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Pertinence of score for neonatal acute physiology-II to prognosticate mortality and organ dysfunction in neonatal sepsis

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ABSTRACT

Introduction: The present investigation was undertaken to correlation between mortality and morbidity (organ dysfunction [OD]) and score for neonatal acute physiology-II (SNAP-II).

Materials and Methods: A prospective investigation of newborns neonates, a total 157 neonates 82 male (52.2%), female 75 (47.8%) were enrolled and disunited into four groups according to gestational age: 28 to 30 weeks (G1), 31 to 33 (G2) 34 to 36 weeks (G3) and >37 weeks (G4) variables analyzed were SNAP II.

Results and Discussion: The receiver operating characteristic curve for SNAP-II score and death is more predictive in correlation to OD (area under curve of death is 0.776 as compared to 0.553 for OD). The sensitivity, specificity, positive predictive value, and negative predictive value of SNAP-II score with mortality (outcome) were 42.8%, 100%, 100%, and 82.3%, respectively.

Conclusion: The SNAP-II revealed efficient to fantabulous ≥40 can prognosticate OD and death when applied on admission to neonates with sepsis.

Keywords: Neonatal, Sepsis, Organ dysfunction, Score for neonatal acute physiology, Mortality

INTRODUCTION

Neonatal deaths constituting about 45% of deaths (World Health Organization, 2015) in children under 5 years, have until recently remained largely unaddressed as a global health concern.[1] Nevertheless, early neonatal mortality, particularly inside the 1st day after birth, is thought to contribute considerably to the general neonatal mortality rates.[2-4] According to recent worldwide estimates neonatal mortality extend from 2.9 to 3.6 million deaths for every year.[3,5-7] Sepsis is as yet a significant reason for morbidity and mortality in neonates, particularly in preterm newborn children, causing roughly 36% of the assessed 4 million neonatal passing annually.[8]

Neonatal sepsis is an overall general medical problem where checked varieties concerning its hazard and prognostic variables have been reported.[9] In spite of the improvement of wide range of antimicrobials and innovative advances in life support therapy, the morbidity and mortality rate because of neonatal sepsis continues to be high in the worldwide. An expected 5.9 million children under 5 years of age died in 2015, with a global under-five mortality rate of 42.5/1000 live births.[1] The incidence of neonatal sepsis in India according to the information from

National Neonatal Perinatal Database 2002–2003 is 30/1000 live births.[10] It is assessed that 20% of all neonates develop sepsis and approximately 1% die of sepsis-related causes.[11]

A wide assortment of etiologic agents taint the infant, including bacteria, viruses, fungi, protozoa, and mycoplasma. Recent investigations in 2015 found that *Staphylococcus aureus*, *Klebsiella pneumoniae,* and *Acinetobacter* were most common organisms isolated for neonatal sepsis.[12] Among intramural births, *K. pneumoniae* was the most frequently isolated pathogen pursued by *S. aureus*. Among extramural neonates (referred from community/other hospitals), *K. pneumoniae* was again the most common organism, trailed by *S. aureus* and *Pseudomonas*.[12]

A scoring framework has been utilized for individual risk prediction and counseling and involves fittingly weighted demographic, physiological, and clinical information gathered on the newborn child to compute a score that quantifies its morbidity. During the 1990s, Richardson *et al*. built up an arrangement of evaluation for the most significant physiological factors influencing mortality in the 1st h following affirmation. Each factor was assigned points based on the values found, and the result was the score for neonatal acute physiology (SNAP).[13] As the factors in SNAP and it cumbersome to calculate the score henceforth, 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) so as to encourage usage of the framework and the time of information assortment to 12 h.[14]

In perspective on the centrality of neonatal sepsis, endeavors have been made to asses and analyze the condition utilizing SNAP-II. Previous studies have applied SNAP-II as a measure of illness severity in precisely ventilated term babies and to anticipate transient unfavorable respiratory results in infants 34 weeks gestation admitted to the neonatal intensive care unit (NICU). Numerous babies may not be very sick at admission to NICU and may develop severe sickness later in the course of NICU stay. SNAP-II score were applied to the babies who developed features of sepsis at the time of admission and during their stay in the NICU and observed them for 14 days for their outcomes in the form of survival, determined organ dysfunction (OD) or death.

