Comparison of PRISM IV and PIM III prognostic scores as mortality indicators among paediatric intensive care unit patients

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Abstract
Introduction: Identifying prognosis of patients admitted in the paediatric intensive care unit (PICU) is of paramount importance to better allocate medical resources, reduce patient-doctor conflict and for overall better patient care. Many scoring systems have been formulated to accomplish this task including paediatric risk of mortality (PRISM) IV and paediatric index of mortality (PIM) III.

Objectives: To compare PRISM IV and PIM III as prognostic scoring tools in the PICU of a tertiary healthcare centre

Method: This prospective observational study was conducted in the PICU, Dhiraj hospital, SBKS MI&RC, Gujarat, India, from March 2021 to September 2022. It included all patients from age 1 month to 18 years who were admitted in the PICU for >24 hours and gave consent for this study. They were thoroughly examined and investigations were done within the first hour of admission as per standard guidelines and their PRISM IV and PIM III scores were calculated and data were analysed.

Results: A total of 74 patients was enrolled in this study. Whilst 43 (58.1%) patients were discharged, 18 (24.3%)] were discharged against medical advice (DAMA) moribund, 4 were DAMA (non-moribund) and 9 (12.2%) died. Receiver Operating Characteristic (ROC) curves were made for both PRISM IV and PIM III scores. Discriminatory powers of PIM III (AUC 0.725; 95% CI: 0.609 to 0.823) and PRISM IV (AUC 0.8; 95% CI: 0.691 to

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0.884) were acceptable. Whilst PRISM IV was the better predictor of mortality at cut off point of >4 with area under curve of 0.8 for correctly predicting mortality, this difference was not statistically significant (p value=0.354). Multivariate logistic regression analysis showed that the duration of stay (days) and PRISM IV value >4 were significant independent risk factors of mortality after adjusting for confounding factors.

Conclusions: Both PRISM IV and PIM III were good prognostic scoring tools in the PICU of the tertiary healthcare centre. Multivariate logistic regression analysis showed that the duration of stay (days) and PRISM IV value >4 were significant independent risk factors of mortality after adjusting for confounding factors.

Introduction
Often in PICUs the underlying illness of a patient is addressed but the prognosis remains unpredictable[1]. For risk classification and best care of these patients, it is crucial to identify predictors and determinants of death in PICU. The goal of all scoring systems is to measure and boil down a variety of distinct but related patient features to a single value. This value can be used to compare and analyse numerous factors, such as the severity of the condition, the treatments utilised, and the outcome[2]. Physiologic stability index was the first grading system created with the goal of being utilised for severely ill paediatric patients[3,4]. It served as the basis for the development of the paediatric risk of mortality (PRISM) score. It was later modified to PRISM-III and PRISM-IV with greater calibration and discrimination efficiency.

The paediatric index of mortality (PIM) score, which was created in Australian PICUs, has been evaluated in intensive care units in the UK and by the same set of authors, and it was discovered to have high discriminatory capacity. The revised version of the PIM i.e., PIM-3 has better calibration and discrimination capability than the previous model, PIM-2, reported in 2013[4]. To provide a better and more accurate assessment of the performances of

these models, additional research with superior designs is required.

Objectives
To compare PRISM IV and PIM III as prognostic scoring tools in the PICU of a tertiary healthcare centre

Method
Study design: Prospective observational study
Place of study: PICU, Department of Paediatrics, Dhiraj Hospital, Sumandeep Vidyapeeth, Vadodara, Gujarat, India, with a sample size of 74.
All patients admitted to PICU for at least 24 hours, between 1 month to 18 years of age, who gave consent/assent for this study were included. Children who stayed for less than 24 hours in PICU or died within 24 hours of admission were excluded.
Complete clinical examination and detailed investigations of the enrolled participants were noted in a pre-structured proforma within the 1st hour of admission. For PRISM IV, patient's complete blood count (CBC), renal function tests (RFTs), arterial blood gas (ABG), prothrombin time (PT)/activated partial thromboplastin time (APTT), serum electrolytes and blood sugar were analysed whereas PIM III only required patient's ABG analysis Their data were entered in online calculators (www.espnic.eu and www.cpccrn.org) of these scores. Participants were followed up only during the hospital stay and outcome was categorised in terms of morbidity, mortality condition at the time of discharge and duration of hospital stay. Data collected from various aspects were analysed and conclusions were drawn.

Ethical issues: The study was approved by the Sumandeep Vidyapeeth Institutional Ethics Committee, Vadodara, Gujarat, India (No. SVIEC/ON/Medi/BNPG/2107). Written informed consent / assent were taken from the parent/patient after explaining nature of the study.

