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# Thrombocytopenia as a Marker of Patient Outcome in Medical Intensive Care Unit

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#### **Abstract**

**Introduction:** Thrombocytopenia is a common hematologic disorder observed in many pathological conditions in critically ill patients. The current study aimed at investigating the prevalence of thrombocytopenia and its relationship with the length of stay and mortality among intensive care unit (ICU) patients.

**Methods:** The current prospective cohort study enrolled 150 patients consecutively admitted to the medical ICU during a nine-month period. Patients' baseline characteristics and underlying diseases were recorded. Laboratory findings and admission mean platelets and platelet counts on the 3rd day of admission were obtained. Patients were divided into thrombocytopenic (platelet count of less than 150×109/L or decrease of platelet to more than 50%) and non-thrombocytopenic groups according to the 3rd day platelet count.

**Results:** Thrombocytopenia was detected in 53(35%) patients while 13 patients (8.6%) had severe thrombocytopenia (platelets count <  $50 \times 109$ /L). ICU stay and mortality were significantly higher in patients with thrombocytopenia compared with non-thrombocytopenic patients ( $16 \pm 2.7$  vs  $12 \pm 2.4$  days, P = 0.01) and (45.5% vs 37.3%, P = 00.1) respectively.

**Conclusions:** Platelet might be considered as a prognosis monitor in ICU settings. Severe thrombocytopenia could be mentioned as a poor prognostic factor for increased mortality and prolonged hospitalization period in ICU patients.

### INTRODUCTION

Thrombocytopenia is a frequent abnormality in intensive care unit (ICU) patients that varies from 13% to 44% [1]. Thrombocytopenia is often multi-factorial and it is not easy to determine the exact cause of thrombocytopenia in ICU. It may cause higher mortality in critically ill patients [2]. Thrombocytopenia is defined as platelet count less than  $150\times10^9$ .L<sup>-1</sup>, but for ICU patients the amount is less than  $100\times10^9$ .L<sup>-1</sup>, and platelet counts less than  $50\times10^9$ .L<sup>-1</sup> is known as severe thrombocytopenia [3, 4]. In addition to platelet count,

mean platelet volume (MPV) is one of the factors that indicate platelet function [5]. Higher MPV values are associated with increased platelet activation. Platelet count and MPV are simple methods to monitor patient's condition [6-10]. Thrombocytopenia may increase the risk of bleeding as well as thrombosis caused by platelets activation, according to the underlying mechanism [11, 12].

Thrombocytopenia in intensive care unit may cause bleeding, organ failure, and increase the length of hospitalization [3, 13, 14].

Etiologies of thrombocytopenia in critically ill patients are widely studied. Mechanisms that can result in thrombocytopenia in critically ill patients are hemodilution (decreased concentration of cells and solids in the blood resulting from gain of fluid), more platelet consumption (due to massive tissue trauma), bleeding, platelet sequestration, decreased platelet production, sepsis, and DIC (disseminated intravascular coagulation) [15-17]. It is necessary to make the etiologic diagnosis to accommodate the patients benefit from appropriate treatment. Association between thrombocytopenia and prognosis of patients admitted in ICU was declared recently. The current study aimed at investigating the prevalence of thrombocytopenia and its relationship with the length of stay in ICU and mortality among ICU patients.

#### **METHODS**

The current histological cohort study enrolled 150 patients above 18 years old consecutively admitted to ICU for more than two days (83 male and 67 female). This study protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences. Patients had normal platelet range (more than  $150 \times 10^9$ .L<sup>-1</sup>) in the beginning, and were followed until they were discharged or died.

Patients' baseline and demographic characteristics such as age, gender, and body mass index (BMI) were evaluated.

Thrombocytopenia was defined as more than 50% decrease in platelet count or platelet count less than 150×10<sup>9</sup>.L<sup>-1</sup> on the 3rd day. Patients were divided to thrombocytopenic and non-thrombocytopenic groups.

