



# The Application of Scoring Systems in Pediatric Intensive Care Unit for Onco-Hematological Patients Who Have Not Undergone Stem Cell Transplantation: A Cross-Sectional Study

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## Abstract

Pediatric onco-hematological patients require intensive care due to the complexity of their conditions, aggressive disease progression, and the immunosuppressive effects of treatments like chemotherapy and immunotherapy, increasing their risk of life-threatening complications. This study aimed to assess and compare the performance of PRISM III (Paediatric Risk of Mortality 3), PRISM IV (Paediatric Risk of Mortality 4), PIM3 (Pediatric Index of Mortality 3), TISS (Therapeutic Intervention Scoring System), and pSOFA (Pediatric Sequential Organ Failure Assessment) in onco-hematological patients after admission to the pediatric intensive care unit (PICU) without a history of hematopoietic stem cell transplantation and to evaluate risk factors of mortality. We included 150 onco-hematological patients without prior stem cell transplantation admitted to PICU. Sociodemographic data, diagnosis, treatment, and causes of PICU admission were recorded. The average age was  $7.2 \pm 4.5$  years, and 55.3% were male. Overall, 43.3% of patients survived. Nonsurvivors showed significantly higher PIM3, PRISM III, PRISM IV, pSOFA, and TISS  $\geq 4$  scores ( $p < 0.001$ ). The pSOFA score demonstrated the highest sensitivity (87.1%), specificity (86.2%), and diagnostic accuracy (area under the curve [AUC]: 0.946) for mortality prediction, followed by PIM3 (AUC: 0.862). Mortality was 56.7%, with pSOFA and PIM3 emerging as the most accurate predictors of outcomes.

## Keywords

- ▶ onco-hematological
- ▶ children
- ▶ PRISM III
- ▶ PRISM IV
- ▶ PIM3
- ▶ TISS
- ▶ pSOFA

## Introduction

Pediatric onco-hematological patients represent a vulnerable population requiring intensive medical management due to the complexities of their underlying conditions, including cancer and hematological disorders. These patients frequently have a higher risk of experiencing life-threatening con-

sequences due to the aggressive nature of their disease, treatment regimens (such as chemotherapy and immunotherapy), and associated immunosuppressive effects.<sup>1</sup>

While hematopoietic stem cell transplantation (HSCT) is a common therapeutic intervention for certain hematological conditions, a significant proportion of onco-hematological

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patients do not undergo this procedure, due to either the nature of their disease or its contraindications. These patients may present with a range of complications, including but not limited to severe infections, multiorgan dysfunction, and treatment-related toxicity, all of which necessitate close monitoring and aggressive intervention in the pediatric intensive care unit (PICU) setting. Fewer studies have been conducted on the characteristics and outcomes of this subgroup of patients admitted to the PICU without a history of HSCT.<sup>2</sup>

The necessity for an accurate modified risk score for children undergoing stem cell transplantation led to the creation of a specialized risk assessment tool; however, an analogous prognostic instrument for the wider population of children with hemato-oncological diseases remains absent.<sup>3</sup> The latest advancements in medical and therapeutic interventions underscore the crucial need for accurate predictive systems. These models have multiple applications, including their use for benchmarking the efficacy of PICU services, the early identification of critically ill patients, and the optimization of resource allocation. This may result in an enhancement of care quality and patient safety, especially in low- and middle-income nations.<sup>4</sup>

The study assessed and compared PRISM III (Paediatric Risk of Mortality 3), PRISM IV (Paediatric Risk of Mortality 4), PIM3 (Pediatric Index of Mortality 3), TISS (Therapeutic Intervention Scoring System), and pSOFA (Pediatric Sequential Organ Failure Assessment) performance and evaluated mortality risk factors in 150 onco-hematological patients admitted to the PICU without prior hematopoietic stem cell transplantation.

## Materials and Methods

This cross-sectional analytic study was performed in an oncology center between September 2021 and September 2023. The Ethical Committee of the Pediatrics Department approved the study protocol. Patients or their guardians gave their consent before enrollment.

### Inclusion and Exclusion Criteria

Pediatric patients under the age of 18 with onco-hematological malignancies requiring PICU admission and no prior history of HSCT participated in the study. Exclusion criteria comprised patients declared “do not resuscitate” by three attending consultants, patients admitted to the PICU for less than 24 hours, and those diagnosed with brain stem death.

### Methods

Data collection was performed within the first 24 hours of PICU admission. Each case underwent a comprehensive assessment, including detailed history-taking, clinical examination, laboratory investigations, and imaging studies.

### History and Clinical Assessment

A thorough history was obtained, documenting demographic data, family history, underlying disease, and causes of PICU admission. The treatment phase before PICU admission was

categorized as untreated, newly diagnosed, or undergoing specific treatment phases such as induction, consolidation, maintenance, or reinduction in relapsed cases.

