

Comparison between paediatric risk of mortality III and paediatric logistic organ dysfunction-2 as mortality predictor in paediatric intensive care

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Abstract

Background: Scoring systems in an intensive care unit (ICU) help in monitoring the patient, evaluating the performance of the ICU and in determining the prognosis of the patient. Pediatric Logistic Organ Dysfunction-2 (PELOD-2) is a new scoring system describing organ dysfunction in paediatric intensive care unit (PICU) which has gained importance as a mortality predictor.

Objectives: To assess the performance of PELOD-2 in predicting mortality and compare it with Pediatric Risk of Mortality-III (PRISM-III) scoring system.

Method: This prospective observational study was carried out in a tertiary care PICU. All consecutive patients with critical illness were scored according to the 2 scoring systems within 24 hours of admission and followed up until discharge or death. Patients admitted for post-surgical care, PICU stay less than 2 hours, death within 8 hours of admission and patients leaving against medical advice were excluded from the study.

Results: A total of 550 patients with critical illness was included in study with a median (IQR) age of 60 (12,132) months and a M: F ratio of 1.6. Predicted mortality using PELOD-2 and PRISM-III score was 62 and 63 patients respectively whereas actual mortality was 67 patients. Area under the ROC was 0.992 for PELOD-2 and 0.98 for PRISM-III with a mean difference of 0.0118 with 95% CI (0.00325 to 0.0204) p value of 0.007. Hosmer and Lemeshow goodness of fit test also showed good calibration in predicting mortality for both scoring systems (PELOD-2: $\chi^2 = 6.051$, p value of 0.301, PRISM-III - $\chi^2 = 9.391$, p value= 0.153)

Conclusions: PRISM-III and PELOD-2 were found to have excellent discrimination and good calibration in our study.

(Key words: Critical illness, Paediatric intensive care, PELOD-2, PRISM-III).

Introduction

Several scoring systems are used to predict mortality and progression of illness in adult¹ and paediatric intensive care units (PICUs)². They help in assessing the performance of the intensive care unit and in monitoring the quality of care delivered to patients. Prognostication based on the scoring system helps in better counseling of patient attenders. Identification of sick patients also helps in more intensive monitoring and prioritization of resources. Performance of the scoring systems vary in different populations because of differences in case mix, facilities available and treatment protocols followed. Hence the newer scoring systems need to be assessed prior to being used in any given population. The two scores which are increasingly being used in PICUs are Paediatric Risk of Mortality-III (PRISM-III) and Paediatric Logistic Organ Dysfunction -2 (PELOD-2).

PRISM-III was developed in 1996 on 11,165 patients from 32 PICUs in North America³. It has 17 variables in 4 subgroups, namely, systolic blood pressure, heart rate, temperature, mental status and pupillary responses in cardiovascular and neurologic subgroup, acidosis, pH, pCO₂, pO₂, total CO₂ in acid bases and blood gases subgroup, blood urea, creatinine, potassium and glucose in biochemistry subgroup, total count, platelet count, prothrombin time and activated partial thromboplastin time in the haematology subgroup. It is scored taking the most abnormal value of each variable in either the first 12 hours (PRISM III-12) or in the first 24 hours (PRISM III-24). PRISM-III-24 has been seen to have good discrimination capacity in predicting the outcome of a critically ill child and has excellent calibration^{4,5}.

PELOD score is a score based on organ dysfunction. It was developed in 1997 in 3 French and Canadian PICUs in 594 patients⁶ and validated in 7 tertiary care PICUs which included 1806 patients⁷. PELOD score is a discontinuous score and was found to have poor calibration in a Brazilian study⁸. This gave rise

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to PELOD-2 which was established in 2013 in France and Belgium. It was developed to update the earlier version and was validated on a larger set of 3671 patients⁹. This score has 10 variables involving 5 organ systems with a maximum possible score of 33. The differences between the two were the addition of mean arterial pressure and lactataemia and the removal of hepatic dysfunction.

Although PELOD score is a descriptive score which describes the course of the illness and organ dysfunction during the hospital stay, it can be used as a surrogate marker for predicting mortality. Unlike PELOD, the newer PELOD-2 score is a continuous scale, and has good calibration and excellent discrimination for mortality. The PELOD-2 score has not been compared with the PRISM-III score in the Asian population.

Objectives

The objective of this study was to compare the performance of PRISM-III and PELOD-2 in predicting outcome among critically ill paediatric patients in PICU.

