Original Research Article

Assessment of pSOFA-L score in predicting the clinical outcome of critically ill children

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ABSTRACT

Background: Recently Pediatric Sequential Organ Failure Assessment (pSOFA) score was adapted and validated in critically ill children to predict the clinical outcome. This study was aimed to evaluate the lactate level association with the outcome and thereby formulating pSOFA-L score to predict the clinical outcome better in critically ill children.

Methods: This hospital based prospective, observational, analytical study was conducted in the Department of Paediatrics, A. J Hospital, Mangalore, Karnataka. Requirement of oxygen, inotrope support and other parameters were studied and compared the score with clinical outcome. A total of 75 cases were studied.

Results: In this study total of 51 children had high serum lactate levels (68%). Out of 28 expired children 23 children had higher serum lactate levels that accounts for about 82.14% which is statistically significant (p<0.001). ROC curve of pSOFA-L score in predicting the mortality yielded AUC: 0.92 and cut off value: 10.5 which is statistically significant (p<0.001). In the present study mortality rate was 26.09% in children whose pSOFA-L score was less than 9 and mortality rate of 38.89% and 50.00% in children whose pSOFA-L score was 9 to 11 and more than 11 respectively.

Conclusions: In this study increase in pSOFA-L score is associated with high mortality and poor outcome. The findings of the present study validate and emphasize that, pSOFA-L score helps in accurate prediction of mortality of critically ill children.

Keywords: Multiorgan dysfunction syndrome, Pediatric sequential organ failure assessment, PELOD score, pSOFA-L score, Quick SOFA score

INTRODUCTION

The evaluation and prognostication of all cases admitted to the Pediatric Intensive Care Unit (PICU) is important for various reasons. Scoring systems aim at providing an objective measure of the severity and hence the prognosis of patients. Almost all patients in Intensive Care Units (ICUs) have some organ dysfunction. Adult and pediatric studies have shown that mortality increases with the number of organs involved. Thus, Multiple-Organ Dysfunction Syndrome (MODS) has been viewed as the inexorable pathway to death. Clinical opinions are more of subjective whereas predictive scoring systems appear to be objective method of assessment. Many Predictors of Mortality Scores exist such as Sequential Organ Failure Assessment (SOFA), Pediatric Logistic Organ Dysfunction (PELOD) and Pediatric Risk of Mortality-III (PRISM-III).

The SOFA score was selected as the scoring system to quantify organ dysfunction in the Third International Consensus Definitions for Sepsis and Septic Shock

(Sepsis-3).[1] TheSepsis-3 Task Force validated the SOFA score in patients with suspected infection and found the SOFA system to be either comparable or superior to other scoring systems at discriminating in-hospital mortality.

One of the major limitations of the SOFA score is that it was developed for adult patients and contains measures that vary significantly with age, which makes it unsuitable for children. The Sepsis-3 Task Force recognized this problem and identified it as an area for further development. Prior studies have attempted to adapt the SOFA score to pediatric patients, mostly focusing on the cardiovascular subscore. However, none have taken into account the age-related variability of the renal sub score criteria despite the increasingly recognized detrimental effect of kidney dysfunction in younger patients.[2-4] In addition, the respiratory sub score criteria-based on the ratio of PaO2 to the Fraction of Inspired Oxygen (FiO2) have not been modified in previous adaptations of the SOFA score even though the decreased use of arterial blood gases in children is a known limitation. Fortunately, the cardiovascular and renal components of the SOFA score were evaluated and adapted to pediatric patients by the PELOD-2 score investigators, and the ratio of peripheral oxygen saturation (SpO2) to FiO2 has been validated as an alternative to the PaO2:FiO2 ratio in children.[1]

In this study, authors sought to adapt and validate a SOFA score for critically ill pediatric patients (pSOFA) using age-adjusted criteria. Multiple organ failure, which can occur in many severe conditions, including trauma, sepsis, burns and severe acute pancreatitis, is an important cause of morbidity and mortality. Blood lactate levels have been associated with the occurrence of organ failure. However, the relationship between lactate levels and the well-validated Sequential Organ Failure Assessment (SOFA) score[5-7] has not yet been studied in children. Although lactate as a biomarker and SOFA as an organ dysfunction scale have different functions, an association between the two might have clinical implications. Blood lactate measurement may act as a real-time marker for the severity of organ failure.[3,4] In view of this authors decided to evaluate the paediatric version of SOFA-LACTATE [pSOFA-L] score in predicting the mortality of critically ill children in set up.

