

# The Incidence of Thrombocytopenia and Its Association with Mortality in Patients with Sepsis Followed in Intensive Care Unit

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## Abstract

**Aim:** Thrombocytopenia is common in intensive care units (ICU) and is associated with high mortality. The aim of this study aimed to determine the incidence of thrombocytopenia in patients diagnosed with sepsis and its relationship with mortality and morbidity.

**Materials and Methods:** This study was conducted in the reanimation ICU of a university hospital. Patients followed and diagnosed with sepsis between January 2014 and January 2018 were collected and the recorded data analyzed retrospectively. Demographic data, comorbidities, disease severity scores, hematological laboratory values, and outcome were recorded. Thrombocytopenia was defined as the platelet count to be less than  $100 \times 10^3/\mu\text{L}$ . Patients were divided into two groups as with or without thrombocytopenia, and statistical analysis was performed.

**Results:** The number of patients followed with the diagnosis of sepsis was 299. The median age of the patients was 68 years, and 62.9% (n=188) was male. The rate of invasive mechanical ventilation was 97.7%. Thrombocytopenia was detected in 36.8% of the patients. The Sequential Organ Failure Assessment score was higher in the thrombocytopenia group ( $p < 0.0001$ ). Additionally, the rate of acute renal failure was 24.1%, which was higher in the thrombocytopenia group ( $p = 0.011$ ). In the thrombocytopenia group, the blood product transfusion rates were higher ( $p = 0.004$ ). Median ICU hospitalization time was 15 (6-28) days. While the total mortality of sepsis patients was 43.1%, this rate was higher in the thrombocytopenia group ( $p = 0.011$ ).

**Conclusion:** Thrombocytopenia, which is commonly seen in ICU's and especially in the septic patients, is thought to be associated with mortality and morbidity.

**Keywords:** Thrombocytopenia, sepsis, intensive care unit, mortality, morbidity

## Introduction

Thrombocytopenia was defined as the platelet count to be less than  $100 \times 10^3/\mu\text{L}$  (1) and is common in intensive care units (ICUs) and closely associated with high mortality. Sometimes, thrombocytopenia may occur due to sepsis. Sepsis is a life-threatening organ dysfunction induced by a dysregulated host response. In septic shock, there is circulatory and cellular metabolic dysfunction (2). The relationship between sepsis-septic shock and thrombocytopenia is known, but the mechanism of thrombocytopenia in sepsis is still unclear (3). This study aimed

to determine the incidence of thrombocytopenia in patients with sepsis in the ICU and its relationship with mortality and morbidity.

## Materials and Methods

This study was conducted in the Anesthesiology and Reanimation ICU of a university hospital. Between January 2014 and January 2018, the data collected from sepsis patients in the ICU were analyzed retrospectively. Demographic data, comorbidities, disease severity scores, some laboratory values, including platelet values, and intensive care results were recorded.



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Thrombocytopenia was defined as the platelet count to be less than  $100 \times 10^3/\mu\text{L}$ . Then, patients were then divided into two groups with or without thrombocytopenia and statistical analysis was performed.

### Statistical Analysis

Data were statistically evaluated using the Statistical Package for the Social Sciences (SPSS) version 22 (SPSS Inc., Chicago, IL, USA) program. Descriptive statistics were performed on the patient group; numerical data were indicated as median (interquartile range), and categorical data as percentages. Later, the patients were divided into two groups as those with and without thrombocytopenia; the characteristics of the patients were compared using the chi-square test for categorical data and the Mann-Whitney U test for numerical data. Logistic regression was applied to find independent risk factors that determine mortality. A p value  $<0.05$  was considered statistically significant.