Method

A prospective observational follow-up study was conducted in the PICU of a tertiary referral hospital attached to a medical college from January 2018 till December 2020. All critically ill patients consecutively admitted to the PICU between the ages of 1 month to 18 years were enrolled in the study. Patients admitted for post-surgical care, PICU stay less than 2 hours, death within 8 hours of admission and patients leaving against medical advice were excluded from the study. Demographic details, diagnosis, the use of vasoactive drugs and the use of ventilatory support were entered in a predesigned proforma. All subjects were followed up till either discharge or death.

All subjects were scored by PELOD-2 and PRISM-III within 24 hours of admission by 2 experienced paediatricians involved in managing the PICU. Daily PELOD-2 was calculated on days 2, 5, 8, 12, 16 and 18 depending on the length of PICU stay. The worst value for each parameter was taken in case of multiple values. Physiologic variables 4 hours prior to death were not included. Neurological component of the PELOD-2 score like Glasgow Coma Scale (GCS) score and pupillary reaction were scored prior to sedation and/or iatrogenic pupillary dilatation. In the case of hypotension, mean arterial pressure was scored prior to starting inotropes. The primary outcome was mortality and the secondary outcome was length of PICU stay, the use of mechanical ventilation and inotropic support.

Sample size: A study carried out by Gonsalves JP, *et al*¹⁰ has revealed that PRISM-III and PELOD-2

scores predicted the outcome as death in 5.5% and 4.4% respectively. Based on above findings, assuming that PELOD-2 score is not inferior to PRISM-III, with a non-inferiority margin of 0.012 and power of 80%, alpha error of 5%, it was estimated that 546 cases are required to evaluate the performance of the 2 scoring systems.

Ethical issues: Approval for the study was obtained from the Institutional Ethics Committee of Ramaiah Medical College, Bangalore, India (No. MSRMC/EC/2018) on 26th of March 2018. Written informed consent was obtained from the primary caregiver before enrollment into the study.

Statistical analysis: All quantitative variables such as age and length of PICU stay were expressed as mean (standard deviation) and median (interquartile range). Categorical variables, such as gender, the use of mechanical ventilation and diagnosis were expressed as percentages. Shapiro test was used to check the normality of data. Mann Whitney test was used when data was not normally distributed. $p < 0.05$ was considered statistically significant

The area under the Receiver Operating Curve (AUC) with 95% confidence interval (CI) was used to test the ability of the 2 scoring systems to differentiate between survivors and non survivors. Youden index was used to find the cut-off value for the 2 scores. The Hosmer Lemeshow goodness of fit test was used to check the calibration of the scoring systems. A p -value > 0.05 is indicative of good calibration. The performance of daily PELOD-2 score was analysed. All analyses were carried out using SPSS, Inc. released 2009.PASW statistics for Windows version 18.0. Chicago.

Results

A total of 550 patients with critical illness was enrolled with a median (IQR) age of 60 (12, 132) months. Sixty two percent of the study sample were boys with a male: female ratio of 1.6. There was no significant difference in the gender between the 2 groups.

The demographic characteristics of the study population are given in Table 1.

Infection was the most frequent reason for admission followed by respiratory and neurological causes like seizures, encephalopathies and Guillain Barre Syndrome. Twenty two percent of the patients required mechanical ventilation. A mortality of 12.2% ($n=67$) was observed in the study, predominantly in infants less than 1 year of age. Infections (35.8%) were the leading cause of death, followed by respiratory causes (20.9%).

Table 1: Baseline characteristics of study population

| Characteristics | Total number (%) | Survivors (n=483) n (%) | Non-survivors (n=67) n (%) |
|--------------------------------------|------------------|----------------------------|-------------------------------|
| <i>Age (months)</i> | | | |
| 1- 12 | 143 (26.2) | 115 (23.8) | 28 (41.8) |
| 13-60 | 139 (25.3) | 126 (26.1) | 14 (20.9) |
| 61-120 | 122 (22.2) | 114 (23.6) | 08 (11.9) |
| >120 | 145 (26.4) | 128 (26.5) | 17 (25.4) |
| <i>Gender</i> | | | |
| Female | 208 (37.8) | 185 (88.9) | 23 (11.1) |
| Male | 342 (62.2) | 298 (87.1) | 44 (12.9) |
| <i>Diagnosis</i> | | | |
| Neurologic | 67 (12.2) | 58 (12.0) | 09 (13.4) |
| Infections | 223 (40.5) | 199 (41.2) | 24 (35.8) |
| Respiratory | 129 (23.5) | 115 (23.8) | 14 (20.9) |
| Cardiovascular | 12 (02.2) | 08 (01.7) | 04 (06.0) |
| Trauma | 14 (02.5) | 12 (02.5) | 02 (03.0) |
| Endocrinologic | 33 (06.0) | 33 (06.8) | 0 (0) |
| Haematologic | 27 (04.9) | 25 (05.2) | 02 (03.0) |
| Others | 45 (8.2) | 33 (06.8) | 12 (17.9) |
| <i>Mechanical ventilation</i> | 122 (22.0) | 56 (11.6) | 66 (98.5) |
| Length of PICU stay median (IQR)* | 4 (3, 6) | 4 (3, 6) | 2 (1, 4) |

*Mann Whitney test IQR- Interquartile range.