Statistical analysis: Categorical variables are presented in the form of numbers and percentages.

Quantitative data are presented as means ± SD and median with 25th and 75th percentiles (interquartile range). Data normality was checked by using Kolmogorov-Smirnov test. In the cases in which data were not normal, we used non parametric tests. The following statistical tests were applied for the results:

- Association of variables which were quantitative and not normally distributed in nature were analysed using Mann-Whitney test (for two groups).
- Association of variables which were qualitative in nature were analysed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.
- Receiver operating characteristic (ROC) curve was used to find cut off point, sensitivity, specificity, positive predictive value and negative predictive value of PIM III and PRISM IV for predicting mortality. DeLong *et al* test was used for comparison of area under curve of PIM III and PRISM IV for predicting mortality.
- Multivariate logistic regression was used to find out significant independent risk factors of mortality.

The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, version 25.0. p-value less than 0.05 was considered statistically significant.

Results
Mean value of PIM III of study subjects was 6.54 ± 11.01 with median (25th-75th percentile) of 1.8 (1.4-7.4). It is shown in Table 1.

Mean value of PRISM IV of study subjects was 4.53 ± 6.4 with median (IQR) of 2 (1- 4.75). It is shown in Table 2.

Table 1: *PIM III values*

Variable	Mean ± SD	Median (IQR)	Range
PIM III	6.54 ± 11.01	1.8 (1.4-7.4)	0.2-65.2

Table 2: *PRISM IV values*

Variable	Mean ± SD	Median (IQR)	Range
PRISM IV	4.53 ± 6.4	2 (1- 4.75)	0-30

ROC curves above the diagonal line are considered to have reasonable discriminating ability to predict mortality. Both parameters had significant discriminatory power to predict mortality. Discriminatory power of PIM III (AUC 0.725; 95% CI: 0.609 to 0.823) and PRISM IV (AUC 0.8; 95%

CI: 0.691 to 0.884) was acceptable. Among both parameters, PRISM IV was the best predictor of mortality at cut off point of >4 with area under curve of 0.8 for correctly predicting mortality. PRISM IV had sensitivity of 55.6% followed by PIM III (44.4%). On the other hand, PIM III had specificity

of 93.6% followed by PRISM IV (91.5%). Highest positive predictive value was found in PIM III (80.0%) and highest negative predictive value was found in PRISM IV (78.2%). There is always a trade-off between sensitivity and specificity (any increase in sensitivity will be accompanied by a decrease in specificity) so we choose that variable as best in which combination of sensitivity and specificity gives the maximum predictive value i.e., maximum area under curve so overall PRISM IV was best predictor of mortality. No significant difference was seen in area under curve of PIM III and PRISM IV for predicting mortality. (p value=0.354) It is shown in Table 3 and Figures 1 and 2.

Table 3: *Receiver operating characteristic curve of PIM III and PRISM IV for predicting mortality*

| Variable	PIM III	PRISM IV
Area under ROC curve (AUC)	0.725	0.8
Standard error	0.0625	0.0523
95% confidence interval	0.609 to 0.823	0.691 to 0.884
p-value	0.0003	<0.0001
Cut-off	>8	>4
Sensitivity (95% CI)	44.4% (25.5%-64.7%)	55.6% (35.3%-74.5%
Specificity (95% CI)	93.6% (82.5%-98.7%)	91.5% (79.6%-97.6%
Positive predictive value (95% CI)	80% (51.9%-95.7%)	78.9% (54.4%-93.9%)
Negative predictive value (95% CI)	74.6% (61.6%-85.0%)	78.2% (65.0%-88.2%)
Diagnostic accuracy	75.7%	78.4%
p-value	0.354	

De Long et al test
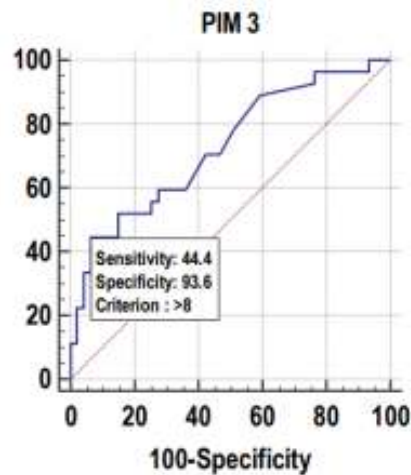
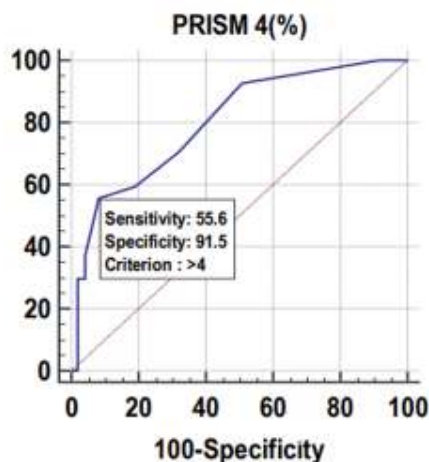Figure 1: *ROC curve of PIM III for predicting mortality*