METHODS

All critically sick children admitting to pediatric intensive care unit of A. J. Institute of Medical Sciences, Mangalore during the study period of one and half year (November 2017-April 2019).

Study design was prospective, observational, analytical study. Sample size was 75. Paediatric intensive care unit of A. J. Institute of Medical Science, Mangalore.

All patients fulfilling the inclusion criteria will be included as study subjects after obtaining the informed consent. pSOFA-L score will be used to predict the outcome of the patients. This includes 7 variables namely Glasgow coma scale, blood pressure, PaO2, FiO2, SPO2, platelet count, bilirubin levels, serum creatinine and lactate levels. For each variable, the most abnormal value of that day is used in calculating the pSOFA-L score. Again pSOFA-L variables are measured at 72 hours. Other factors such as the age and sex distribution of the patients, total counts are also documented (Table 1).

Inclusion criteria

- Children between the age of 1 month to 18 years admitted to PICU.
- PICU stay more than 48 hours.
- Presence of paediatric MODS [>1 organ system failure] irrespective of the cause.

Exclusion criteria

- Admission for scheduled procedures normally cared for in a PICU [e.g. Haemodialysis, IVIG administration].
- PICU stay less than 48 hours.

Ethical clearance

The ethical clearance was obtained from Ethical and research committee, A J Institute of medical sciences, Mangalore, Karnataka.

Blood samples of 5ml is collected which includes 0.5 ml of arterial blood will be collected at the time of admission, as well as at 72 hours after admission and relevant investigations were measured to determine the variables for pSOFA-L score.

Data analysis

The data obtained was coded and entered into Microsoft excel spreadsheet. Categorical data was expressed as rates, ratios and percentages. Continuous data was expressed as mean±standard deviation. The comparison of categorical data was done by chi-square test and/or Fishers exact test and independent sample 't' test was used to compare mean values. The discrimination of pSOFA and pSOFA-L score in the diagnosis of sepsis and survival was done using was made by area under the curve (AUC) using the receiver operating characteristic curve (ROC curve). If the AUC (Area under curve) is 0.9 or more it considered excellent discrimination, 0.80-0.89 it considered good and 0.70-0.79 as fair. The accuracy of pSOFA and pSOFA-L score in discriminating the survival was expressed in terms of sensitivity, specificity, Positive Predictive Value (PPV), negative predictive value (NPV). At 95% confidence interval, a probability (p) value of ≤0.050 was considered as statistically significant. At 95% Confidence Interval (CI), a probability value of less than or equal to 0.05 was considered as statistically significant.

Table 1: Pediatric sequential organ failure assessment score.[1]

Variables		Score				
		0	1	2	3	4
Respiratory	PaO$_2$:FiO$_2$ or	≥400	300-399	200-299	100-199 with respiratory support	<100 with respiratory support
	SpO2:FiO$_2$	≥292	100-149	50-99	20-49	<20
Coagulation	Platelet count (x10^3/μL)	≥150	100-149	50-99	20-49	<20
Hepatic	Total bilirubin (mg/dL)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular - MAP by age group or vasoactive infusion, mmHg or μg/kg/mind	<1 mo	≥46	<46	Dopamine hydrochloride ≤5 ordobutamine hydrochloride (any)	Dopamine hydrochloride >5or epinephrine ≤0.1or norepinephrine bitartrate ≤0.1	Dopamine hydrochloride >15or epinephrine >0.1or norepinephrine bitartrate >0.1
	1-11 mo	≥55	<55			
	12-23 mo	≥60	<60			
	24-59 mo	≥62	<62			
	60-143 mo	≥65	<65			
	144-216 mo	≥67	<67			
	>216 mo	≥70	<70			
Neurologic	Glassgow coms score	15	13-14	10-12	6-9	<6
Renal - Creatinine by age group	<1 mo	<0.8	0.8-0.9	1.0-1.1	1.2-1.5	≥1.6
	1-11 mo	<0.3	0.3-04	0.5-0.7	0.8-1.1	≥1.2
	12-23 mo	<0.4	0.4-0.5	0.6-1.0	1.1-1.4	≥1.5
	24-59 mo	<0.6	0.6-0.8	0.9-1.5	1.6-2.2	≥2.3
	60-143 mo	<0.7	0.7-1.0	1.1-1.7	1.8-2.5	≥2.6
	144-216 mo	<1.0	1.0-1.6	1.7-2.8	2.9-4.1	≥4.2
	>216 mo	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	≥5
Lactate level		<2 mmol/	>2 mmol/lt			

