



# Prognostic Value of Admission Red Cell Distribution Width and Mean Platelet Volume in Pediatric Sepsis and Septic Shock: Comparison with CRP, Procalcitonin, Lactate, PRISM IV and pSOFA

Pediatric Sepsis ve Septik Şokta Başvuru Sırasındaki Eritrosit Dağılım Genişliği ve Ortalama Trombosit Hacminin Prognostik Değeri: CRP, Prokalsitonin, Laktat, PRISM IV ve pSOFA ile Karşılaştırma

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## ABSTRACT

**Objective:** In this study, we aimed to evaluate the relationship between red cell distribution width (RDW) and mean platelet volume (MPV) levels and disease severity in pediatric patients followed in the pediatric intensive care unit with a diagnosis of sepsis or septic shock, to investigate the correlations of these biomarkers with procalcitonin, C-reactive protein (CRP), lactate, PRISM, and pSOFA scores, and to assess their diagnostic performance.

**Methods:** This retrospective observational study included 243 pediatric patients aged 1 month to 18 years admitted to the pediatric intensive care unit with sepsis or septic shock. RDW, MPV, procalcitonin, CRP, lactate, PRISM, and pSOFA scores obtained at admission were analyzed. Non-parametric tests were used for group comparisons. Receiver operating characteristic analysis for 28-day mortality, and age-based subgroup analyses, were performed.

## ÖZ

**Amaç:** Bu çalışmada sepsis ve septik şok tanısı ile çocuk yoğun bakımda izlenen çocuk hastalarda eritrosit dağılım genişliği (RDW) ve ortalama trombosit hacmi (MPV) düzeylerinin hastalık şiddeti ile ilişkisini değerlendirmek, bu biyobelirteçlerin prokalsitonin, C-reaktif protein (CRP), laktat, PRISM ve pSOFA skorları ile korelasyonunu incelemek ve tanılarda performanslarını değerlendirmeyi amaçladık.

**Yöntemler:** Bu retrospektif gözlemsel çalışmaya çocuk yoğun bakım ünitesinde sepsis veya septik şok tanısı ile izlenen, 1 ay-18 yaş arası toplam 243 hasta dahil edildi. Hastaların başvuru anındaki RDW, MPV, prokalsitonin, CRP ve laktat değerleri ile PRISM ve pSOFA skorları kaydedildi. Gruplar arası karşılaştırmalar non-parametrik testler ile yapıldı. Biyobelirteçlerin 28 günlük mortaliteyi öngörmedeki performansı alıcı işletim karakteristiği analizi ile değerlendirildi ve yaşa göre alt grup analizleri yapıldı.

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**ABSTRACT**

**Results:** RDW, CRP, MPV, procalcitonin, and lactate levels were significantly higher in the septic shock group than the sepsis group ( $p<0.001$ ). All biomarkers showed positive correlations with PRISM and pSOFA scores. For predicting 28-day mortality, lactate [area under the curve (AUC): 0.99] and CRP (AUC: 0.98) showed the highest discriminative power, followed by pSOFA (0.89), procalcitonin (0.87), and RDW (0.85), while MPV (0.73) showed the lowest performance. The combined RDW+CRP+MPV model improved discrimination (AUC: 0.99). CRP performed relatively better in infants ( $<12$  months), while RDW and MPV performed relatively better in children aged  $\geq 12$  months.

**Conclusion:** RDW, CRP, MPV, procalcitonin, and lactate are readily available, cost-effective biomarkers associated with disease severity and mortality in pediatric sepsis and septic shock. CRP and lactate alone show strong performance, while RDW appears to be a more consistent prognostic marker than MPV. Their combined, age-specific use may support early risk stratification in clinical practice.

**Keywords:** Pediatric sepsis, RDW, PRISM IV, pSOFA

**ÖZ**

**Bulgular:** Septik şok grubunda RDW, CRP, MPV, prokalsitonin ve laktat düzeyleri sepsis grubuna kıyasla anlamlı olarak daha yüksek bulundu ( $p<0,001$ ). Tüm biyobelirteçler PRISM ve pSOFA skorları ile pozitif korelasyon gösterdi (en güçlüsü prokalsitonin-pSOFA,  $r=0,87$ ). Yirmi sekiz günlük mortaliteyi öngörmeye laktat [eğri altında kalan alan (AUC): 0,99] ve CRP (AUC: 0,98) en yüksek ayırt edici güce sahipti; bunu pSOFA (0,89), prokalsitonin (0,87) ve RDW (0,85) izledi; MPV (0,73) en düşük performansı gösterdi. RDW, CRP ve MPV'nin kombine modeli ayırt edici gücü artırdı (AUC: 0,99).  $<12$  ay grubunda CRP'nin,  $\geq 12$  ay grubunda ise RDW ve MPV'nin görece daha güçlü performans gösterdiği saptandı.

