

Original Research Article

Comparative prognostic performance of the neonatal sequential organ failure assessment and score for neonatal acute physiology with perinatal extension-II score for predicting in-hospital mortality among neonates with sepsis: a retrospective cohort study

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ABSTRACT

Background: Accurate risk stratification is essential for identification of neonates with sepsis at high risk of mortality. The neonatal sequential organ failure assessment (nSOFA) score reflects dynamic organ dysfunction, whereas the score for neonatal acute physiology with perinatal extension-II (SNAPPE-II) assesses baseline illness severity at admission.

Methods: This retrospective cohort study included neonates with clinical sepsis admitted to a tertiary neonatal intensive care unit between September 2024 and March 2025. SNAPPE-II scores were calculated using admission data within the first 12 hours of NICU stay. nSOFA scores were calculated using the worst physiological parameters within 24 hours of sepsis diagnosis. The primary outcome was in-hospital mortality. Discriminative performance was assessed using receiver operating characteristic (ROC) curve analysis, correlation analysis, and binary logistic regression.

Results: Among 175 neonates, 35 (20.0%) died during hospitalization. Mean nSOFA and SNAPPE-II scores were higher among the non-survivors than survivors (nSOFA: 5.7 ± 2.1 vs 2.3 ± 1.9 ; SNAPPE-II: 56.4 ± 19.8 vs 31.7 ± 17.3 ; both $p < 0.001$). The area under the ROC curve was 0.754 for nSOFA and 0.877 for SNAPPE-II. On logistic regression analysis, higher values of both scores were independently associated with increased odds of mortality.

Conclusions: Both nSOFA and SNAPPE-II are effective predictors of in-hospital mortality in neonates with sepsis. SNAPPE-II demonstrated higher discriminative accuracy while nSOFA provides a dynamic insight of organ dysfunction. The complementary use of these scoring systems may enhance early risk stratification in neonatal intensive care units, particularly in resource-limited settings.

Keywords: Neonatal sepsis, nSOFA, SNAPPE-II, In-hospital mortality, Neonatal intensive care unit

INTRODUCTION

Sepsis is a life-threatening condition that arises when the body's response to an infection becomes dysregulated, leading to widespread inflammation, tissue damage, and organ dysfunction. Despite advances in neonatal intensive

care, predicting outcomes in septic neonates remains challenging due to the complex and rapidly evolving nature of the disease. Early identification of neonates at higher risk of adverse outcomes is crucial for guiding clinical decision-making and optimizing resource allocation. Life-threatening organ dysfunction is

substantiated by a SOFA score, which is a clinical tool used to track a patient's organ function over time, particularly in cases of infection.¹ An increase of 2 or more points from a patient's baseline SOFA score indicates significant organ dysfunction, helping to identify individuals who may be experiencing severe complications related to infection. In contrast to adult and pediatric intensive care settings, the distinction between infection and sepsis, as well as the integration of organ dysfunction into diagnostic criteria, remains underdeveloped in neonatal intensive care units (NICUs). Current definitions of neonatal sepsis largely rely on identifying bacterial pathogens in blood cultures or the duration of antimicrobial therapy, rather than clinical indicators of organ dysfunction. This lack of emphasis on organ failure in preterm infants hinders the ability to categorize patients by severity of illness and mortality risk, an essential step for advancing research efforts and improving clinical outcomes in this vulnerable population.² The nSOFA score was developed to address the need for an organ dysfunction-based framework applicable to neonatal sepsis.³ The SOFA score has shown promise in predicting mortality among very preterm infants who develop late-onset sepsis, as confirmed by positive blood culture findings.⁴ In contrast, the SNAPPE-II is a well-established tool based on physiological variables measured within the first 12 hours of admission, traditionally used for risk stratification in critically ill neonates. Higher scores indicate a greater risk, assisting healthcare providers in identifying critically ill infants who need intensive care interventions. Neonates with elevated SNAP-II scores are at greater risk of developing long-term complications from septicemia, often requiring extended medical care and ongoing follow-up.⁵

Aim

Aim was to compare the discriminative ability of nSOFA and SNAPPE-II scores in predicting in-hospital mortality and assess the correlation between these scores and examine their association with mortality in septic neonates.

