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Original Article

Clinical Outcomes and Mortality Predictors in Patients Hospitalized in the Pediatric Intensive Care Unit due to Sepsis

Çocuk Yoğun Bakım Kliniğine Sepsis Nedeniyle Yatan Hastaların Klinik Sonuçları ve Mortalite Belirteçleri

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ABSTRACT

Objective: Sepsis is a serious disease in children and necessitates accurate mortality risk assessment. This study aims to evaluate the effectiveness of clinical findings, laboratory parameters, and scoring systems in predicting mortality and morbidity in pediatric sepsis cases in the pediatric intensive care unit (PICU).

Method: Clinical and laboratory parameters, Pediatric Index of Mortality (PIM) II, Pediatric Risk of Mortality III, Pediatric Logistic Organ Dysfunction (PELOD) and Vasoactive Inotropic Scoring (VIS) scores of 219 patients, aged between 1 month and 18 years, diagnosed with sepsis and septic shock between 2010 and 2016 were retrospectively evaluated.

Results: The mortality rate of the patients was 32.9% (72/219). The specified percentages of patients had an underlying disease (73.1%), required invasive mechanical ventilation (IMV) support (80%), and had a median hospitalization time of 11 days, while 77.2% of the patients were diagnosed with septic shock. In the multivariate logistic regression analysis, higher PIM II [odds ratio (OR): 1.027, p=0.010], PELOD OR: 1.024, p=0.001), Vasoactive-Inotropic Score (VIS) (OR: 1.016, p<0.001) scores, and lactate levels (OR: 1.143, p=0.032) were identified as significant predictors of mortality in pediatric sepsis patients. In receiver operating characteristic analysis, VIS had the highest predictive power [area under the curve: 0.820]. The partial pressure of carbon dioxide (PCO_2) significantly correlated with the length of stay in PICU (r=0.407). PIM II remarkably correlated with the duration of IMV support (r=0.516).

Conclusion: The most efficient parameters to assess mortality in pediatric sepsis were VIS, PIM II and PELOD, respectively. PCO_2 correlated with the length of stay in the PICU, and PIM II with the duration of IMV support.

Keywords: Sepsis, mortality, VIS, PIM II, PICU

ÖZ

Amaç: Sepsis çocuklarda mortalite riskinin doğru değerlendirmesini gerektiren ciddi bir hastalıktır. Bu çalışmada çocuk yoğun bakım ünitesindeki (ÇYBÜ), pediyatrik sepsis olgularında mortalite ve morbiditeyi tahmin etmede klinik bulguların, laboratuvar parametrelerinin ve puanlama sistemlerinin etkinliğini değerlendirmeyi amaçladık.

Yöntem: 2010-2016 yılları arasında sepsis ve septik şok tanısı alan, yaşları 1 ay ile 18 yıl arasında değişen 219 hastanın klinik ve laboratuvar parametreleri, Pediyatrik Mortalite İndeksi (PIM) II, Pediyatrik Mortalite Riski III, Pediyatrik Lojistik Organ Disfonksiyonu (PELOD) ve Vazoaktif İnotropik Skor (VIS) değerleri retrospektif olarak değerlendirilmiştir.

Bulgular: Mortalite oranı %32,9 (72/219) idi. Hastaların altta yatan bir hastalığı (%73,1) ve invaziv mekanik ventilasyon (İMV) desteğine (%80) ihtiyacı olup, ortalama hastanede kalış süresi 11 gündü. Hastaların %77,2'sine septik şok tanısı konuldu. Çok değişkenli lojistik regresyon analizinde, yüksek PIM II [Olasılık oranı (OR): 1,027, p=0,010], PELOD (OR: 1.024, p=0,001), VIS (OR: 1.016, p<0,001) skorları ve laktat düzeyleri (OR: 1.143, p=0,032) pediyatrik sepsis hastalarında mortalitenin önemli öngördürücü parametreleri olarak belirlendi. ROC analizinde, VIS en yüksek öngörü gücüne sahipti (eğrinin altındaki alan: 0,820). PCO_2, ÇYBÜ'de kalış süresi (r=0,407), PIM II ise İMV uygulama süresiyle önemli ölçüde ilişkiliydi (r=0,516).

Sonuç: Pediyatrik sepsiste mortaliteyi değerlendirmek için en etkili parametreler sırasıyla VIS, PIM II ve PELOD skorları idi. PCO_2, ÇYBÜ'de kalış süresi, PIM II ise İMV uygulama süresiyle ilişkiliydi.