**Sonuç:** RDW, CRP, MPV, prokalsitonin ve laktat pediatrik sepsis ve septik şokta hastalık şiddeti ve mortalite ile ilişkili, kolay erişilebilir ve düşük maliyetli biyobelirteçler olarak kullanılabilir. CRP ve laktatın tek başına güçlü prognostik belirteçler olduğu, RDW'nin ise MPV'ye kıyasla daha tutarlı bir prognostik belirteç olduğu görülmektedir; bu parametrelerin birlikte ve yaşa özgü kestirim değerleriyle kullanımı, erken risk sınıflamasında klinik olarak yararlı olabilir.

**Anahtar Kelimeler:** Pediatrik sepsis, RDW, PRISM IV, pSOFA

**Introduction**

Sepsis and septic shock remain major causes of morbidity and mortality in pediatric intensive care units (PICUs). Early recognition and accurate risk stratification constitute the cornerstone of clinical management. The clinical course of pediatric sepsis is highly variable and may rapidly progress to multiple organ dysfunction syndrome. Therefore, accurate assessment of disease severity at the time of intensive care unit admission is of critical importance.

Several scoring systems have been developed to assess disease severity and prognosis in pediatric critical care practice (1). The Pediatric Risk of Mortality IV (PRISM IV) score is a widely used prognostic tool for predicting mortality risk. The Pediatric Sequential Organ Failure Assessment (pSOFA) score was adapted to evaluate organ dysfunction and is considered a valid instrument for predicting disease severity and adverse outcomes in children with sepsis (2). However, the calculation of these scoring systems requires numerous clinical and laboratory variables and may be time-consuming in routine clinical practice.

In recent years, increasing attention has been directed toward the prognostic value of biomarkers that can be readily obtained from routine laboratory tests in patients with sepsis and septic shock. C-reactive protein (CRP), a classical acute-phase reactant, reflects the degree of infection and systemic inflammation. Previous studies have demonstrated that elevated CRP levels are associated with increased disease severity and unfavorable clinical outcomes in patients with sepsis and septic shock (3). Red cell distribution width (RDW), a parameter reflecting the heterogeneity of erythrocyte volume distribution, has been

reported to be associated with inflammation, oxidative stress, and bone marrow dysfunction (4). Although growing evidence suggests that RDW is associated with mortality and disease severity in adult intensive care and sepsis populations, data regarding its prognostic significance in pediatric patients remain limited. Mean platelet volume (MPV), which reflects platelet size and activity, is considered an indirect marker of platelet activation during inflammatory processes. Given the established role of platelets in inflammation, microthrombosis, and endothelial injury during the pathophysiology of sepsis, the clinical relevance of MPV has gained increasing attention (5).

Although the prognostic roles of RDW, CRP, and MPV in sepsis and septic shock have been investigated individually, studies evaluating these biomarkers in conjunction with PRISM and pSOFA scores and incorporating age-specific subgroup analyses in pediatric populations remain scarce.

The aim of this study was to evaluate the association of RDW, CRP, and MPV with disease severity in pediatric patients diagnosed with sepsis and septic shock, to investigate their correlations with PRISM and pSOFA scores, and to determine their performance in predicting the mortality using receiver operating characteristic (ROC) curve analysis.

**Methods****Study Design and Patient Selection**

This retrospective observational study was conducted in a tertiary PICU using medical records from October 2020 to November 2025. During the study period, 1,440 patients

were admitted to the PICU, and 243 pediatric patients aged 1 month to 18 years who met the eligibility criteria were included. Demographic characteristics, laboratory parameters obtained from the initial blood samples collected at PICU admission, and the calculated pSOFA and PRISM IV scores were recorded.