METHODS

Study design

It was a retrospective Cohort study.

Study population

Both early-onset and late-onset sepsis cases were included; however, the timing of sepsis did not affect SNAPPE-II calculation, as the score was derived exclusively from admission data.

Inclusion criteria

Neonates admitted to the neonatal intensive care unit with

a clinical diagnosis of sepsis, Clinical sepsis was defined as suspected infection with compatible clinical signs and at least one supportive laboratory abnormality irrespective of blood culture positivity, during the study period. Availability of complete clinical and laboratory data required to calculate both nSOFA and SNAPPE-II scores within the defined scoring windows included.

Exclusion criteria

Neonates with incomplete clinical or laboratory data precluding calculation of either scoring system, neonates with major congenital anomalies likely to independently affect survival outcomes were excluded from the study.

Definition of neonatal sepsis

Neonatal sepsis was defined in accordance with the International Pediatric Sepsis Consensus Conference criteria, as the presence of suspected or proven infection accompanied by systemic clinical signs and supportive laboratory abnormalities. Neonates were included if they exhibited clinical features suggestive of infection such as cardiorespiratory instability, abnormal temperature regulation, neurological symptoms, petechiae or purpura, signs of poor perfusion and an overall appearance of being unwell together with at least one supportive laboratory parameter, including elevated C-reactive protein, positive blood culture, or hematological abnormalities such as thrombocytopenia. All cases were initiated on antimicrobial therapy by the treating team.

Study settings

Pediatrics department unit 1 at Lahore General Hospital, Lahore.

Study duration

The study population included neonates admitted to the neonatal intensive care unit between September 1, 2024 and March 31, 2025. The medical records of eligible neonates were reviewed to collect demographic and clinical data, including nSOFA and SNAPPE 2 scores. Primary outcomes of interest was in-hospital mortality.

Data collection

Demographic data were gestational age, birth weight, gender. Clinical data includes vital signs, presence of shock, need for mechanical ventilation. Laboratory data had complete blood count, blood gas analysis, serum biomarkers (e.g., CRP). Outcomes were in-hospital mortality, length of hospital stay, requirement for mechanical ventilation, and inotropic support.

Sampling technique

Non-probability consecutive purposive sampling technique was used for this study.

Sample size calculator

Sample size adequacy was assessed based on available cases during the study period and event rates reported in prior studies evaluating prognostic accuracy of neonatal severity scoring systems.

Calculation and timing of nSOFA and SNAPPE-II scores

The SNAPPE-II score was calculated using the worst physiological and perinatal variables recorded within the first 12 hours of neonatal intensive care unit admission, in accordance with the original score description. SNAPPE-II was therefore used as a measure of baseline illness severity at admission, irrespective of the timing of subsequent sepsis episodes. Variables used for SNAPPE-II calculation included gestational age, birth weight, Apgar score, and early physiological parameters routinely documented at admission.

The nSOFA score was calculated at the time of clinical sepsis diagnosis, using the worst recorded values for respiratory, cardiovascular, and hematologic parameters within the subsequent 24-hour period. This approach reflects the dynamic nature of nSOFA as a measure of evolving organ dysfunction during critical illness.

Given the different design purposes of SNAPPE-II (baseline illness severity assessment) and nSOFA (organ dysfunction-based severity assessment), the two scores were evaluated for their individual and comparative ability to discriminate in-hospital mortality, rather than as temporally equivalent measures.