MATERIALS AND METHODS

As part of progressing examinations of present investigation, the plan and clinical criteria was carried as per literature procedure.[15-19] In the present examination was an imminent medical clinic based companion study led at NICU of a Tertiary Care Teaching, a referral hospital in Pune for 18 months. Parents or caretakers of neonates who were fulfilling inclusion criteria were approached for total 157 neonates were enrollment in this study, out of normal birth weight neonates were 11 (7%), low birth weight (LBW) were 55 (35%), very LBW (VLBW) were 72 (45.9%), and extremely LBW (ELBW) were 19 (12.1%), and the mean weight in this investigation was 1571.9 ± 613.22 g. Written informed consent or assent was taken as necessary.

All inborn and outborn infants determined to have clinical sepsis or sepsis screen positive or with evidence of systemic inflammatory response syndrome (SIRS) and OD were enrolled during the course of NICU stay. When they were diagnosed to have sepsis before antibiotics course or analyzed to have sepsis on affirmation not received antibiotics for more than 2 days (if referred from outside), SNAP-II score was calculated within 12 h after enrollment.

Sepsis screen comprised C-reactive protein (CRP), micro erythrocyte sedimentation rate (mESR), total leukocyte count (TLC), absolute neutrophil count (ANC), and immature to total ratio (ITR), and viewed as positive if any two or more out of these five were abnormal. CRP was considered positive above 10 mg/L, mESR above 10 mm in 1st h or "age in days +3" mm in the first 7 days, and TLC <5000/mm^3, ANC and ITR 20% charts were prepared as per literature method.[15] The presence of at least two of the accompanying four criteria, one of which must be abnormal temperature or leukocyte check and OD criteria systemic inflammatory respiratory response syndrome[16] were utilized.

SNAP-II

Score was applied with 12 h of beginning sepsis, this score comprises six physiological parameters, to be specific most minimal mean arterial pressure (MAP), most exceedingly terrible proportion of partial pressure of oxygen (PaO_2) to fraction of inspired oxygen (FiO_2), lowest temperature (in °F), lowest serum pH, and event of various seizures and urine output (<1 mL/kg/h). Scores were given dependent on the presence or absences of each parameter. The seriousness of the illness was reviewed by SNAP-II score 69 as mild: 1–20, moderate: 21–40, and extreme: >40.

Neonates with major congenital malformations, extreme asphyxia APGAR <4 at 5 min, neonate with hereditary issues, post-operative surgical cases, neonates referred from the outside hospital who have been mostly treated (more than 2 days) for serious sepsis were excluded from this investigation. All neonates satisfying the criteria were enlisted and SNAP-II score was applied within 12 h of sepsis, neonates were followed up for 14 days or death whichever was later for the ultimate result as endurance, OD, or death.

Statistical analysis

Information examination was finished by utilizing Statistical Package for the Social Sciences (SPSS) version 20:0. *P*-value

was determined utilizing the Chi-square test on numerical data. The receiver operating characteristic (ROC) curve was used to display the relationship between sensitivity and specificity for OD and death. Moral endorsement of the examination convention was acquired from the Institutional Ethics Committee.

RESULTS AND DISCUSSION

In the present investigation, a total of 157 patients were selected out of 1984 absolute confirmations in NICU between September 2014 and June 2016 who met the incorporation criteria for sepsis. Neonates with features clinical sepsis or sepsis screen positive or SIRS positive at the time of admission or during the course of NICU stay were enrolled. SNAP-II score was applied within 12 h of development of sepsis and score was determined, neonate was observed for 14 days from the beginning of sepsis to search for the result on 14th day as endurance, death, or OD.

Mean values:

- In the examination, the mean gestational age was 33.5 ± 3.36 weeks (28–30 weeks) similar results were observed.[15,20] The mean gestational age was 30.2 ± 2 weeks and 34.95 weeks (28–40 weeks), respectively.
- In this study, the mean weight on admission was 1571.9 ± 613.22 g and in another Indian study.[20] Mean birth weight was 1188.3 ± 282.8 g, however, in the study.[15] The mean weight on affirmation was 2320 g. This difference in mean weight might be because of various geographical locations and socioeconomic status.
- The median day of onset of illness was 3 in our study this is corresponding with results that were acquired.
- Day of illness was 4 and 3.5, respectively. This could be a reason why early-onset sepsis more when compared to late-onset sepsis. In investigation sepsis screen was positive in 63.7% of neonates which was generally normal, comparable perceptions were done, where sepsis screen was positive in 91.3% neonates. In the blood culture positive in 19.1% of neonates in contrast to study, where blood culture was positive in 28.75% neonates. This might be a direct result of the experimental utilization of antibiotics.