The associations of RDW and MPV with CRP, lactate, procalcitonin, pSOFA score, and PRISM IV score were evaluated in critically ill patients diagnosed with sepsis or septic shock. Sepsis and septic shock were defined according to the criteria established by the International Pediatric Sepsis Consensus Conference. These criteria were selected because they were the sepsis/septic shock definitions used in the study institution during the study period and allowed consistent retrospective identification of eligible patients.

For PRISM IV calculation, laboratory variables obtained from the 2 hours preceding PICU admission through the first 4 hours after admission were included, whereas physiological variables were limited to those measured during the first 4 hours following PICU admission. The PRISM IV score incorporates patient age, source of admission (operating room, emergency department, hospital ward, or referral from another hospital), cardiopulmonary resuscitation within the 24 hours preceding PICU admission, presence of acute or chronic malignancy, primary dysfunction of low-risk organ systems (including endocrine, hematologic, musculoskeletal, and primary renal disorders), and the neurological/non-neurological diagnostic category.

The pSOFA score consists of six organ system components: respiratory ( $\text{PaO}_2/\text{FiO}_2$  or  $\text{SpO}_2/\text{FiO}_2$  ratio), hepatic (serum bilirubin concentration), hematologic (platelet count), cardiovascular (age-adjusted mean arterial pressure or the requirement for vasoactive agents such as dopamine, dobutamine, epinephrine, or norepinephrine), neurological (Glasgow Coma Scale score), and renal (age-adjusted serum creatinine level). Each organ system was assigned a score ranging from 0 to 4 according to the worst recorded value within the first 24 hours of PICU admission, and the total pSOFA score (range, 0-24) was calculated by summing the individual organ scores. Variables not measured during the first 24 hours were considered normal, consistent with the original pSOFA criteria.

Patients were followed until discharge from the PICU. The primary outcome was 28-day all-cause mortality. Secondary outcomes included a PICU length of stay of at least 48 hours and the total duration of PICU hospitalization.

### Inclusion and Exclusion Criteria

Patients with hematologic or oncologic disorders (patients with primary non-malignant chronic hematologic disorders (e.g., hemoglobinopathies, hereditary anemias) or those who had received erythrocyte or platelet transfusions within the preceding three months were excluded, as

these factors independently alter baseline RDW and MPV parameters. Patients with hematologic malignancies (such as leukemias or lymphomas) presenting with acute sepsis were included, provided they had no recent transfusion history. Patients with cyanotic congenital heart disease, chronic liver disease, chronic kidney disease, or inherited metabolic disorders were excluded because these underlying conditions could independently influence RDW and MPV values. Patients who had received erythrocyte or platelet transfusions within the preceding three months for any reason, had a previous PICU admission with sepsis or septic shock during the study period, or had incomplete clinical or laboratory data were also excluded.

The admission-diagnosis categories were retained as recorded in the clinical dataset. The hematological admission-diagnosis category therefore refers to the coded reason for admission and does not alter the prespecified exclusion of patients with underlying hematologic or oncologic disorders.

### Ethical Approval

The study protocol was approved by the Clinical Research Ethics Committee of the University of Health Sciences, İzmir Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital (protocol no: 2017/122; decision no: 2017/01-03, date: 26.01.2017). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

### Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and Python (pandas, SciPy, and scikit-learn libraries). The distribution of continuous variables was assessed using the Shapiro-Wilk test. Variables that did not follow a normal distribution were expressed as median (minimum-maximum). Comparisons between groups were performed using the Mann-Whitney U test. Associations between variables were evaluated using Spearman's rank correlation analysis.

The diagnostic performance of each biomarker for 28-day mortality was assessed using ROC curve analysis. The area under the ROC curve (AUC) and corresponding 95% confidence intervals were estimated using bootstrap resampling with 2,000 iterations. Optimal cut-off values were determined using the Youden index ( $J$ : sensitivity + specificity - 1). A two-sided p-value <0.05 was considered statistically significant.

## Results

### Demographic and Clinical Characteristics

A total of 243 pediatric patients were included in the study. The median age was 24 months (range, 1-216 months), and 146 patients (60.1%) were male, while 97 (39.9%) were female.

Respiratory diseases were the most common primary admission diagnosis (32.5%), followed by sepsis (21.8%) and neurological disorders (11.1%).

Vasoactive medications were administered to 60 patients (24.7%). Microbiological evaluation revealed no pathogen growth in 168 patients (69.1%). Among patients with positive cultures, blood cultures (11.9%) and urine cultures (10.3%) were the most frequently identified sources of microbiological positivity.