### Results

In this period, the number of patients followed with the diagnosis of sepsis in the ICU was 299. The median age of the patients was 68 (52-77) years, and 62.9% (n=188) was male. The rate of invasive mechanical ventilation was 97.7%. Thrombocytopenia was detected in 36.8% of sepsis patients. The Sequential Organ Failure Assessment (SOFA) score was higher in the thrombocytopenia group ( $p < 0.0001$ ). The rate of acute renal failure was 24.1%, and this rate was higher in the thrombocytopenia group ( $p = 0.011$ ). The blood product

transfusion rates were higher in the thrombocytopenia group (76.4% vs. 59.3% and  $p = 0.004$ ). White blood cell ( $p = 0.028$ ), procalcitonin ( $p = 0.001$ ), and lactate ( $p = 0.002$ ) levels were significantly higher in the thrombocytopenia group. Median ICU hospitalization time was 15 (6-28) days. While the total mortality of sepsis patients was 43.1%, this rate was higher in the thrombocytopenia group ( $p = 0.011$ ) (Table 1).

Data that were significant in univariate analysis (acute renal failure, blood transfusion, platelets, white blood cell, procalcitonin and lactate) were evaluated in multivariate analysis. The high SOFA score and the development of acute renal failure were independent risk factors for mortality [ $p = 0.001$ , Odds ratio (OR): 1.139, 95% confidence interval (CI): 1.058-1.226 and  $p = 0.001$ , OR: 2.704, 95% CI: 1.541-4.743, respectively] (Table 2).

### Discussion

In this retrospective study, 299 patients with sepsis were admitted to the ICU between 2014 and 2018 were evaluated. Local Ethics Committee approval was taken from the Selçuk University Ethics Committee (no: 2019/02, date: 20.03.2019). The development of thrombocytopenia in sepsis is well known. At the same time, the presence of changes in platelet counts is a common clinical condition in ICU. In a previous review, the incidence of thrombocytopenia was found to be 8.3-67.6% in ICUs (4). 20-50% of patients with sepsis in the ICUs suffer from thrombocytopenia (5-8). The differences in the incidence of thrombocytopenia may be due to differences in the definition of thrombocytopenia

	<b>Total patients n=299 (100%)</b>	<b>Thrombocytopenia group n=110 (36.8%)</b>	<b>Non-thrombocytopenia group n=189 (63.2%)</b>	<b>p value</b>
Age (year)	68 (52-77)	68 (54.7-78)	67 (48-77)	0.382
Gender (male)	188 (62.9%)	67 (60.9%)	121 (64%)	0.234
APACHE 2 score	23 (17-28)	24 (19-29)	22 (16-26)	0.156
SOFA score	10 (8-13)	13 (11-14)	10 (7-11)	<b>&lt;0.0001</b>
Mechanical ventilation	292 (97.7%)	108 (98.2%)	184 (97.4%)	1.000
Acute renal failure	72 (24.1%)	36 (32.7%)	36 (19%)	<b>0.011</b>
Blood transfusion	196 (65.6%)	84 (76.4%)	112 (59.3%)	<b>0.004</b>
<b>Laboratory parameters</b>				
Platelets ( $\times 10^3/\mu\text{L}$ )	130 (73-193)	49.5 (31.5-80)	170 (135-230)	<b>&lt;0.0001</b>
Hemoglobin (g/dL)	8.7 (7.2-10.5)	8.4 (7-10)	8.7 (7.5-11)	0.059
White blood cell ( $\times 10^3/\text{L}$ )	18 (13-27)	20.3 (14-30)	16.7 (12.6-25)	<b>0.028</b>
Procalcitonin (ng/mL)	4.5 (1.1-19.09)	9.8 (2.07-31.9)	3.3 (1-15.2)	<b>0.001</b>
Lactate (mEq/L)	4.4 (3-8.6)	4.8 (3.4-9.8)	3.8 (3-6.8)	<b>0.002</b>
Length of ICU stay (days)	15 (6-28)	16 (7-28)	15 (6-29)	0.774
Mortality	129 (43.1%)	58 (52.7%)	71 (37.6%)	<b>0.011</b>
APACHE 2: Acute Physiologic Assessment and Chronic Health Evaluation 2, SOFA: Sequential Organ Failure Assessment, ICU: Intensive care units				

(9). Some studies defined thrombocytopenia as a platelet count of  $<100 \times 10^3/\mu\text{L}$  and reported that the incidence was 33-36% (10,11). However, a previous study defined thrombocytopenia as a platelet count of  $<150 \times 10^3/\mu\text{L}$  and found that the incidence was 47.6% (9). In our study, thrombocytopenia was defined as the platelet count to be less than  $100 \times 10^3/\mu\text{L}$  and found that the incidence of thrombocytopenia was 36.8%.