At the time of enrollment, the median SNAP-II score was 12 (interquartile range [IQR] 5–22) and median SNAP-II score was 12.5 (IQR O-32). Another comparable examination done by had a median score of 37 (IQR 18.5–37.5) at the time of enlistment. The median SNAP-II score for birth weight was calculated and it was found that ELBW neonates had median value of 14 (IQR 5–25), similarly, for VLBW the median value was 5 (IQR 5–20.25), for LBW neonates the median value was 19 (IQR 4.5–23), and for normal weight neonates the median value was 19 (5–22.5). The median SNAP-II score in VLBW babies was 12 (IQR 0–32), in LBW babies, it was 12.5 (IQR 0–60).

Table 1: Baseline characteristics.

Baseline characters	Values
Gestational age in weeks (mean±SD)	33.5±3.36
Birth weight in grams (mean±SD)	1571.9±613.22
Sex (%)	
Male	82 (52.2)
Female	75 (47.8)
Day of onset illness (median)	3 (1–6)

SD: Standard deviation

Table 2: Correlation between SNAP-II score with outcome.

SNAP-II score category	Death (*n*), (%)	Organ dysfunction (*n*) (%)	Alive (*n*), (%)	Total number, (%)	*P*-value
Mild (1–20)	9 (21.4)	16 (64.0)	70 (77.8)	95 (60.5)	**<0.001
Moderate (21–40)	15 (35.7)	9 (36.0)	20 (22.2)	44 (28.0)	
Severe (>40)	18 (42.9)	0	0	18 (11.5)	
Total	42 (26.8)	25 (15.9)	90 (57.3)	157 (100.0)	

SNAP: Score for neonatal acute physiology

Table 3: Correlation between individual parameter of score for neonatal acute physiology-II score with outcome.

Parameters	Survival (*n*=90)	Death (*n*=42)	Organ dysfunction (*n*=25)	*P*-value
MAP ≤29 mmHg	3	29	8	**<0.001
Lowest blood pH (<7.20)	25	28	13	0.0002
PaO_2/FiO_2 ratio (<2.50)	22	20	4	0.0188
Urine output (<1 mL/kg/h)	4	15	3	**<0.001
Lowest temperature (35.6°C)	5	10	4	0.0244
Multiple seizures	25	12	8	0.9821

***P*-value <0.05 is considered significant. MAP: Mean arterial pressure

The calculated median values according to the outcome and found that median value for survival was 5 (IQR 5–19), median value for OD was 10 (IQR 5–23), and median value for death was 20 (IQR 9–20.75). The median value of death was more when compared to survival and OD (20 IQR 9–20.5 vs. 5 IQR 5–19) with $P < 0.001$. A study had median score for death neonates which was higher than the neonates who survived (median [IQR] 43 [36–53.5] vs. 18 [16–37], respectively; $P < 0.001$). Similar results were observed.

Out of 157 neonates, 60.5% had mild illness (SNAP-II = 1–20), moderate illness in 28% (SNAP-II = 21–40), and severe illness in 11.5% (SNAP-II >40). Similar were observation that 57.7% neonates had mild illness (SNAP-II = 1–20), 27.5% had moderate illness (SNAP-II = 21–40), and 14.8% had severe illness (SNAP-II >40) by Helal *et al.*[15]

The death percentage by SNAP-II category in mild illness was 9.47%, moderate illness was 34.1%, and in severe illness was 100%. A similar observation that the death percentage by SNAP-II category was 21.7% for mild illness, 40.9% for moderate illness, and 66.7% for severe illness, on the other hand, the death percentage by SNAP-II category was 20% for mild, 64% for moderate, and 87.5% for severe. This shows that there are higher chances of mortality if the score is more.

The study analyzed mild, moderate, and severe SNAP-II score to predict the result in the form of survival, OD and death, the results were statistically noteworthy ($P < 0.001$), comparable perception was available in an examination.

Table 4: Specificity of SNAP-II score with mortality (outcome).

SNAP-II Score	Mortality		Total
	Yes	No	
Severe (>40)	18	0	18
Mild + Moderate (≤ 40)	24	115	139
Total	42	115	157

SNAP: Score for neonatal acute physiology

Table 5: Blood culture.

Organism	*n* (%)
Acinetobacter species	10 (33.3)
Klebsiella pneumoniae	9 (30)
Pseudomonas aeruginosa	3 (10)
Escherichia coli	2 (6.7)
Citrobacter species	2 (6.7)
Enterococcus species	2 (6.7)
Enterobacter species	1 (3.3)
Methicillin-resistant *Staphylococcus aureus*	1 (3.3)
Total	30 (100)

Table 6: Cerebrospinal fluid culture.