At the end of the 28-day follow-up period, 221 patients (90.9%) were discharged alive, whereas 22 patients (9.1%) died. The median length of PICU stay was 5 days (range, 1-136 days), and the median duration of mechanical ventilation was 0 days (range, 0-70 days).

At admission, the median serum albumin concentration was 3.7 g/dL (range, 1.0-5.1 g/dL), the median PRISM IV score was 3 (range, 0-39), and the median pSOFA score was 3 (range, 0-13). The median RDW was 14.4% (range, 12.4-17.4%), median MPV was 10.5 fL (range, 9.1-12.4 fL), median procalcitonin level was 3.22 ng/mL (range, 0.76-12.50 ng/mL), median CRP concentration was 46.3 mg/L (range, 3.0-249.6 mg/L), and median lactate level was 1.6 mmol/L (range, 0.5-7.3 mmol/L) (Table 1).

### Comparison Between the Sepsis and Septic Shock Groups

Patients with septic shock exhibited significantly higher RDW, MPV, CRP, procalcitonin, and lactate levels, as well as significantly higher PRISM IV and pSOFA scores, compared with patients with sepsis (all  $p < 0.001$ ) (Table 2).

### Correlation Analyses

Spearman correlation analysis performed in the overall study population ( $n=243$ ) demonstrated statistically significant positive correlations between RDW, MPV, CRP, procalcitonin, and lactate levels and both PRISM IV and pSOFA scores (all  $p < 0.001$ ). The strongest correlation was observed between procalcitonin and the pSOFA score ( $r=0.87$ ), whereas the weakest correlation was found between MPV and the PRISM IV score ( $r=0.31$ ). RDW demonstrated a stronger correlation with clinical severity scores ( $r=0.49-0.53$ ) than MPV ( $r=0.31-0.33$ ) (Table 3).

### ROC Curve Analyses for Predicting 28-day Mortality

Among the individual biomarkers evaluated for predicting 28-day mortality, lactate (AUC: 0.99) and CRP (AUC: 0.98) demonstrated the highest discriminative performance. These were followed by the pSOFA score (AUC: 0.89), procalcitonin (AUC: 0.87), RDW (AUC: 0.85), and the PRISM IV score (AUC: 0.82), whereas MPV showed the lowest discriminative ability (AUC: 0.73). A combined logistic regression model incorporating RDW, CRP, and MPV predicted mortality with excellent discriminatory performance (AUC: 0.99) (Table 4).

**Table 1.** Demographic, clinical, and laboratory characteristics of the patients included in the study

|                                                                                                                                | n (%) / median (min-max)         |
|--------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
| <b>Age (months)</b>                                                                                                            | 24 (1-216)                       |
| Male, n (%)                                                                                                                    | 146 (60.1%)                      |
| Female, n (%)                                                                                                                  | 97 (39.9%)                       |
| <b>Patients with underlying comorbidities</b>                                                                                  |                                  |
| Respiratory                                                                                                                    | 79 (32.5%)                       |
| Sepsis                                                                                                                         | 53 (21.8%)                       |
| Neurological                                                                                                                   | 27 (11.1%)                       |
| Shock                                                                                                                          | 17 (7.0%)                        |
| Metabolic                                                                                                                      | 17 (7.0%)                        |
| Cardiac                                                                                                                        | 15 (6.2%)                        |
| Hematological                                                                                                                  | 8 (3.3%)                         |
| Other (trauma/postoperative)                                                                                                   | 4 (1.6%)                         |
| <b>Patients with no underlying comorbidities</b>                                                                               | 23 (0.09%)                       |
| <b>Vasoactive drugs (yes)</b>                                                                                                  | 60 (24.7%)                       |
| <b>Positive microbiological culture</b>                                                                                        | 75 (30.9%)                       |
| Blood                                                                                                                          | 29 (11.9%)                       |
| Urine                                                                                                                          | 25 (10.3%)                       |
| Body fluid                                                                                                                     | 9 (3.7%)                         |
| CSF                                                                                                                            | 6 (2.5%)                         |
| Tracheal aspirate                                                                                                              | 6 (2.5%)                         |
| <b>28-day mortality</b>                                                                                                        | 22 (9.1%)                        |
| <b>Length of PICU stay (days)</b>                                                                                              | 5 (1-136)                        |
| <b>Duration of mechanical ventilation (days)</b>                                                                               | 0 (0-70) (IQR)-(mean: 4.25 days) |
| <b>Serum albumin (g/dL)</b>                                                                                                    | 3.7 (1.0-5.1)                    |
| Note: Data are presented as n (%) or median (minimum-maximum)<br>PICU: Pediatric intensive care unit, IQR: Interquartile range |                                  |