Statistical analysis

Statistical analysis was performed using the statistical package for the social sciences (SPSS). Continuous variables were summarized using mean and standard deviation or median and interquartile range, as appropriate, while categorical variables were expressed as frequencies and percentages. Comparisons between survivors and non-survivors were conducted using the independent samples t test or Mann-Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. A two-sided $p < 0.05$ was considered statistically significant.

The discriminative ability of the nSOFA and SNAPPE-II scores for predicting in-hospital mortality was assessed using ROC curve analysis, with calculation of the area under the ROC curve (AUC). AUC values were interpreted as measures of discrimination, with higher values indicating better ability to distinguish between survivors and non-survivors.

The relationship between nSOFA and SNAPPE-II scores was evaluated using Pearson correlation analysis. Binary logistic regression analysis was performed to examine the

association of each scoring system with mortality. Regression results are presented as odds ratios with 95% confidence intervals, reflecting the strength of association between increasing score values and mortality risk. Optimal cutoffs were determined using the Youden Index. Calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test. ROC curves were compared using the DeLong method.

RESULTS

A total of 175 neonates admitted to the neonatal intensive care unit with a diagnosis of sepsis during the study period were included in the analysis. Their baseline demographic characteristics are mentioned in Table 1.

Among these, 35 neonates (20.0%) died during their hospital stay, while 140 (80.0%) survived to discharge. Of the 175 neonates included, 116 (66.3%) had early-onset sepsis and 59 (33.7%) had late-onset sepsis. Among culture-positive cases, 26 (43.3%) were caused by Gram-positive organisms, 32 (53.3%) by Gram-negative organisms, and 2 (3.3%) by fungal pathogens. Mortality during the index hospitalization was the primary outcome assessed. The mean nSOFA score among non-survivors was significantly higher (5.7 ± 2.1) compared to survivors (2.3 ± 1.9), with a $p < 0.001$. Similarly, the mean SNAPPE-II score was also significantly higher among non-survivors (56.4 ± 19.8) compared to survivors (31.7 ± 17.3), with a $p < 0.001$.

ROC curve analysis demonstrated that both scoring systems showed good discrimination for in-hospital mortality. The area under the ROC curve (AUC) for the nSOFA score was 0.754, while the AUC for the SNAPPE-II score was 0.877 (ROC curves for nSOFA and SNAPPE-II are shown in Figure 1). These findings indicate that both scores were able to distinguish survivors from non-survivors with a high degree of accuracy. A moderate positive correlation was observed between nSOFA and SNAPPE-II scores (Pearson $r = 0.514$, $p < 0.001$), suggesting that although the two scores assess overlapping aspects of illness severity, they are not redundant and may capture distinct dimensions of neonatal critical illness. Mechanical ventilation, shock and culture-positive sepsis were significantly more common among non-survivors compared to survivors. Detailed distributions of the individual components contributing to nSOFA and SNAPPE-II scores are presented in Supplementary Tables 1 and 2, however, the difference between ROC curves was not statistically significant (DeLong test $p = 0.071$). On binary logistic regression analysis, both nSOFA and SNAPPE-II scores were significantly associated with in-hospital mortality. Odds ratios are presented per unit increase in score; values less than 1 reflect inverse coding of the dependent variable, with higher scores corresponding to increased mortality risk. (Results of logistic regression analysis are presented in Table 2). Increasing values of each score were associated with a higher likelihood of death,

reflecting their relationship with illness severity. SNAPPE-II demonstrated a stronger statistical association with mortality compared with nSOFA, although both scores remained independently associated with the outcome. ROC analysis demonstrated an AUC of 0.754 for nSOFA and 0.877 for SNAPPE-II as shown in Table 3. The optimal cutoff for mortality prediction was ≥ 8 for nSOFA (sensitivity 88.5%, specificity 56.3%) and ≥ 50 for SNAPPE-II (sensitivity 73.1%, specificity 91.7%). SNAPPE-II achieved a higher Youden index (0.647 vs 0.447), suggesting better overall classification performance at the selected cutoff (Table 4). Calibration analysis using the Hosmer-Lemeshow goodness-of-fit test demonstrated acceptable calibration for SNAPPE-II ($p=0.252$), whereas nSOFA showed evidence of poorer calibration ($p=0.029$). Calibration should be interpreted cautiously given limited event counts (Table 5).