Organism	*n* (%)
Acinetobacter species	3 (50)
Enterococcus species	2 (33.3)
Enterobacter species	1 (16.7)
Total	6

Individual parameter of SNAP-II score

All parameters identified with circulatory instability such as MAP, decreased urine output <1 ml/kg/h, lowest blood pH, hypothermia, and hypoxia were significantly associated with OD and death and these parameters have statistical significance ($P < 0.05$), 28.7% of neonates had multiple seizures, however, multiple seizures was associated with 12 deaths and 8 OD but it was not statistically significant. These results were consistent. With the study done by Helal *et al.*,[15]

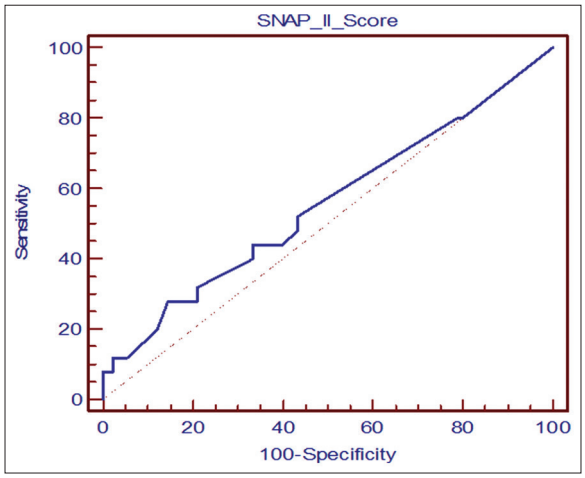

Figure 1: Receiver-operator characteristic curve of score for neonatal acute physiology-II in neonates with organ dysfunction.

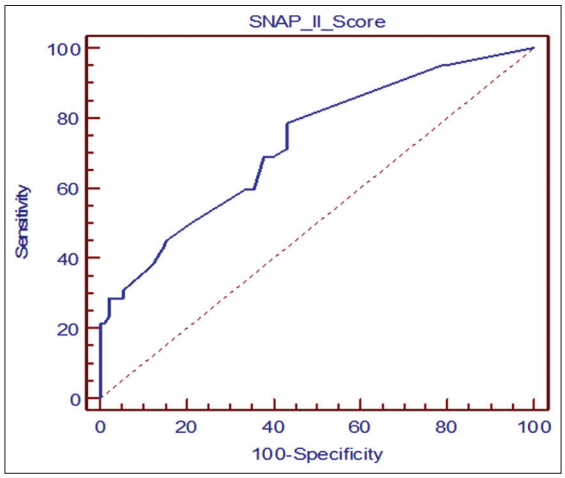

Figure 2: Receiver operating characteristic curve for score for neonatal acute physiology-II in neonates with death as outcome.

Table 7: Correlation between score for neonatal acute physiology-II and ROC curve for organ dysfunction and death.

Measurement	Organ dysfunction	Death
Sensitivity	28% (95% CI 12.1–49.4)	78.6% (CI 95% 63.2–89.7)
Specificity	85.6% (95% CI 76.6–92.1)	56.7% (CI 95% 45.8–67.1)
Positive likelihood ratio	1.94	1.81
Negative likelihood ratio	0.84	0.38
Area under ROC curve	0.553 (95% CI 0.457–0.645)	0.726 (95% CI 0.641–0.800)

ROC: Receiver operating characteristic, CI: Confidence interval

Sundaram *et al*.[20] The results of sensitivity, specificity calculation of SNAP-II score with mortality (outcome), and the sensitivity were seen as 42.8% with a specificity of 100% and positive predictive value (PPV) was 100% and negative predictive value (NPV) was 82.3%.

It is intriguing to call point out ROC curve for SNAP-II score with OD found that area under the ROC curve = 0.553 (95% confidence interval [CI] = 0.457–0.645), with sensitivity of 28% (95% CI 12.1–49.4), and specificity of 85.6% (95% CI 76.6–92.1), +LR = positive likelihood ratio of 1.94, and −LR = negative likelihood ratio of 0.84. The area under the (ROC) curve for SNAP-II and Organ Dysfunction (OD) was 0.829 (95% CI 0.731–0.926), sensitivity for OD was 23.1% (95% CI 11.2–34.9), and specificity was 100%. The sensitivity for OD showed that 58% (95% CI 39–74.5) and specificity of 86% (95% CI 60–95.9).