### Age-based Subgroup ROC Analyses

In patients younger than 12 months, CRP (AUC: 1.00) and RDW (AUC: 0.81) demonstrated high discriminative performance, whereas MPV showed relatively poor predictive ability (AUC: 0.62). In contrast, among patients aged  $\geq 12$  months, both CRP (AUC: 0.98) and RDW (AUC: 0.87) maintained strong predictive performance, while the discriminative ability of MPV increased modestly compared with the infant subgroup (AUC: 0.78). In both age groups, the combined biomarker model (RDW+CRP+MPV) achieved comparable or superior discriminative performance compared with the individual biomarkers alone (Table 5).

### Comparison of Admission Biomarkers and Severity Scores According to 28-day Mortality

When baseline parameters were compared between survivors and non-survivors at 28-days, non-survivors demonstrated significantly higher admission RDW, MPV, CRP, procalcitonin, and lactate levels, as well as higher

PRISM IV and pSOFA scores compared with survivors (all  $p < 0.001$ ) (Table 6).

## Discussion

In the present study, we investigated the associations of RDW, CRP, MPV, procalcitonin, and lactate with disease severity and mortality in 243 pediatric patients diagnosed

with sepsis or septic shock. Disease severity was evaluated using the PRISM IV and pSOFA scoring systems, ROC curve analysis, and age-based subgroup analyses. All evaluated biomarkers demonstrated significant positive correlations with both PRISM IV and pSOFA scores. Lactate and CRP exhibited the greatest discriminative ability for predicting 28-day mortality, whereas RDW proved to be a

**Table 2.** Comparison of the sepsis and septic shock groups

|                       | Sepsis (n=183)      | Septic shock (n=60)  | p-value |
|-----------------------|---------------------|----------------------|---------|
| RDW (%)               | 14.20 (12.40-16.60) | 14.95 (13.40-17.40)  | <0.001  |
| MPV (fL)              | 10.50 (9.10-12.40)  | 10.80 (9.50-12.20)   | <0.001  |
| CRP (mg/L)            | 41.20 (3.00-140.00) | 73.10 (14.70-249.60) | <0.001  |
| Procalcitonin (ng/mL) | 2.74 (0.76-9.12)    | 5.15 (1.35-12.50)    | <0.001  |
| Lactate (mmol/L)      | 1.50 (0.50-5.30)    | 2.30 (0.50-7.30)     | <0.001  |
| PRISM IV              | 2 (0-16)            | 6 (0-39)             | <0.001  |
| pSOFA                 | 2 (0-9)             | 4.5 (0-13)           | <0.001  |

Data are presented as median (minimum-maximum). Comparisons between groups were performed using the Mann-Whitney U test. RDW: Red cell distribution width, MPV: Mean platelet volume, CRP: C-reactive protein, PRISM IV: Pediatric Risk of Mortality IV, pSOFA: Pediatric Sequential Organ Failure Assessment

**Table 3.** Correlation of biomarkers with PRISM IV and pSOFA scores

|                          | r-value | p-value |
|--------------------------|---------|---------|
| RDW - PRISM IV           | 0.49    | <0.001  |
| RDW - pSOFA              | 0.53    | <0.001  |
| MPV - PRISM IV           | 0.31    | <0.001  |
| MPV - pSOFA              | 0.33    | <0.001  |
| CRP - PRISM IV           | 0.73    | <0.001  |
| CRP - pSOFA              | 0.79    | <0.001  |
| Procalcitonin - PRISM IV | 0.79    | <0.001  |
| Procalcitonin - pSOFA    | 0.87    | <0.001  |
| Lactate - PRISM IV       | 0.62    | <0.001  |
| Lactate - pSOFA          | 0.64    | <0.001  |

Note: r-value = Spearman's correlation coefficient. PRISM IV: Pediatric Risk of Mortality IV, pSOFA: Pediatric Sequential Organ Failure Assessment, RDW: Red cell distribution width, MPV: Mean platelet volume, CRP: C-reactive protein