Anahtar kelimeler: Sepsis, mortalite, VIS, PIM II, ÇYBÜ

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INTRODUCTION

Sepsis is a leading cause of morbidity and mortality among children[1]. Sepsis is a life-threatening condition caused by an aberrant response to infection that could lead to organ dysfunction[2]. Since sepsis persists as a prevalent cause of mortality and morbidity in pediatric patients, it is vital to be able to detect and categorize the severity of the disease effectively[3]. The International Pediatric Sepsis Consensus Conference previously announced the criteria of pediatric sepsis in 2005. The criteria defined sepsis as a possible or verified infection that leads to a systemic inflammatory response syndrome. Even though these standards are widely applied in day-to-day practice, this definition has limits that have been known since it was first used[4,5]. The Society of Critical Care Medicine Pediatric Sepsis Definition Task Force recently identified The Phoenix Pediatric Sepsis criteria for sepsis and septic shock in children[6]. "An infection with life-threatening organ dysfunction" is the final new definition for pediatric sepsis. This definition comprises respiratory, cardiovascular, coagulation, and neurological components of pediatric sepsis[7]. Early diagnosis of sepsis and septic shock in children and predicting the prognosis are very important; therefore, studies on this subject continue intensively[8,9].

The aim of the study was to determine clinical markers and investigate the effectiveness of standard scoring systems used in pediatric intensive care units (PICUs) in predicting mortality and morbidity in patients hospitalized due to sepsis.

MATERIALS and METHODS

Medical records of patients aged between one month and eighteen years with the established diagnosis of sepsis, who were followed up at the University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital between January 1, 2010, and December 31, 2016, were retrospectively evaluated. Data were collected and extracted retrospectively from medical records in compliance with the ethical principles for medical research. The conduction of the study was permitted by the University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital Clinical Research Ethics Committee. Sepsis, septic shock, and organ failures were diagnosed according to sepsis criteria defined in 2005[4]. Demographic data, medical history, vital parameters, physical examination findings, laboratory and radiological outcomes, medications utilized, disease outcomes, and duration of stay in the PICU of the patients were critically evaluated. Assessment of disease severity and prediction of mortality risk in pediatric sepsis patients were performed based on Pediatric Index of Mortality (PIM) II, Pediatric Risk of Mortality (PRISM) III, Pediatric Logistic Organ Failure (PELOD), and Vasoactive Inotrope (VIS) Scores calculated for each patient. The PRISM III score evaluates physiological parameters collected within the first 24 hours of PICU admission, including neurological status (Glasgow Coma Scale, pupillary reactions), cardiovascular and respiratory function (blood pressure, heart rate, PaO_2/FiO_2 ratio), acid-base balance (pH, bicarbonate), and metabolic markers (glucose, potassium, creatinine) of the patients. The PIM II score is calculated at the time of PICU admission and incorporates variables such as systolic blood pressure, oxygenation status, base excess, need for mechanical ventilation, and the presence of high-risk diagnoses (e.g., cardiac arrest, severe neurological impairment). The PELOD score quantifies multi-organ dysfunction by assessing six organ systems: neurological (Glasgow Coma Scale), cardiovascular (hypotension, lactate), respiratory (PaO_2/FiO_2 ratio, ventilator dependence), hematologic (platelet count), hepatic (bilirubin), and renal (serum creatinine) functions. Higher scores in each of these systems correlate with increased disease severity and a greater risk of mortality[10-13]. VIS scoring system predicts mortality and morbidity of the patients, and is calculated by considering the following parameters in combination estimated during the first 24 hours of the patients in the PICU: dopamine dose (μg/kg/min), dobutamine dose (μg/kg/min), 100 x adrenaline dose (μg/ kg/min), 100 x noradrenaline dose (μg/kg/min), 10 x milrinone dose (μg/kg/min), and 10.000 x vasopressin dose (U/kg/min). The length of the PICU stay was calculated as the interval in days between the date of admission and discharge from the PICU. The cumulative hours required for invasive mechanical ventilation (IMV) were used to determine the duration of IMV support. Morbidity indicators encompassed the duration of IMV support and the length of stay in the PICU. Patients followed up with a diagnosis of sepsis were divided into two groups: those who died during follow-up and those who were discharged. Additionally, patients were separated into two groups as those that did and did nor require IMV support. All groups were also compared in terms of clinical, laboratory parameters, and scoring systems.

