DOI:10.34084/bshr.843462 e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Araştırma Makalesi/Research Article

http://dergipark.org.tr/tr/pub/bshr

Frequency of Thombocytopenia in Intensive Care Patients and Related Factors

Yoğun Bakım Hastalarında Trombositopeni Sıklığı Ve İlişkili Faktörler

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Geliş Tarihi / Received : 19-12-2020 **Kabul Tarihi / Accepted:** 04-03-2021 **Yayın Tarihi / Online Published:** 30-04-2021

Ece C. Frequency of Thombocytopenia in Intensive Care Patients and Related Factors, J Biotechnol and Strategic Health Res. 2021;5(1):33-43

Abstract

Objective Thrombocytopenia is a common hematological disorder in intensive care patients with serious consequences. Determining the etiology as well as detecting thrombocytopenia is important in terms of patient management and treatment planning. In our study, it was aimed to examine the incidence of thrombocytopenia and related factors in patients hospitalized in our general intensive care unit.

Materials and Methods In our retrospective study, the information of patients hospitalized in the Intensive Care clinic was retrospectively and randomly scanned. Deep thrombocytopenia was considered to be less than 50.000 / µL of the patients, and the development of thrombocytopenia in the first five days of hospitalization in the intensive care unit was accepted as early stage thrombocytopenia. Statistical analyzes were performed using SPSS version 17.0 software. Mann-Whitney U test, Pearson's Chi Square or Fisher's Exact Chi Square test were used for comparisons. Logistic regression analysis was performed to determine the risk factor. The cases where the p-value was less than 0.05 were considered statistically significant.

Results 83 female (53.2%), 73 male (46.8%) 156 patients were included in our study. While the number of patients with thrombocytopenia was found in 26 (16.7%) during the first admission to intensive care, it was observed that thrombocytopenia developed in 23 (14.7%) of the patients during the days of hospitalization in the intensive care unit. Deep thrombocytopenia was detected in 9 (5.8%) patients.
The mean time to onset of thrombocytopenia was 5.8 ± 5.1 days and the median was 4 (IQR = 6) (min-max 1-20) days. The number of patients who developed early thrombocytopenia was 7 (4.48%). It was observed that 30.4% of the patients who developed thrombocytopenia during the days of intensive care hospitalization were thrombocytopenic in the early period. The incidence of thrombocytopenia in patients with sepsis was 48.1% (n = 26), and the rate of thrombocytopenia in those who did not develop was found to be 22.5% (n = 23). The rate of development of thrombocytopenia (n = 1) in patients using linezolid was found to be 4.3%.

Discussion In our study, the incidence of thrombocytopenia developed during admission to intensive care and during hospitalization is consistent with other studies. The rate of deep thrombocytopenia found during hospitalization in intensive care is higher than in other studies. This rate may be due to the fact that our study was conducted in tertiary care patients, the proportion of patients diagnosed with sepsis and the use of multiple drugs.
In our study, the mortality rate in patients with early thrombocytopenia (n = 7) was not found to be statistically significant compared to those with late thrombocytopenia; It was observed that the presence of sepsis significantly increased the incidence of thrombocytopenia.

Conclusion Thrombocytopenia is a parameter that should be followed in terms of etiology and prognosis in intensive care patients.

Keywords intensive care, thrombocytopenia, sepsis, deep thrombocytopenia, early thrombocytopenia

Özet

Amaç *Trombositopeni yoğun bakım hastalarında sık görülen ve ciddi sonuçlara yol açabilen bir hematolojik bozukluktur. Trombositopeniyi tespit etmek kadar etiyolojisini saptamak hasta yönetimi ve tedavinin planlaması açısından önemlidir. Çalışmamızda genel yoğun bakım ünitemizde yatan hastalarda trombositopeni insidansının ve ilişkili faktörlerin incelenmesi amaçlandı.*