**Table 4.** Results of ROC analysis in predicting 28-day mortality

|                        | AUC (95% CI)     | Cut-off     | Sensitivity (%) | Specificity (%) |
|------------------------|------------------|-------------|-----------------|-----------------|
| CRP (mg/L)             | 0.98 (0.96-1.00) | $\geq 88.5$ | 95.5            | 92.8            |
| RDW (%)                | 0.85 (0.75-0.92) | $\geq 14.7$ | 90.9            | 65.6            |
| MPV (fL)               | 0.73 (0.62-0.82) | $\geq 10.7$ | 77.3            | 64.3            |
| Procalcitonin (ng/mL)  | 0.87 (0.76-0.96) | $\geq 6.05$ | 72.7            | 92.8            |
| Lactate (mmol/L)       | 0.99 (0.99-1.00) | $\geq 3.20$ | 100.0           | 97.3            |
| PRISM IV               | 0.82 (0.69-0.93) | $\geq 9$    | 72.7            | 83.7            |
| pSOFA                  | 0.89 (0.79-0.97) | $\geq 7$    | 77.3            | 94.1            |
| RDW+CRP+MPV (combined) | 0.99 (0.97-1.00) | -           | -               | -               |

Optimal cut-off values were determined using the Youden index. ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval, CRP: C-reactive protein, MPV: Mean platelet volume, RDW: Red cell distribution width, PRISM IV: Pediatric Risk of Mortality IV, pSOFA: Pediatric Sequential Organ Failure Assessment

**Table 5.** ROC analysis of biomarkers for predicting 28-day mortality according to age groups

| Age groups                  |                        | AUC (95% CI)     | Cut-off | Sensitivity (%) | Specitifiity (%) |
|-----------------------------|------------------------|------------------|---------|-----------------|------------------|
| <b>&lt;12 months (n=77)</b> | RDW (%)                | 0.81 (0.63-0.95) | ≥15.2   | 72.7            | 87.9             |
|                             | CRP (mg/L)             | 1.00 (0.98-1.00) | ≥98.7   | 100.0           | 97.0             |
|                             | MPV (fL)               | 0.62 (0.45-0.78) | ≥10.6   | 81.8            | 43.9             |
|                             | Combined (RDW+CRP+MPV) | 1.00 (1.00-1.00) | -       | -               | -                |
| <b>≥12 months (n=166)</b>   | RDW (%)                | 0.87 (0.79-0.95) | ≥14.7   | 100.0           | 67.7             |
|                             | CRP (mg/L)             | 0.98 (0.93-1.00) | ≥88.5   | 90.9            | 92.9             |
|                             | MPV (fL)               | 0.78 (0.60-0.91) | ≥10.8   | 81.8            | 74.2             |
|                             | Combined (RDW+CRP+MPV) | 0.99 (0.96-1.00) | -       | -               | -                |

ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval, CRP: C-reactive protein, MPV: Mean platelet volume, RDW: Red cell distribution width

**Table 6.** Comparison of admission biomarkers and severity scores according to 28-day mortality

| Variable              | Survivors (n=221), median (min-max) | Deaths (n=22), median (min-max) | p-value |
|-----------------------|-------------------------------------|---------------------------------|---------|
| RDW (%)               | 14.30 (12.40-16.70)                 | 15.50 (13.60-17.40)             | <0.001  |
| MPV (fL)              | 10.50 (9.10-12.00)                  | 10.80 (10.00-12.40)             | <0.001  |
| CRP (mg/L)            | 43.90 (3.00-123.50)                 | 139.70 (67.90-249.60)           | <0.001  |
| Procalcitonin (ng/mL) | 3.01 (0.76-7.67)                    | 7.18 (1.96-12.50)               | <0.001  |
| Lactate (mmol/L)      | 1.60 (0.50-5.20)                    | 4.90 (3.20-7.30)                | <0.001  |
| PRISM IV              | 3.00 (0.00-21.00)                   | 12.50 (0.00-39.00)              | <0.001  |
| pSOFA                 | 2.00 (0.00-9.00)                    | 8.00 (1.00-13.00)               | <0.001  |

Continuous variables were compared between the sepsis and septic shock groups using the Mann-Whitney U test and are presented as median (interquartile range) (p<0.01)  
RDW: Red cell distribution width, MPV: Mean platelet volume, CRP: C-reactive protein, PRISM IV: Pediatric Risk of Mortality IV, pSOFA: Pediatric Sequential Organ Failure Assessment

more consistent and robust prognostic marker than MPV. Furthermore, combining these biomarkers significantly improved diagnostic performance, and their predictive value varied according to patient age.