Clinical examination included vital signs (blood pressure, heart rate, respiratory rate, capillary refill time, oxygen saturation, temperature, and random blood glucose levels). The Glasgow Coma Scale Borgialli et al<sup>5</sup> was applied to assess neurological status. Signs of cardiac dysfunction, such as tachypnea, sinus tachycardia, hepatomegaly, and poor feeding in infants, were documented, along with symptoms of fatigue, exercise intolerance, and respiratory distress in older children. Fluid overload was monitored using pulmonary edema, liver enlargement, congested neck veins, and changes in body weight. It was quantitatively assessed using the formula:

$$[\text{Total fluid input in 24 hours (mL)} - \text{total fluid output in 24 hours (mL)} / \text{weight at admission (g)}] \times 100.^6$$

Additional assessments included the presence of complications such as neutropenic enterocolitis (typhlitis), disseminated intravascular coagulation, hepatic failure, and acute kidney injury (AKI) were evaluated according to KDIGO (Kidney Disease, Improving Global Outcomes) guidelines.<sup>7</sup>

### Laboratory Investigations

Blood and urine samples were collected at admission and subsequently as required. Laboratory tests included a complete blood count, blood gases, and electrolyte levels (sodium, potassium, calcium, phosphorus, and magnesium). Kidney function (urea, creatinine) and liver function (alanine transaminase, aspartate transaminase, albumin) were assessed, along with coagulation parameters (prothrombin time, partial thromboplastin time, platelets concentration (PC), international normalized ratio). Additional tests, such as serum lactate, cardiac enzymes, lactate dehydrogenase, D-dimer, and serum ferritin, were performed when clinically indicated. Blood, urine, and sputum cultures were obtained to identify infectious agents.

### Imaging Studies

Routine imaging included chest X-rays and computed tomography scans of the chest. Echocardiography was performed before initiating chemotherapy and repeated if signs of heart failure or fluid overload were present. Pelvic-abdominal ultrasound was utilized to assess the bowel wall thickening in cases of typhlitis and evaluate organomegaly and ascites.

The five scoring systems (PRISM III, PRISM IV, PIM3, pSOFA, and TISS-76) were calculated based on data from the first 24 hours of PICU admission. The key physiological and laboratory components utilized by each score were summarized in **Table 1**.

### Statistical Analysis

Data were analyzed using SPSS 26.0. Normality was tested with Shapiro–Wilk test. Qualitative variables were shown as frequencies/percentages and compared using chi-square or Fisher’s exact test. Quantitative data were presented as mean  $\pm$  standard deviation for normal or median (range)

**Table 1** Key components of the assessed scoring systems

| Scoring System | Full name                                     | Key assessed components                                                                                                                                                                                                               |
|----------------|-----------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PRISM III      | Pediatric Risk of Mortality III               | Systolic BP, Diastolic BP, Heart Rate, Respiratory Rate, PaO <sub>2</sub> /FiO <sub>2</sub> ratio, GCS, Pupillary reflexes, pH, PaCO <sub>2</sub> , Bicarbonate, Potassium, Calcium, Glucose, BUN, Creatinine, WBC, Platelets, PT/PTT |
| PRISM IV       | Pediatric Risk of Mortality IV                | Similar to PRISM III with updated variable weights and coefficients                                                                                                                                                                   |
| PIM3           | Pediatric Index of Mortality 3                | Systolic BP, PaO <sub>2</sub> /FiO <sub>2</sub> ratio, Base Excess, Pupillary reflexes, Elective/Urgency of admission, Recovery from surgery, Cancer diagnosis, Low risk diagnosis, High risk diagnosis                               |
| pSOFA          | Pediatric Sequential Organ Failure Assessment | Respiration (PaO <sub>2</sub> /FiO <sub>2</sub> ), Coagulation (Platelets), Liver (Bilirubin), Cardiovascular (Hypotension/Vasoactive meds), CNS (GCS), Renal (Creatinine/Urine output)                                               |
| TISS-76        | Therapeutic Intervention Scoring System       | Scores interventions (e.g., mechanical ventilation, vasoactive drips, frequent lab draws, renal replacement therapy) to quantify nursing workload and care intensity                                                                  |

**Table 2** Underlying oncological diagnoses and primary reasons for pediatric intensive care unit admission

| Characteristic                                      | n = 150     |
|-----------------------------------------------------|-------------|
| Primary onco-hematological diagnoses and conditions |             |
| Acute lymphoblastic leukemia (ALL)                  | 61 (40.7%)  |
| Acute myeloid leukemia (AML)                        | 31 (20.7%)  |
| Hemophagocytic lymphohistiocytosis (HLH)            | 29 (19.3%)  |
| Lymphoma                                            | 14 (9.3%)   |
| Other tumors                                        | 15 (10%)    |
| Primary reason for PICU admission                   |             |
| Metabolic causes and electrolyte disturbance        | 112 (74.7%) |
| Respiratory failure                                 | 102 (68%)   |
| Septic shock                                        | 59 (39.3%)  |
| Gastrointestinal and hepatic                        | 47 (31.3%)  |
| Hematological                                       | 47 (31.3%)  |
| Central nervous                                     | 46 (30.7%)  |
| Cardiovascular                                      | 37 (24.7%)  |
| Acute kidney injury                                 | 11 (7.3%)   |

Abbreviation: PICU, pediatric intensive care unit.