It should be noted that SNAPPE-II reflects baseline physiological risk at admission, whereas nSOFA captures evolving organ dysfunction at sepsis onset; thus, their predictive performance represents complementary rather than identical constructs. In conclusion, both nSOFA and SNAPPE-II scores are effective in predicting mortality in neonates, with SNAPPE-II showing slightly better predictive accuracy. However, due to its simplicity, nSOFA remains a practical and reliable tool, especially in resource-limited settings.

Given different intended applications of 2 scoring systems SNAPPE-II representing baseline illness severity and nSOFA representing evolving organ dysfunction at time of sepsis, observed predictive performance should be interpreted as complementary rather than directly interchangeable measures of mortality risk.

Table 1: Baseline demographic and clinical characteristics of the study population according to survival status.

Variables	Overall, (n=175)	Survivors, (n=140)	Non-survivors, (n=35)	P value
Gestational age (in weeks), mean $\pm$ SD	36.2 $\pm$ 2.5	36.5 $\pm$ 2.3	34.5 $\pm$ 2.7	<0.001
Birth weight (g), mean $\pm$ SD	2,650 $\pm$ 550	2,720 $\pm$ 520	2,300 $\pm$ 600	0.002
Male sex, N (%)	95 (54.3)	74 (52)	21 (58)	0.69
Mechanical ventilation, N (%)	50 (28.6)	30 (21.4)	20 (57.1)	<0.001
Shock, N (%)	40 (22.9)	20 (14.3)	20 (57.1)	<0.001
Inotrope requirement, N (%)	45 (25.7)	22 (15.7)	23 (65.7)	<0.001
SpO ₂ /FiO ₂ ratio, median (IQR)	240 (160-320)	275 (210-340)	115 (80-180)	<0.001
Culture-positive sepsis, N (%)	60 (34.3)	40 (28.6)	20 (57.1)	0.001
CRP elevated, N (%)	120 (68.6)	85 (60.7)	35 (100)	<0.001
Platelet count ($\times 10^9/L$), median (IQR)	150 (110-210)	160 (120-220)	90 (60-130)	<0.001
Late-onset sepsis, N (%)	59 (33.7)	45 (32.1)	14 (40.0)	-
Early-onset sepsis, N (%)	116 (66.3)	95 (67.9)	21 (60.0)	-

Table 2: Association of nSOFA and SNAPPE-II scores with in-hospital mortality.

Variables	OR	95% CI	P value
nSOFA score	0.74	0.57-0.97	0.031
SNAPPE-II score	0.90	0.86-0.95	<0.001

*Odds ratios are reported for survival as the dependent variable. Therefore, values below 1 indicate an increased risk of mortality with increasing score values.

Table 3: Discriminative performance of nSOFA and SNAPPE-II scores for mortality.

Score	AUC	95% CI	P value
nSOFA	0.754	0.642-0.865	<0.001
SNAPPE-II	0.877	0.794-0.959	<0.001