Sepsis and septic shock remain major causes of morbidity and mortality in both pediatric and adult populations, particularly when diagnosis and treatment are delayed. Consequently, there is a growing need for readily available, inexpensive biomarkers capable of identifying disease severity at an early stage (6). Although prognostic scoring systems such as PRISM IV and pSOFA are widely used in clinical practice, their calculation requires numerous clinical and laboratory variables and may therefore be time-consuming. In this context, evaluating the prognostic value of parameters routinely obtained from complete blood count analysis and acute-phase reactants is of considerable clinical importance.

In our cohort, lactate and CRP demonstrated the highest AUC values among the individual biomarkers for predicting 28-day mortality. Notably, the combined model incorporating RDW, CRP, and MPV achieved a discriminative performance comparable to that of lactate alone. As lactate is a direct indicator of tissue hypoperfusion and cellular metabolic

stress, its strong association with mortality during the early stages of septic shock is biologically plausible. However, lactate measurement may not be readily available in all healthcare settings, particularly in secondary-care hospitals. Our findings suggest that routinely available laboratory parameters may provide comparable prognostic information, thereby facilitating early risk assessment in resource-limited settings.

Previous pediatric studies have demonstrated that CRP reflects the severity of systemic inflammation and is associated with mortality in patients with sepsis and septic shock (7). The significantly elevated CRP levels observed in patients with septic shock in our study further support its role as a marker of systemic inflammatory response, consistent with previous reviews evaluating biomarkers in sepsis (8).

Procalcitonin is one of the most extensively investigated biomarkers for the diagnosis and risk stratification of bacterial infections and sepsis (9). Numerous studies have demonstrated that elevated procalcitonin concentrations correlate with the presence of systemic infection, greater disease severity, and increased mortality risk (10). Furthermore, elevated procalcitonin levels at clinical

presentation have been associated with intensive care admission and adverse clinical outcomes across various infectious diseases, particularly community-acquired pneumonia (11). Consistent with these reports, procalcitonin levels were significantly elevated in patients with septic shock compared to those with sepsis in our cohort, and ROC curve analysis demonstrated strong discriminative performance for 28-day mortality. While these findings highlight the utility of procalcitonin as a marker of disease severity and short-term prognosis in critically ill children, prospective case-control studies are required to directly evaluate and compare its baseline diagnostic sensitivity relative to CRP and hematological indices.

RDW has recently emerged as an indirect marker of inflammation, oxidative stress, and bone marrow dysfunction (12). In our study, RDW demonstrated significant positive correlations with both PRISM IV and pSOFA scores and showed superior predictive performance for mortality compared with MPV (AUC: 0.85 vs. 0.73). These findings suggest that RDW may represent a more reliable prognostic biomarker than MPV in pediatric sepsis. Although several studies have reported an association between RDW and mortality in adult patients with sepsis (13,14), evidence in pediatric populations remains limited. Our findings, therefore, provide additional support for the use of RDW as an inexpensive, readily available biomarker reflecting disease severity and mortality in pediatric sepsis and septic shock.

MPV is considered a marker of platelet activation and systemic inflammatory response and is therefore biologically relevant in the pathophysiology of sepsis, in which platelets contribute to inflammation, microvascular thrombosis, and endothelial injury (15). In the present study, MPV demonstrated statistically significant but relatively weak correlations with PRISM IV and pSOFA scores ( $r=0.31-0.33$ ) and showed the lowest discriminative ability for predicting mortality (AUC: 0.73). These findings indicate that the prognostic value of MPV alone may be limited. The dynamic nature of platelet activation and peripheral platelet consumption during sepsis may explain the greater biological variability of MPV compared with RDW and CRP. Accordingly, MPV appears to be more informative when interpreted in combination with other inflammatory biomarkers rather than as an isolated parameter.