Notes: Data were analyzed using SPSS 26.0. Normality was tested with Shapiro–Wilk test. Qualitative variables were shown as frequencies/percentages and compared using chi-square or Fisher's exact test. Quantitative data were presented as meanstandard deviation for normal or median (range) for non-normal distributions. Significance was set at  $p \leq 0.05$ , highly significant at  $p < 0.001$ .

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### Ethical Approval

The Research Ethical Committee of the Faculty of Medicine, Cairo University, provided approval for the research protocol (code: MD-34-2021). The study was conducted in accor-

dance with the Helsinki Declaration of 1964, as revised in 2000. Written informed consent was procured from the patient's guardian prior to their inclusion in the study, and from all patients.

### Results

The average age of patients was  $7.2 \pm 4.5$  years. A total of 55.3% were males (►Table 2).

►Table 3 shows the cardiovascular and respiratory assessment among the participants. Heart failure was present among 12.7% of the participants. Almost all the participants (94%) did not have any symptoms of the severity of fluid overload. Nearly half of the participants (48.7%) had PARDS (Paediatric Acute Respiratory Distress Syndrome); of them, 52.1% had severe PARDS. Also, 74% of the participants need respiratory support; of them, 74.8% need mechanical ventilation.

►Table 4 shows the neurological, gastrointestinal, and hematological assessments among the participants. A total of 25.3% had signs suggestive of typhilitis; 39.3% of the participants had septic shock.

►Table 5 shows the outcome among the studied group; 43.3% of the participants were improved and still alive by the end of the study.

As shown in ►Table 6, the clinical data revealed significant mortality patterns across conditions and admission causes. Septic shock demonstrated 100% mortality among 59 cases, whereas respiratory failure showed 73.5% mortality. Acute myeloid leukemia patients experienced higher mortality (74.2%) compared with acute lymphoblastic leukemia (55.7%). Metabolic disturbances, hematological complications, and gastrointestinal issues were associated with significantly elevated mortality rates, with  $p$ -values indicating statistical significance across multiple clinical parameters.

As shown in ►Table 7, PIM3, PRISM III, PRISM IV, pSOFA, and class  $\geq 4$  TISS scores were significantly higher among

**Table 3** Cardiovascular and respiratory assessment among the participants

| Cardiovascular assessment                     |             |
|-----------------------------------------------|-------------|
| Heart failure                                 | 19 (12.7%)  |
| Myocarditis                                   | 11 (7.3%)   |
| Cardiomyopathy                                | 2 (1.3%)    |
| Inotropic drug administration                 | 53 (35.3%)  |
| Number of inotropic drugs ( <i>n</i> = 53)    | 2 (1–3)     |
| Presence and severity of fluid overload       |             |
| No                                            | 141 (94%)   |
| Yes                                           | 5 (6%)      |
| Respiratory assessment                        |             |
| PARDS                                         |             |
| No                                            | 77 (51.3%)  |
| Yes                                           | 73 (48.7%)  |
| Severity of PARDS ( <i>n</i> = 73)            |             |
| Mild                                          | 13 (17.8%)  |
| Moderate                                      | 22 (30.1%)  |
| Severe                                        | 38 (52.1%)  |
| Respiratory support                           |             |
| No                                            | 39 (26%)    |
| Yes                                           | 111 (74%)   |
| Type of respiratory support ( <i>n</i> = 111) |             |
| Mechanical ventilation                        | 83 (74.8%)  |
| High-velocity nasal insufflation              | 5 (4.5%)    |
| Oxygen mask                                   | 20 (18%)    |
| Nasal oxygen                                  | 3 (2.7%)    |
| PaO <sub>2</sub>                              |             |
| Mean ± SD                                     | 73.7 ± 24.8 |
| Median (range)                                | 80 (21–100) |
| FiO <sub>2</sub>                              |             |
| Mean ± SD                                     | 41.6 ± 18.2 |
| Median (range)                                | 40 (21–121) |

Abbreviations: PARDS, pediatric acute respiratory distress syndrome; SD, standard deviation.

children who died than among children who improved ( $p < 0.001$ ).

As shown in ►Table 8, pSOFA score with cutoff point 6.5 had the highest sensitivity and specificity and the highest diagnostic accuracy in predicting outcome compared with other scores (►Fig. 1).

