Increased mean platelet volume in children with sepsis as a predictor of mortality

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Our aim is to investigate the correlation between the mean platelet volume (MPV) levels and platelet counts of the septic children with 28-day mortality risk. MPV at admission (MPV_{adm}), MPV at 72nd hour (MPV_{72h}) and the difference between these two parameters ($\Delta MPV_{72h\text{-}adm}$) and platelet counts were recorded retrospectively. The control group consisted of 100 healthy children matched for age, gender, and ethnicity. One hundred eighty six children were enrolled into the study. The study group had significant higher MPV values than those of control group. There were 156 survivors and 32 nonsurvivors in study group with a mortality rate of 17%. Nonsurvivors had significantly higher MPV_{adm} (p: 0.001), MPV_{72h} (p: 0.001), $\Delta MPV_{72h\text{-}adm}$ (p<0.001) and lower platelet count (p: 0.002) than survivors. MPV_{adm} (OR 2.39), MPV_{72h} (OR 4.23), $\Delta MPV_{72h\text{-}adm}$ (OR 6.4), platelet count (OR 7.3), and need for mechanical ventilation support (OR 9.76) had significant effect on 28-day mortality risk at logistic regression analysis. At the receiver operating characteristic analysis (ROC) the cutoff values for MPV_{adm}, MPV_{72h}, and $\Delta MPV_{72h\text{-}adm}$ were found to be 9 fL, 9.86 fL, and 0.79, respectively. Kaplan-Meier analysis and log-rank test proved that these cutoff values were significantly associated with the time of survival. Septic children who had high MPV levels at admission and whose MPV levels increased during follow up had higher risk of mortality. With the results of further researches targetting large groups of pediatric patients, MPV_{adm}, MPV_{72h}, and $\Delta MPV_{72h\text{-}adm}$ values can be fast and reliable markers for early diagnosis of sepsis and mortality prediction.

Key words: mean platelet volume, sepsis, mortality, child.

Platelets are the main component of the blood. They play a major role in physiological and pathological processes, such as coagulation, thrombosis, inflammation, and maintaining the integrity of vascular endothelial cells[1]. Inflammation associated endothelial dysfunction is one of the causes of organ failure and it is related with platelet activation and consumption. According to this relation, changes in platelet counts have been reported to be closely associated with the prognosis of critically ill patients[2-4].

Inflammatory and thrombotic conditions may change platelet sizes. Mean platelet volume (MPV) is the most commonly used platelet indice and is routinely measured in the complete blood count by the automatic analyzer. MPV is the ratio of plateletcrit to platelet count and is measured in femtoliters[5]. Larger platelets are more reactive than smaller ones, as they can more easily release chemical mediators in response to endogenous or exogenous stimuli [6-8]. Therefore, several studies have reported that alteration of MPV levels is associated with morbidity and mortality in patients with various disease[9-14]. However especially in childhood, only a few study have revealed the relationship between MPV and early diagnosis[15-22] or mortality[23-25] of sepsis.

Besides, all of these studies were performed in neonatal period.

Sepsis, severe sepsis and/or septic shock are major healthcare problems affecting millions of children worldwide each year[26]. Mortality rate of the sepsis cases are 6-8% who were admitted to pediatric intensive care unit (PICU), depending on the severity of the illness and organ failure[26, 27]. Therefore, it will be very useful to detect the risk of mortality associated with sepsis, with an inexpensive, fast and reliable test. In this retrospective study we investigated platelet count, MPV value at admission (MPV_{adm}), MPV value at 72th hour (MPV_{72h}), difference of MPV values at admission and 72th hour ($\Delta MPV_{72h-adm}$) and the relation of these values with the 28-day mortality rates.

Material and Methods

Hospital Settings, Patients and Study Design

Dr. Behçet Uz Children's Research and Training Hospital, Pediatric Intensive Care is a tertiary unit with 30 beds, serving 1,100 patients annually. Patients who were admitted to our PICU with sepsis and stayed more than 72 hours between January 2012 and January 2016 were enrolled into our study.

Table I. Comparison of Demographic, Clinical and Laboratory Variables between Survivors and Non-survivors.