## **Statistical Analysis**

Data were presented as means  $\pm$  SD and qualitative variables as frequency (percentage). Statistical analyses were performed with SPSS software for Windows (Statistical Product and Service Solutions, version 20.0, SSPS Inc., Chicago, IL, USA). Student t test for quantitative variables and chi-squared test for quantitative variables were used. P values less than 0.05 were considered as statistically significant.

# **RESULTS**

Mean age of patients was  $58.8 \pm 11.9$  years (range 46-73). Patients' characteristics are shown in Table 1. From 150 patients (83 male and 67 female) thrombocytopenia was detected in 53(35%) patients while 13 (8.6%) patients had severe thrombocytopenia (platelet count  $<50 \times 10^9/L$ ). Thrombocytopenia on the 3rd day of admission was detected in 40.2% and 31.3% of females and males, respectively, which was not

statistically different (P = 0.1). As shown in Table 2, admission mean platelets were similar in patients with thrombocytopenia and non-thrombocytopenic patients (243674x10<sup>6</sup>  $\pm$  7648  $\times$  10<sup>6</sup>/L and 26154  $\times$  10<sup>6</sup>  $\pm$  8031  $\times$  10<sup>6</sup>/L, respectively; P = 0.6), while the platelet counts on days 3-5 after admission significantly decreased in patients with thrombocytopenia (243674  $\times$  10<sup>6</sup>  $\pm$ 7648  $\times$  10<sup>6</sup>/L and 26154  $\times$  10<sup>6</sup>  $\pm$  8031  $\times$  10<sup>6</sup>/L, respectively; P = 0.6). Overall duration of hospitalization was 13.41 $\pm$ 2.6 days, which was significantly higher in patients with thrombocytopenia compared with non-thrombocytopenic patients (16  $\pm$  2.7 vs 12  $\pm$  2.4 days, respectively P = 0.01).

Table 1: Patients baseline characteristics

	Thrombocytopenic
	(n = 150)
Age (years)	58.74± 11.93
Gender (male)	83(55.3%)
BMI (Kg/m2)	$34.63 \pm 6.72$
Creatinine (mg/dl)	$1.23 \pm\ 0.68$
Platelet on admission (×10°/L)	$259364 \pm 7438$
Admission cause	
Respiratory failure	63 (42%)
Septic shock	34 (22.7%)
Renal failure / ESRD	53 (35.3%)
Systolic blood pressure (mmHg)	$137.2 \pm 11.1$
Heart rate (bpm)	$73.6 \pm 6.7$
Hospitalization duration (days)	13.6± 2.5
Mortality (%)	60 (40%)

Data in are presented as No. (%) or Mean ± SD. ESRD: end stage renal disease; bpm: beat per min

The current study results demonstrated significant difference in ICU mortality between thrombocytopenic and non-thrombocytopenic patients (45.5% vs 37.3%, P = 0.01). The current study investigated the effect of sever thrombocytopenia (platelet count  $<50 \times 10^9/L$ ) on ICU mortality. As shown in Table 3, sever thrombocytopenia was associated with increased mortality compared with thrombocytopenic patients who had platelet count more than  $50 \times 10^9/L$  (OR 1.4; 95% confidence interval (CI): 1.2-1.8; P = 00.1).

# **DISCUSSION**

The prevalence of thrombocytopenia among 150 patients (83 male and 67 female) admitted to ICU was detected in 53(35%) patients while 13 patients (8.6%) had severe thrombocytopenia (platelet count <50  $\times$   $10^9/L$ ). The current study results were consistent with those of previous studies reporting that thrombocytopenia can vary from 30% to 50% [1]. The wide range of prevalence might be due to different inclusion or exclusion criteria, condition or stage of patients, and quality of hospitalization.