## Discussion

Due to the implementation of rigorous, combined treatment procedures that include chemotherapy, immunotherapy, radiation, and surgery, the prognosis for children with onco-hematological illnesses has improved dramatically

**Table 4** Neurological, gastrointestinal, and hematological assessment among the participants

| Neurological assessment      |            |
|------------------------------|------------|
| GCS*                         |            |
| Mean ± SD                    | 12.5 ± 3.4 |
| Median (range)               | 15 (3–15)  |
| Pupils                       |            |
| Round, regular, reactive     | 129 (86%)  |
| Dilated fixed pupils         | 11 (7.3%)  |
| Unequal pupils               | 10 (6.7%)  |
| Gastrointestinal examination |            |
| Typhlitis                    | 38 (25.3%) |
| Hepatic failure              | 4 (2.7%)   |
| Coagulation disorder         | 55 (36.7%) |
| Septic shock                 | 59 (39.3%) |
| KDIGO classification*        |            |
| Stage 1                      | 5 (3.3%)   |
| Stage 2                      | 3 (2%)     |
| Stage 3                      | 2 (1.3%)   |

GCS, Glasgow coma scale; KDIGO, Kidney Disease, Improving Global Outcomes; SD, standard deviation.

**Table 5** Outcome among the studied group

| Outcome     | <i>n</i> = 150 (100%) |
|-------------|-----------------------|
| Nonsurvival | 85 (56.7%)            |
| Survival    | 65 (43.3%)            |

over time. However, these intensive therapies can result in life-threatening complications. Severe infections are responsible for the hospitalization of up to 40% of oncology patients in PICU.<sup>7</sup> Despite ongoing advancements in survival rates for these patients, their mortality remains higher compared with the general population.<sup>8</sup>

This study presents a comprehensive analysis of 150 PICU patients, aimed to assess and compared the performance of PRISM III, PRISM IV, PIM3, TISS, and pSOFA in onco-hematological patients after admission to the PICU without a history of hematopoietic stem cell transplantation and to evaluate the different risk factors of mortality in those patients.

The slight male predominance (55.3%) is consistent with the known epidemiological trends in pediatric oncology, where certain malignancies, such as leukemia, show a higher incidence in boys, and the average age was 7.2 years, with a wide range of 0.2 to 17 years. This aligns with previous studies, which report that pediatric onco-hematological patients are often young, with a slightly higher prevalence of male patients.<sup>7</sup>

Overall, the study reported a mortality rate of 56.7% (85 patients), which is higher than the rates observed by

**Table 6** Relation between diagnosis and causes of pediatric intensive care unit admission to outcome

| Characteristics                                 | n = 150 | Dead (n = 85) | Improved (n = 65) | p-Value        |
|-------------------------------------------------|---------|---------------|-------------------|----------------|
| Diagnosis                                       |         |               |                   |                |
| ALL                                             | 61      | 34 (55.7%)    | 27 (44.3%)        | 0.850          |
| AML                                             | 31      | 23 (74.2%)    | 8 (25.8%)         | <b>0.027</b>   |
| HLH                                             | 29      | 17 (58.6%)    | 12 (41.4%)        | 0.813          |
| Lymphoma                                        | 14      | 8 (57.1%)     | 6 (42.9%)         | 0.975          |
| Others                                          | 15      | 3 (20%)       | 12 (80%)          | 0.003          |
| Treatment phase at the moment of PICU admission |         |               |                   |                |
| No                                              | 24      | 8 (33.3%)     | 16 (66.7%)        | <b>0.012</b>   |
| Yes                                             | 126     | 77 (61.1%)    | 49 (38.9%)        |                |
| Causes of PICU admission                        |         |               |                   |                |
| Metabolic causes and electrolyte disturbance    |         |               |                   |                |
| No                                              | 38      | 13 (34.2%)    | 25 (65.8%)        | <b>0.001</b>   |
| Yes                                             | 112     | 72 (64.3%)    | 40 (35.7%)        |                |
| Septic shock                                    |         |               |                   |                |
| No                                              | 91      | 26 (28.6%)    | 65 (71.4%)        | < <b>0.001</b> |
| Yes                                             | 59      | 59 (100%)     | 0 (0%)            |                |
| Hematological                                   |         |               |                   |                |
| No                                              | 103     | 52 (50.5%)    | 51 (49.5%)        | <b>0.024</b>   |
| Yes                                             | 47      | 33 (70.2%)    | 14 (29.8%)        |                |
| Respiratory failure                             |         |               |                   |                |
| No                                              | 48      | 10 (20.8%)    | 38 (79.2%)        | < <b>0.001</b> |
| Yes                                             | 102     | 75 (73.5%)    | 27 (26.5%)        |                |
| Gastrointestinal and hepatic                    |         |               |                   |                |
| No                                              | 103     | 51 (49.5%)    | 52 (50.5%)        | <b>0.009</b>   |
| Yes                                             | 47      | 34 (72.3%)    | 13 (27.7%)        |                |
| Central nervous                                 |         |               |                   |                |
| No                                              | 104     | 60 (57.7%)    | 44 (42.3%)        | 0.703          |
| Yes                                             | 46      | 25 (54.3%)    | 21 (45.7%)        |                |
| Cardiovascular                                  |         |               |                   |                |
| No                                              | 113     | 64 (56.6%)    | 49 (43.4%)        | 0.990          |
| Yes                                             | 37      | 21 (56.8%)    | 16 (43.2%)        |                |
| Acute kidney injury                             |         |               |                   |                |
| No                                              | 139     | 78 (56.1%)    | 61 (43.9%)        | 0.628          |
| Yes                                             | 11      | 7 (63.6%)     | 4 (36.4%)         |                |

Abbreviations: ALL, acute lymphoblastic leukemia; AMH, acute myeloid leukemia; HLH, hemophagocytic lymphohistiocytosis; PICU, pediatric intensive care unit.