Variables	Total (n=188)	Survivors (n=156)	Non-survivors (n=32)	p
Age, month (median, IQR, min-max)	50, 68.6, 3-162.5	50, 65, 3-162	56, 75, 4.5-129	0.65
Gender (female, n/%; male, n/%)	102/54.3; 86/45.7	84/53.8; 72/46.2	18/56.3; 14/43.8	0.85
PRISM 3 score (median, IQR, min-max)	9, 9, 2-49	8, 5, 2-17	25,12, 17-49	<0.001*
PELOD score (median, IQR, min-max)	11, 3, 1-42	10, 6, 1-20	30, 9, 20-42	<0.001*
Comorbidities (n/%)				
None	74/39.4	57/36.5	4/12.5	0.008*
Cerebral palsy	33/17,6	28/17.9	10/31.3	0.08
Epilepsy	23/12.2	19/12.2	7/21.9	0.16
Chronic lung disease	17/9	17/10.9	1/3.1	0.31
Congenital cardiopathy	16/8,5	16/10.3	1/3.1	0.31
Metabolic disease	13/6,9	11/7.1	4/12.5	0.29
Genetic syndrome	9/4,8	5/3.2	4/12.5	0.04
Immune deficiency	3/1,6	3/1.9	1/3.1	0.31
Laboratory results				
Hb, gr/dl (mean±SDg)	10.7±1.5	10.7±1.5	10.6±1.5	0.67
WBC, $\times 10^3/\mu L$ (mean±SD)	14.1±7.9	13.8±7.6	15.8±9.1	0.24
CRP, mg/dl (mean±SD)	13.6±12.5	11.8±3.6	22.1±5.7	0.002*
Procalcitonin, ng/ml (median, IQR, min-max)	5, 5.9, 1.1-5.4	4.6, 4.8, 1.1-16	9.9, 9.4, 4.2-54	0.004*
Lactate, mmol/L, (median, IQR, min-max)	1.1, 1, 0.4-4.2	1, 0.8, 0.4-2.2	2.7, 1.2, 1.6-4.2	0.008*
MPV_{adm}, fL (mean±SD)	8.9±1.02	8.7±0.97	9.6±0.94	0.001*
MPV_{72h}, fL (mean±SD)	9.5±1.09	9.3±0.97	10.7±0.92	0.001*
$\Delta MPV_{72h-adm,}$ fL (mean±SD)	0.59±0.37	0.5±0.2	1.03±0.5	<0.001*
Platelet count, $\times 10^3/\mu L$ (mean±SD)	268.3±89.5	286.6±87.1	179.1±21.8	0.002*
Secondary outcomes				
Mechanical ventilation (n/%)	58/30.9	29/18.6	29/90.6	<0.001*
PICU LOS, day (median, IQR, min-max)	15, 14, 2-32	17, 15, 7-32	7, 10, 2-26	<0.001*

*: $p<0.05$

IQR: interquartile range; PRISM 3: pediatric risc of mortality 3; PELOD: pediatric logistic organ dysfunction; Hb: hemoglobin; SD: standard deviation; WBC: white blood cell; CRP: C reactive protein; MPVadm: mean platelet volume at admission; MPV72h: mean platelet volume at 72th hour; ΔMPV72h-adm: difference of mean platelet volume at admission and 72th hour; PICU LOS: pediatric intensive care unit length of stay.

Children who had obesity, hyperlipidemia, diabetes mellitus, hypertension, hypothyroidism, chronic renal failure, nephrotic syndrome, inflammatory bowel disease, connective tissue disorders, malignity or previously known hematologic diseases were excluded from our study as it was previously reported that these diseases affected MPV values[8, 14, 28]. Septic shock or severe sepsis cases and the patients who died or received platelet transfusion in the first 72 hours of admission were also excluded.

Sepsis is defined as the presence (probable or documented) of infection together with systemic manifestations of infection[29, 30].

The presence of two or more of the following criteria (one of which must be abnormal temperature or leukocyte count) defines systemic inflammatory response syndrome (SIRS) [31]:

- Core temperature (measured by rectal, bladder, oral, or central probe) of > 38.5°C or < 36°C.

- Tachycardia, defined as a mean heart rate more than two standard deviations above normal for age; or for children younger than one year of age, bradycardia defined as a mean heart rate < 10th percentile for age.

- Mean respiratory rate more than two standard deviations above normal for age or mechanical ventilation for an acute pulmonary process without neuromuscular disease or general anesthesia.

