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Performance of pediatric index of mortality-2, pediatric index of mortality-3and pediatric risk of mortality IV in an Egyptian pediatric intensive care unit.

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Abstract:

Introduction: Severity of illness (SOI) scores have been developed to predict the outcome and to provide a better quality of care with available resources.

Objective of the study: was to evaluate the predictive ability of pediatric index of mortality-2 (PIM-2), pediatric index of mortality-3(PIM-3) and pediatric risk of mortality IV (PRISM IV) in a resource-limited pediatric intensive care unit (PICU).

Materials and methods: We conducted a prospective cohort study in PICU in Sohag University Hospital in the period from March 2018 to June 2020. We recorded the baseline patient characteristics, admission diagnoses, variables of PIM-2, PIM-3 and PRISM IV models and outcomes of children admitted to the PICU. We utilized area under receiver operating characteristics (AU-ROC) curves and Goodness-of-fit (GOF) test to evaluate the discrimination and calibration of the three models.

Results: Of 451 patients enrolled, 171 (37.9%) died. Sepsis was the major admission diagnosis. The discrimination was acceptable for PRISM IV, while it was poor for both PIM-2 and PIM-3 as indicated by the AU-ROC which was (0.74; 95%CI: 0.62- 0.86 for PRISM IV) *vs* (0.69; 95% CI: 0.58- 0.81 for PIM-2) and (0.69; 95% CI: 0.57-0.81for PIM-3) ($p < 0.0001$). The calibration was poor for all scores as the *p*-value of GOF test for was < 0.0001 for all scores.

Conclusion: The discrimination of PRISM IV was acceptable and the best among the three models. All scores had poor calibration and under-predict mortality in our setting. We suggest utilizing them as quality indicators rather than in mortality prediction.

Key words: Severity of illness assessment scores, discrimination, calibration.

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Introduction:

The Pediatric intensive care unit (PICU) is a specialized facility designed primarily to provide the best possible care for seriously ill children, with the goal of reducing both mortality and morbidity.(1) Since it was developed in the early 1960s, it has it has played a crucial role in decreasing childhood mortality rates in developed countries. (2) Over the past twenty years, there has been notable progress in expanding access to pediatric critical care in developing nations.(1)

Due to the limited availability of PICU facilities, particularly in developing countries, pediatric intensivists must evaluate the severity of illness (SOI) in order to prioritize critical care for the most critically ill patients. To enhance the quality of care with the limited resources available, numerous SOI scoring systems have been developed to forecast outcomes. Among the most commonly used SOI scores are revised versions of the pediatric risk of mortality (PRISM III and PRISM IV) and pediatric index of mortality (PIM-2 and PIM-3). These models utilize physiological abnormalities as a foundation for determining illness severity .[3]

In addition to predicting mortality, these models are valuable in assessing the quality of medical care in intensive care units. As such, they can serve as quality indicators to compare outcomes among different units and assist individual units in monitoring and enhancing their performance. [4]

Although both PRISM and PIM models have been developed and validated in PICUs in Western countries, their predictive accuracy has been found to vary significantly in different populations worldwide, especially in resource-limited developing countries. [5]

A limited number of studies have assessed the predictive ability of these scores in Egypt. Thus, the objective of our study was to determine the predictive capacity of the PIM-2, PIM-3, and PRISM IV models in our population within a PICU setting with limited resources.

Patients and methods:

We conducted this observational prospective cohort study in our 10-bedded PICU in Sohag University Hospital in the period from March 2018 to June 2020. Sohag University Hospital is a tertiary care university-affiliated hospital that serves Sohag governorate with about 5 million populations. It also receivers referral from nearby governorates in Upper Egypt.

Each bed is equipped with an electronic monitor, one infusion pump, one syringe pump, and one mechanical ventilator. Central oxygen source and suction are available for each bed. Moreover, there is one portable X-ray machine, one portable ultrasound machine, one electrocardiogram machine, and two defibrillator-cardioversion machines. There is no blood gas analyzer within the unit which could facilitate the rapid yield of blood gas analysis; instead all laboratory investigations are performed in the central laboratory in the hospital. Invasive hemodynamic monitoring and continuous renal replacement therapy are not performed in our unit because of expensive supplies that are not available. All medications necessary for resuscitations and managing most of acute childhood illnesses, according to the World Health Organization standards .[6], are available in our unit.

The PICU team consists of residents, general pediatric specialists, pediatric consultants, and 23 senior-level nurses, but there are no respiratory therapists, physiotherapists, pharmacists, and dieticians. Twenty-four-hour shifts are covered by two residents and one specialist. The consultants lead daily morning rounds and are on call 24 hours. The nurse-to-patient ratios range from 1:2 to 1:4 which are the minimally accepted international recommendation .[7] However, their number is insufficient to carry out the ideal 8 hour-shifts; instead there are only 2 shifts, each lasts 12 hours.