Statistical Analysis

The Statistical Package for Social Sciences version 20.0 (SPSS 20.0, IBM Corp., Armonk, NY, USA) was employed to analyze the data. The normality of continuous variables was evaluated using the Kolmogorov-Smirnov

test. In addition, graphical methods including histograms and Q-Q plots were examined. Skewness and Kurtosis values were also calculated to assess the shape of the distribution. Variables with normal distribution were presented as mean ± standard deviation, while non-normally distributed variables as median interquartile range (IQR). The chi-square or Fisher's exact test was used for the comparison of categorical data. Variables that showed statistically significant differences ($p<0.05$) were then included in a multivariate logistic regression analysis (Backward logistic regression method) to identify independent predictors of mortality. The model was adjusted for potential confounders, and multicollinearity was assessed using the Variance Inflation Factor <5 to avoid overestimation or underestimation of coefficients. Adjusted odds ratios (OR) with 95% confidence intervals were reported. Receiver Operating Characteristic (ROC) analysis was performed to measure the predictive power of mortality parameters that were found to be significant in logistic regression analysis. The area under the curve (AUC) refers to the area under the ROC curve, representing the overall ability of a model to distinguish between survivors and non-survivors (0.50-0.60: poor discrimination; 0.61-0.70: fair discrimination; 0.81-0.90: very good discrimination; 0.91-1.00: excellent discrimination). The correlation between two numerical data was calculated using the Spearman test [Spearman Correlation coefficient (r) <0.25 very weak correlation; 0.26-0.49 weak correlation; 0.50-0.69 medium correlation; 0.70-0.89 high correlation; 0.90-1.0 very high correlation] since the data did not conform to normal distribution. In all analyses, p-value of <0.05 was considered statistically significant.

RESULTS

The study population of 219 participants comprised 104 (47.5%) female, and 115 (52.5%) male patients hospitalized in the PICU with a diagnosis of sepsis. The demographic features of these patients are detailed in Table 1. The median age of the patients was 12 months (max: 204 months; min: 1 month; IQR: 6 months - 33 months). The underlying disease was present in 160 (73.1%) cases. Infection foci were detected in 123 patients (56.2%) (Table 1). Respiratory system infections were the most prevalent manifestations of sepsis. The most prevalent microorganisms that were cultivated were coagulase-negative *S. aureus* (29.5%) in blood, *E. coli* (38.2%) in urine, and *P. aeruginosa* (75%) in bronchoalveolar lavage culture media. Most (n=169; 77.2%) of the patients received the diagnosis of septic shock throughout the follow-up. IMV was applied to

Table 1. Demographic characteristics of patients with sepsis hospitalized in PICU

Characteristics	Total number of patients, n=219 (%)/ mean ± SD
Sex, n (%)	
Male	104 (47.5)
Female	115 (52.5)
Age, month	Median 12 (IQR: 6-33)
Transferred from	
Another hospital, n (%)	101 (46.1)
Emergency department, n (%)	84 (38.4)
Ward, n (%)	34 (15.5)
Hospitalized during	
Day shift, n (%)	118 (53.9)
Night shift, n (%)	101 (46.1)
Nationality, n (%)	
Turkish	207 (94.5)
Refugee patient	12 (5.5)
Parental consanguiuity, n (%)	75 (34.2)
Underlying diseases, n (%)	160 (73.1)
Neurological diseases	88 (40.3)
Endocrine/metabolic diseases, n (%)	31 (15.1)
Respiratory diseases	20(9.2)
Hematological/oncological diseases	16 (7.4)
Cardiac diseases	13 (6.0)
Gastroenterological diseases	8 (3.7)
Genetic diseases	4 (1.9)
Rheumatological diseases	2 (0.9)
Identified focus of infection, n (%)	123 (56.2)
Septic shock, n (%)	169 (77.2)
MV support, n (%)	171 (78.1)
Duration of mechanical ventilation	144 hours (1 hour to 7200 hours)
Inotropic medication use, n (%)	167 (76.2)
CRRT, n (%)	17 (7.8)
Mortality scores, median (IQR)	
PIM II	9.2 (4-22.2)
PRISM III	6 (3-13)
PELOD	1.7 (0.2-26.1)
Organ failures, n (%)	
Respiratory	172 (78.5)
Cardiovascular	158 (72.1)
Neurological	72 (32.9)
Hematological	42 (19.2)
Renal	32 (14.6)
Hepatic	20 (9.1)
Mortality, n (%)	72 (32.9)
PICU length of stay (median)	11 (1 to 311 days)