- Leukocyte count elevated or depressed for age, or > 10% immature neutrophils, without chemotherapy induced leukopenia.

The control group consisted of 100 healthy children matched for age, gender, and ethnicity. One hundred healthy children without any chronic diseases who were referred to our hospital for general medical examination, were chosen as the control group.

Institutional Ethical Committee approved the study (No: 2015/02-05).

Data Collection

Demographic data and comorbidities (underlying diseases) of the patients were recorded. Pediatric risk of mortality 3 (PRISM 3) scores were acquired via using the worst values during the first 24 hours. Following criteria were used to calculate PRISM 3 score[32]:

Systolic blood pressure, body temperature, Glasgow coma score, heart rate, pupillary reflexes, parameters of blood gas, plasma glucose, potassium, blood urea nitrogen, creatinine, white blood cell (WBC) count, platelet count, prothrombin time and activated partial thromboplastin time.

Pediatric logistic organ dysfunction (PELOD) scores of the patients which were used to determine the organ failure recorded. Following criteria were used to calculate PELOD score[33]:

Systolic blood pressure, Glasgow coma score, pupillary reflexes, heart rate, parameters of blood gas, need for mechanical ventilation, plasma creatinine, WBC, platelet count, prothrombin time and aspartate aminotransferase levels.

We have also recorded hemoglobin (Hb), C reactive protein (CRP), procalcitonin, lactate levels. We measured the MPV values at admission (MPV_{adm}) and at 72th hour (MPV_{72h}). Then we calculated the difference between them ($\Delta MPV_{72h\text{-}adm}$). In additon, need for mechanical ventilation and the length of stay in PICU were also assessed.

Table II. Multivariate Logistic Regression Analysis for the Prediction of 28-day Mortality.

Variables	p value	Odds Ratio	95% Confidence Interval
MPV_{adm} (fL)	0.003	2.39	1.5-3.6
MPV_{72h} (fL)	<0.001	4.23	2.5-17.06
$\Delta MPV_{72h\text{-}adm}$ (fL)	<0.001	6.4	5.9-187.1
Platelet count ($\times 10^3/\mu L$)	0.001	7.3	4.8-34.7
Mechanical ventilation need	<0.001	9.76	8.1-55.3

MPV adm: mean platelet volume at admission
MPV 72h: mean platelet volume at 72nd hour
$\Delta MPV_{72h\text{-}adm}$: difference of mean platelet volume at admission and 72nd hour

Data were acquired from patient files and electronic hospital data management system.

Laboratory analyses

Venous blood samples for laboratory tests were collected from all patients in tubes containing ethylenediamine tetra-acetic acid (EDTA) and analysed with a Beckman Coulter LH 780 hematology analyser [The Advanced Medical Technology Association (AdvaMed), USA] within maximum 1 hour of sample collection. The reference range for MPV was between 7.4 and 10.4 fL.

Statistical analysis

All variables were assessed with descriptive statistics. The normality of data distribution was checked with the Kolmogorov-Smirnov test and the graphics. Continuous variables were expressed as mean ± standart deviation (SD) or median, interquartile range (IQR), minimum and maximum values according to normal or abnormal distributions. Categorical variables were presented as absolute values and percentages. Demographic data and MPV values of control group consisted of 100 cases were analyzed. Patients were divided into 2 groups: Survivors and nonsurvivors (for 28th day mortality). The demographic, clinical and laboratory variables were compared between the two groups. Differences in continuous variables were evaluated by the Mann-Whitney U test and unpaired Student t test, where appropriate. Categorical variables were compared using the Chi-square test. The correlations between the [MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$, platelet count] with [PRISM 3 score, PELOD score, WBC, CRP, procalcitonin, lactate] were analysed by Spearman's correlation test. For the multivariate analysis, possible factors identified with univariate analyses were further entered into the logistic regression analysis (stepwise forward) to determine independent predictors of 28-day mortality. "Hosmer-Lemeshow goodness of fit" statistics were used to assess logistic regression model fit. Receiver operating characteristic (ROC) curve analysis was performed to show the utility of the MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$, Plt_{adm}, Plt_{72h}, $\Delta Plt_{adm\text{-}72h}$ for 28-day mortality. Survival functions, according to the optimal cutoff values of the MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$, were estimated using the Kaplan-Meier method and the outcomes were compared using the log-rank test. For all tests, a p value < 0.05 was considered statistically significant. All analyses were performed using SPSS version 15.0 statistical software program (SPSS Inc., Chicago, Ilinois).