Materyal ve Metod *Retrospektif yapılan çalışmamızda Yoğun Bakım kliniğinde yatan hastaların bilgileri retrospektif, randomize olaracak tarandı. Hastaların 50.000/µL altı trombosit değeri derin trombositopeni, yoğun bakıma yatışın ilk beş gününde trombositopeni gelişmesi ise erken dönem dönem trombositopeni kabul edildi. İstatistiksel analizler SPSS versiyon 17.0 yazılımı kullanılarak yapıldı. Karşılaştırmalar için Mann-Whitney U testi, Pearson's Chi Square veya Fisher's Exact Chi Square testi kullanıldı. Risk faktörü belirlemek için logistic regression analizi yapıldı. p-değerinin 0.05'in altında olduğu durumlar istatistiksel olarak anlamlı kabul edildi.*

Bulgular *Çalışmamıza 83'ü kadın (%53,2), 73 'ü erkek (%46,8) 156 hasta dahil edildi. Yoğun bakıma ilk yatış anında trombositopenisi olan hasta sayısı 26 (%16,7) bulunurken, Hastaların 23'ünde (%14,7) yoğun bakımda yattığı günler içerisinde trombositopeni geliştiği görüldü. Dokuz (%5,8) hastada ise derin trombositopeni saptandı.*
Trombositopeninin ortaya çıkış süresi ortalama 5,8±5,1 gün ve medyan 4 (IQR=6) (min-maks 1-20) gün bulundu. Erken dönem trombositopeni gelişen hasta sayısı 7 (%4,48) bulundu. Yoğun Bakıma yattığı günler içerisinde trombositopeni gelişen hastaların %30,4'ünün erken dönemde trombositopenik olduğu görüldü. Sepsis gelişen hastalarda trombositopeni görülme oranı %48,1 (n=26), gelişmeyenlerde trombositopeni görülme oranı %22,5 (n=23) olarak bulumdu. Linezolid kullanan hastalarda trombositopeni gelişme oranı (n=1) %4,3 olarak bulundu.

Tartışma *Çalışmamızda yoğun bakıma başvuruda ve yatış süresince gelişen trombositopeni insidansı diğer çalışmalarla uyumludur. Yoğun bakımda yatış süresince saptanan derin trombositopeni oranı diğer çalışmalara göre daha yüksektir. Bu oran çalışmamızın üçüncü basamak yoğun bakım hastalarında yapılmış olması, sepsis tanılı hasta oranına ve çoklu ilaç kullanımına bağlı olabilir. Çalışmamızda erken dönem trombositopeni gelişen hastalardaki mortalite oranı geç dönem trombositopeni gelişenlere göre istatistiksel olarak anlamlı bulunmazken; sepsis varlığının trombositopeni görülme oranını istatistiksel olarak anlamlı arttırdığı görüldü*

Sonuç *Yoğun bakımda hastalarında trombositopeni etiyoloji ve prognoz açısından takip edilmesi gereken bir parametredir.*

Anahtar Kelimeler *yoğun bakım, trombositopeni, sepsis, derin trombositopeni, erken trombositopeni*

INTRODUCTION

Thrombocytopenia is a common hematological disorder in intensive care patients with serious consequences. There are different definitions for thrombocytopenia. Generally, a platelet count below 150.000 / μL in the complete blood count is considered as thrombocytopenia. However, some authors accept the thrombocytopenia limit as 100.000 / μL[1-3].

It is important to detect thrombocytopenia, determine its etiology, patient management and treatment planning.

The incidence of thrombocytopenia in intensive care patients is reported in a very wide range from 13% to 44%[4,5]. Sepsis is reported to be the most common cause, especially in intensive care patients. Disseminated intravascular coagulation (DIC) and drug-related causes are among other common causes[6,7].

The variety of thrombocytopenia etiology and the clinical conditions it may cause require close monitoring in intensive care units. In our study, we aimed to investigate the incidence of thrombocytopenia in patients hospitalized in our tertiary general intensive care unit and to examine the factors associated with thrombocytopenia.

MATERIALS and METHODS

Patients hospitalized in the 3rd step intensive care clinic of Cigli Regional Training Hospital between 1 June 2016 and 30 August 2018 were included in our study. The data of the patients were evaluated retrospectively and randomly using the hospital electronic recording systems. Institution permission was obtained before the study and the study was carried out in accordance with the Declaration of Helsinki Principles (www.wma.net/e/policy/b3.htm). Patients under 18 years of age, hospitalized for less than 24 hours, patients diagnosed with hematologica and liver malignancy and pregnant patients were excluded from the study.