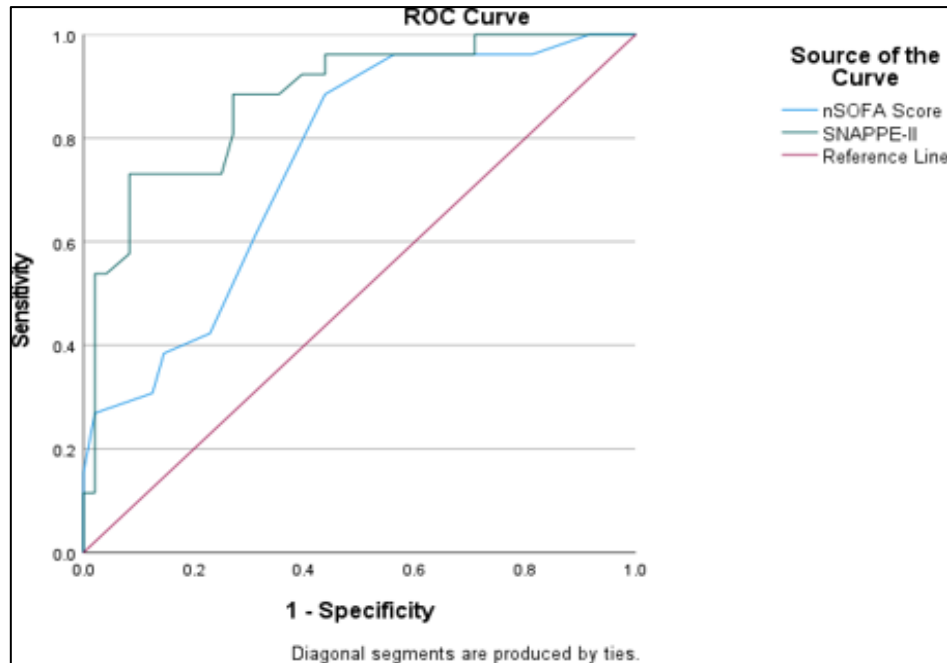
Table 4: Optimal cutoff values, sensitivity, specificity, and overall diagnostic performance of nSOFA and SNAPPE-II scores for predicting in-hospital mortality among neonates with sepsis.

Score	Optimal cutoff	Sensitivity	Specificity	Youden Index
nSOFA	≥ 8	88.5%	56.3%	0.447
SNAPPE-II	≥ 50	73.1%	91.7%	0.647

Table 5: Calibration performance of nSOFA and SNAPPE-II scores assessed using the Hosmer-Lemeshow goodness-of-fit test.

Score	HL χ^2	P value
nSOFA	14.07	0.029
SNAPPE-II	10.20	0.252

*A non-significant p value (>0.05) indicates acceptable agreement between predicted and observed mortality outcomes

**Figure 1: ROC curves demonstrating the discriminative ability of nSOFA and SNAPPE-II scores for predicting in-hospital mortality among neonates with sepsis.**

DISCUSSION

In this study, both the nSOFA and SNAPPE-II scores demonstrated strong prognostic value for hospital mortality in septic neonates. SNAPPE-II showed higher observed AUC than nSOFA (0.754 for nSOFA and 0.877 for SNAPPE-II); however, the difference between the two ROC curves did not reach statistical significance on DeLong testing ($p=0.071$). Hence, these findings support the prognostic value of both scores rather than superiority of one over the other. Another important consideration is the difference in timing and intent of the two scores. SNAPPE-II was designed to quantify initial severity of illness within the first 12 hours of NICU admission, whereas nSOFA is a dynamic score reflecting ongoing organ dysfunction.⁶

Upon consideration of individual score components, more cardiovascular and respiratory dysfunction was observed among non-survivors as illustrated by increased cardiovascular support requirements, higher composite organ dysfunction scores and lower oxygenation indices (Supplementary Table S1). Similarly, higher SNAPPE-II values were found in non-survivors, mostly attributed to a worse physiological state at admission (Supplementary Table S2). In newborns with late-onset sepsis, SNAPPE-II

is mainly utilized to measure underlying vulnerability rather than acute severity of sepsis. Despite this limitation, SNAPPE-II demonstrated good predictive ability, suggesting baseline physiological risk as a vital mortality predictor even in late-onset sepsis. The present study should not be considered as a superiority comparison because SNAPPE-II and nSOFA were developed for different goals and measured at different time points. In fact, findings report both nSOFA and SNAPPE-II related to mortality.