Results

The study group comprised 86 boys and 102 girls with a median age of 50 months. The control group consisted of 44 boys 56 girls with a median age of 47 months. The age and gender distribution was not different between two groups (p: 0.82). The mean MPV level of the study group at admission was higher then that of the control group (8.9±1.02 fL vs 7.9±0.9 fL; p:0.004). The mean platelet count of the study group was lower than that of the control group (268.3±89.5×$10^3/\mu$L vs 302.4±74.1×$10^3/\mu$L; p: 0.002). There were 156 survivors and 32 nonsurvivors, with a mortality rate of 17%. There was no difference between age and gender distribution of survivor and

Table III. Correlation between MPV_{adm}, $MPV_{72h,}$ $\Delta MPV_{72h\text{-}adm.}$, Platelet Counts and All Numeric Variables.

Variables	MPV_{adm}		MPV_{72h}		$\Delta MPV_{72h\text{-}adm}$		Platelet count	
	r	p	r	p	r	p	r	p
PRISM 3 score	0.172	0.01	0.32	<0.001	0.48	<0.001	-0.37	<0.001
PELOD [b] score	0.29	<0.001	0.41	<0.001	0.43	<0.001	-0.32	<0.001
WBC [c] (×$10^3/\mu$L)	0.42	0.05	0.07	0.3	0.06	0.4	-0.05	0.45
CRP [d] (mg/dl)	0.28	<0.001	0.38	<0.001	0.37	<0.001	-0.37	<0.001
Procalcitonin (ng/ml)	0.15	0.03	0.19	0.008	0.41	0.005	-0.27	<0.001
Lactate (mmol/l)	0.23	0.001	0.34	<0.001	0.42	<0.001	-0.31	<0.001

CRP: C reactive protein; PELOD: pediatric logistic organ dysfunction; PRISM: pediatric risk of mortality; MPV_{adm}: mean platelet volume at admission; MPV_{72h}: mean platelet volume at 72nd hour; $\Delta MPV_{72h\text{-}adm.}$: difference of mean platelet volume at admission and 72nd hour; WBC: white blood cells

nonsurvivor groups (p: 0.65, p: 0.85). However, nonsurvivors group had higher comorbidity rates and higher PRISM 3 and PELOD scores (p:0.008; p<0.001; p<0.001). According to laboratory parameters, nonsurvivors had significantly higher CRP, procalcitonin, lactate, MPV_{adm} (9.6±0.94 vs 8.7±0.97 fL; p:0.001), MPV_{72h} (10.7±0.92 vs 9.3±0.97 fL; p:0.001), and $\Delta MPV_{72h\text{-}adm}$ (1.03±0.5 vs 0.5±0.2 fL; p<0.001) values than those of survivors. In contrast, the platelet count (179.1±21.8 vs 286.6±87.1×$10^3/\mu$L; p:0.002) was significantly lower in nonsurvivors than in survivors and nonsurvivors had high rate of mechanical ventilation support. (p<0.001; Table I).

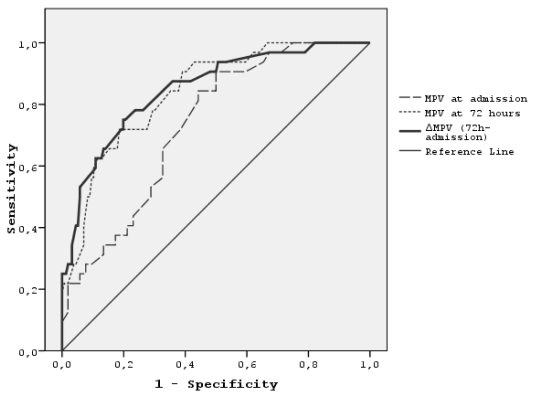


Fig. 1. Receiver operating characteristic curve for MPV values to predict 28-day mortality. Areas under the curve for MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$, are 0.73 (95%CI: 0.64-0.81), 0.81 (95%CI: 0.77-0.90) and 0.85 (95%CI: 0.77-0.92); respectively. The cutoff values for MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$, are 9 fL, (sensitivity 72%, specificity 61.5%); 9.86 fL, (sensitivity 78%, specificity 70.5%) and 0.79 (sensitivity 72%, specificity 80.8%); respectively.
CI: confidence interval; MPV_{adm}: mean platelet volume at admission; MPV_{72h}: mean platelet volume at 72nd hour; $\Delta MPV_{72h\text{-}adm}$: difference of mean platelet volume at admission and 72nd hour

