sepsis screen. The most common causative organism was *coagulase negative Staphylococci* (10%) (Table 3).

Twenty seven (33.8%) neonates died within the 14-days observation period due to septicemia, while 35 (43.8%) babies had organ dysfunction. Ten (12.5%) babies had improved OD and 25 (31.3%) babies had persistent OD.

The study population had a median SNAP II score of 12.5 (IQR 0-32) at enrollment. Forty six (57.7%) neonates had mild illness [SNAP II=1-20], 22 (27.5%) had moderate illness [SNAP II=21-40] and 12 (14.8%) had severe illness [SNAP II>40].

In term babies median SNAP II score was 19 (IQR 0-65) versus 12 (IQR 0-60) in preterm babies; P value=0.476.

The median SNAP II score in very low birth weight (VLBW) babies was 12 (IQR 0-32), in low birth weight (LBW) babies it was 12.5 (IQR 0-60) and in appropriate for gestational age babies (AGA) it was 19 (IQR 0-65) with; P value=0.71.

The death percentage by SNAP II category was 21.7% for mild illness, 40.9% for moderate illness and 66.7% for severe illness, as shown in table 4.

The median number of organs with dysfunction involved during the 14 days observation period was 2 (IQR 1-3). In 10 (12.5%) babies, OD improved by day 14.

Respiratory system was the most frequently involved organ at enrollment as 27 (33.8%) neonates presented with respiratory distress syndrome and pneumonia, followed by the hematologic system (30%) with 9 (11.3%) babies had (DIC). Seventeen (21.3%) babies had cardiovascular involvement. Shock requiring vasoactive drug support was present in 16 (20%) babies and renal failure was diagnosed in 8 (10%) babies at enrollment.

There was a significant difference in the median SNAP II in babies with persistent OD; it was 21 (IQR 11-36) versus 12 (IQR 0-37.5) in those with improving or normalized OD; P=0.001.

When the individual SNAP-II parameters were analyzed, it was found that parameters related to perfusion (mean arterial pressure

SNAP II score category	Alive (n=), (%)	Death (n=), (%)	Total number, (%)	Overall P value	
Mild (1-20)	36 (78.3%)	10 (21.7%)	46 (100.0%)		
Moderate (21-40)	13 (59.1%)	9 (40.9%)	22 (100.0%)	**0 001	
Severe (>40)	4 (33.3%)	8 (66.7%)	12 (100.0%)	0.001	
Total	53 (66.3%)	27 (33.8%)	80 (100.0%)		

**P value <0.05 is considered significant.

 Table 4: The relationship between death percentage of studied babies and SNAP II category.

Parameters	Improved and discharged (n=18)	Improved OD (n=10)	Persistent OD (n=25)	Died (n=27)	P value
MAP ≤ 29 mmHg	0	3	8	8	0.064
Lowest blood pH (<7.20)	1	5	12	17	**0.002
PaO ₂ /FiO ₂ ratio (<2.50)	2	4	20	22	**<0.001
Urine output (<1 mL/kg/hr)	1	1	4	8	0.175
Lowest temperature(35.6°C)	0	0	1	2	#
Multiple seizures	1	2	8	10	0.101

**P value <0.05 is significant

*Number of study subjects with hypothermia was too small for valid analysis Table 5: Individual SNAP II parameters and outcome.

Measurement	OD		Death	
	%	(95%CI)	%	(95%CI)
Sensitivity	23.1	11.2-34.9	29.6	11.2-48.0
Specificity	100		92.5	85.1-99.8
Positive predictive value (PPV)	100		66.7	35.4-98.0
Negative predictive value (NPV)	41.2	29.2-53.2	72.1	61.1-83.0

 Table 6: SNAP II score more than 40 as a prognostic test for death and organ dysfunction.







and acidosis) were significantly associated with death as well as organ dysfunction at day 14 as shown in table 5.