Automated nSOFA scores in very-low-birthweight infants with late-onset sepsis were considerably higher in non-survivors, yielding AUCs up to 0.93 by 12 h after evaluation.⁷ In the same way, SNAPPE-II was linked to effective prediction of neonatal mortality (AUC $\approx$ 0.857 in very-low-birthweight infants).⁸ Thus, our findings are consistent with the existing literature showing that both physiological (nSOFA) and perinatal-physiological (SNAPPE-II) scoring systems can stratify risk in critically ill newborns. Additionally, SNAPPE-II has shown high performance in other settings (e.g. AUC $\approx$ 0.917 in a recent NICU cohort) and a SNAPPE-II threshold ≥ 20 was associated with significantly increased mortality.^{9,10} These results indicate that addition of birth weight and Apgar scores (as in SNAPPE-II) may enhance early risk stratification to some extent. On the other hand,

markedly lower nSOFA scores were observed in a cohort of survivors compared to non-survivors, with each incremental one-point elevation in the nSOFA corresponding to a 1.6-fold increase in the odds of mortality (95% CI: 1.2-2.1). An optimal nSOFA threshold of 3.5 was determined to predict mortality, yielding 100% sensitivity and 83.9% specificity.¹¹ A study conducted by Harsha et al described the SNAPPE-II score's predictive validity in relation to mortality and morbidity in neonates. SNAPPE-II score was found to be higher among non-survivors compared to survived ones. A mean score of 37 was associated with higher mortality. However, it didn't accurately predict the length of stay.¹²

Another prospective observational research conducted by Niranjana et al comparing neonatal outcomes with the degree of SNAPPE II scores. SNAPPE II score demonstrated efficacy in predicting mortality (AUC: 0.837, 95% CI: 0.73-0.91). The cutoff score with the highest sensitivity and specificity for predicting mortality was 29 and the odds ratio estimate was 15.27, indicating higher scores were associated with 15 times increased risk of dying, as do those with low scores.¹³ Clinically, these results reinforce the utility of both tools for early risk stratification. The nSOFA score, which quantifies respiratory, cardiovascular, and hematologic dysfunction over time, provides a dynamic measure of evolving organ failure. In contrast, the SNAPPE-II integrates perinatal factors and initial physiology. Although SNAPPE-II showed a modestly higher predictive accuracy in our mixed sepsis cohort, nSOFA's simplicity and focus on active organ dysfunction remain valuable, particularly in settings with limited resources. Importantly, the moderate correlation between the scores suggests they capture overlapping but distinct aspects of illness severity. Our data support using either score to identify high-risk neonates; in practice, the choice may depend on availability of data and timing (SNAPPE-II is calculated within 12 h of birth, whereas nSOFA can be updated during the course of illness). Although SNAPPE-II demonstrated a numerically higher AUC than nSOFA, the difference between ROC curves did not reach statistical significance on DeLong testing.

Strengths of this study include a sizable sample of septic neonates and the direct head-to-head comparison of two validated scoring systems. By examining all-cause mortality, we focused on a robust and clinically meaningful endpoint. This work extends previous single-score analyses by demonstrating that both nSOFA and SNAPPE-II retain good prognostic value in a general NICU population with sepsis. Our results are particularly relevant given the increasing recognition of organ dysfunction criteria in neonatal sepsis.