The demographic data of the patients, diagnose at intensive care admission, Acute Physiology and Chronic Health Evaluation Score (APACHE II), the duration of hospitalization in the intensive care unit, the duration of intubation, the drugs used during the stay at the intensive care unit, the status of immunosuppressive drug use, whether they were diagnosed with sepsis and their prognosis were recorded. Thrombocyte values of the patients were recorded as days during their hospitalization in the intensive care unit.

In our study, in order to evaluate the effects of thrombocyte value and the day of thrombocytopenia on the prognosis, a platelet value below 50.000 / μL was accepted as deep thrombocytopenia. Development of thrombocytopenia in the first five days of admission to intensive care unit was accepted as early stage thrombocytopenia.

Statistical analysis

Statistical analyzes were performed using SPSS version 17.0 software. The suitability of variables to normal distribution was analyzed using analytical methods (Kolmogorov-Smirnov / Shapiro¬Wilk tests). Descriptive analyzes were given as median (IQR) for variables that were not normally distributed. Descriptive statistics were made by giving demographic characteristics, frequency and percentage values. In continuous data, Mann-Whitney U test was used to compare paired groups such as with or without thrombocytopenia. Pearson's Chi Square or Fisher's Exact Chi Square test was used in the analysis of categorical data. Logistic regression analysis was performed to determine the risk factor. The cases where the p-value was less than 0.05 were considered statistically significant.

RESULTS

Eighty three female (53.2%), 73 male (46.8%) (a total of 156 patients) were included in our study. The mean age of the patients was 65.9 ± 20.4 years (min-max, 16-100).

Considering the cause for admission to intensive care, 117 patients were in intensive care unit due to respiratory failu-

re, 63 patients with respiratory system disease, 39 patients with neurological disease, 17 patients with metabolic disease, 10 patients postoperative, 10 patients with gastrointestinal bleeding, 8 patients with cardiovascular disease, 4 patients with drug intoxication and 3 patients due to other reasons. It was seen that he was lying.

The mean APACHE-II score of all patients was 19.3 ± 7.5; The average duration at the intensive care unit was 9.3 ± 14.5 days.

Demographic data of the patients and general data of intensive care admission are shown in Table 1. Reasons for hospitalization are shown in Table 2.

Table-1. Demographic data and descriptive statistical analysis

Parameters	Minimum	Maximum	Median	IQR	Mean±SD
Age	16	100	82	18,75	65.8±20.4
APACHE II Score	5	41	22	5,5	19.3±7.5
Admission PLT	23000	1430000	170000	56750	263121.8±167452.2
Diamisted PLT	16000	2920000	107500	73000	277859±267007.4
Hospitation Day	1	107	5	5.75	9.3±14.5
The day of thrombocytopenia	1	20	4	6	5.8±5.1

IQR; Interquartile range

Table-2. Cause of ICU admission

Parameters	n =117	%
Respiratory Failure	75	64.1
Respiratory System Disease	63	40.3
Neurological Disorder	39	25
Metabolic Disease	17	10.8
Postop Patient	10	6.4
Gastrointestinal System Bleeding	10	6.4
Cardiovasculer System Disease	8	5.1
Drug Intoxication	4	2.6
Other	3	1.9

While the number of patients with thrombocytopenia was found in 26 (16.7%) at the time of initial admission to intensive care, it was observed that thrombocytopenia developed in 23 (14.7%) of the patients during the days of hospitalization in the intensive care unit. Deep thrombocytopenia was detected in 9 (5.8%) patients.

The mean time to onset of thrombocytopenia was 5.8 ± 5.1 days and the median 4 (IQR = 6) min-max 1-20 days. The number of patients who developed early thrombocytopenia was found to be 7 (4.48%). It was observed that 30.4% of the patients who developed thrombocytopenia during the days of intensive care hospitalization were thrombocytopenic in the early period.