MV: Mechanical ventilation, CRRT: Continuous Renal Replacement Therapy, PIM: Pediatric Index of Mortality, PRISM: Pediatric Risk of Mortality, PELOD: Pediatric Logistic Organ Dysfunction, PICU: Pediatric Intensive Care Unit, IQR: Interquartile range

171 (78.1%) cases. The median value of the duration of IMV support was 144 hours (IQR: 72-360 hours) (max.: 7200-min.: 1 hour). At least one inotropic treatment was started in 167 patients (76.2%). Seventeen patients (7.8%) received dialysis treatment including hemodiafiltration (n=16), and peritoneal dialysis (n=1). The most common organ failures were respiratory (n=172; 78.5%) and cardiovascular (n=158; 72.1%) system failures.

Seventy-two (32.9%) patients did not survive. The median intensive care unit stay was 11 days (max.: 311 days-min.: 1 day), and the median hospital stay was 23 days (max.: 327 days-min.: 1 day).

There was no significant relationship between mortality and age, body weight, gender, refugee status of the patients, the presence of an underlying disease, and being admitted to the intensive care unit outside working hours (p>0.05). However, the survival rate was higher among those admitted to the emergency department (p=0.017). Survival was also significantly higher in patients with an infection focus (p<0.001), although no significant relationship was found between positive culture results and survival rates (p= 0.158) (Table 2). A significant association was observed between mortality, the necessity for IMV support and high scores obtained (p<0.05). Nevertheless, there was no statistically significant association between the necessity for a blood transfusion and survival (p>0.05). Mortality was found to be significantly higher in those with low Glasgow Coma Scores, bradypnea, low mean arterial pressure, hypothermia, low oxygen saturation and high FiO_2 requirement (p<0.05) (Table 3). An analysis of laboratory data revealed that deceased patients exhibited a higher prevalence of several adverse medical conditions, and laboratory parameters compared to those who survived including anemia, thrombocytopenia, hypocalcemia, elevated levels of lactate dehydrogenase, troponin, international normalized ratio (INR), prothrombin time, activated partial thromboplastin time (aPTT), and D-dimer, along with low levels of fibrinogen. Additionally, the deceased patients showed lower pH and HCO_3 values, along with increased lactate levels and base deficit. All these findings were statistically significant (p<0.05) (Table 4). In the logistic regression analysis, higher PIM II, PELOD, and VIS scores, and higher lactate levels were identified as significant predictors of mortality (p<0.05). The significant parameters identified in the logistic regression analysis were evaluated using ROC analysis. The parameters with the highest predictive power for mortality were PIM II, PELOD, and VIS scores (Table 5, Figure 1).

The pCO_2 value showed the strongest correlation with the duration of PICU stay (r=0.407), while the PIM II score indicated the highest correlation with the length of stay on IMV support (r=0.516) (Table 6). The relationships between the duration of patient's stay on IMV support and intensive care, the presence of chronic disease, his/her refugee status, and living place were examined. It was found that only patients with underlying chronic diseases were monitored longer on IMV (p=0.003) and stayed longer in PICU (p<0.001).

DISCUSSION

In this study, we examined the predictive markers of mortality for 219 patients diagnosed with sepsis.

Table 2. Relationships between demographic data, baseline characteristics of patients and survival

Parameters median (IQR) or n (%)	Non-survivors (n=72)	Survivors (n=147)	p-value
Age, months, median (range)	11.5 (5-36)	12 (5-36)	0.365
Body weight (kg) median (range)	8 (5-16)	8 (5.5-12)	0.834
Sex, n (%) Female Male	 36 (50) 36 (50)	 68 (46.3) 79 (53.7)	 0.602
Refugee patient, n (%)	5 (6.9)	7 (4.8)	0.535
Presence of an underlying disease, n (%)	45 (71.4)	81 (66.4)	0.486
Admission during night shift, n (%)	67 (45.6)	34 (47.2)	0.819
Transferred from Emergency department, n (%) Ward, n (%) Another hospital, n (%)	18 (25) 40 (55.6) 14 (19.4)	66 (44.9) 61 (41.5) 14 (19.4)	 **0.017***
Identified focus of infection, n (%)	28 (38.9)	95 (64.6)	**<0.001**
Positive culture results, n (%)	30 (41.7)	47 (32)	**0.158**