Azevedo et al<sup>9</sup> who reported 41% mortality. Also, Wu et al<sup>10</sup> who found observed mortality in 35.9% among 155 children with acute leukemia. Additionally, Rubnitz et al<sup>11</sup> who reported 7.7% mortality. Furthermore, Pechlaner et al<sup>12</sup> found that the mortality was present in 11% of an Austrian cohort, including HSCT patients. These differences may be attributed to variations in the level of care across countries and delays in initiating induction therapy, potentially due to extended waiting lists in our region. Moreover, Pechlaner

et al<sup>12</sup> attributed improved outcomes to advancements in intensive care interventions, such as the prompt administration of the sepsis treatment bundle, lung-protective ventilation strategies, and early initiation of extracorporeal therapies like continuous renal replacement therapy and extracorporeal membrane oxygenation.

In the present cohort study, respiratory failure ( $p < 0.001$ ) and septic shock ( $p < 0.001$ ) emerged as the primary determinants of PICU mortality, whereas metabolic and

**Table 7** Relation between mortality scores and outcome of the participants

|                                                              | Dead (n = 85)     | Improved (n = 65) | p-Value |
|--------------------------------------------------------------|-------------------|-------------------|---------|
| Paediatric Index of Mortality score 3 (PIM3)                 |                   |                   |         |
| Mean $\pm$ SD                                                | 38.14 $\pm$ 23.73 | 13.1 $\pm$ 28.6   | <0.001  |
| Median (range)                                               | 35.5 (3.8–95.1)   | 6.7 (0.2–20.2)    |         |
| Paediatric risk of mortality (PRISM III)                     |                   |                   |         |
| Mean $\pm$ SD                                                | 18 $\pm$ 6        | 10 $\pm$ 5        | <0.001  |
| Median (range)                                               | 19 (2–34)         | 9 (0–25)          |         |
| Paediatric risk of mortality (PRISM IV) (%)                  |                   |                   |         |
| Mean $\pm$ SD                                                | 42.9 $\pm$ 23.9   | 17.8 $\pm$ 13.8   | <0.001  |
| Median (range)                                               | 40 (5–98)         | 13 (3–77)         |         |
| Therapeutic Intervention Scoring System (TISS) 76            |                   |                   |         |
| <4                                                           | 6 (7.1%)          | 62 (95.4%)        | <0.001  |
| =4                                                           | 79 (92.9%)        | 3 (4.6%)          |         |
| Paediatric Sequential Organ Failure Assessment (pSOFA) score |                   |                   |         |
| Mean $\pm$ SD                                                | 11 $\pm$ 3        | 4 $\pm$ 2         | <0.001  |
| Median (range)                                               | 11 (3–18)         | 4 (0–11)          |         |

Abbreviation: SD, standard deviation.

**Table 8** Diagnostic accuracy of PIM3, PRISM III PRISM IV, and pSOFA scores in predicting outcome using the receiver operating characteristic curve

|           | Cutoff point | Sensitivity (%) | Specificity (%) | The area under the curve (95% CI) | p-Value |
|-----------|--------------|-----------------|-----------------|-----------------------------------|---------|
| PIM3      | 12.3         | 80              | 81.5            | 0.862 (0.799–0.926)               | <0.001  |
| PRISM III | 11.5         | 84.7            | 69.2            | 0.843 (0.780–0.905)               | <0.001  |
| PRISM IV  | 18           | 83.5            | 67.7            | 0.842 (0.780–0.906)               | <0.001  |
| pSOFA     | 6.5          | 87.1            | 86.2            | 0.946 (0.913–0.979)               | <0.001  |

Abbreviations: CI, confidence interval, PIM3, Paediatric Index of Mortality score 3, PRISM III, Paediatric Risk of Mortality 3, PRISM IV, Paediatric Risk of Mortality 4, pSOFA, Paediatric Sequential Organ Failure Assessment score.

electrolyte disturbances ( $p=0.001$ ), gastrointestinal and hepatic complications ( $p=0.009$ ), and hematological issues ( $p=0.024$ ) also contributed substantially to adverse outcomes.