RESULTS

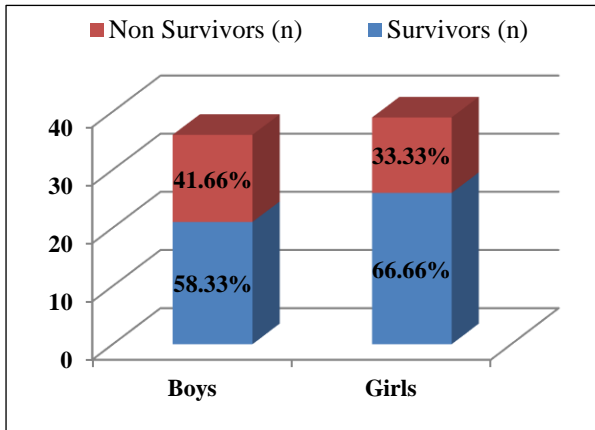### Clinical profile of the study populations is as shown in the table

The clinical profile of the study population is as shown in Table 2. Age of the study population ranged between 0.01 to 16 years. The mean age was 4.07(+5.29) years and median was 1.32 years.

The mean pSOFA-L score was 9.38 (+3.07) with a median score of 10.00. Score ranged from 2.00 to 18.00 in the study population.
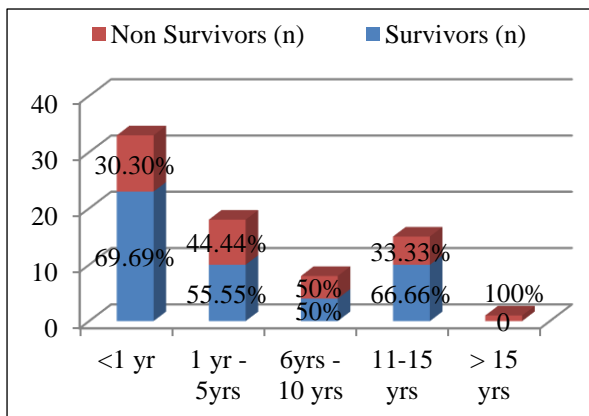
Table 2: Clinical profile of study population.

Parameters	Mean (n=75)		Median	Range	
	Mean	SD		Minimum	Maximum
Age (Years)	4.07	5.29	1.32	0.08	16
Total count (x1000/cumm)	13.42	5.68	11.24	3.70	34.2
Platelet count (x lakhs/cumm)	2.51	1.53	2.14	0.16	6.35
Total Bilirubin (mg/dl)	1.11	1.20	0.82	0.20	7.90
Inotrope dose (mcg/kg/min)					
Dopamine	8.13	4.98	10	0	15
Dobutamine	2.2	4.37	10	0	15
Mean Aretrial Pressure (mmhg)	49.60	13.54	49.1	27.60	88.00
Serum Creatinine (mg/dl)	0.81	0.54	0.63	0.30	4.20
FiO2	0.53	0.25	0.55	0.21	1.00
GCS	8.22	3.18	9.00	3.00	15.00
pSOFA - L score	9.38	3.07	10.00	2.00	17.00
Length of hospital stay (days)	10.84	8.45	8.00	3.00	43.00

Figure 1: Comparison of children according to the sex and its association with outcome.

It was observed that out of 36 (48%) male children, 21 (58.33%) survived and 15 (41.66%) expired. Among 39 (52%) girls, 26 (66.66%) survived and 13 (33.33%) expired. This was statistically not significant (p value: 0.41) so in this study there is no association between mortality and gender (Figure 1).

Figure 2: Comparison of age and outcome in the study population.

It was observed that majority of children included in the study population were less than 1 year (44%). Mortality rate was highest in children aged >15 years (100%) and survival rate was higher in children <1 year (69.69%). However, no statistically significant correlation was seen between mortality and the age of the patient (p value: 0.513), so all the children are vulnerable (Figure 2).