*Statistical significance due to pediatric emergency department admissions. IQR: Interquartile range

Worldwide cooperative cross-sectional research carried out in 2013 determined that 8.2% of the children under the age of 18 were treated for severe sepsis in intensive care units (ICUs) with a corresponding hospital mortality rate of 25%. The research revealed no substantial difference in the incidence of sepsis between industrialized and developing countries[14,15]. In our study, 72 out of 219 patients exited, with an associated mortality rate of 32.9%. This high mortality rate could be attributed to the significant age distribution in infancy, a large percentage of underlying illnesses (73.1%), and majority-almost two-thirds - of the patients suffering from septic shock. Furthermore, the fact that nearly 80% of our patients needed IMV support and stayed in the PICU for a median duration of 11 days indicates that they were suffering from severe sepsis.

Table 3. Comparisons of clinical features between non-survivors and survivors

Clinical parameters median (IQR) or n (%)		**Non-survivors (n=72)**	**Survivors (n=147)**	**p-value**
Vital signs				
GCS scores, median (IQR)		8 (4-12)	13 (10-15)	**<0.001**
Pulse rate, n (%)	Normal	3 (4.2)	9 (6.1)	0.067
	Tachycardia	65 (90.3)	137 (93.2)	
	Bradycardia	4 (5.6)	1 (0.7)	
Respiratory rate, n (%)	Normal	9 (12.5)	18 (12.2)	**0.028***
	Tachypnea	58 (80.6)	128 (87.1)	
	Bradypnea	5 (6.9)	1 (0.7)	
Blood pressure, n (%)	Normal	29 (40.3)	82 (55.8)	0.089
	Hypotension	40 (55.6)	59 (40.1)	
	Hypertension	3 (4.2)	6 (4.1)	
Mean arterial pressure, n (%)	Normal	51 (70.8)	134 (91.2)	**<0.001****
	Low	20 (27.8)	11 (7.5)	
	High	1 (1.4)	2 (1.4)	
Body temperature, n (%)	Normal	7 (9.7)	23 (15.6)	**<0.001*****
	Hyperthermia	39 (54.2)	107 (72.8)	
	Hypothermia	26 (36.1)	17 (11.6)	
Oxygen saturation, median (range)		88 (78-95)	92 (86-98)	**0.003**
FiO_2 support, median (range)		80 (60-100)	50 (40-60)	**<0.001**
Organ failure, n (%)	Respiratory	69 (95.8)	103 (70.1)	**<0.001**
	Cardiovascular	64 (88.9)	94 (63.9)	**<0.001**
	Neurological	46 (63.9)	26 (17.7)	**<0.001**
	Renal	15 (20.8)	17 (11.6)	**0.068**
	Hepatic	13 (18.1)	7 (4.8)	**<0.001**
	Hematological	28 (38.9)	14 (9.5)	**<0.001**
Scoring systems, n (%)	PIM II	19.8 (9.2-65.6)	6.9 (2.4-12.7)	**<0.001**
	PRISM III	14 (6.2-22.7)	5 (3-9)	**<0.001**
	PELOD	29 (2-87.7)	1.3 (0.1-16.2)	**<0.001**
	VIS	95 (33.7-120)	10 (0-25)	**<0.001**
IMV Support, n (%)		71 (98,6)	100 (68)	**<0.001**
RBC transfusion, n (%)		61 (84,7)	117 (79.6)	**0.361**

Statistical significance due to *bradypnea, **low arterial pressure, ***hypothermia. IQR: Interquartile range, GCS: Glasgow Coma Scale, FiO_2: Fraction of inspired oxygen, PIM: Pediatric Index of Mortality, PRISM: Pediatric Risk of Mortality, PELOD: Pediatric Logistic Organ Dysfunction, VIS: Vasoactive Inotropic Scoring, RBC: Red blood cell

Leukocytosis, anemia, thrombocytopenia, and endothelial activation are some of the hematologic alterations that can be brought on by severe sepsis[16]. A study conducted on 1073 patients to develop a new mortality scoring system of meningococcal sepsis, thrombocytopenia, aPTT, and INR elevation were shown to be among the most significant parameters in terms of predicting mortality[17]. It has been previously demonstrated D-dimer levels increase at an early stage of the disease in individuals with severe sepsis and disseminated intravascular coagulation[18]. According to our findings, anemia, thrombocytopenia, and coagulopathy were more commonly found in deceased individuals. None of these factors showed statistical significance when analyzed with logistic regression. The latest diagnostic tool, the Phoenix Sepsis Score, incorporates criteria such as thrombocytopenia, elevated INR, D-Dimer, and decreased fibrinogen levels.