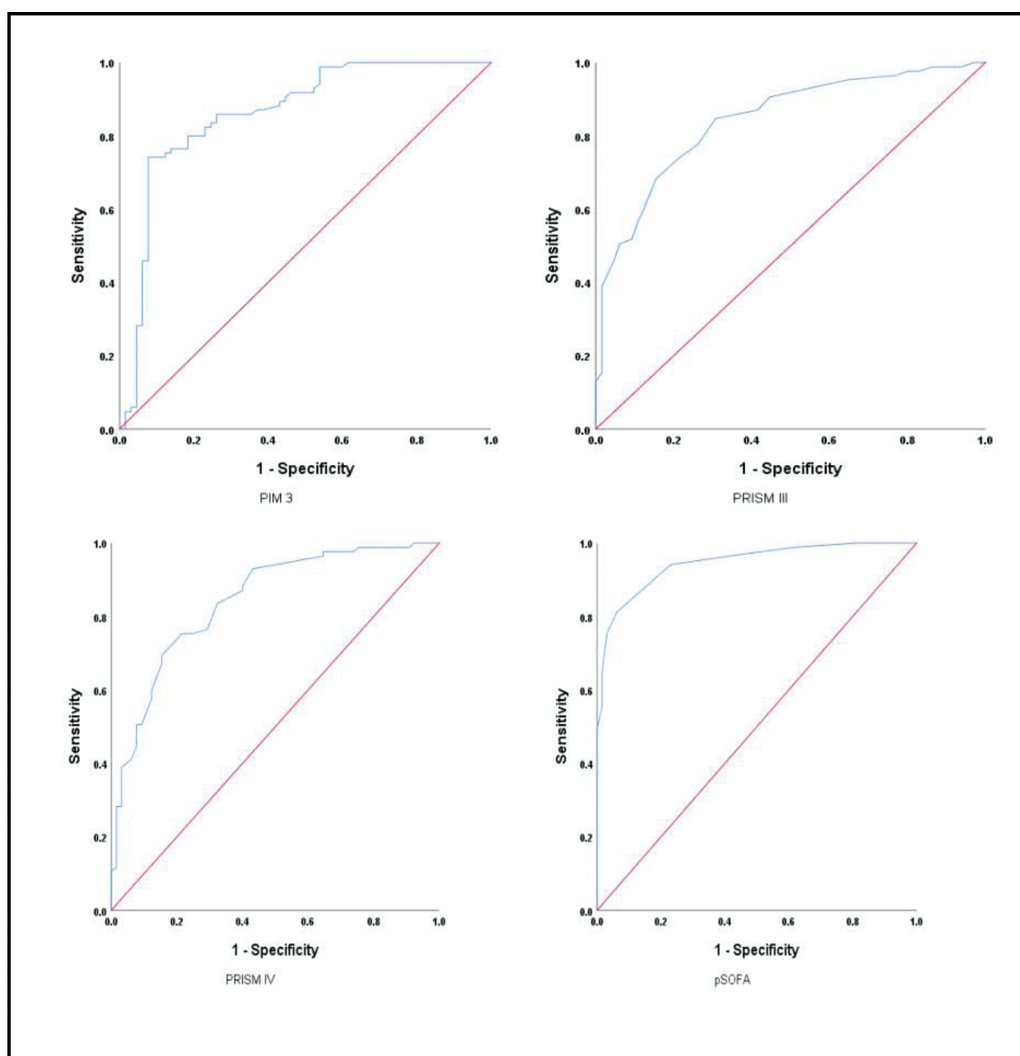
Notably, nonsurviving children exhibited markedly elevated TISS scores (above 4) compared with survivors (92.9 vs. 4.6%), underscoring that patients requiring more intensive interventions generally have more severe underlying illnesses.<sup>13</sup> Although not originally designed as a prognostic tool, the TISS score indirectly reflects illness severity, as more critically ill patients necessitate a broader and more intensive array of interventions.<sup>14,15</sup> These observations are consistent with Ginter et al,<sup>16</sup> who demonstrated the utility of TISS and SOFA scores in estimating mortality and morbidity. Furthermore, Kao et al<sup>17</sup> reported that higher TISS scores are linked to longer intensive care unit stays and increased mortality risk.

Additionally, the TISS quantifies care intensity by assigning scores to specific therapeutic interventions,<sup>18</sup> alterations in hemodynamic parameters—such as blood pressure

and heart rate—and the need for vasoactive drugs serve as clear markers of cardiovascular instability. This instability triggers advanced monitoring and interventions that are systematically integrated within the TISS framework.<sup>19–21</sup> Empirical evidence consistently shows that patients requiring continuous cardiovascular support, including inotropes or vasopressors, present with higher TISS scores,<sup>22</sup> which correlate with increased severity of illness, greater nursing workload, and higher resource utilization in intensive care settings.<sup>23,24</sup>

Among the evaluated scoring systems, the pediatric Sequential Organ Failure Assessment (pSOFA) score exhibited the highest diagnostic accuracy for mortality prediction in our study (area under the curve [AUC]: 0.946). The elevated pSOFA scores are strongly associated with increased mortality risk, reflecting profound impairments in vital functions.<sup>25</sup> For instance, respiratory failure is quantified using oxygenation indices such as the PaO<sub>2</sub>/FiO<sub>2</sub> ratio, with lower ratios indicating significant gas exchange impairment, as seen in acute respiratory distress syndrome.<sup>26,27</sup> Moreover, the