Similarly constructed ROC curve for SNAP-II score with death and found that area under the ROC curve = 0.726 (95% CI = 0.641–0.800) with sensitivity of 78.6 (CI 95% 63.2–89.7), with specificity of 56.7 (CI 95% 45.8–67.1), +LR = Positive likelihood ratio of 1.81, and −LR = Negative likelihood ratio of 0.38. The area under the (ROC) curve for SNAP-II and death was 0.699 (95% CI 0.58–0.818), sensitivity for death was 29.6% (CI 95% 11.2–48.0), and specificity was 92.5% (95% CI 85.1–99.8). The sensitivity showed that for death was 60 (95% CI 40.7–76.6) and specificity of 86.6 (95% CI 62.1–96.3). Hence, the ROC curve for SNAP-II score and death is more predictive in correlation to ROC curve for SNAP-II score and OD (area under the curve of death is 0.776 as compared to 0.553 for OD).

Furthermore, 157 neonates with features of neonatal sepsis were enrolled data analysis was done using SPSS version 20:0, and graphs were prepared using Microsoft Excel. Scientific evidence suggests that quantitative data variables expressed using mean and standard deviation, median. Comparisons between categorical data were done using the Chi-square test/Fisher's exact test (if expected cell frequency <5). The results are delineated in Table 1.

The results clearly signify that correlation between the mild, moderate, and severe SNAP-II score with the outcome on 14th day from the onset of neonatal sepsis and have statistical significance ($P < 0.05$). Similar results were observed.[15] The results are indicated in Table 2.

In Table 3 found that five the parameters related to circulatory failure had attained statistical significance $P < 0.05$, and the majority of neonates were associated with death as the outcome. However, the multiple seizures were found in 25 neonates who survived and eight neonates who had OD and 12 neonates had death as the outcome even then the multiple seizures parameter did not have statistical significance, which were consistent with the results.[15,20] The calculated sensitivity was found to be 42.8% with a specificity of 100% and PPV was 100% and NPV was 82.3%. The results are shown in Table 4.

Further confirmed that the most common organism in blood culture was *Acinetobacter* (33.3%) followed by *K. pneumoniae* and least common was methicillin-resistant *S. aureus* 3.3%. The most common organism in cerebrospinal fluid culture was *Acinetobacter* species (50%) and the least common was *Enterobacter* species 1 (16.7%), as shown in Tables 5 and 6.

The ROC curve was used to display the relationship between sensitivity and specificity for OD and death. The ROC curve is for SNAP-II score with OD. It was found that area under the ROC curve = 0.553 (95% [CI] = 0.457–0.645), with sensitivity of 28% (95% CI 12.1–49.4), and specificity of 85.6% (95% CI 76.6–92.1), +LR = Positive likelihood ratio of 1.94, −LR = Negative likelihood ratio of 0.84. The results are shown in Figure 1. The ROC curve is for SNAP-II score with death as outcome and found that area under the ROC curve = 0.726 (95% CI = 0.641–0.800) with sensitivity of 78.6% (CI 95% 63.2–89.7) with specificity of 56.7% (CI 95% 45.8–67.1), +LR = Positive likelihood ratio of 1.81, and −LR = Negative likelihood ratio of 0.38. The results are indicated in Figure 2. Table 7 indicated ROC curve for SNAP-II score and death is more predictive in correlation to the ROC curve for SNAP-II score and OD (area under the curve of death is 0.776 as compared to 0.553 for OD).

CONCLUSION

The study reports, refusal to feed was the most common clinical feature of neonatal sepsis. SNAP II ≥40 can predict OD and death when applied on admission to neonates with sepsis. Higher the SNAP II score higher the chances of death and OD. However, the ROC curve for SNAP II score and death is more predictive in correlation to the ROC

curve for SNAP II score and OD (area under the curve of death is 0.776 as compared to 0.553 for OD). MAP, acidosis, decreased urine output, low PaO_2/FiO_2, and hypothermia were significantly associated with death as well as OD. Sepsis screen test was the most common investigation positive for neonatal sepsis followed by blood culture. *Acinetobacter* species were the most common organism isolated in blood culture and CSF culture. The sensitivity, specificity, PPV, and NPV of SNAP-II score with mortality (outcome) were 42.8%, 100%, 100%, and 82.3%, respectively.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms.

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Conflicts of interest

There are no conflicts of interest.

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