Serial Evaluation of Sequential Organ Failure Assessment Score (SOFA) as a Predictor of Outcome in Children Admitted in Pediatric Intensive Care Unit (PICU) at Tertiary Care Hospital

Amoolya Lois[1], Sushma Save[2]

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Abstract

Background: Sequential organ failure assessment score (SOFA) is a score to quantify organ system dysfunction. This study was done to evaluate SOFA as a predictor of outcomes in children in pediatric intensive care unit (PICU).

Objective: (A) To determine whether initial SOFA, Delta SOFA, and SOFA score at 72 hours are better predictors of outcome in terms of sensitivity and specificity. (B) To compare the initial SOFA, Delta SOFA, and SOFA score at 72 hours.

Materials and methods: A prospective observational study was conducted on 160 patients aged from 29 days to 12 years admitted in PICU of a Tertiary Care Hospital in a metropolitan city in India for a period of 1 year. Then, the initial SOFA score, 72-hour SOFA, and Delta SOFA (T0 SOFA - T72 SOFA) were calculated and patients were followed up till discharge from PICU or deceased.

Results: The best threshold to differentiate between discharged and deceased corresponds to as initial SOFA of 7.50 with a sensitivity of 64.71%, and specificity of 89.51%. The similar threshold for 72 hours SOFA is 10.50 which correspond to a sensitivity of 76.47% and specificity of 96.50%. The study showed strong evidence (p-value < 0.05) that, patients whose Delta SOFA values increased from the previous value (–1.5), had a greater chance to succumb to illness. Delta SOFA had the best sensitivity (82.35%) and 72-hour SOFA had the best specificity (96.50%) in predicting the outcome of PICU patients.

Conclusion: This study emphasizes the use of SOFA score as a prognostic indicator in critically ill children, as variables measured are easily available.

Keywords: Morbidity, Mortality, Multiorgan dysfunction syndrome, Pediatric intensive care unit, Sequential organ failure Assessment score.

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Highlights

- Sequential organ failure assessment score (SOFA) is a good predictor of outcome in children admitted to pediatric intensive care unit (PICU) since there is a strong correlation between a rise in the score and mortality in all stages of admission.
- Early prediction of outcome using SOFA score is useful to aid suitable modification of management strategies among critically ill children admitted to PICU.
- Delta SOFA has the best sensitivity and 72-hour SOFA has the best specificity in predicting the outcome of PICU patients.

Introduction

Accurate evaluation of disease severity and the likelihood of mortality plays a crucial role in determining the prognosis of patients within the intensive care unit (ICU).[1] In the PICU, children often encounter multiple organ dysfunction syndromes (MODS). The mortality rate in the ICU is associated with two factors: (A) The number of failing organ systems, and (B) The extent of dysfunction within each individual organ system.[2] Among PICU admissions, MODS prevails in approximately 25% of cases, with mortality rates reaching up to 50%.[3] Notably, nearly all deaths in the PICU, ranging from 97 to 100%, are attributed to MODS.[3] To predict outcomes in critically ill children, the SOFA and pediatric logistic organ dysfunction (PELOD) scoring systems, which are based on MODS, are employed.[4,5] These scoring systems facilitate the assessment of illness severity, appropriate monitoring, proper management, and family counseling. During a consensus meeting held by the European Society of Intensive Care Medicine in 1994, the SOFA system made its initial debut, and subsequently underwent revisions in 1996 to enhance its functionality and effectiveness. It assesses multiple organ dysfunctions through a six-organ dysfunction/failure score, assigning a grade from 0 (normal) to 4 (most abnormal) for each organ. Consequently, it provides a daily

[1]Department of Pediatric Intensive Care Unit, Manipal Hospital, Bengaluru, Karnataka, India

[2]Department of Pediatrics, Topiwala National Medical College and Bai Yamunabai Laxman Nair Charitable Hospital, Mumbai, Maharashtra, India

Corresponding Author: Sushma Save, Department of Pediatrics, Topiwala National Medical College and Bai Yamunabai Laxman Nair Charitable Hospital, Mumbai, Maharashtra, India, Phone: +91 9819096819, e-mail: sushmasave73@gmail.com