The demographic information, hospitalization day, APACHE II score, sepsis and prognosis comparisons of patients with thrombocytopenia during the first admission to intensive care and those who developed thrombocytopenia during the days in intensive care are given in Table 3.

The drugs used by patients who developed thrombocytopenia (n = 23) during the days of intensive care are shown in Table 4, respectively. According to this; LMWH

Table 3. Comparison of parameters according to thrombocytopenia status				
	Presence of Thrombocytopenia at First Admission	Development of Thrombocytopenia in ICU	p value §	z score
	n=26	n=23		
	Median (IQR)	Median (IQR)		
Age	73.5 (40)	74 (16)	0.810	-0.241
APACHE II Score	23 (14)	21 (8)	0.514	-0.652
Hospital Duration	5 (7)	7 (12)	0.479	-0.708
	n (%)	n (%)	p value	$\chi 2$
Gender				
Male	14 (53.8)	12 (52.2)	0.907	0.014
Female	12 (46.2)	11 (47.8)		
Sepsis				
None	15 (57.7)	8 (34.8)	0.109	2.572
Yes	11 (42.3)	15 (65.2)		
Prognosis				
Ex	11 (42.3)	17 (73.9)	0.026	4.978
Transfer Another unit	15 (57.7)	6 (26.1)		
§ Mann-Whitney U test was used. Pearson's Chi Square and Fisher's Exact Chi-Square test were used. p<0.05 was considered significant.				

in 69.6% patients, clopidogrel in 4.3%, warfarin sodium in 8.7%, methylprednisolone in 39.1%, acetylsalicylic acid in 39.1%, linezolid in 4.3%, and It was found that succinylated gelatin was used in 57.1 patients, PPI in 90.5%, H2 Receptor Blocker (H2RB) in 4.8% and N-Acetyl Cysteine in 81.0%.

When the drugs used by the patients were examined, no significant difference was observed between the patients with thrombocytopenia and those without thrombocytopenia in the use of other drugs except succinylated gelatin and H2RB. During this evaluation, patients with thrombocytopenia on admission to intensive care were excluded (Table 4).

Table 4. Medication use in thrombocytopenia				
	Trombocytopenia existance	No trombocytopenia	p value	χ2
	n=23	n=107		
	n (%)	n (%)		
DMAH				
No	7 (30.4)	26 (24.3)	0.540	0.376
Yes	16 (69.6)	81 (75.7)		
Clopidogrel				
No	22 (95.7)	96 (89.7)	0.692	0.795
Yes	1 (4.3)	11 (10.3)		
Warfarin sodium				
No	21 (91.3)	95 (88.8)	1.000	0.125
Yes	2 (8.7)	12 (11.2)		
Methylprednisolone				
No	14 (60.9)	66 (61.7)	0.942	0.005
Yes	9 (39.1)	41 (38.3)		
Acetylsalicylic acid				
No	14 (60.9)	60 (56.1)	0.674	0.177
Yes	9 (39.1)	47 (43.9)		
Linezolid				
No	22 (95.7)	106 (99.1)	0.324	1.456
Yes	1 (4.3)	1 (0.9)		
Succinylated Gelatin				
No	9 (42.9)	71 (66.4)	0.042	4.136*
Yes	12 (57.1)	36 (33.6)		
Heparin Sodium				
No	19 (90.5)	102 (95.3)	0.323	0.799
Yes	2 (9.5)	5 (4.7)		
PPI				
No	2 (9.5)	25 (23.4)	0.242	2.020
Yes	19 (90.5)	82 (76.6)		
H2RB				
No	20 (95.2)	80 (74.8)	0.043	4.305*
Yes	1 (4.8)	27 (25.2)		
N Acetyl Cystein				
No	4 (19.0)	34 (31.8)	0.243	1.362
Yes	17 (81.0)	73 (68.2)		
Pearson's Chi Square and Fisher's Exact Chi-Square test were used. p<0.05 was considered significant.				

Patients with thrombocytopenia (n = 26) during their first admission to intensive care unit, mean length of stay in intensive care unit was 6.6 ± 4.9 days, median was 5 IQR 7. Of the patients with thrombocytopenia at the time of first hospitalization (n = 12), this period was 9.8 ± 5.2 (median 9.5 IQR 9 days) in those who were discharged from the hospital (n = 12), and 3.9 ± 2 in those who died (n = 14), 4 days, (median 2.5 IQR days).