**Fig. 1** ROC curve for the diagnostic accuracy of PIM3, PRISM III, PRISM IV, and pSOFA in predicting outcome. PIM3, Pediatric Index of Mortality 3; pSOFA, Pediatric Sequential Organ Failure Assessment; PRISM III, Paediatric Risk of Mortality 3; PRISM IV, Paediatric Risk of Mortality 4; ROC, receiver operating characteristic.

pSOFA score integrates cardiovascular parameters, including blood pressure and vasopressor requirements, to assess septic shock, collectively correlating with a higher probability of adverse outcomes.<sup>28–31</sup>

Furthermore, in the pSOFA scoring system, the neurological component is principally evaluated using the Glasgow Coma Scale,<sup>32</sup> which quantitatively assesses a patient's level of consciousness through responses in eye, verbal, and motor domains<sup>33</sup>; a decrease in the Glasgow Coma Scale reflects a significant impairment in central nervous system function and, consequently, contributes directly to a higher pSOFA score.<sup>34,35</sup> Scientific studies have consistently demonstrated that diminished Glasgow Coma Scale values correlate with elevated mortality risk,<sup>36,37</sup> thereby substantiating the prognostic relevance of neurological assessment in critical care.<sup>38</sup> Specifically, in pediatric populations, the lower Glasgow Coma Scale indicated worsened neurological status that proportionally raises the overall pSOFA score.<sup>39,40</sup>

Within the pSOFA score, the hepatic component is assessed primarily through serum bilirubin levels, which

directly indicate liver function.<sup>41</sup> Elevated bilirubin reflects impaired hepatic clearance, cholestasis, or hepatocellular injury, leading to higher pSOFA scores.<sup>42–44</sup> Evidence from pediatric critical care demonstrates that increased bilirubin levels correlate with worsening liver dysfunction, greater overall organ failure, and elevated mortality.<sup>45,46</sup> In parallel, renal dysfunction is evaluated using serum creatinine and urine output<sup>35</sup> as critical markers of AKI.<sup>47</sup> Research consistently shows that abrupt declines in kidney function, as in AKI, reflected by elevated creatinine or diminished urine output<sup>48</sup> are associated with increased morbidity and mortality.<sup>49,50</sup> Moreover, AKI often signals broader systemic derangements, frequently resulting from sepsis or multi-organ failure, which further worsen patient outcomes.<sup>51,52</sup> Consequently, higher pSOFA scores driven by deteriorating hepatic and renal parameters underscore a more severe disease state and a greater risk of adverse clinical events.

It is important to note, however, that in pediatric oncology patients, thrombocytopenia may also result from cytotoxic chemotherapy, bone marrow suppression, or disease

infiltration, rather than organ failure per se.<sup>53,54</sup> Therefore, while a low platelet count contributes to higher pSOFA scores,<sup>55,56</sup> its prognostic specificity for mortality in this subgroup may be attenuated. Adjusted or context-specific interpretations are warranted when applying the pSOFA score in children receiving chemotherapy.<sup>57</sup>

These findings align with Malik et al,<sup>58</sup> who observed that pSOFA's predictive accuracy improved from 81.6% at admission to 90.8% on day 3 and peaked at 97.4% by day 7 (AUC: 0.77). Likewise, Maheshwari and Agarwal<sup>59</sup> reported an AUC of 0.882 for pSOFA in mortality prediction. Additionally, Wu et al<sup>10</sup> reported that pSOFA score had the greatest predictive validity for hospital mortality (AUC: 0.83), whereas Baloch et al<sup>60</sup> further substantiated its superior predictive validity for hospital and 30-day mortality, respectively.

In contrast, Rubnitz et al<sup>11</sup> reported suboptimal performance of the pSOFA score (AUC: 0.73 at 1 and 24 hours), attributing the lower accuracy to delayed attributable mortality from secondary infections or complications in ICU care. They hypothesized that pSOFA and PRISM III might perform better in pediatric oncology populations in low- or middle-income countries, where acute, nonsurvivable organ failure predominates.

Regarding the PIM3, our study demonstrated a robust predictive performance with an AUC of 0.862. The PIM3 score has been extensively validated as a prognostic tool for estimating mortality risk in PICUs.<sup>61</sup> Empirical evidence consistently demonstrates that elevated PIM3 scores are closely linked to a heightened risk of mortality, thereby reflecting the aggregate burden of critical illness. Severe conditions, such as respiratory failure and septic shock, which result in marked hypoxemia and systemic inflammatory responses, are key factors contributing to increased PIM3 scores.<sup>4,62</sup> Similarly, disturbances in metabolic and electrolyte balance, as well as hematological irregularities, serve as indicators of multiorgan dysfunction that further deteriorate the clinical prognosis.<sup>63,64</sup> In support of these findings, Buranapattama et al<sup>65</sup> reported a discriminative ability for mortality prediction with an AUC of 0.804 using the PIM3 score, whereas Jiménez-Textalpa et al<sup>66</sup> documented an acceptable performance with an AUC of 0.77.