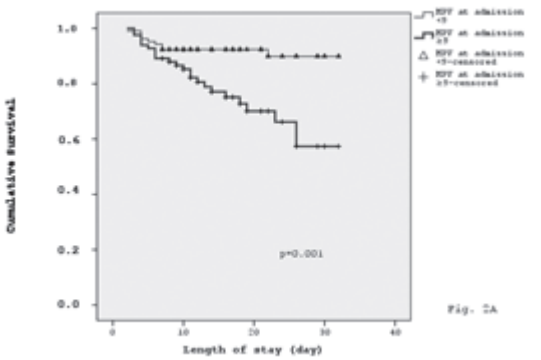
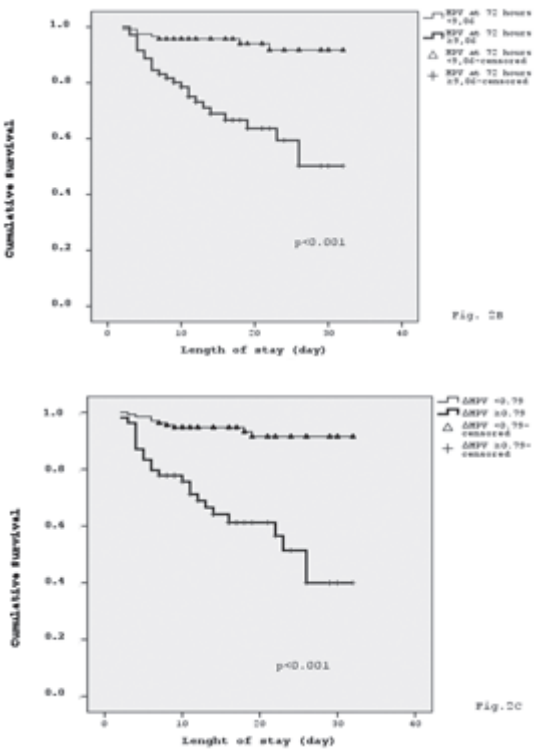


Fig. 2. Kaplan-Meier survival curves for patients with (2A) MPV_{adm} less than 9fL and ≥ 9fL (p: 0.001 with log-rank test); (2B) MPV_{72h} less than 9.86 fL and ≥9.86 fL (p<0.001with log-rank test); and (2C) $\Delta MPV_{72h\text{-}adm}$ less than 0.79 fL and ≥0.79 fL (p<0.001with log-rank test). MPV_{adm}: mean platelet volume at admission; MPV_{72h}: mean platelet volume at 72nd hour; $\Delta MPV_{72h\text{-}adm}$: difference of mean platelet volume at admission and 72nd hour

Comorbidity, need for mechanical ventilation support, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$ and platelet count variables were added to the multivariate logistic regression model via forward stepwise technique. As a conclusion MPV_{adm} (OR 2.39), MPV_{72h} (OR 4.23), $\Delta MPV_{72h\text{-}adm}$ (OR 6.4), platelet count (OR 7.3), and need for mechanical ventilation support (OR 9.76), had a significant effect on 28-day mortality risk. $\Delta MPV_{72h\text{-}adm}$ had the highest odds ratio in all platelet indices (Table II). All tests for Hosmer-Lemeshow goodness of fit were statistically significant. Presence of comorbidity had no significant effect on 28-day mortality risk (p: 0.45; OR 0.62; 95%CI 0.38-1.77).