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Table 1: Components of SOFA score

SOFA score	*0*	*1*	*2*	*3*	*4*
Respiration					
PaO_2/FiO_2	>400	<400	<300	<20	<100
SaO_2/FiO_2		221–301	142–220	67–141	<67
Coagulation					
Platelets ($10^3/mm^3$)	>150	<150	<100	<50	<20
Liver					
Bilirubin (mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
Cardiovascular					
Hypotension	No hypotension	MAP < 70	Dopamine </= 5 or dobutamine (any)	Dopamine >5 or norepinephrine</=0. 1	Dopamine >15 or norepinephrine>0.1
CNS					
Glasgow coma scale	15	13–14	10–12	6–9	<6
Renal					
Creatinine (mg/dL) or urine output (mL/d)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9 or <500	>5.0 or <200

total score ranging from 0 to 24 points, as illustrated in Table 1 above.[6]

The variables included in the SOFA score are readily available and routinely measured in the ICU setting.[7] Several studies have been conducted to assess the predictive value of the SOFA score and other sepsis prediction scores in evaluating the outcomes of patients admitted to the ICU. However, most of these studies have primarily focused on the adult population, neglecting the evaluation of these scores in critically ill children. Despite the existing research, uncertainties persist regarding the utility of the SOFA score as a predictor of mortality among children admitted to the PICU. Therefore, a study titled "Serial Evaluation of Sequential Organ Failure Assessment Score (Sofa) as a Predictor of Outcome in Children Admitted to a Tertiary Care Hospital's Pediatric Intensive Care Unit" was undertaken. The objective of this study was to determine whether the initial SOFA score, Delta SOFA score, and SOFA score at 72 hours are superior predictors of outcome in terms of sensitivity and specificity, and to compare these scores among themselves.

Materials and Methods

This prospective observational study was conducted over a 12-month period, spanning from September 2019 to September 2020, in the PICU of a Tertiary Care Institution. Ethical approval was obtained from the institutional ethics committee before the commencement of the study. All patients between the ages of 29 days and 12 years, who met the inclusion criteria, were enrolled in the study. Excluded from the study were children with PICU stays shorter than 72 hours and those previously admitted to any other hospital's PICU and subsequently referred to the study institution. Upon admission, the patient's clinical details, including age, sex, provisional clinical diagnosis, duration of PICU stay, organ system primarily involved, SOFA score at admission, SOFA score at 72 hours, and outcome (discharge or death), were recorded using a predefined proforma.

The values were entered into a calculator to calculate the SOFA score. Following recruitment, patients were followed up until their discharge from the PICU or until death. The initial SOFA score was calculated within 24 hours of admission, and a subsequent calculation was performed after 72 hours. The difference between the SOFA score at 72 hours (T0 SOFA - T72 SOFA) was recorded as the Delta SOFA score.[8] For each organ system, the highest score among all variables was considered the score for that specific organ system. The sum of these six scores for each organ system provided the overall SOFA score, ranging from 0 to 24, which was used to predict the risk of mortality in the PICU. The SOFA score was calculated by entering the data obtained at admission and 72 hours after admission into online software available at clincalc.com/icumortality/SOFA.aspx, which did not require authentication from the software developer. The results were documented in a case record form. The study adhered to the ICMR guidelines for Biomedical Research during the COVID-19 pandemic in 2020.

A total of 160 children were included in the study to assess the involvement of specific organ systems. Initial SOFA, 72-hour SOFA, Delta SOFA scores, and outcomes were calculated and tabulated, followed by a precise analysis of the results. The data were processed and analyzed using the IBM statistical packages for social sciences (SPSS) software version 22. The Shapiro-Wilk test was employed to assess the normality of the data. Continuous measurements were reported as frequency, mean, and standard deviation, while categorical measurements were presented as numbers and percentages. The association between various systems and the outcome (deceased or discharged) was analyzed using the Chi-square test. The receiver operating characteristic (ROC) curve was utilized to determine the threshold, sensitivity, and specificity of the clinical measurements. The Mann-Whitney *U* test was applied to assess the differences in clinical measurements between deceased and discharged patients.