The median (IQR) length of PICU stay was 4 (3, 6) days with a range of 1-109 days. The length of PICU stay was significantly less among the non survivors with a median of 2 (1, 4) days compared to the survivors with a median of 4 (3, 6) days. Forty six

percent of patients who were mechanically ventilated survived. The median (IQR) of the day 1 PELOD-2 and PRISM-III was significantly higher in the non-survivor group compared to the survivors (Table 2) (p value <0.05).

Table 2: Day1 PELOD-2 and PRISM-III scores among survivors and non survivors

| Score | Non survivors | Survivors | p value* |
|------------|---------------|--------------|----------|
| | Median (IQR) | Median (IQR) | |
| PELOD 2 | 12 (10,15) | 2 (2,4) | <0.001 |
| PRISM -III | 17 (14,21) | 5 (2,6) | <0.001 |

IQR-interquartile range, *Mann Whitney test

The 2 scoring systems were analysed for power of discrimination and calibration. The analysis of the ROC curve showed that the area under curve (AUC) for PELOD-2 was 0.992 (0.986-0.998) while that for

PRISM-III was 0.98 (0.97-0.99) (Figure 1) with a mean difference of 0.0118 with 95% CI (0.00325 to 0.0204) (p value of 0.007).

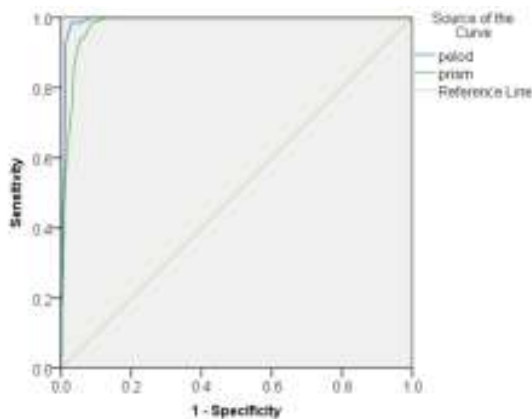


Figure 1: ROC of PRISM-III AND PELOD2 in predicting mortality

The Hosmer-Lemeshow goodness of fit test showed good calibration in predicting mortality for PELOD-2 ($\chi^2 = 6.051$, p value of 0.301) and for PRISM-III ($\chi^2 = 9.391$, p value= 0.153) as shown in Table 3. The predicted mortality using PELOD-2 and PRISM-III score was 62 and 63 patients respectively

whereas the actual mortality was 67 patients. The cut-off value of PELOD-2 for mortality was 7.5 with sensitivity of 98.5% and specificity of 97.1%. The cut-off value of PRISM-III for mortality of 9.5 showed a sensitivity of 98.5% and specificity of 91.3%.

Table 3: Performance of PELOD-2 and PRISM-III in predicting mortality

| Score | PELOD-2 | PRISM-III | p value |
|------------------------|---------------------------|--------------------------|---------|
| AUC | 0.992 | 0.98 | <0.001 |
| 95%CI | 0.986-0.998 | 0.97-0.99 | |
| Cut off | 7.5 | 9.5 | |
| Sensitivity | 98.5 | 98.5 | |
| Specificity | 97.1 | 91.3 | |
| Hosmer – Lemeshow test | $\chi^2=6.051$ (p= 0.301) | $\chi^2=9.391$ (p=0.153) | |

AUC- area under the curve, CI-confidence interval

The PELOD-2 was scored on days 2, 5, 8, 12, 16 and 18 (Table 4). The PELOD scores were significantly higher in the non survivors than the survivors on all

the days. The AUC was highest on the day of admission.

Table 4: PELOD performance on day 2,5,8,12,16 and 18

| | Day 1 | Day 2 | Day 5 | Day 8 | Day 12 | Day16 | Day 18 |
|----------------------------|------------|-------------|------------|-------------|----------|----------|----------|
| No of patients | 550 | 430 | 235 | 97 | 36 | 18 | 13 |
| Survivors | 483 | 394 | 220 | 90 | 32 | 15 | 10 |
| Non survivors | 67 | 36 | 15 | 7 | 4 | 3 | 3 |
| Survivors median (IQR) | 2 (2, 4) | 2 (0, 2) | 1 (0, 2) | 0 (0, 1.25) | 0 (0, 0) | 0 (0, 0) | 0 (0, 2) |
| Non survivors median (IQR) | 12 (10,15) | 9 (7,11) | 10 (7, 11) | 7 (4, 9) | 7 (5, 9) | 7 (7, 7) | 7 (7, 7) |
| p value* | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.009 | 0.032 |
| AUC | 0.992 | 0.965 | 0.8 | 0.9 | 0.9 | 0.9 | 0.9 |
| 95% CI | .986-.998 | 0.938-0.992 | 0.56-1 | 0.714-1 | 0.714-1 | 0.714-1 | 0.714-1 |
| p value | <0.001 | <0.001 | 0.128 | 0.043 | 0.026 | 0.026 | 0.026 |