ROC analysis was performed to predict 28-day mortality and the results showed that areas under the ROC curve for MPV_{adm}, MPV_{72h}, and $\Delta MPV_{72h\text{-}adm}$, Plt_{adm}, Plt_{72h}, $\Delta Plt_{adm\text{-}72h}$ were



0.73 (95%CI: 0.64-0.81), 0.81 (95%CI: 0.77-0.90), 0.85 (95%CI: 0.77-0.92), 0.76 (95%CI: 0.62-0.91), 0.84 (95%CI: 0.79-0.88) and 0.82 (95%CI: 0.79-0.93), respectively. The cutoff values for MPV_{adm}, Plt_{adm}; MPV_{72h}, Plt_{72h}; $\Delta MPV_{72h\text{-}adm}$, $\Delta Plt_{adm\text{-}72h}$ were 9 fL, $194\times10^3/\mu L$ (sensitivity 72%, specificity 61.5%), 9.86 fL, $159\times10^3/\mu L$ (sensitivity 78%, specificity 70.5%), and 0.79 fL, $21\times10^3/\mu L$ (sensitivity 72%, specificity 80.8%), respectively (Fig. 1).

Correlation analysis was performed between MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm,}$ platelet count, WBC, CRP, procalcitonin and lactate levels with PRISM 3 and PELOD scores. Low or medium grade positive significant correlation was found between MPV values and all numerical variables except WBC. For MPV measurements the highest correlation was found at $\Delta MPV_{72h\text{-}adm}$ value. Low or medium grade negative significant correlation was found between platelet count and PRISM 3 score, PELOD score, CRP, procalcitonin and lactate levels (Table III).

In order to determine the effects of cutoff values calculated by ROC analysis of MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$ variables on survey, Kaplan-Meier analysis was performed.

Owing to log-rank test, MPV_{adm} greater than or equal to 9 fL, MPV_{72h} greater than or equal to 9.86 fL and $\Delta MPV_{72h\text{-}adm}$ greater than or equal to 0.79 fL were significantly associated with the time of survival (Fig. 2).

Discussion

In the present study, we have evaluated the relevance of platelet count and platelet indices, particularly MPV, on mortality of children with sepsis. Our results indicated that patients who had high MPV values both at admission and at 72th hour, higher $\Delta MPV_{72h\text{-}adm}$, and low platelet count had higher mortality risk. In additon, compared with the control group, our study group had higher MPV_{adm} and lower platelet count.

Platelet indices are a group of measurements used to determine the count and morphology of platelets. Under physiological conditions, the amount of platelets in blood can be maintained in an equilibrium state by regeneration and elimination. Therefore, both the number of platelets and their morphology stays relatively constant. Under pathophysiological conditions, any factor which could inhibit platelet regeneration, increase their activation or accelerate their death once overwhelming the capacity of self-regulation will cause changes in both platelet count and morphology and thus results in a change in platelet indices[34]. Researches demonstrated that the activation of the coagulation system, thrombotic diseases and inflammatory conditions can change platelet indices. One of the independent risk factor for ICU patients is the decrease in the platelet count[4]. MPV is a measure of the volume of platelets and when platelet consumption increases, the bone marrow produces more immature platelets. This causes an increase in MPV value[34]. There are few studies in adults stating that increase in the MPV level is correlated with the severity of the illness[35]. Therefore, not only the platelet counts but the MPV is also tought to be a good marker of prognosis and survey of the patient.

A study including 1,556 adults, made by Zhang et al.,[34] showed that platelet distribution width (PDW) ≥17% and MPV ≥11.3 fL is an independent risk factor for mortality. However, the study group was heterogenous because all patients in ICU were enrolled into the study[5]. Similarly, another study, with 361 critical patients, showed that low platelet count, high MPV, and high PDW were related with more severe disease and high risk of mortality. However, a spesific disease was not targetted; and it was not possible to differentiate the causative disease affecting the platelet indices[34]. One of the studies focusing on sepsis, septic shock and severe sepsis found $\Delta MPV_{72h\text{-}adm}$; and another one found PDW as an independent risk factor for mortality[36, 37]. Besides, the mortality risk at sepsis, severe sepsis and septic shock are not the same and these two studies did not specify the distribution of these diseases in survivors and nonsurvivors groups. Thus it was not possible to say platelet indices are effective on mortality alone. In our study, PDW was not included in the evaluation and it was aimed to investigate only the relation of MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$ parameters with mortality. Ates et al.[38] found MPV and MPV/PLT ratio higher in patients with sepsis and SIRS than those of the control group. Gao et al.[39] stated that MPV may be the most useful prognostic forecaster platelet indice,

because they found that MPV was higher in nonsurvivors group of septic shock patients.