Results

During the length of the study 160 children have been admitted within the PICU and included in the study. About 36.9% of the study participants were more than 5 years. Admissions in the age-group of 29 days-1 year was 57/160; (35.6%) and 1–5 years was 44/160 (27.5%). Out of 160 patients, males comprised 63.70% (102/160)

Table 2: Association of effect on each system and outcome

Organ system	Systems involved and percentage		Outcome: Deceased (n = 17)	Outcome: Discharged (n = 143)	Total	Chi-square	p
Respiratory system	No	*N*	4	41	45	0.199	0.45
		%	23.5	28.7	27.5		
	Yes	*N*	13	102	115		
		%	76.5	71.3	72.5		
Coagulation	No	*N*	10	119	129	5.788	0.02*
		%	58.8	83.2	80.6		
	Yes	*N*	7	24	31		
		%	41.2	16.8	19.4		
Hepatic system - Liver	No	*N*	9	119	128	8.704	0.00*
		%	52.9	83.2	80.0		
	Yes	*N*	8	24	32		
		%	47.1	16.8	20.0		
Cardiovascular system	No	*N*	11	112	123	1.584	0.17
		%	64.7	78.3	76.9		
	Yes	*N*	6	31	37		
		%	35.3	21.7	23.1		
Central nervous system	No	*N*	6	87	93	4.073	0.04*
		%	35.3	60.8	58.1		
	Yes	*N*	11	56	67		
		%	64.7	39.2	41.9		
Renal system	No	*N*	12	117	129	1.227	0.21
		%	70.6	81.8	80.6		
	Yes	*N*	5	26	31		
		%	29.4	18.2	19.4		

Chi-square test; *Statistically significant; $p < 0.05$; NS, not significant

outnumbering the female population that comprised 36.30% (58/160) of the study population.

The association of each system with the effect on the outcome of mortality is shown in above Table 2.

Table 2 illustrates the association of the effect involvement of different systems and outcomes. Chi-square test was applied to the data and the *p* value was calculated. A *p*-value of < 0.05 was statistically significant. There was a statistically significant association found between the outcome and effect on coagulation, hepatic system, and central nervous system involvement which means to imply that if these systems were affected, more chance of getting deceased, and when not involved more chance of getting discharged. The association between the outcome and effect on the respiratory, cardiovascular, and renal systems was not statistically significant.

The following Table 3, Figures 1 and 2 show the result of a receiver operating characteristic or ROC curve analysis for initial SOFA, 72 hours SOFA, and Delta SOFA between the study participants who were discharged and deceased. The y and x axes are chosen as vertical for sensitivity (true-positive rate), and horizontal 1-specificity (false-positive rate) respectively (Figs 1 and 2).

Table 3: Area under the curve for SOFA scores

Test result variable	Area	Std. error	p-value	Asymptotic 95% confidence interval: Lower bound	Asymptotic 95% confidence interval: Upper bound
Initial SOFA	0.852	0.05	0.00*	0.752	0.952
72-hour SOFA	0.932	0.04	0.00*	0.854	1.000
Delta SOFA	0.080	0.03	0.00*	0.011	0.148

*Statistically significant

The best threshold to differentiate between discharged and deceased corresponds to initial SOFA of 7.50. This initial SOFA threshold value corresponds to a sensitivity of 64.71%, and a specificity of 89.51%. The best threshold to differentiate between discharged and deceased corresponds to 72 hours SOFA of 10.50, which has a sensitivity of 76.47%, and specificity of 96.50%. The best threshold to differentiate between discharged and deceased corresponds to Delta SOFA of –1.50. The Delta SOFA threshold value

of –1.50 corresponds to a sensitivity of 82.35%, and specificity of 93.01% and differentiates between diseased and discharged.

Figure 3 illustrates the clinical characteristics of the study population. Mann–Whitney *U* test was applied that depicted a significant difference between initial SOFA, 72 hours SOFA, and Delta SOFA of deceased and discharged.