Table 2: Variables between Groups

	Thrombocytopenic (n = 53)	Non-Thrombocytopenic (n = 97)	P value
Age (years)	$61.3 \pm 12.6$	57.2± 11.7	0.4
Gender (male)	26(49%)	57(58.7)	0.1
BMI (Kg/m2)	$36.5 \pm 7.6$	$33.2 \pm 6.5$	0.3
Creatinine (mg/dl)	$1.2\pm~0.8$	$1.3 \pm 0.6$	0.2
Platelet on admission ( $\times 10^9/L$ )	$243674 \pm 7648$	$326154 \pm 8031$	0.6
Systolic blood pressure (mmHg)	$142.8 \pm 11.4$	$138.7 \pm 9.6$	0.2
Heart rate (bpm)	$78.2 \pm 5.3$	$83.6 \pm 4.7$	0.1
Hospitalization duration (days)	16.1± 2.7	12.3±2.4	0.01
Mortality (%)	24 (45.4%)	36 (37.5%)	0.001

Data in are presented as No.(%) or Mean  $\pm$  SD.

BMI: Body Mass Index; bpm: beat per min

Table 3: Severe Thrombocytopenia and Intensive Care Unit Admission Outcome

	Severe Thrombocytopenia Platelet $< 50 \times 10^9/L$	Thrombocytopenia Platelet: 50-150×10°/L	P
	(n=13)	(n=40)	value
Discharge (%)	5 (39%)	24 (60%)	0.01
Expire (%)	8 (61%)	16 (40%)	0.01

Data in are presented as No. (%)

In the current study, thrombocytopenia was detected in 35% of patients, which was lower than that of the study by Thiery-Antier et al. reporting that 48.4% of patients had thrombocytopenia and 14.8% of them had platelet count  $<50\times10^9/L$  [18]. According to the current study, thrombocytopenia was associated with increased hospitalization period and mortality rate in critically ill patients. The current study findings were similar to those of some studies suggesting that thrombocytopenia increases ICU length of stay and mortality in patients admitted to ICU [19].

Thrombocytopenia is a common disorder in ICU patients and prolonged thrombocytopenia is assumed to be associated with increased mortality. Due to the importance, many studies investigated the etiology of thrombocytopenia and its role on the prognosis in critically ill patients, but the exact reason is not clarified. It is believed that thrombocytopenia is multi-factorial and the fall in platelet count is caused by different mechanisms. Five major mechanisms such as hemodilution, increased platelet consumption, decreased platelet production, increased platelet sequestration, and platelet destruction due to immune mechanisms seem responsible for thrombocytopenia [20]. According to the authors' best knowledge there are limited data on sever thrombocytopenia in ICU patients [21, 22]. The current study also investigated the effect of sever thrombocytopenia (platelet count  $<50 \times 10^9/L$ ) on ICU mortality. The study observed sever thrombocytopenia in 8.3% of patients associated with increased mortality among patients with thrombocytopenia (OR 1.4; CI95% 1.2-1.8; P=00.1). Marco-Schulke et al., demonstrated a total of 11.7% developed sever thrombocytopenia in ICU patients, which was higher than our results [23].

The current study results showed that sever thrombocytopenia increased with mortality rate and low platelet scale was known as a poor prognostic factor. Although decrease in platelet count in critically ill patients is common and can be observed in different conditions, occurrence of sever thrombocytopenia reflects DIC and is correlated with coagulation disorders [24]. One of the most important causes of thrombocytopenia in ICU patients is bacterial infection, known as sepsis. During a septic shock, platelets can also be either activated by inflammatory mediators or directly by microorganism components [25]. Some studies show higher mortality in patients with acute kidney injury undergoing dialysis thrombocytopenia fortifying inflammatory process [26]. The role of platelet in increasing mortality range is possibly due to its important role in inflammatory procedure and not in coagulation pathway.

#### CONCLUSIONS

Platelet alternation is one of the common hematologic abnormalities occurred by various conditions that might be considered as a prognosis monitor in ICU setting. Severe thrombocytopenia could be mentioned as a poor prognostic factor for increased mortality and prolonged hospitalization period in ICU patients.

#### **Author's Contribution**

Abbas Fadaei: data collection and supervision Seyed Mojtaba Heidari: data collection Mohammad Amin Abbasi: data analysis and writing Maryam Alizadeh Chamkhaleh: data collection and writing

#### **Conflicts of Interests**

None declared.

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