Several factors are responsible for tubular lesions in sepsis-related acute kidney injury (AKI), such as metabolic changes, mitochondrial dysfunction, autophagy, and cell cycle arrest (12-15). Additionally, the role of immune response pathways and particularly inflammation in AKI progression is increasingly stressed (16,17). Platelets can also be activated by ischemic blood flow disturbances in the septic kidney, and the rate of acute renal failure was found to be higher in patients with thrombocytopenia (3). In our study, the rate of acute renal failure was 32.7%. Patients with sepsis are prone to the propagation of homeostasis, thrombosis, and bleeding disorders due to injured endothelium (18,19). It is important to know that critically ill patients with thrombocytopenia are prone to bleeding. Various studies have found that patients with thrombocytopenia were more likely to develop major bleeding and received more blood product transfusions (9). In our study, we found that the blood product transfusion rate was higher in the thrombocytopenic group. Because thrombocytopenia causes many undesirable events, patients with thrombocytopenia can be expected to have a longer hospital stay. In our study, the median ICU hospitalization time was 15 (6-28) days, but there was no significance between the two groups ( $p=0.774$ ).

It is shown that thrombocytopenia is associated with poor outcome (4,9,20-23). Platelets are central to coagulation metabolism. Therefore, thrombocytopenia may cause bleeding and/or the need for more blood transfusions. Additionally, platelets contribute to vascular and tissue injury in acute or chronic inflammation (24-26). Many previous studies have show that thrombocytopenia is an independent risk factor for mortality in ICU patients and sepsis was found to be the most common risk factor for thrombocytopenia (27-30). There are several studies on the mortality of patients with thrombocytopenia in ICUs. Strauss et al. (31) found that thrombocytopenia alone was not a predictor of mortality. In another study found that ICU mortality increased significantly

when the initial platelet count was less than  $50 \times 10^3/\mu\text{L}$  (32). Venkata et al. (9) found that thrombocytopenia was associated with a high mortality rate. In a previous study, the overall mortality was found to be 42.5% (33). In our study, we found that overall mortality was 43.1%, which was higher than the non-thrombocytopenic group ( $p=0.011$ ).

**Study Limitations**

There were several limitations to our study. First, this study was a retrospective, single-center study. Second, we did not differentiate sepsis and septic shock. Finally, we evaluated overall mortality not as early and/or long-term mortality.

**Conclusion**

Thrombocytopenia, which is commonly seen in ICUs and particularly in the sepsis patient group, is thought to be associated with mortality and morbidity.

**Ethics**

**Ethics Committee Approval:** The study was approved by the Selçuk University of Local Ethics Committee (no: 2019/02, date: 20.03.2019).

**Informed Consent:** Retrospective study.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions**

Surgical and Medical Practices: Y.Ş.B., İ.K., J.Ç., Concept: A.D., J.Ç., Design: İ.K., A.D., Data Collection or Processing: Y.Ş.B., A.A., H.E., H.H.B., Analysis or Interpretation: İ.K., A.D., Literature Search: Y.Ş.B., A.A., İ.K., Writing: Y.Ş.B., A.A., İ.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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Parameters	p value	OR (95% CI)
SOFA score	0.001	1.139 (1.058-1.226)
Acute renal failure	0.001	2.704 (1.541-4.743)

SOFA: Sequential Organ Failure Assessment, OR: Odds ratio, CI: Confidence interval

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