In patients who developed thrombocytopenia during the days of intensive care (n = 23), this period was 10.9 ± 14.1 days; 9.2 ± 5.7 days in those who were discharged / transferred to the service (n = 6) and 11.5 ± 16.2 days in those who died (n = 17).

Considering the mortality rates, the mortality rate (n = 11) of patients with thrombocytopenia during the first admission to intensive care (n = 26) was found to be 42.3%. This rate was 37.7% in patients who developed thrombocytopenia (n = 23), mortality (n = 17; 73.9%), and no thrombocytopenia (n = 107) during the days of hospitalization (n = 40).

The rate of death in patients who developed during the days of hospitalization in the intensive care unit was found to be statistically significantly higher than those with thrombocytopenia at the time of first hospitalization and those who did not develop at all (p = 0.026).

The mortality rate (n = 4) in patients (n = 7) who developed early thrombocytopenia (in the first five days of intensive care) was found to be 57.14%. This rate was 81.25% in patients with late thrombocytopenia (n = 13). There was no statistically significant difference between mortality rates (p> 0.05).

In those with deep thrombocytopenia, the mortality rate was 6 (66.7%), and the transfer to other unit rate was 3 (33.3%), and the rate of transfer to another unit was 62 (42.5%), and the rate of transfer to another unit was 84 (57.5%). This rate was not statistically significant (p = 0.156; $\chi 2 = 2.016$).

No statistically significant difference was found in terms of age, gender, GCS and length of hospital stay in patients who developed thrombocytopenia during the days of intensive care (p> 0.05).

No statistically significant difference was found when the patients who developed thrombocytopenia during the days of intensive care were compared with the patients who did not develop their age, gender, APACHE II score, prognosis (ex / discharge), coraspirin, clopidogrel, linezolid, PPI and H2RB usage rate.

The incidence of thrombocytopenia was found to be 48.1% (n = 26) in patients with sepsis, and 22.5% (n = 23) in those who did not. It was observed that the presence of sepsis significantly increased the incidence of thrombocytopenia (p = 0.001; $\chi 2 = 10.740$)

The rate of development of thrombocytopenia (n = 1) in patients using linezolid was found to be 4.3%. When this ratio was compared to 2.3% of patients who used linezolid but did not develop thrombocytopenia (n = 3), no significant difference was found (p = 0.475; $\chi 2 = 0.344$).

Risk factors affecting mortality in patients with thrombocytopenia were evaluated by logistic regression analysis. In single logistic regression analysis, mortality increased 1.4 times with each unit increase in APACHE-II score (p = 0.019). There was no statistically significant difference in other variables examined.

Logit (YMortalite) = 5.617- 0.35 x APACHE-II

While the incidence of thrombocytopenia (n = 8) (30.76%) was found in patients in the surgical group (n = 26) during their hospitalization in intensive care, this rate was found (n = 15) (11.53%) in other patients (n = 130).

DISCUSSION

Intensive care units are units in which patients with many underlying disorders and multiple drug use are followed up and numerous invasive procedures are performed. Thrombocytopenia is a common problem in these units. In addition to detecting thrombocytopenia, determining the etiology is important for mortality and treatment planning.

There are congenital and acquired causes of thrombocytopenia. The etiology of thrombocytopenia can generally be explained by decreased production and abnormal distribution or increased destruction.

Platelet aggregation (Pseudotrombocytopenia) and thrombocyte satellitism caused by immunoglobulin due to anticoagulant can be shown among the causes of unreal thrombocytopenia.

Megakaryocytic hypoplasia, ineffective thrombopoiesis, impairment in the mechanisms controlling thrombopoesis and hereditary thrombocytopenias are among the causes of thrombocytopenia due to decreased thrombocyte production.

Thrombocytopenias caused by increased platelet destruction can be examined in 2 groups as immunological and non-immunological. Idiopathic thrombocytopenic purpura primary immunological, infections, pregnancy, collagen vascular disorders, lymphoproliferative diseases, and drugs are among the causes of secondary immunological thrombocytopenia.