Table 6 shows the sensitivity, the specificity and the predictive values of SNAP II score greater than 40 in the prognosis of neonatal sepsis.

The area under the (ROC) curve for SNAP II and OD was 0.829 (95% CI 0.731-0.926), as shown in figure 1. While the area under the (ROC) curve for SNAP II and death was 0.699 (95% CI 0.58-0.818), as shown in figure 2.

Discussion

The study of illness severity and mortality risk measurement

among newborns admitted to NICUs is attaining an increasing level of importance. In order to compare mortality levels of different NICUs, even after making adjustments for factors such as gender, birth weight, gestational age and ethnicity, it is still necessary for subject disease severity to be similar [17].

Given the median SNAP II score in our study was lower than that described by Sundaram et al. [9] (12.5 versus 37), we attribute this finding to their inclusion criteria of only severely septic neonates.

We found that the median SNAP II was significantly higher in the babies who died (n=27) compared to those who survived (n=53). These results were similar to the results of Sundaram and his colleagues [9] who noticed a significantly higher median SNAP II in babies who died versus in those who survived [median (IQR) 43 (36-53.5) *vs.* 18 (16-37), respectively; P<0.001].

Maiya et al. [18] had reported the mean SNAP in babies who survived versus who died as 4.88 vs. 17.38 (P<0.001). Sutton et al. [8] and Maiya et al. [18] who used the older generation SNAP in babies at the point of admission to the NICU, being a physiological score of severity of illness found that the higher the score the greater would be the physiologic derangement and the organ involvement.

Consistent with this, we observed higher SNAP II in babies with persisted/worsened organ dysfunction and *vice versa*. This indicates that organ function recovery was better in babies with a lower severity of illness.

In the current study, we found that respiratory system was the most frequently system involved at enrollment followed by the hematologic system then the cardiovascular system and when the individual SNAP II parameters were analyzed, it was found that parameters related to circulatory instability like low mean arterial pressure and lowest blood pH were significantly associated with death as well as organ dysfunction at day 14, P= 0.002. Also hypoxemia was significantly observed in babies with persistent OD and who died vs. those who survived, P<0.001.

Regarding hypothermia, the number of babies with hypothermia was too small for valid analysis. Multiple seizures were observed more commonly in babies who died but did not attain statistical significance. These results indicate that individual parameters of the SNAP II did not contribute equally to the risk of death.

When we constructed ROC curves for the SNAP II score \geq 40, they showed moderate predictive accuracy. The area under the (ROC) curve was 0.829 with sensitivity (90.4%) for OD and was 0.699 with sensitivity (88.9%) for death.

In contrast, Sundaram et al. study [9] had found that the area under the (ROC) curve for SNAP II curve for death was 0.82 (95% CI 0.68-0.95, P<0.001).

In comparison, Richardson and his colleagues [5] found that in all birth weights, SNAPPE II (Score for Neonatal Acute Physiology-Perinatal Extension) had excellent discrimination. Area under the (ROC) curve was 0.91 \pm 0.01. Accordingly SNAP II and SNAPPE II are empirically validated illness severity and mortality risk scores for newborn intensive care.

The strengths of our study are: SNAP II is a simple, objective and physiology-based measure of illness severity that is relatively easy to obtain. The six items in SNAP II are readily available in neonatal medical records and a score can be assessed in 4 to 6 minutes. An easily calculated illness severity score can be used by clinicians to predict patient outcomes and resource use.

Pge 4 of 5

Conclusion

SNAP II \geq 40 can predict OD and death with moderate predictive accuracy when applied on admission to neonates with sepsis. Parameters related to perfusion (mean arterial pressure and acidosis) were significantly associated with death as well as organ dysfunction at day 14.

From the results of the present study, we recommend application of the score on neonates on the first day of admission and serially in different institutions that may be helpful in making comparison between hospitals for outcomes of admitted neonates.

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Pge 5 of 5

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