CI- confidence interval, IQR-interquartile range, AUC- area under the curve *Mann Whitney test

Discussion

Scoring systems used to predict mortality and progression of illness are valuable tools for assessing quality of management of critically ill children in intensive care units. Application of a scoring system which has been developed elsewhere, to a particular population requires that the scores be checked for discrimination and calibration.

This study was conducted to compare the performance of PELOD-2 with PRISM III scores among paediatric patients in a developing country. The median age of our study population was 60 months which was similar to other studies^{10,11}. There was a predominance of males with a M: F ratio of 1.6: 1.0. This predominance of critical illness in boys is also seen in other studies^{10,11}.

Infection was the commonest reason for admission as well as mortality in our study. Neurological illness was the commonest reason for admission and haematological illness was the commonest reason for mortality in a study by Deshmukh T, *et al*¹¹. Respiratory illness was the main reason for admission in a study by El Nawawy A, *et al*¹². The mortality rate in our study was similar to that of other Indian studies^{13,14}. Mortality was more in

infants which was also observed in other studies^{11,12,15}.

The mean PRISM-III was significantly higher in non survivors as compared to survivors. This is similar to studies from Brazil¹⁶, where the mean scores were 7 and 15, Portugal¹⁰, where the scores were 5.6 and 19.7 and an Indian study¹⁷, where the scores were 5.72 and 19.01 among survivors and non survivors respectively. A PELOD-2 score of >15, associated with increased risk of mortality in our study, was also observed in other studies¹¹.

In our study the PRISM-III was found to have good discrimination and calibration as has been seen in many studies^{4,5}. In the study by Gonsalves JP, *et al*¹⁰, the PRISM III was found to have good discrimination and calibration (AUC-0.92, $\chi^2 = 3.82$, p value-0.282). Zhang L, *et al*¹⁸ also showed similar results for PRISM-III (AUC-0.858 and $\chi^2 = 5.667$, p value-0.368). However, a study conducted in India¹⁹ observed the PRISM-III to have poor discrimination with AUC 0.667 but good calibration. This could be because the interpretation of the performance of the scoring systems depends to some extent on the sample size, population characteristics and the standard of care in the PICUs.

PELOD-2, a newer organ dysfunction score developed by Leteurtre S, *et al*⁹ was found to have good discrimination and calibration (AUC-0.934, χ^2 -9.31, p-0.317) and has the advantage of fewer variables compared to the PRISM-III and so is easier to calculate. Gonsalves JP, *et al*¹⁰ also showed PELOD-2 to have good discrimination with AUC-0.94. El Nawawy A, *et al*¹² who compared PELOD with PELOD-2 also found PELOD-2 to be better in discrimination (AUC-0.907).

The cut-off score for mortality derived from the ROC analysis in PELOD-2 in our study was 7.5. Similar cut-off scores were seen in a study by Deshmukh T, *et al*¹¹ who observed that a score of >8 had a sensitivity of 80% and specificity of 80.7% for mortality. Schlapbach LJ, *et al*²⁰ also found that a value of >8 was best in identifying patients at higher risk of mortality. The PRISM-III cut-off score for mortality in our study was 9.5. Hasan ZE, *et al*²¹ concluded that a PRISM-III score >8 was a significant predictor of mortality with an odd's ratio of 9.28 for mortality. An Egyptian study²² done in patients with end stage liver disease and fulminant hepatic failure also got a PRISM cut-off score of 9.5.

The strength of this study is that it is prospective with a good sample size. One major limitation of the study is that the nutritional status of the study population was not analysed which could have an important bearing on the outcome of the illness. Secondly, the number of patients staying in PICU beyond 1 week was low to draw conclusions regarding the scores on those days. Finally, this study shows results from a single centre. A multicentric study would help in generalizing the results to the entire population. There is scope for further studies, preferably multicentric ones to assess the comparative performance of the 2 scoring systems in the paediatric population.

Conclusions

Both PRISM-III and PELOD-2 were found to have excellent discrimination and good calibration in paediatric patients with critical illness in our centre.

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