Age-stratified subgroup analyses provided additional exploratory insights in our study. Among patients younger than 12 months, CRP demonstrated high discriminative performance, which may reflect the relatively pronounced acute-phase response during infancy. Conversely, the lower performance of MPV in this age group might be related to the immaturity of the hematopoietic system and age-dependent differences in platelet kinetics. In children aged  $\geq 12$  months, the discriminative performance of RDW and MPV appeared to improve, potentially aligning

with the progressive maturation of erythropoietic and thrombopoietic functions with age. However, given the limited number of outcome events within these age subgroups, these findings—and the potential utility of age-specific cut-off values—should be interpreted with caution and regarded primarily as hypothesis-generating, warranting further validation in larger cohorts (16).

The excellent AUC values obtained from the combined RDW, CRP, and MPV model indicate that the simultaneous assessment of these biomarkers provides superior predictive performance compared with their individual use. Similar findings have been reported in previous studies investigating multimarker approaches (17,18). From a practical perspective, this finding suggests that disease severity and mortality may be predicted with high accuracy using only routinely available laboratory parameters, thereby facilitating early clinical risk stratification without requiring complex or costly investigations.

### Study Limitations

Several limitations of this study should be acknowledged. First, the retrospective, single-center design may limit the generalizability of our findings to broader pediatric populations. Second, because only laboratory values obtained at PICU admission were analyzed, dynamic changes and temporal trends in biomarker levels during the clinical course could not be evaluated. Third, as the primary objective of this study was early risk stratification among critically ill children with sepsis requiring intensive care, an independent control group consisting of healthy children or patients with non-septic mild infections was not included. Consequently, the diagnostic specificity of the evaluated biomarkers could not be fully assessed. Finally, the combined model analysis in patients younger than 12 months and the ROC analyses for disease were exploratory in nature because of the limited number of outcome events. In this study, the “International Pediatric Sepsis Consensus Conference” criteria were used for the diagnosis of sepsis and septic shock. However, while the study was ongoing, a new study was also planned using the new “Phoenix” diagnostic criteria published in 2024. Nevertheless, we believe that our study makes a meaningful contribution to the existing literature by demonstrating strong associations between inexpensive, routinely available biomarkers and validated clinical severity scores in a homogeneous pediatric intensive care population.

### Future Research

In light of the present findings and the limitations identified, future investigations should focus on larger, multicenter prospective cohort studies to validate these results. New studies should be conducted using the Phoenix diagnostic criteria published in 2024. Serial assessment of biomarker kinetics throughout the PICU stay may provide a more dynamic approach to predicting treatment response and

clinical outcomes. In addition, studies incorporating well-defined control groups are needed to further establish the diagnostic specificity of these biomarkers. Finally, combined biomarker models and age-specific cut-off values, particularly for vulnerable populations such as infants, should be externally validated in independent pediatric cohorts before being incorporated into routine clinical practice.

## Conclusion

This study demonstrates that RDW, CRP, MPV, procalcitonin, and lactate are readily available and cost-effective biomarkers associated with disease severity and 28-day mortality in pediatric sepsis and septic shock. Among the individual biomarkers evaluated, procalcitonin, lactate, and CRP exhibited the strongest discriminative performance, whereas RDW proved to be a more consistent prognostic marker than MPV. Moreover, the combined assessment of RDW, CRP, and MPV provided superior discriminative performance compared with the use of each biomarker individually.

From a clinical perspective, the combined application of these biomarkers using age-specific cut-off values may facilitate early risk stratification in pediatric patients with sepsis and septic shock. Nevertheless, these findings should be confirmed by large-scale, prospective, multicenter studies, particularly those including a greater number of patients with disease, to further validate the clinical utility and generalizability of these biomarkers. This study does not establish diagnostic accuracy for sepsis or the value of serial biomarker monitoring, and the reported prognostic findings require validation in larger, prospective, multicenter cohorts.

### Ethics

**Ethics Committee Approval:** The study protocol was approved by the Clinical Research Ethics Committee of the University of Health Sciences, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital (protocol no. 2017/122; decision no. 2017/01-03, date: 26.01.2017).

**Informed Consent:** Retrospective study.

### Footnotes

#### Authorship Contributions

Surgical and Medical Practices: F.S., Ö.S., G.A., E.S., Concept: F.S., H.A., Design: F.S., H.A., Data Collection or Processing: F.S., Analysis or Interpretation: G.C., G.A., Literature Search: G.C., Ö.S., G.A., Writing: F.S.

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