In our study we have focused on MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$ instead of all platelet indices and only sepsis cases were investigated. In univariate analyses, similar to the literature, non survivors group had higher PRISM 3 and PELOD scores, MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$, CRP, WBC, procalcitonin and lactate levels, compared to those of the survivors group. In addition, comorbidity and mechanical ventilation use were higher than those of nonsurvivors group. Conversely platelet count was lower than survivors group. In the multivariate logistic regression analysis MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$, platelet count and mechanical ventilation support were identified as independent risk factors for 28-day mortality.

PRISM 3, PELOD scores, CRP, WBC, procalcitonin and lactate levels were higher in the nonsurvivors group by univariate analysis. All numeric variables, except WBC count, had a mild or moderate significant positive corrrelation with platelet indices. Detected correlation between platelet count was negative. Our results were compatible with the literature[36]. PRISM 3 and PELOD scores, which had been used to predict the mortality and organ dysfunction, were correlated with platelet indices and this correlation supported our hypothese. $\Delta MPV_{72h\text{-}adm}$ had the strongest correlation with platelet indices. There are studies in adults, and neonates supporting our study, which report that MPV increases in repetitive measurements in sepsis, septic shock, and critical patients. They also stated that the group with higher increase had higher risk of mortality[13, 24, 35].

In our study we classified the patients as culture proven, non culture proven groups and we made another classification according to isolated microorganisms. Powerful analyses could not be performed if we have divided into subgroups due to relatively small number of patients because of the inclusion and exclusion criteria. Guida et al.[16] made analyses after grouping the adult patients according to causative agent and they found that patients with gram negative sepsis had lower platelet counts than the patients with gram positive sepsis, however the groups did not differentiate according to MPV values. Similarly, Catal et al.[24] found that platelet indices didn't differentiate between different microorganisms or between culture proven or non-culture proven in preterm infants with sepsis. Also, Akarsu et al.[17] reported that according to causative microorganisms they found no difference in neonates with sepsis. On the other hand, Aydemir et al.[13] found that increased MPV value was more common in adult cases with fungal sepsis.

In our study, ROC analysis showed that highest area under curve (AUC) value (0.85, 95%CI: 0.77-0.92) belongs to $\Delta MPV_{72h\text{-}adm}$. Also AUC levels of MPV_{adm}, and MPV_{72h} were statistically significant (0.73, 95%CI: 0.64-0.81; 0.81, 95%CI: 0.77-0.90, respectively).

We found that patients who had equal or higher MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$ values than 9 fL, 9.86 fL ve 0.79 fL, had significantly shortened length of survival than those with values below. In neonatal studies, the cutoff values of MPV to predict mortality or to diagnose the sepsis early is reported to be between 9.3 fL and 12 fL[21-25].

Adult and pediatric studies commonly suggest that platelet indices are beneficial to predict mortality or to diagnose the sepsis early[37-40]. However numerical data is so variable and our knowledge of the pediatric age group is limited[18, 21, 24]. For this reason further studies with larger numbers which target patients between 1 months-18 years old are required.

Our study has also several limitations. First, this is a retrospective study that inevitably had a risk to introduce selective bias. Second, this is a single-center study; and the results may not be generalizable to other institutions. As the third, due to inclusion and exclusion criteria of this study, we could only enroll limited number of patients. For this reason, detailed subgroup analyses could not be performed.

However, we were able to create a homogeneous group with sepsis diagnose and to exclude the patients who had diagnoses that can effect platelet indices. Besides, we have a control group with similar age and gender distribution, in order to compare the study group by terms of MPV values at admission. Considering that all pediatric studies have targetted only neonates, our study will have a contribution to the literature.

One of the most important cause of mortality

in PICUs is sepsis, and MPV levels were found to be higher whereas platelet counts were found to be lower in these patients when compared to healthy control group. Platelet count measurements such as MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$ had significant effect on mortality in patients with sepsis. We have determined that patients had shorter survival if they had MPV_{adm}, ≥ 9 fL, MPV_{72h}, ≥ 9.86 fL and $\Delta MPV_{72h\text{-}adm}$, ≥ 0.79 fL.

In conclusion, platelet indices are valuable indicators of sepsis severity and effective predictors of mortality. MPV_{adm}, MPV_{72h}, $\Delta MPV_{72h\text{-}adm}$ values could be a fast and reliable marker used for early diagnosis of sepsis and mortality prediction.

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