Table 4. Laboratory findings in non-survivors and survivors

Laboratory parameters		**Non-survivors (n=72)**	**Survivors (n=147)**	**p-value**
White blood cell count, n (%)	Normal	26 (31.1)	62 (42.2)	0.401
	Leukocytosis	29 (40.3)	61 (41.5)	
	Leukopenia	17 (23.6)	24 (16.3)	
Anemia, n (%)		54 (75)	76 (51.7)	**0.001**
Neutrophil count, median (IQR)		6200 (4100-10300)	14400 (8000-39800)	0.193
Lymphocyte count, median (IQR)		4900 (4100-7400)	1900 (1150-12900)	0.935
Thrombocytopenia, n (%)		34 (47.2)	29 (19.7)	**<0.001**
Eosinophil count, median (IQR)		200 (150-5350)	100 (50-3000)	0.772
RDW, median (IQR)		21 (14.5-24.2)	17.2 (15.5-19.3)	0.573
MPV, median (IQR)		8.9 (7.5-9.5)	8.2 (7.5-10.8)	0.567
CRP, median (IQR)		6.2 (1.1-21.2)	11.2 (5.4-23.3)	0.712
Procalcitonin, median (IQR)		6.9 (0.3-42)	10.5 (2.3-45.2)	0.216
Glucose, median (IQR)		58 (30-77)	98 (83-182)	0.072
Urea, median (IQR)		45 (14-49)	26 (14-35)	0.176
Creatinine, median (IQR)		0.4 (0.4-0.8)	0.5 (0.4-0.8)	0.120
Sodium, median (IQR)		140 (137-146)	134 (133-139)	0.532
Potassium, median (IQR)		4.3 (3.8-6.5)	3.9 (3.7-4.5)	0.405
Calcium, median (IQR)		7.4 (7-8)	8.6 (8.3-9.3)	**0.004**
Alanine transaminase, median (IQR)		41 (17-559)	19 (15-91)	0.325
Albumin, median (IQR)		2.6 (2.4-2.9)	3.1 (2.9-3.5)	**<0.001**
Lactate dehydrogenase, median (IQR)		821 (377-5685)	336 (292-533)	**<0.001**
Troponin, median (IQR)		0.2 (0-7.1)	0.03 (0.01-0.05)	**0.001**
INR, median (IQR)		2 (1.2-5)	1.2 (1.2-1.3)	**0.010**
Prothrombin time, median (IQR)		23.3 (15.4-47.7)	15.7 (15.2-16.2)	**0.024**
aPTZ, median (IQR)		43.3 (22-54.6)	36.8 (32.1-42.8)	**0.012**
D-dimer, median (IQR)		5000 (2352-5000)	1535 (682-3823)	**0.010**
Fibrinogen, median (IQR)		285 (115-385)	414 (293-368)	**0.045**
pH, median (IQR)		7.17 (7.10-7.30)	7.43 (7.32-7.49)	**0.001**
pCO_2, median (IQR)		47 (38-55)	29 (29-48)	0.846
HCO_3, median (IQR)		17 (13-19)	22 (19-29)	**<0.001**
Lactate, median (IQR)		2.1 (1.4-5.7)	1.2 (0.9-1.6)	**0.013**
Base excess, median (IQR)		-8.3 (-13.8 - -5.8)	-3.4 (-6.4 + 5)	**<0.001**

IQR: Interquartile range, RDW: Red cell distribution width, MPV: Mean platelet volume, CRP: C-reactive protein, aPTZ: Activated partial thromboplastin time, pCO_2: Carbon dioxide partial pressure, INR: International normalized ratio

Table 5. Logistic regression analysis of statistically significant parameters and analysis of prognostic factors by ROC analysis for sepsis-related mortality in the PICU

	Logistic regression analysis of the statistically significant parameters for sepsis-related mortality in the PICU			Analysis of prognostic factors by ROC analysis for sepsis-related mortality
Parameters	**p-value**	**Odds ratio**	**95% confidence, interval**	**AUC**
PIM II	**0.010**	1.027	1.006-1.048	0.797
PELOD	**0.001**	1.024	1.010-1.038	0.794
VIS	**<0.001**	1.016	1.009-1.024	0.820
Lactate	**0.032**	1.143	1.011-1.292	0.636