Estimation of pSOFA-L score and its association with mortality is as shown in the following table

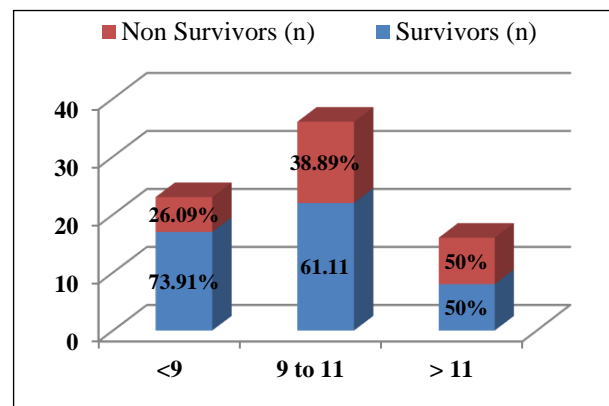Method: Fisher's Exact Test for Count Data with simulated p-value (based on 1e+06 replicates).

pSOFA-L score <9 is associated with mortality rate of 26.09% in comparison to 50% mortality with a pSOFA-L score of >11 and 38.39% mortality with a pSOFA-L

score of 9 -11 which was statistically significant (p 0.04). Score reveals that higher the score higher the chances of mortality (Table 3).

Table 3: Comparison of pSOFA - L score with mortality.

pSOFA-L Score	Outcome				Total	
	Survivors		Non-Survivors			
	No.	%	No.	%	No.	%
<9	17	73.91	6	26.09	23	30.66
9-11	22	61.11	14	38.89	36	48.00
>11	8	50.00	8	50.00	16	21.34
Total	47	62.66	28	37.33	75	100.00

p value: 0.04

Figure 3: Comparison of pSOFA-L score and outcome in the study population.

It was observed in this study that higher the pSOFA- L score worse was the prognosis. Mortality was 26.09% with score <9, 38.89% with score between 9-12 and 50% with score >11. p value was 0.04 which was statistically significant and patients with higher pSOFA-L score needs immediate intervention (Figure 3).

Comparison of change in lactate level and its association with outcome is explained in the following table

Table 4: Comparison of change in lactate levels and outcome.

	Change in lactate levels		p value
	Mean	Standard deviation	
Survivors	- 0.76	1.3	
Non-Survivors	0.81	1.76	<0.001

Method: Kruskal-Wallis rank sum test.

In this study it was observed that a decrease in lactate level is associated with a better outcome and increase in lactate levels is associated with higher risk of mortality.

Out of 28 expired children 23 had high lactate levels, which accounts for about 82.14% which was statistically significant (p<0.001) (Table 4).
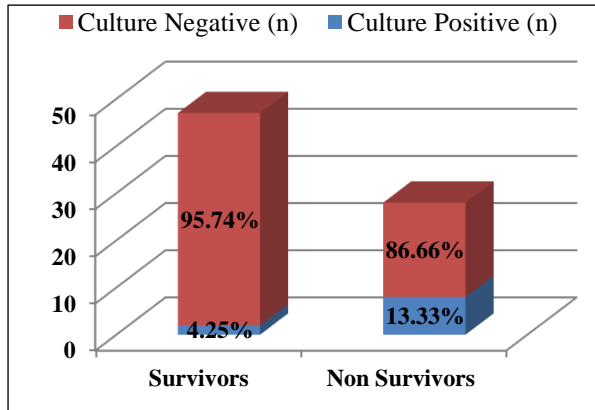

Figure 4: Comparison of blood culture and outcome.

In this study it was observed that mortality rate was 28.57% in culture positive patients and 4.25% in culture negative patients. p value was 0.004 which was statistically significant. This represents culture positive sepsis patients are more vulnerable and high mortality was noted in patients with septic shock (Figure 4).
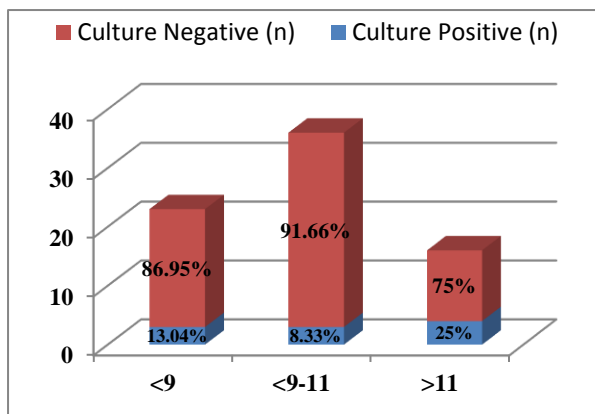

Figure 5: Comparison of blood culture and pSOFA-L score.