Table 4 illustrates the association between the number of systems and outcome. Chi-square test was applied and a *p* value was obtained, showing a statistically significant association found between the outcome and the number of systems.

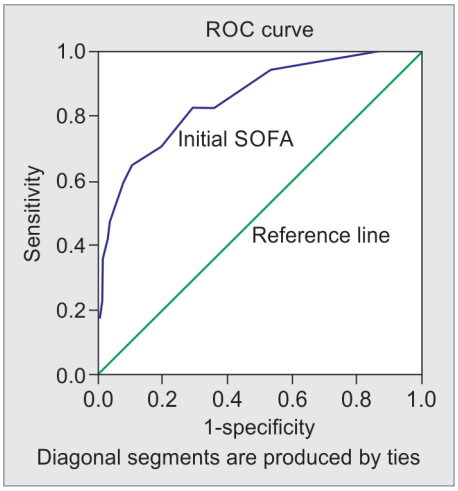

Fig. 1: ROC curve analysis for initial SOFA

Discussion

The SOFA scoring system, initially described by Vincent et al.,[9] provides a quantitative and objective assessment of organ dysfunction in both individual patients and groups of patients. It has undergone extensive validation and has been widely used for prognostication in large cohorts of critically ill patients. In the current era of rising healthcare costs, the ability to assess a patient's prognosis during the course of treatment becomes vital. Therefore, scoring systems have been employed to predict outcomes, with the SOFA scoring system being widely utilized in critical situations due to its simplicity and ease of application. It has proven to be a useful bedside tool in many ICUs.

Among the 160 study participants, the majority were children over 5 years old, constituting 36.9% of the cases, followed by infants aged 29 days to 1 year (35.6%). Male patients accounted for 63.7% (102/160), while females accounted for 36.3% (58/160). This gender distribution of cases aligns with the study population in a previous study conducted by Mishra R et al.[10] Respiratory system involvement was the most common (72.5%), followed by the central nervous system (41.9%). This is consistent with the findings of Khilnani P et al.,[5] where the majority of admissions were also due to respiratory system involvement, including acute respiratory distress syndrome (ARDS) and pneumonia.