There are several limitations. The retrospective, single-center design may limit generalizability and introduces potential bias from incomplete records. We did not adjust for all possible confounders (e.g. severity of sepsis or comorbidities beyond the scores). Additionally, SNAPPE-

II was originally developed for the first day of life, whereas many of our infants may have had late-onset sepsis, so the timing of score calculation could affect its performance. SNAPPE-II was not recalculated at the time of sepsis and therefore may not fully capture acute physiological derangement in late-onset sepsis; however, this reflects appropriate use of the score according to its original validation. The sample size, while adequate for detecting differences in AUC, may be insufficient for detailed subgroup analyses such as stratification by birth weight or pathogen type therefore no stratified analysis by early- versus late-onset sepsis was performed, which may have provided additional insight into score performance across different sepsis phenotypes. Approximately two-thirds of the cohort had early-onset sepsis. Although both early and late-onset sepsis cases were included, the study was not powered for separate subgroup analyses comparing score performance between these populations. Finally, like all predictive models, neither score is perfectly sensitive or specific; clinical judgment remains essential. Future research should prospectively validate these findings across multiple centers and varied patient populations. It would be valuable to assess whether combining scores or integrating biomarkers (e.g. lactate, procalcitonin) improves prognostic precision. Additionally, studies could examine whether using nSOFA or SNAPPE-II to guide therapy (for example, earlier aggressive support in high-score infants) actually improves outcomes. Exploration of these scores' ability to predict other outcomes, such as prolonged organ dysfunction or neurodevelopmental impairment, would also be informative.

CONCLUSION

In conclusion, our study confirms that both nSOFA and SNAPPE-II are effective prognostic tools in neonatal sepsis. The slightly higher predictive accuracy of SNAPPE-II must be balanced against nSOFA's practicality and focus on dynamic organ failure. Although the cohort represents one of the larger neonatal sepsis datasets reported from our region, the sample size remains modest and limits subgroup analyses. Given the high stakes of neonatal sepsis, the use of such validated scores can aid clinicians in identifying critically ill infants early and allocating resources appropriately, while also informing future efforts to refine neonatal sepsis definitions and care protocols.

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ANNEXURE

Table 1: Components of the nSOFA score.

Variables	Survivors	Non-survivors
SpO ₂ /FiO ₂ ratio, mean	195.4	135.0
Respiratory subscore, mean	2.96	3.77
Cardiovascular subscore, mean	1.56	3.23
Hematologic subscore, mean	1.4	2.7

Table 2: Components of the SNAPPE-II score.

Variables	Survivors	Non-survivors
Mean arterial pressure (mmHg), mean	64.2	48.4
pH, mean	7.35	7.33
Urine output (mL/kg/h), mean	2.60	2.56
PaO ₂ /FiO ₂ ratio component, mean	1.52	1.43

Table 3: Distribution of microbiological isolates among culture-positive cases.

Category	N
Culture positive	60
Culture negative	115
Gram positive	26
Gram negative	32
Fungal	2

Table 4: SNAPPE 2 score.

Variables	Range or condition	Points
Mean arterial pressure (mmHg)	≥30	0
	20-29	9
	<20	19
Lowest temperature (°C)	>35.6	0
	35.0-35.5	8
	<35	15
P _a O ₂ /FiO ₂ ratio (mmHg)	>2.5	0
	1.0-2.49	5
	0.3-0.99	16
	<0.3	28
Lowest serum pH	≥7.20	0
	7.10-7.19	7
	<7.10	16
Multiple seizures	No	0
	Yes	19
Urine output (mL/kg/hr)	≥1	0
	0.1-0.9	5
	<0.1	18
Apgar score	≥7	0
	<7	18
Birth weight (g)	≥1000	0
	750-999	10
	< 750	17
Small for gestational age (SGA)	< 3 rd percentile	12

Table 5: nSOFA score.

Organ system	Score 0	Score 1	Score 2	Score 3	Score 4
Respiratory	S/F ≥300, not intubated	S/F <300, not intubated	S/F <200 or intubated	S/F <150 and intubated	S/F <100 and intubated
Cardiovascular	No support	1 inotrope	≥2 inotropes	≥2 inotropes+systemic steroids	Refractory shock
Hematologic	Platelets ≥150 ×10 ⁹ /L	100-149 ×10 ⁹ /L	50-99 ×10 ⁹ /L	<50 ×10 ⁹ /L	Active bleeding + <50 ×10 ⁹ /L