The number of patients admitted averages 350 -500 patients annually. Because our unit is a referral unit from many hospitals, there is an urgent need to

increase the number of well-equipped beds together with sufficient number of qualified nurses to meet the demands of admitting more critically-ill children waiting for an empty bed in the PICU.

Ethical consideration:

Approval of the Sohag Faculty of Medicine research ethics committee has been obtained. Informed written consent was obtained from the parents or authorized legal representatives of the children participating in the study.

Patients' selection:

Inclusion Criteria:

Patients admitted to the PICU aged from one month to 16 years old who stayed more than 6 hours in the PICU.

Exclusion Criteria:

- Readmission to the PICU during the study period.
- Patients with incomplete or missing data.

All patients enrolled in the study were subjected to the following assessments on the first day of admission.

I- Demographic data: including age, gender, residence, and any associated comorbid conditions.

II-Clinical data including:

-Vital signs, capillary refill time, Glasgow coma scale, and anthropometric measures.
- Systemic examination with special attention to the system affected.
- Clinical diagnosis.

III- Laboratory investigations including: serial blood gases, serum electrolytes, blood glucose, C- reactive protein, complete blood counts, serum createnine, liver enzymes, serum albumin, total proteins, etc.

IV- Radiological investigations including: chest X-ray, echocardiography, abdominal ultrasound, etc.

V- The severity of illness assessment scores (PIM and PRISM models):

PRISM IV was measured from the information collected within the first 4 hours of PICU admission .[8] The calculator of PRISM IV and the predicted mortality is available at

https://www.cpccrn.org/calculators/prismiiicalculator/

PIM-2 and PIM-3scores calculator available on the website of **the French Society of Anesthesia and Intensive Care http:// www.sfar.org** was used to construct the formula into the study electrical chart system. The system computes the predicted mortality rate based on standard methods using a logistic regression equation .[9]

VI- Length of stay (LOS): referred to the duration of stay in days from the date of admission to the date of discharge.

VII-Outcome assessment: at the end of the PICU stay regarding survival.

Statistical analysis:

Upon completion of data collection, variables included in each data collection sheet were

organized and tabulated then coded prior to computerized data entry. The data were then imported into IBM Statistical Package for the Social Sciences (SPSS version 26.0, IBM Crop., Armonk, NY, USA, 2019) software for statistical analysis.

Kolmogorov–Smirnov, and Shapiro–Wilk tests were used to assess the normality of the distribution. The data were described as medians and interquartile ranges (IQR) for continuous numerical data, whereas frequencies and percentages were used for categorical data.

For assessing the risk factors of mortality, univariable logistic regression analysis was used. A probability level

(*p*-value) of 0.05 was adopted as the level of significance.

The performance of the PRISM IV and PIM-2 and PIM-3 models in mortality prediction was assessed by their discriminatory power and calibration in all patients. Discrimination power (i.e., the ability to predict survival and death at admission for each patient) was assessed by calculating the area under the receiver operating characteristic (AU-ROC) curve. We defined excellent discrimination as AU-ROC between 0.9–1.0, good as 0.8–0.9, acceptable as 0.7–0.8, poor as 0.6–0.7, and unacceptable as 0.5–0.6. [10]

The Hosmer–Lemeshow GOF chi-square (χ^2) test was used to evaluate the calibration of the scoring system, which refers to the correlation between predicted and actual outcomes over the entire range of risk. A good calibration is represented by a $p \geq 0.05$. [11] Finally, the standardized mortality ratio (SMR), which is the ratio of the observed to the expected deaths, was calculated using each model.

Results:

A total of 451 patients out of 506 admitted during the 28-month study period were included in the final analysis. The median age at admission was 7 months with IQR (3 – 24) months. Other baseline information of our cohort is summarized in **Table 1.**

Table1. Baseline characteristics of the studied population admitted to the PICU.