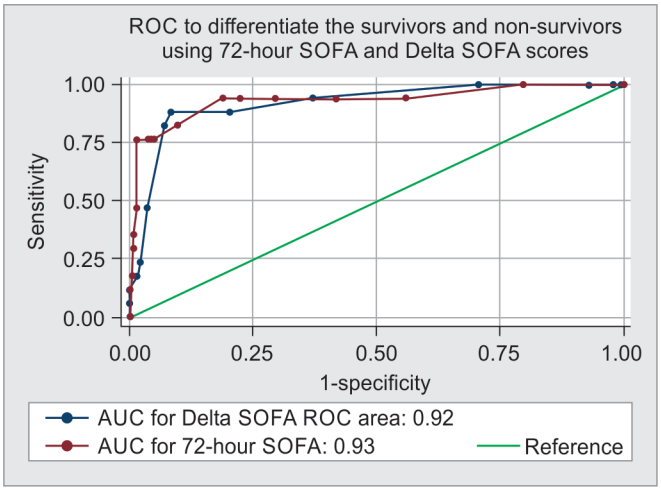

Fig. 2: ROC curve analysis for 72-hour SOFA and Delta SOFA

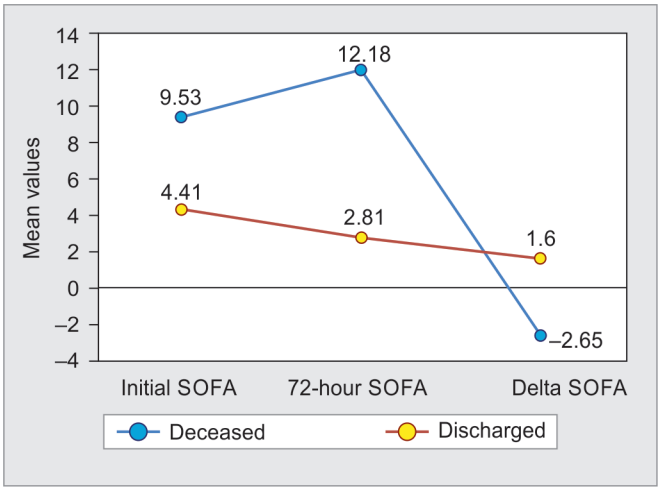

Fig. 3: Clinical characteristics of the study population

Table 4: Association of number of systems affected and outcome

		Outcome				
Number of systems involved		*Deceased (n = 17)*	*Discharged (n = 143)*	*Total*	*Chi-square*	*p*
One	*N*	0	55	55	20.574	0.00*
	%	0.0	38.5	34.4		
Two–four	*N*	14	86	100		
	%	82.4	60.1	62.5		
Five and six	*N*	3	2	5		
	%	17.6	1.4	3.1		

Chi-square test; * Statistically significant; $p < 0.05$; NS, not significant

The coagulation system was involved in 19.4% of cases (31/160), followed by the renal system (19.4%), hepatic system (20%), and cardiovascular system (23.1%). Similar results were observed in a study by Tan GH et al.[1] Studies have shown that cardiovascular, neurological, respiratory, renal, hematological, and hepatic dysfunctions, as assessed by the SOFA scores, are independent risk factors for mortality. In our study, we observed similar results for coagulation, hepatic, and neurological variables. However, renal, respiratory, and cardiovascular parameters did not differ significantly between deceased and discharged patients, possibly due to the predominant respiratory and cardiovascular system involvement in the study population, which included a large number of COVID-19-positive cases.

There was a significant increase in mortality when the initial SOFA score was 7.50, and the 72-hour SOFA score exceeded 10.5. The mortality curve demonstrated a steep rise at these thresholds. Admission SOFA (initial SOFA), 72-hour SOFA, and Delta SOFA were all statistically significant ($p < 0.001$), as shown in Table 3. There is strong evidence that an increase in Delta SOFA values from the previous value (–1.5) indicates a greater likelihood of mortality.

The initial SOFA threshold value of 7.5 corresponded to a sensitivity of 64.71% and specificity of 89.51%. The best threshold for differentiating between discharged and deceased patients was a 72-hour SOFA score of 10.50, which corresponded to a sensitivity of 76.47% and specificity of 96.50%. This is in line with the study by Sayed AS et al.,[11] which demonstrated that the SOFA score at 72 hours is a statistically strong predictor of mortality in the PICU. The optimal threshold for differentiating between discharged and deceased patients based on Delta SOFA was –1.50, which corresponded to a sensitivity of 82.35% and specificity of 93.01%.

In a research study by Priya Gogia et al.,[12] the SOFA score was calculated to evaluate the severity of sepsis and multiorgan failure at presentation and after 48 hours. This was compared with a study conducted in adult patients. The group of patients with an initial SOFA score <7 had an 86.49% survival rate, while those with SOFA >7 had a 65.08% survival rate. Among the subjects with a 48-hour SOFA score <7, 98.59% survived, compared to 1.41% who did not. In the inpatient group with SOFA scores of 8–15, the non-survival rate was 89.66%. The adjusted mortality was significantly higher with SOFA >8 compared to SOFA <8 on Day 1, and it doubled on Day 3, as shown in a study by Lalitha et al.[13] The optimal SOFA cutoff for discriminating non-survivors from survivors was seven points in an Egyptian study by El-Mashada GM et al.,[14] compared to the cut-off of 8 points reported in a different pediatric study by TJ Matics et al.[15]

In our study, the mean initial SOFA score (T0) was 9.53 ± 4.26 in non-survivors and 4.41 ± 2.52 in survivors. T0 was significantly higher in non-survivors ($p = 0.00$). This is similar to the initial SOFA value obtained in the study by Nair R et al., conducted in a Medical Intensive Care Unit in South India, which showed a significant increase in mortality in patients with an initial SOFA score of 11 or higher.[16] The mean SOFA score at 72 hours (T72) was 12.18 ± 4.8 in non-survivors and 2.81 ± 2.98 in survivors. About T72 was significantly higher in non-survivors ($p < 0.001$). The mean Delta SOFA score was –2.65 ± 2.34 in non-survivors and 1.6 ± 1.79 in survivors, with the mean Delta SOFA score being significantly higher in non-survivors ($p < 0.001$). These findings are similar to the study by Gogia et al.[17] for the initial and 72-hour SOFA scores, which showed similar results. The SOFA score at 72 hours demonstrated the highest positive and negative predictive values, comparable to the PELOD score.[17]