Other causes such as thrombotic microangiopathy, Disseminated intravascular coagulation, Thrombotic thrombocytopenic purpura, Hemolytic-uremic syndrome and drug and infection are among the causes of non-immunological thrombocytopenia.

It should also be kept in mind that diseases such as infections and malignancies involving the spleen, and hypothermia may cause abnormal distribution.

According to the meta-analysis results in which the etiology of thrombocytopenia was investigated in intensive care patients and a total of 24 studies, 12 of which were prospective, the rate of patients with thrombocytopenia during intensive care admission was reported to be between 8-67% (4,5). In another meta-analysis, this rate is between 20% and 30% 3,8 .

When we examined the studies conducted in our country, the rate of thrombocytopenia detected at the time of first admission to intensive care was reported with a rate of 20.4% [9].

In another study, this rate was found to be 16%. Thrombocytopenia development rate was reported to be 44.7% during the hospitalization of patients in intensive care. In the study, the rate of patients developing thrombocytopenia after hospitalization is 28% [10].

In our study, 16.7% of the patients admitted to our intensive care unit had thrombocytopenia during the first hospitalization. The rate of patients who developed thrombocytopenia during the days of intensive care was 14.7%. The results of our study are consistent with other studies.

Some studies have classified thrombocytopenia according to its severity and investigated its effects on prognosis.

In a study in which the degree of thrombocytopenia was classified as mild, moderate and severe, the frequency of thrombocytopenia was found to be 15.3%, 5.1% and 1.6%, respectively [11].

In the study in which thrombocyte count below 50.000 / ul was evaluated as severe thrombocytopenia, the rate of patients with thrombocyte count below 100.000 / uL was between 20-40%; It has been shown that those with a pla-

telet count of less than 50.000 / uL range between 5-20% [12]. In our study, a platelet value of less than 50.000 / uL was accepted as deep thrombocytopenia. Accordingly, deep thrombocytopenia was detected in 9 patients (5.8%). It was observed that 39.13% of the patients who developed thrombocytopenia during the ICU stay had deep thrombocytopenia. This rate is higher than other studies. This rate may be due to the fact that our study was conducted in tertiary intensive care patients, the proportion of patients diagnosed with sepsis and the use of multiple drugs.

In our study, although the mortality rate was higher in those who developed deep thrombocytopenia, this rate was not statistically significant. ($p = 0.156$; $\chi 2 = 2.016$).

In various studies, the incidence of thrombocytopenia was found to be higher in surgical and trauma patients. It has been shown that thrombocytopenia occurs especially in the first four days in this group of patients [13].

In our study, intensive care patients were classified as internal and surgical patients according to their hospitalization diagnoses. In addition, among the patients who developed thrombocytopenia during the days of hospitalization in the intensive care unit, those who developed thrombocytopenia within the first five days were accepted as those who developed early thrombocytopenia.

The incidence of thrombocytopenia (n = 8¸30.76%) was found to be higher (n = 15¸11.53%) compared to the other patients (n = 130) during hospitalization in the surgical group (n = 26).

In our study, the mortality rate in patients with early thrombocytopenia (n = 7) was not statistically significant compared to those with late thrombocytopenia.

In studies investigating the etiology of thrombocytopenia in intensive care patients, although no etiology was found in some patients with thrombocytopenia, sepsis, drugs, diffuse intravascular coagulation and thrombocytopenia secondary to massive transfusion were observed as the leading causes.

Thrombocytopenia is also seen in the course of many infectious diseases such as viral, mycoplasma, mycobacteria and malaria. Although thrombocytopenia in most of these diseases is due to the decrease in thrombocyte production, some of them occur by immune mechanism. Sepsis is reported to be the most important cause of thrombocytopenia, especially in intensive care units [7,14,15]. The most important cause of thrombocytopenia in patients with sepsis is thrombocyte phagocytosis caused by the effect of increased M-CSF.