Baseline patient characteristics	**N = 451**	**(%)**
Age		
< 1 year	268	66.1
1 – 5 years	95	21.1
> 5 years	58	12.8
Gender		
Male	250	55.4
Female	201	44.6
Residence		
Rural	**269**	**59.7**
Urban	**182**	**40.3**
Comorbidity	257	57
Severity of illness scores*		
PIM-2 probability	**6.8**	**1.8-18.7**
PIM-3 probability	**1.7**	**0.8-4**
PRISM IV probability	**3**	**2-7**
Clinical data		
Type of patient's case		
Medical	407	90.2
Surgical	44	9.8
Main medical diagnosis		
Sepsis, severe sepsis, septic shock	271	60.1
Diabetic ketoacidosis	28	6.2
Dysrhythmia	19	4.2
Renal disease	19	4.2
Poisoning	11	2.4
Trauma	8	1.8
Multiorgan dysfunction syndrome	217	48.1
Mechanical ventilation	156	34.6
Length of PICU stay, d*	4	2-8
Outcome		
Survivors	280	62.1
Non-survivors	171	37.9

PIM-2: pediatric index of mortality-2, PIM-3: pediatric **in**dex of mortality-3, PRISM IV: pediatric risk of mortality IV.

The values are presented as median and interquartile ranges.
We found that the following factors were significantly associated with increase-drisk of mortality: age younger than one year, probability of death based on the SOI assessment scores (PIM-2, PIM-3, and PRISM IV), sepsis diagnosis, presence of MODS and the need for MV **(Table 2)**

Table 2. Comparison between survivors and non-survivors regarding baseline data.

Baseline patient characteristics	**Survivors** N= 280	**Non-survivors** N= 171	***p* value†**
Age			**<0.001**
<1 year	156(55.7)	120(70.2)	
1-5 years	73(26.1)	42(24.6)	
>5 years	51(18.2)	9(5.3)	
Gender			0.967
Male	155(55.4)	95(55.6)	
Female	125(44.6)	76(44.4)	
Residence			0.114
Rural	159(56.8)	110(64.3)	
Urban	121(43.2)	61(35.7)	
Comorbidity	158(56.4)	99(57.9)	0.76
Severity of illness scores*			
PIM-2 probability	2.8 (1.4-8.3)	20.3 (8.6-48.6)	**<0.001**
PIM-3 probability	1.3 (0.4-1.2)	4 (2-12.2)	**<0.001**
PRISM IV probability	2 (1-3)	8 (4-19)	**<0.001**
Clinical data			
Diagnosis			**<0.001**
Sepsis, severe sepsis, septic shock.	125(44.6)	146(85.4)	
Surgical operation.	40(14.3)	4(1.8)	
Diabetic ketoacidosis.	27(9.6)	1(0.6)	
Renal disease	13(4.6)	6(3.5)	
Dysrhythmias.	19(6.8)	0	
Poisoning	11(3.9)	0	
Trauma	6(2.5)	2(1.2)	
Multiorgan dysfunction syndrome	57(20.4)	160(93.6)	**<0.001**
Mechanical ventilation	46(16.4)	110(64.3)	**<0.001**
Length PICU of stay, d*	4 (2-8)	4 (1-8)	0.192

PIM-2: pediatric index of mortality-2, *PIM-3*: pediatric index of mortality-3, *PRISM IV*: pediatric risk of mortality IV.

*The values are presented as median and interquartile ranges.
†*p* value was calculated using univariable logistic regression analysis. *p* - value ≤ 0.05 was adopted as the level of significance.

The most common probable causes of deaths were irreversible shock with respiratory failure in 70 (40.9%) patients and multi-organ system failure in 57 (33.3%) patients. Other causes included marked increased intracranial pressure in 27(15.8%) patients and pulmonary edema in 17 (9.9%) patients.

Performance of severity of illness assessment scores

The discrimination power for each score was measured by the AU-ROC curve **(Table 3 and Fig. 1)**. It was acceptable for PRISM IV, while it was poor for both PIM-2 and PIM-3 as indicated by the AU-ROC which was (0.74; 95%CI:

0.62- 0.86 for PRISM IV) *vs* (0.69; 95% CI: 0.58- 0.81 for PIM-2) and (0.69; 95% CI: 0.57-0.81for PIM-3) (p < 0.0001). Hence, PRISM IV had the best discriminatory power among all utilized scores in this study.

The Hosmer and Lemeshow GOF test showed poor calibration for PIM-2 (χ^2 = 649.7), PIM-3(χ^2 = 1792), and PRISM IV (χ^2 = 1667) with p-value being < 0.0001 for all scores.

Table 3. Cutoff value and coordinates of the receiver operating characteristic curve.