A pSOFA-L score of >11 was associated with 25% culture positive sepsis in this study. Whereas a score <9 was associated with only 13.04% culture positive sepsis which was not statistically significant (p=0.09). In this study culture positive sepsis patients are more vulnerable for MODS and need immediate intervention. High mortality was noted in culture positive sepsis patients (Figure 5). AUC: 0.92, Cut off value: 9.5. in the present study ROC curve yielded AUC of 0.92 and cut off value of 9.5 in predicting mortality for pSOFA score with sensitivity of 95.3 and specificity of 76.32 which is statistically significant (p<0.001) (Figure 6).

AUC =0.925, Cut off value = 10.5 for pSOFA-L score. In the present study, ROC curve yielded an Area under curve

of 0.925. Cut off value was 10.5 in predicting mortality for pSOFA-L score with sensitivity of 96.428 and specificity of 80.851 which is statistically significant (p<0.001). This study shows that pSOFA-L score is a better objective assessment in predicting the mortality (Figure 7).
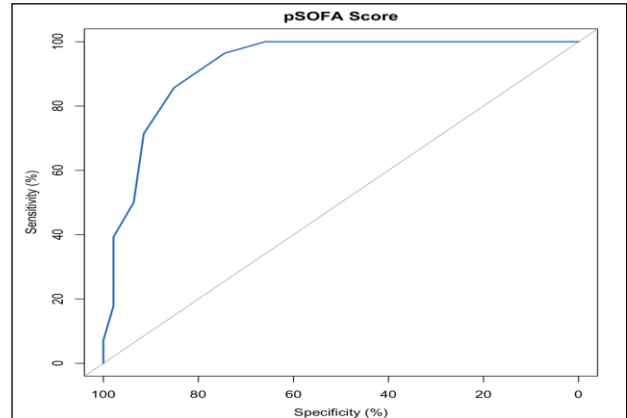

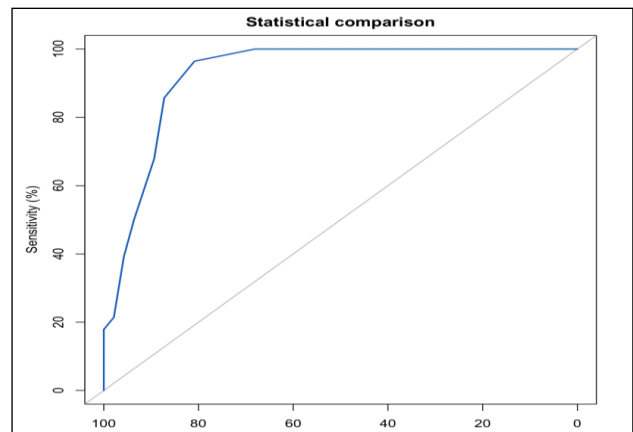**Figure 6: ROC curve of pSOFA score in predicting the mortality.**

Figure 7: ROC Curve of pSOFA-L score in predicting mortality.

DISCUSSION

It is important to predict the outcome of the critically ill children admitted to the PICU with the help of advances in critical care technology so that timely intervention can be done. Various methods are available for mortality prediction, including the Pediatric Risk of Mortality (PRISM, PRISM III)8, Pediatric Index of Mortality (PIM and PIM2) and the Paediatric logistic organ dysfunction score which are validated in different settings.[8,10-13] In critically sick children organ dysfunction assessment helps in predicting outcome, timing of resuscitation and also to improve quality care. MODS is characterized by physiological dysfunction of two or more organ systems after an acute insult to systemic homeostasis. Numerous studies have documented that intensive care mortality rate correlates with the number of failing organ system. Recently Mattics TJ and Sanchez-Pinto LN1 adapted and

validated pSOFA score with age-adjusted variables in critically ill children. Using the pSOFA score, the Sepsis-3 definitions were assessed in children with confirmed or suspected infection. The present study was planned to evaluate the feasibility of addition of lactate level parameter to paediatric version of SOFA score so as to formulate the pSOA-LACTATE [pSOFA-L] score and to adapt and validate with reference to pSOFA score in predicting the mortality of critically ill children in pediatric intensive care unit, which is first of its kind.

In the present study, though there was wide variation in the clinical presentation and diagnosis. Nearly two third of the patients improved (62.7%) and more than one third (37.3%) expired. The mortality rate noted in the present study was high compared to the study by Mattics TJ and Sanchez-Pinto LN1 (2017) who reported in hospital mortality rate as 2.6%.[14] Recently another study from Hyderabad, India reported mortality rate of 2.1% giving an ICU survival rate of 97.9%. A recent study by Rashma RP et al, from Kochi, Kerala, India to study the Mortality Rate and Mortality profile of children admitted to the PICU of a tertiary care centre of Kerala and reported mortality rate of 10.58%.[15] The higher mortality rate noted in the present study can be explained by varied selection criteria and different sample size in the different studies.