PICU: Pediatric Intensive Care Unit, AUC: Area under the curve, PIM: Pediatric Index of Mortality, PRISM: Pediatric Risk of Mortality, PELOD: Pediatric Logistic Organ Dysfunction, VIS: Vasoactive Inotropic Scoring

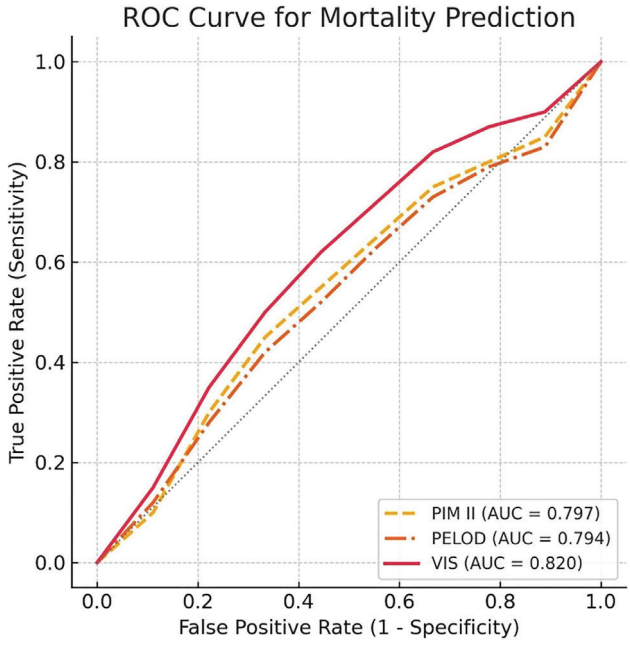

Figure 1. Receiver Operating Characteristics (ROC) curve for mortality prediction in PICU

PICU: Pediatric Intensive Care Unit, PIM: Pediatric Index of Mortality, PELOD: Pediatric Logistic Organ Dysfunction, VIS: Vasoactive Inotropic Scoring, AUC: Area under the curve

However, our findings did not validate this score, as the Phoenix Sepsis Score is designed for diagnosis rather than predicting mortality.

Hyperlactatemia seen in the critically ill patient group diagnosed with sepsis and septic shock, is a product of anaerobic metabolism that develops secondary to inadequate oxygen distribution, resulting in cellular stress. The study conducted on 87 patients diagnosed with septic shock reported that the serum lactate levels of patients who died in the first 24 hours of admission were higher than those who died after the 24th hour with a notable reduction in the serum lactate levels in the first 24 hours of admission in surviving patients and that the longevity of lactic acidosis was the reliable indicator of non-survival[19]. According to a recent study, specifically, a lactate level of ≥4.95 mmol/L upon admission was associated with 32.5 times greater odds of developing severe outcomes, including mortality or the requirement for assisted ventilation[20]. In our logistic regression analysis, elevated lactate levels were found to be a significant predictor of mortality in pediatric sepsis patients (OR: 1.143). This OR indicates that for each unit increase in lactate levels, the odds of mortality increase by approximately 14.3%. The blood lactate AUC indicated that higher lactate levels had a fair but limited ability to discriminate between survivors and non-survivors. This finding aligns with previous studies demonstrating the prognostic value of lactate as a marker of tissue hypoxia, impaired oxygen delivery, and metabolic dysfunction in critically ill patients.

In our study, approximately 2/3 of the patients were started on at least one inotropic treatment, and most frequently dopamine was used. The estimated vasoactive inotropic score was considerably elevated in the deceased patients. In the ROC analysis, the AUC values for PIM II, PELOD, and VIS were 0.797, 0.794, and 0.820, respectively, indicating good discriminative ability in predicting mortality in pediatric sepsis patients. The VIS score demonstrated the highest predictive performance (AUC =0.820), suggesting that requirements for vasoactive support play a crucial role in mortality risk stratification. The PIM II (AUC =0.797) and PELOD (AUC =0.794) scores also showed good discrimination, reflecting the impact of multi-organ dysfunction and physiological derangement on patient outcomes. While all three scoring systems exhibited reliable predictive

Table 6. Correlations between the length of stay in the pediatric intensive care unit and the duration of mechanical ventilation support