Figure 2: *ROC curve of PRISM IV for predicting mortality*

Proportion of non survivors was significantly higher in PIM III >8 (80%) as compared to PIM III ≤8 (25.4%) (p=0.0002). Median (IQR)) of PIM III of non survivors was 6.2 (1.6-14.45) which was significantly higher as compared to survivors 1.6 (1.4-3.85) (p =0.001). It is shown in Table 4.

Table 4: *Association of PIM III with outcome*

PIM III	Non survivors (n=27)	Survivors (n=47)	Total	p-value
≤ 8	15 (25.4%)	44 (74.6%)	59 (100.0%)	
>8	12 (80.0%)	03 (20.0%)	15 (100.0%)	0.0002*
Mean ± SD	11.8 ± 15.44	3.52 ± 5.66	6.54 ± 11.01	
Median (IQR)	6.2 (1.6-14.45)	1.6 (1.4-3.85)	1.8 (1.4-7.4)	0.001**
Range	0.4-65.2	0.2-34.9	0.2-65.2	

**Mann-Whitney test; *Fisher's exact test

Proportion of non survivors was significantly higher in PRISM IV >4 (79.0%) as compared to PRISM IV ≤4 (21.8%). (p <0.0001) Median (IQR) of PRISM IV in non survivors was 5 (2-11) which was significantly higher as compared to survivors 2 (1-3) (p <0.0001) It is shown in Table 5.

Table 5: *Association of PRISM IV with outcome*

PRISM IV	Non survivors (n=27)	Survivors (n=47)	Total	p-value
≤4	12 (21.8%)	43 (78.2%)	55 (100.0%)	
>4	15 (79.0%)	04 (21.0%)	19 (100.0%)	<0.0001*
Mean ± SD	7.81 ± 8	2.64 ± 4.41	4.53 ± 6.43	
Median (IQR)	5 (2-11)	2 (1-3)	2 (1-4.75)	<0.0001**
Range	1-28	0-30	0-30	

**Mann-Whitney test; *Fisher's exact test

On performing multivariate regression, duration of stay (days), PRISM IV >4 were significant independent risk factors of mortality after adjusting for confounding factors. With the increase in duration of stay (days), risk of mortality significantly decreases with adjusted odds ratio of 0.889 (0.814 to 0.970). Patients with PRISM IV >4 had significantly high risk of mortality with adjusted odds ratio of 14.232 (2.451 to 82.654). It is shown in Table 6.

Table 6: *Multivariate logistic regression to find out significant risk factors of mortality*

Variable	Beta coefficient	Standard error	p-value	Odds ratio	Odds ratio Lower bound (95%)	Odds ratio Upper bound (95%)
Age (years)	-0.098	0.076	0.194	0.906	0.781	1.051
Duration of stay (days)	-0.118	0.045	0.009	0.889	0.814	0.970
PIM III						
≤8				1.000		
>8	1.340	1.050	0.202	3.819	0.488	29.893
PRISM IV						
≤4				1.000		
>4	2.655	0.898	0.003	14.232	2.451	82.654
Ventilatory support	1.333	0.845	0.115	3.794	0.724	19.890
Inotropes	0.679	0.830	0.413	1.972	0.388	10.038

Discussion

In the present study, the primary system involved was the central nervous system in 26 (35.1%) patients, the gastrointestinal system, in 11 (14.9%) patients, the respiratory system in 11 (14.9%) patients, the haematological system in 11 (14.9%) patients, the autoimmune system in 10 (13.5%) patients and the endocrine system in 2 (2.7%) patients. We found that the association of new morbidity with physiological status was similar to that of mortality, increasing as the physiological dysfunction increased and only decreasing as the physiological dysfunction became sufficiently large to change potential morbidities into mortalities. Critical care mortality is usually associated with physiological abnormalities in the cardiovascular, respiratory, neurological and hematological systems[5-10]. This was similarly stated by Rahmatinejad Z, *et al*[11]. Also, Pollack MM, *et al*[12] stated the predominant organ systems of primary dysfunction were respiratory (33.5%), cardiovascular (24.1%), and neurological (20.1%). In the study by Rahmatinejad Z, *et al*[11], the mean score of PIM-3 was 3 ± 2.8. Gemke RJ, *et al*[13] stated that the expected mortality based on PIM was 7.5% (SMR 0.88; 0.55–1.20).