In a study conducted in the intensive care unit, sepsis ranked first among the causes of thrombocytopenia with 47.8%, while other reasons were reported as DIC, primary hematological diseases, hypersplenism, cytotoxic agents, drugs, and massive blood transfusions, respectively. In the study, a multifactorial cause was found with a rate of 27.4%[14].

In another study in which hematological malignancies were excluded, sepsis was found to be the most common cause of thrombocytopenia with a rate of 52%; Other reasons were listed as DIC, drugs, massive transfusion heparin and ITP, respectively [7].

Multiple drug use is also among the factors causing development of thrombocytopenia. A study excluding hematological diseases showed that multiple drug use is the third most common cause of thrombocytopenia after sepsis and DIC [14].

In another study, the use of multiple drugs, especially H2 receptor antagonists, heparin and derivatives and antibiotic use, was associated with thrombocytopenia. In our study, many factors such as sepsis status and the drugs used were investigated in order to determine the causes of

thrombocytopenia.

In our study, no statistically significant difference was found when the age, gender, APACHE II score, prognosis (ex / discharge), coraspirin, plavix, linezolid, PPI and H2RB usage rates of patients who developed thrombocytopenia during the days of hospitalization were compared with those who did not. In single logistic regression analysis, mortality increased 1.4 times with each unit increase in APACHE-II score (p = 0.019). It was observed that the presence of sepsis significantly increased the incidence of thrombocytopenia .

When the relationship between drug use and thrombocytopenia was examined, it was seen that the drugs with the highest rate of thrombocytopenia in our study were Proton Pump Inhibitors (PPI), Low Molecular Weight Heparin (LMWH) and N-Acetyl Cysteine, but no drug caused statistically significant thrombocytopenia.

There are many studies showing that the use of linezolid may cause thrombocytopenia. In our study, although the rate of developing thrombocytopenia in patients using Linezolid (4.3%) was higher than those who did not (2.3%), this rate was not statistically significant. ($p = 0.475; \chi 2 = 0.344$).

In studies examining the effect of thrombocytopenia on mortality, the degree of thrombocytopenia was found to be determinative, especially in terms of bleeding risk. These studies have also shown that thrombocytopenia is a stronger independent predictor of mortality than standard scoring systems (Acute Physiology and Chronic Evaluation (APACHE) II score) (relative risk 1.9–4.2) [1,5,13,16.]

In another study, it was observed that the predictors of thrombocytopenia category were the APACHE-II score for each group, the use of inotrope or vasopressor, and renal replacement therapy. The study showed that the risk of developing thrombocytopenia is higher in surgical patients and patients with liver disease and lower in patients receiving LMWH thromboprophylaxis. It was also shown in the study that thrombocytopenia that develops in intensive care patients has a negative effect on prognosis [9].

In a review investigating the effects of thrombocytopenia on prognosis, the mortality rate of thrombocytopenic patients was reported as 31-46%, while the mortality of non-thrombocytopenic patients was presented as 16-20%[8]. In a study conducted; The mortality of patients without thrombocytopenia in the ICU was 9.3% and the mortality of patients with thrombocytopenia was 33%. The mortality of patients with thrombocytopenia during admission to the ICU was 34%, and the mortality of patients who developed thrombocytopenia during ICU follow-up was 31.9% [14].

In another study, intensive care mortality of thrombocytopenic patients was 17.6%, while intensive care mortality of non-thrombocytopenic patients was 4.4%. In the same study; Hospital mortality of thrombocytopenic patients was 22.1%, and hospital mortality of non-thrombocytopenic patients was 7.8% [17]. In the study conducted by Strauss et al., the mortality of thrombocytopenic patients was 44%, non-thrombocytopenic patients were 16% and the overall mortality of intensive care was 31% [5].

In our study, the mortality rate (n = 11) of patients with thrombocytopenia (n = 26) during the first admission to intensive care was found to be 42.3%. This rate was 73.9% in patients who developed thrombocytopenia during hospitalization (n = 23), mortality (n = 17) was 73.9%, and mortality (n = 40) was 37.7% in those without thrombocytopenia (n = 107) The mortality of rate in patients who developed thrombocytopenia during intensive care admission was statistically significantly higher than those with thrombocytopenia at the time of first hospitalization and those who did not develop at all (p = 0.026).