	The length of stay in the pediatric intensive care unit		The duration of mechanical ventilation support	
Parameters	**p**	**r**	**p**	**r**
PIM II	**<0.001**	0.345	**<0.001**	0.516
PRISM III	-	-	**0.001**	0.265
PELOD	**<0.001**	0.352	**<0.001**	0.354
GCS	**0.023**	-0.224	**0.010**	-0.253
Oxygen saturation	**<0.001**	-0.337	**0.002**	-0.259
Hemoglobin	**0.008**	0.216	**-**	-
Glucose	**0.003**	0.246	**0.002**	0.259
pH	**0.015**	-0.200	**-**	-
pCO2	**<0.001**	0.407	**<0.001**	0.301
HCO3	**0.001**	0.268	**0.009**	0.215
Base excess	**0.011**	0.210	**-**	-
VIS	**0.001**	0.269	**<0.001**	0.358

GCS: Glasgow Coma Scale, PIM: Pediatric Index of Mortality, PRISM: Pediatric Risk of Mortality, PELOD: Pediatric Logistic Organ Dysfunction, VIS: Vasoactive Inotropic Scoring

values, the superior performance of VIS highlights the importance of hemodynamic instability in the prognosis of patients with sepsis. According to the results of ROC analysis, the vasoactive inotropic score was the most efficient parameter in predicting mortality in our patient group. This finding is consistent with literature; many studies show that VIS correlates with high mortality[21,22].

Patients admitted from the emergency department had a significantly higher survival rate in our study. This may reflect earlier recognition of pediatric sepsis symptoms and timely initiation of interventions such as fluid resuscitation, antibiotherapy, and airway management. The presence of pediatric emergency physicians familiar with sepsis protocols may contribute to this improved outcome, as supported by previous studies emphasizing early diagnosis and management in emergency settings. Multiple organ failure developing based on sepsis causes a significant increase in patient mortality rates. PELOD is a scoring system that assesses the impact of organ dysfunctions in the PICU and correlates with mortality rates in research studies[23,24]. The PELOD score, which evaluates the severity of organ failures, was also found to have a mortality predictive power similar to the PIM II score in our study.

Our study supports the Phoenix Sepsis Score, which has been recently formulated with data acquired from more than 3 million pediatric patients worldwide. Phoenix Sepsis Score applies the definition of infection with life-threatening organ dysfunction, including the respiratory, cardiovascular, coagulation, and neurological systems. Cardiovascular dysfunction is based on hypotension, elevation of lactate, and the need for vasoactive medication[6,7]. The VIS score, related to the need for vasoactive medication, which is emphasized in determining these very new criteria, is the most significant criterion in our study. The four-organ failure and elevation of lactate mentioned were also found to be significant in our study.

In our study, PCO_2 correlated with the length of stay in the PICU. PIM II scores correlated with the duration of IMV support. A longitudinal study including over 10,000 patients established a comparison model for length of stay in the PICU, identifying mechanical ventilation as one of the four primary determinants among the therapeutic modalities[25]. Furthermore, a recent investigation of patients with bronchiolitis hospitalized in the PICU demonstrated a correlation between the length of stay and pH, pCO_2, and bicarbonate levels[26]. In a study of 536 patients, the parameters with the highest mortality prediction were identified as the prolonged duration of MV support, the presence of MODS, and the PIM II score. However, the correlation between PIM II and the duration of MV support was not specified[27].

Study Limitations

Our study has some limitations. The primary limitation of the current study is that it was conducted at a single center and utilized a retrospective design. Furthermore,

we were unable to apply the Phoenix Sepsis Score, which has been recently established, to our patients. However, there is a good agreement between these very new diagnostic criteria and our results. We think that additional large-scale prospective and multicenter studies are required to substantiate our findings.

CONCLUSION

In our study, the most reliable parameters to estimate mortality in children with sepsis and septic shock were VIS, PIM II and PELOD, respectively. The initial PCO_2 value showed the highest correlation with the PICU length of stay, and PIM II showed the highest correlation with the duration of IMV support.

Ethics

Ethics Committee Approval: The study approved by the University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital, Clinical Research Ethics Committee (approval number: 15, dated: 26.06.2016).

Informed Consent: Retrospective study.

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Footnotes

Author Contributions

Concept: E.U., A.B.A., Design: E.U., A.B.A., M.A., Data Collection or Processing: E.U., F.K., Ü.A., G.Ö., N.Z., F.D., Analysis or Interpretation: A.B.A., M.A., F.K., G.Ö., Literature Search: E.U., F.K., Ü.A., N.Z., F.D. Writing: E.U., A.B.A., M.A.

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