	AUC	*p* - value	SE	95% CI		Cutoff	Sp	Sn	+PV	-PV	Acc.
PIM-2	0.694	<0.0001	0.059	0.5 79	0.810	14.2	87.5	59.6	78.0	74.5	76.9
PIM-3	0.687	<0.0001	0.061	0.5 68	0.807	2.3	79.6	68.4	80.5	67.2	75.4
PRISM-IV	0.740	<0.0001	0.061	0.6 21	0.859	4	86.8	67.3	81.3	75.7	79.4

Acc.: Accuracy, AU-ROC: Area under the receiver operating characteristic curve, 95% CI: 95% confident interval, PIM-2: pediatric index of mortality-2, PIM-3: pediatric index of mortality-3, PRISM IV: pediatric risk of mortality IV, +PV: positive predictive value,PV :negative predictive value, SE: standard error, Sn: Sensitivity,Sp: Specificity.

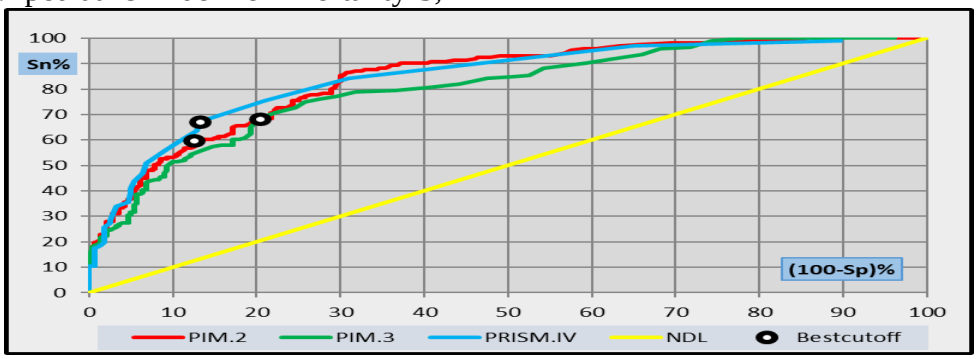

Figure 1. Mortality indices by the area under the receiver operating characteristic curve.

In all models, predicted mortality was lower than observed mortality, as reflected by an SMR of 2.2, 4.75, and 4.5 for the PIM-2, PIM-3, and PRISM IV predictions, respectively **(Table 4)**.

Table 4. Analysis of expected outcome of children using Pediatric Index of Mortality-2, Pediatric Index of Mortality-3, and Pediatric Risk of Mortality IV scores.

	Observed		**Total**
	Non-survivors *n (%)*	Survivors *n (%)*	
Predicted by PIM-2			
Non- survivors *n(%)*	77 (45)	0	77 (17.1)
Survivors *n(%)*	94(55)	280(100)	374 (82.9)
Predicted by PIM-3			
Non-survivors *n(%)*	36(21.1)	0	36 (8)
Survivors *n(%)*	135(78.9)	280(100)	415 (92)
Predicted by PRISM IV			
Non-survivors *n(%)*	38 (22.2)	0	38 (8.4)
Survivors *n(%)*	133(77.8)	280(100)	413 (91.6)
Total	171(100)	280(100)	451(100)

PIM-2: pediatric index of mortality-2, *PIM-3*: pediatric index of mortality-3, *PRISM IV*: pediatric risk of mortality IV.

Discussion:

PIM-2, PIM-3, and PRISM IV were used as the SOI scores that predict mortality in our unit as these scores are the most commonly utilized scores worldwide.[3] The results of the current study revealed that PRISM IV had the best discrimination power among all utilized scores. However, none of the scores had good calibration.

In our study population, the median probability of death when utilizing PIM-2 (6.8) was greater than that reported in multicenter studies where the model was developed (5.3%)[9] and validated (4.9%) .[12] This indicates that the children admitted to our unit were more severely ill upon admission and likely further advanced in their disease progression. However, the median probability of death when using PIM-3 in our study (1.7%) was lower than that observed in both the development set (3.5%) . [9] and validation set (3.9%) .[12] Similarly, the median PRISM IV in the current study was lower than in a recent Chinese study (3 *vs* 5). [13]

The performance of these scores was assessed by measuring discrimination and calibration of each score. The results demonstrated that the discrimination power of PRISM IV was acceptable while poor for both PIM-2 and PIM-3. Likewise, **Zhang et al** reported that PRISM IV had an acceptable discrimination as the AU-ROC curve was 0.76. [13]

Our results are somewhat comparable with other Egyptian studies that revealed better discrimination ability of PRISM over PIM models in predicting PICU mortality. One study stated that the discriminatory performance of PRISM III was better than PIM-3 (AU-ROC = 0.99 *vs* 0.97), both scores had excellent overall discrimination.[14] Another study concluded that PRISM III had better discrimination ability in comparison with PIM2 (AU-ROC = 0.94 *vs* 0.87) .[15] However, these studies demonstrated better discriminatory ability for both models than in our study. This discrepancy could be attributed to the differences in the patient characteristics and disease status.