The PIM3 score, while not directly incorporating the Glasgow Coma Scale, relies significantly on the patient's neurological status. A low Glasgow Coma Scale, indicative of depressed consciousness,<sup>67</sup> is commonly associated with neurological dysfunction<sup>34</sup> that contribute to increase mortality risk in PICU.<sup>68</sup> Moreover, the need for mechanical ventilation serves as an indicator of severe respiratory injury and elevated mortality risk.<sup>69,70</sup> Clinical studies consistently show that patients requiring ventilation face a significantly higher risk of death,<sup>71</sup> which contributes to higher PIM3 score as the risk of mortality correlated with PIM3 score.<sup>72</sup>

Nonsurvivors in our cohort also exhibited significantly higher PRISM III and PRISM IV scores compared with survivors, with AUCs of 0.843 and 0.842, respectively—the latter demonstrating an optimal cutoff value of 18. The metabolic

disturbances—such as acid–base imbalances reflected by aberrant pH and bicarbonate levels—and electrolyte abnormalities, characterized by deviations in sodium, potassium, and other essential ions, indicate underlying cellular dysfunction and systemic stress.<sup>73,74</sup> Empirical evidence consistently associates these pronounced deviations with increased PRISM scores, which in turn correlate strongly with heightened mortality risk.<sup>75,76</sup> In support of these findings, Anjali et al<sup>77</sup> reported that elevated PRISM scores are linked to increased mortality and serve as an excellent predictor of both mortality and illness severity (AUC: 0.99). This observation was further corroborated by Azevedo et al,<sup>9</sup> who noted that survivors exhibited significantly lower PRISM IV scores compared with nonsurvivors (10.9 vs. 14.1). Similarly, Muthupandi et al<sup>78</sup> demonstrated that the PRISM III score effectively predicts mortality risk in patients requiring PICU admission, achieving an AUC of 0.881, whereas Srinivas et al<sup>79</sup> reported robust discriminatory performance of the PRISM III score for mortality prediction in a South Indian tertiary care PICU setting (AUC: 0.888).

Conversely, Wittmann et al,<sup>8</sup> in a cohort of 233 children with hemato-oncological diseases or poststem cell transplant, reported limited predictive accuracy of the PRISM III score (AUC: 0.78) among children admitted to the PICU with sepsis, potentially due to the inclusion of both hemato-oncological and posttransplant patients. Also, Rubnitz et al<sup>11</sup> observed that the PRISM III score performed poorly in predicting mortality among pediatric patients receiving conventional cancer therapy in the ICU.

Abnormal elevations in creatinine and blood urea nitrogen (BUN) serve as indicators of AKI which heighten overall illness severity.<sup>80</sup> Research consistently shows that higher creatinine and BUN levels independently correlate with increased mortality risk in PICU,<sup>81–83</sup> which results in higher the PRISM III score.<sup>77</sup>

In our study, the pSOFA and PIM3 scores demonstrated the highest predictive accuracies for mortality, with AUCs of 0.946 and 0.862, respectively, followed by PRISM III (AUC: 0.843) and PRISM IV (AUC: 0.842). Notably, PIM3 is the sole score incorporating hematological malignancies, with very high-risk diagnoses—including cardiac arrest, severe combined immunodeficiency, leukemia or lymphoma, bone marrow transplant recipients, and liver failure—integral to its framework.<sup>4</sup> These findings align with those of Srinivas et al,<sup>79</sup> who, in a single-center prospective study of 214 PICU patients in South India, demonstrated that the PIM3 score (AUC: 0.934) provided superior mortality discrimination compared with PRISM III (AUC: 0.888). Further supporting our results, Agrwal et al<sup>84</sup> reported that the pSOFA score exhibited a better predictive ability for PICU mortality than PRISM III, whereas Angurana et al<sup>85</sup> highlighted the enhanced accuracy of pSOFA over PRISM III. Additionally, Baloch et al<sup>60</sup> noted that the pSOFA score is an effective predictor of 30-day mortality in critically ill children, outperforming PRISM III in this regard.

This study is limited by its observational design, which validates pSOFA and PIM3 as mortality predictors but does



not establish causal impact on outcomes. Future research should pursue prospective interventional trials to evaluate whether applying these scores in real-time care, including escalation or goals-of-care discussions, can improve clinical outcomes across diverse settings. We did not incorporate advanced hemodynamic monitoring data, such as inferior vena cava status, point-of-care echocardiography, or dynamic indices of fluid responsiveness (e.g., Pulsatility Index, Pleth Variability Index). The potential added prognostic value of these advanced parameters in conjunction with established scores represents an important avenue for future prospective research.

#### Data Availability Statement

Data are accessible via a reasonable request directed to the corresponding author.

#### Authors' Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by R.S.B.M., E.H.A.E., and S.A.M.M. The first draft of the manuscript was written by H.I.A.F.R., and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

#### Patient Consent

All patients provided written informed consent.

#### Conflict of Interest

None declared.

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