Taha El-keiy M et al.[18] demonstrated significant positive correlations between SOFA scores on Days 1 and 3 and PICU mortalities ($p < 0.0001$). The SOFA score exhibited the highest discrimination ability (area under the ROC curve: 0.765) compared to other scores used in the study, which aligns with our findings.[18]

In conclusion, sequential assessment of organ dysfunction in sepsis patients admitted to the ICU proves to be a good indicator of prognosis. A study by Balasubramanian et al. on critical illness scoring systems in India concluded that the SOFA score correlated with mortality and could be used as a predictor of outcome in patients with organ dysfunction, in comparison to the APACHE II and quick SOFA scores.[19]

The initial SOFA score was higher among deceased patients and lower among discharged patients, which was statistically significant (9.53 vs 4.41, $p = 0.00$). However, the most significant difference was observed at 72 hours. The 72-hour SOFA score was substantially higher among deceased patients compared to discharged patients, which was highly statistically significant (12.18 vs 2.81, $p = 0.00$). This is consistent with many previous studies. Gogia P et al.,[12] in their study of 100 critically ill children admitted to the ICU, demonstrated that the SOFA score at 72 hours is a superior predictor of mortality compared to the initial and Delta SOFA scores. Ferreira FL et al.[6] found that increasing SOFA values predicted a higher risk of mortality while decreasing SOFA values were associated with lower mortality rates. Although Ferreira FL et al.[6] conducted serial evaluations of the SOFA score at 48, 72, and 96 hours after admission, they concluded that Delta SOFA and the highest SOFA score held the greatest significance. Similarly, Taha El-keiy M et al.[18] observed the correlation between patient outcomes and SOFA scores on days 1, 3, and 7 after admission. All scores exhibited positive correlations with PICU mortalities. Thus, the SOFA score calculated up to 72 hours after admission can accurately predict the outcome of PICU patients, as consistent outcomes were observed even with later evaluations of the SOFA score in other studies. Therefore, we emphasize the use of the SOFA score as a prognostic indicator in critically ill children, as the variables measured are readily available.

There are certain limitations to our study. We calculated the SOFA score at admission to the PICU and at 72 hours, but we did not calculate it every 24 hours. Thus, we may have missed earlier predictions of mortality 48 hours after admission to the PICU. Children who survived less than 72 hours in the PICU were excluded from our study, and therefore, the data from children who died within 72 hours of admission to the PICU could not be analyzed.

Our study was conducted in a Tertiary Care Center that serves as a referral center for many peripheral hospitals. As a result, our PICU receives a high number of critically ill children from across the city. The sample size included in our study was smaller than expected due to the COVID-19 pandemic. Therefore, the results may not be generalizable to the overall population or other peripheral center hospitals. Randomized controlled trials are needed to apply these findings to the general population.

Conclusion

The SOFA proves to be a valuable prognostic indicator for evaluating the outcome of children admitted to the PICU. This is due to the significant correlation observed between the initial, 72-hour, and Delta SOFA scores and mortality rates across all stages of admission. Additionally, a statistically significant association was identified between the outcome and the number of affected systems.

Notably, Delta SOFA demonstrates the highest sensitivity at 82.35%, while the 72-hour SOFA exhibits the best specificity at 96.50% in predicting the outcome of PICU patients. Utilizing the SOFA score for early outcome prediction proves beneficial as it enables appropriate modifications to management strategies for critically ill children in the PICU, potentially reducing mortality rates.

Orcid

Amoolya Lois https://orcid.org/0000-0002-7343-3363
Sushma Save https://orcid.org/0000-0002-6498-7962

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