Moreover, studies from the Middle East showed similar results to ours. **Alkhalifah and colleagues** reported that both PRISM III and PIM-3 showed sufficient discrimination although PRISM III generally showed better discrimination than PIM-3.[16]

Rahmatinejad and coauthors demonstrated that the PRISM III had significantly higher discrimination power in comparison with the PIM-3 (AU-ROC = 0.83 *vs* 0.75) for PICU.[17] In contrast, some studies from china reported that the discrimination ability for PIM-2 and PIM-3 scores was better than the PRISM III. [18,19]

Nevertheless, PIM-2 was the most specific score in the present study (specificity was 87.5% with PIM-2 *vs* 79.6% with PIM-3 and 86.8% with PRISM IV). This might explain the lower values of PIM-3 and PRISM IV scores despite the higher actual mortality in our study.

In addition, we propose that the PIM scoring system presents an advantage over PRISM due to its limited number of variables, which simplifies the measurement process and could be more financially viable in resource-limited settings, such as developing countries. The reduced number of variables also facilitates the training of PICU staff in a standardized manner. Consequently, the PIM model has the greatest potential for reproducibility.[20–22]

In contrast to the satisfactory level of discrimination achieved by at least one score, calibration was found to be inadequate for all scores in our set, which is consistent with observations made in certain units in Egypt and other developing nations .[14,16,17,23] The poor calibration of these scores in our and other units may be attributed to variations in patient characteristics, the need of managing a significant number of critically ill children with limited resources, and potential differences in the standard of care between these units and the ones where the scoring models were originnally developed. Consequently, these models appear to be underestimating mortality rates in resource-limited PICUs, and require recalibration to suit the specific patient population and accurately determine illness severity in such settings.

The SMR looks at the overall calibration of a score .[24] SMR based on PIM-2 was 2.2 while PRISM IV was 4.4 in our study population. SMR > 1 means that the number of observed deaths is more than that of the expected deaths. Our SMR based on both scores was similar to studies performed in Egypt and other resource-restricted PICUs . [23,14,16,17,22] However, it was much higher than that observed in the European and American countries where these scores originated. [8,12]

The cause of this discrepancy is attributable to the elevated mortality rate in our unit and other comparable units relative to resource-rich facilities. Another possible explanation for this variation could be differences in the disease patterns between our unit and others. Both the PIM and PRISM models were developed and tested in mixed ICU units that receive both medical and surgical patients, with approximately one-third of admissions in the development sets being post-surgical cases, including those undergoing cardiac bypass and post-transplant procedures .[8,12] In contrast, our PICU primarily admits patients with acute infectious or medical conditions, and occasionally accepts post-surgical cases. These factors were not taken into consideration by the variables employed to compute the scores.

As an illustration, the PIM-2 and PIM-3 models do not take into account certain diagnoses that are prevalent in our patient population, such as sepsis, which resulted in a substantial number of patients receiving low scores despite potentially qualifying for the high- or very-high-risk categories in our unit. However, due to the limited size of our study cohort, it was not feasible to con-duct an accurate assessment of this issue. Similarly, **Hendricks and McKerrow** noted that PIM does not encompass diagnoses commonly observed in their patient population in South Africa, such as HIV infection, malnutrition, tuberculosis, and other communicable diseases, which resulted in a significant proportion of patients being assigned a score of zero. [22]

Therefore, it may not be appropriate to utilize these scores as predictors of mortality in our unit. Instead, the PRISM and PIM scores may be useful for calculating the SMR to monitor the unit's performance over time or to compare the performance of different units with similar resources. According to **Hendricks and McKerrow**, PRISM and PIM should not be employed as mortality-prediction tools due to their inadequate accuracy, and instead, units should use SMR to evaluate and compare their performance. [22]

A limitation of the study is that it was a single center study which restricts the generalizability of the findings to other

healthcare facilities in Egypt or other nations. Additionally, the poor calibration restricts the applicability of the results. It is suggested that future multicenter research in resource-limited settings be conducted to adjust the SOI scores for use in resource- poor PICUs.

Conclusion:

PRISM IV demonstrated the best discrimination among the utilized scores. Nevertheless, all scores exhibited inadequate calibration and underestimated mortality rates in our setting. Despite this, these scores could be utilized as quality indicators to track and compare the performance of different units.

Conflicts of interest: none stated.
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Contributors: MMM, RGA, MAMB, RAM: designed the study and developed the protocol; RGA: collected the data; MMM, RAM: performed the statistical analysis and drafted the article; MAMB: critically reviewed the article for the important intellectual content. All authors contributed to the article and approved the submitted version.

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