In the present study 46% of the children were boys and 52% girls. Boy to girl ratio was almost equal (1:1.2) suggesting no gender prediction for PICU admission. Further, mortality was high (53.57%) among the girls compared to boys (46.43%) but the difference was statistically not significant, suggesting lack of association between mortality and gender. The gender distribution pattern noted in the present study was sharply in agreement with a recent study by Reshma RP et al.[15] from Kochi, Kerala, India to study the mortality rate and mortality profile of children admitted to the PICU of a tertiary care centre of Kerala and reported 48% of the females and 52% of the males. Similar patterns of the gender distributions were reported by studies from developing countries. With regard to the mortality and gender predilection, the results of the present study were in agreement with a recent study by Mattics TJ and Sanchez-Pinto LN1 where no association was found between mortality and sex (p=0.090).

In this study the age of the children ranged between 1 month to 16 years. Although the mortality was high in children aged between 13 to 18 years (72.73%) and less than one year (68%). Association between age and mortality was not significant statistically (p=0.5). A study by Mattics TJ and Sanchez-Pinto LN1 reported significantly lower mean age in children who expired compared to those who survived. In the present study ionotrope administration was noted in 77.3% of the children. Mortality (47.2%) was significantly high in children who were on inotrope support. In the present study blood culture was positive in 10 (13.33%) children. Out of 10 children with positive culture, streptococcal species and MRSA were the common isolates noted in 6 children (30% each). The positive blood culture was significantly high in children who underwent ionotrope administration (18.18%; p=0.041), the culture positive sepsis was independent of age and gender while it was significantly associated with ionotrope administration or lower MAP.

In the present study serum lactate analysis was done to explore the accuracy in predicting outcome which indicates anaerobic metabolism at tissue level. Notably patients in the lower lactate (<2 mmol/L) group had better outcome and survival rates. In this study total of 51 children had high serum lactate levels (68%) and out of 28 expired children 23 children had higher serum lactate levels that accounts for about 82.14% which is statistically significant p value <0.001. In this study it was observed that a decrease in serum lactate level is associated with better outcome and increase in serum lactate level is associated with higher chance of mortality. A study prognostic accuracy of serum lactate level, the SOFA score and qSOFA score for mortality among adults with sepsis conducted by Zhiqiang Liu, Zibo et al, documented that higher the lactate level poorer the outcome interms of mortality in sepsis patients.[16] Serum Lactate level is considered as a key tool in assessing the metabolic acidosis, hypoxia at tissue level which is mediated by shock either it can be septic shock or hypovolemic or cardiogenic shock. Increase in lactate levels is associated with multi-organ dysfunction and predicts the outcome in terms of length of hospital stay and mortality.

In predicting the mortality of critically ill children and timing of intervention or resuscitation pSOFA-L score is beneficial. In this study ROC curve for pSOFA-L score in predicting the mortality showed threshold 10.5 and area under the curve (AUC) is 0.925 with sensitivity of 96.428 and specificity of 80.851 and p value <0.001 which is statistically significant. In this study increase in pSOFA-L score is associated with high mortality and high score is associated with poor outcome. Overall, this study confirms that addition of lactate to pSOFA score helps in accurate discrimination of mortality in critically ill children. Hence pSOFA-L score can be applied in the PICU settings.

Strength

The strength of the study was that, the scores involves all the vital systems and lactate levels helps in better assessment of oxygen deprivation at tissue level which adds on to accurate prediction of outcome.

Limitations of the study was this study were based on the data from a single center involving relatively a smaller sample which limits it general application to the entire population. The validity of a score need to be observed by a multicentric trial which will allow for larger case mix and hence more representative of an average Indian PICU.

CONCLUSION

The findings of the present study validate and emphasize that, addition of lactate parameter to pSOFA score is highly useful and accurate in discrimination of PICU mortality and morbidity. pSOFA-L score provides an objective assessment of the severity of illness; hence a pSOFA-L can be applied in the PICU settings more often thus helping us in quick assessment of outcome of the action, intervention and treatment taken up for individual cases.

Recommendations

Further large multicentric studies involving large sample size with longer duration of follow up and validating with other organ dysfunction scoring systems like PELOD, P-MODS helps in improving the accuracy of pSOFA-L score but also PICU outcomes.

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