Mean value of PRISM IV of study subjects was 4.53 ± 6.4 with a median (IQR) of 2 (1- 4.75). Proportion of non survivors was significantly higher in PRISM IV >4 (79.0%) as compared to PRISM IV ≤4 (21.8). Ventilatory support was required in only 27 out of 74 patients (36.5%) within the first hour of admission. Also, in most of the studies, it has been reported that a higher risk of mortality is associated with mechanical ventilation[4-7]. Inotrope was required in only 22 out of 74 patients (29.7%) within first hour of admission. Of the 31 patients who needed mechanical ventilation, 17 (55%) died, and when they needed inotropic support as well, the mortality increased to 69%. Krmpotic K, *et al*[14] did a 2-year study and of the 39 children included in the analysis only 1 patient required inotropic support. The remaining 28% of the study population was admitted for monitoring but did not require any of the aforementioned interventions.

In our study of 74 patients, 43 (58.1%) were discharged, 18 (24.3%) were discharged against medical advice (DAMA) in a moribund condition, 4 (5.4%) were DAMA (non-moribund) and 9 (12.2%) died. In the study by Pollack MM. *et al*[12] of the patients discharged alive, 1.7% were discharged to other acute care hospitals and 5% were discharged to other inpatient care facilities (rehabilitation, chronic care, skilled nursing, psychiatric). However, overall, 2.7% patients were dead after discharge.

No significant difference was seen in area under curve of PIM III and PRISM IV for predicting mortality. (p =0.354) The ability to discriminate between survivors and deaths was estimated by the area under the receiver operating characteristic curve as stated by Pollack MM, *et al*[5] in his study which indicated excellent discrimination by PIM in the sample (0.950 ± 0.007).

Shen Y, *et al*[15] did a meta-analysis of combined PRISM-III/IV studies and showed pooled sensitivity of 0.78 (95% CI: 0.72–0.83), and a pooled specificity of 0.75 (95% CI: 0.68–0.81). In the case of PIM III, they reported pooled sensitivity of 0.75 (95% CI: 0.71–0.79) and combined specificity of 0.76 (95% CI: 0.73–0.79). Also, the summary area under the curve suggested 84% discriminatory power of PRISM-III/IV for mortality (SROC 0.84, 95% CI: 0.80–0.87). They could not compute the pooled sensitivity and pooled specificity of the PRISM-IV due to the small number of studies, insufficient for subgroup analysis. The summary area under the curve indicated that the PIM-III scoring system had 82% prediction power to predict mortality (SROC 0.82, 95% CI: 0.78–0.85).

Horvat CM, *et al*[16] conducted a retrospective, single-centre cohort study derived from structured electronic health record data in the large quaternary PICU at a freestanding, university-affiliated children's hospital. This study, which had a large sample size (21,335 subjects in the entire cohort) demonstrated good to excellent discrimination measured by area under the curve (electronic-PRISM-IV had an area under the curve of 0.90 (95% CI 0.86–0.94).

Multivariate logistic regression was done to find out the significant risk factors for mortality. On performing multivariate regression, duration of stay (days), PRISM IV >4 were significant independent risk factors of mortality after adjusting for confounding factors. Multivariate logistic regression analysis using the variables and their ranges selected in the univariate procedure in the study by Pollack MM, *et al*[5] showed that mortality increases as the PRISM III-APS score increases. Most patients have PRISM III-APS scores less than 10, and these patients have a mortality risk of less than 1%. At the other extreme, the mortality rate of the 137 patients with a PRISM III-APS score of more than 80 was greater than 97%. But the multivariable analysis of Balkin EM, *et al*[17] study showed that the ventilation support had the highest odds ratio among all covariates (OR: 2.1, 95% CI: 1.7–2.6). whereas, Shen Y, *et al*[15] stated meta-regression analysis did not observe the significant influence of differences in mortality rates among different populations, study design, mean age of PICU patients, female gender, and setting (specialized children hospital/tertiary care hospitals), study period, and length of hospital stay on the discriminatory and predictive performance of PRISM III/IV.

Conclusions
Both PRISM IV and PIM III were good prognostic scoring tools in the PICU of the tertiary healthcare centre. Multivariate logistic regression analysis showed that the duration of stay (days) and PRISM IV value >4 were significant independent risk factors of mortality after adjusting for confounding factors.

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