In a study investigating the effect of the day developing thrombocytopenia on mortality, the mortality rate in the

group with late thrombocytopenia (14th day) was found to be higher than the group with early thrombocytopenia (4th day). The study also showed a relative increase in the number of platelets in the living group [18].

In another study conducted with intensive care patients, when the median platelet values were examined, no significant difference was found between the survivors and the deceased. However, it has been shown that a decrease in thrombocyte count provides prognostic information in patients who stay in the intensive care unit for more than 5 days and have normal platelet count during admission to the ICU [19].

In our study, although the mortality rate was higher in those who developed deep thrombocytopenia, this rate was not statistically significant. ($p = 0.156$; $\chi 2 = 2.016$).

LMWH and Heparin are among the commonly used drugs in intensive care units.

In a multi-center randomized study comparing low molecular weight heparin (LMWH) and unfractionated heparin (UFH) for DVT prophylaxis in intensive care patients, heparin-induced thrombocytopenia (HIT) developed in 0.5% of the patients [12].

In our study, when classical heparin and low molecular weight heparin were compared, no significant difference was found between them in terms of development of thrombocytopenia.

CONCLUSION

Thrombocytopenia is an important problem in critically ill patients. Mortality rate is very high in those with thrombocytopenia. Is thrombocytopenia more frequently in critically ill patients or patients with thrombocytopenia become more critical; The answer to this question is not clear. If thrombocytopenia developed in patients followed up in intensive care, its causes should be well investigated and care should be taken in terms of mortality.

References

1. Stephan F, Hollande J, Richard O, et al. Thrombocytopenia In Surgical ICU. Chest 1999;115:1363-70.
2. Drews RE, Weinberger SE. Thrombocytopenic disorders in critically ill patients. Am J Respir Crit Care Med 2000;162:347-51.
3. Chakraverty R, Davidson S, Peggs K, et al. The incidence and cause of coagulopathies in an intensive care unit population. Br J Haemotology 1996;93:460-3.
4. Crowther MA, Cook DJ, Meade MO, et al. Thrombocytopenia in medicalsurgical critically ill patients: prevalance, incidence and risk factors. J Crit Care 2009;20:348-53.
5. Strauss R, Wehler M, Mehler K, et al. Thrombocytopenia ın patients in medical intensive care unit: bleeding prevelance, transfusion requirrements and outcome. Crit Care Med 2002;30:1765-9
6. Vanderschueren S, De Weerdt A, Malbrain M, et al. Thrombocytopenia and Prognosis in intensive care. Crit Care Med 2000;28:1871-6.
7. Levi M, Löwenberg EC. Thrombocytopenia in critically ill patients. Semin Thromb Hemost 2008;34:417-24.
8. Greinacher A, Sallange K. Thrombocytopeniae in the intensive care unit patient. ASH Education Program Book. 2010;135-43
9. Haksöyler, V at al. Dahiliye yoğun bakım ünitesinde trombositopeni ve mortalite ve morbidite ilişkisi . Cukurova Medical Journal 44 (2019): 632-41
10. Coşkun R. at al. Yoğun Bakım Ünitesinde Trombositopeni Yoğun Bakım Derg 2016; 7: 3-8
11. Hui P, Cook DJ, Lim W, et al. The frequency and clinical significance of thrombocytopenia complicating critical illness: a systematic review. Chest 2011;139:271-8.
12. Garrard C, Littlewood TJ. The incidence and cause of coagulopathies in an intensive care popülation Br J Haematol 1996 May;93(2):460-3.
13. Vanderschueren S, De Weerdt A, Malbrain M, Vankersschaever D, Frans E, Wilmer A, Bobbaers H: Thrombocytopenia and prognosis in intensive care. Crit Care Med 2000, 28:1871-76.
14. Rice TW, Wheeler AP. Coagulopathy in critically ill patients: Part 1: Platelet disorders. Chest 2009; 136: 1622-1630
15. Thiolliere F, Serre-Sapin AF, Reignier J, et al. Epidemiology and outcome of thrombocytopenic patients in the intensive care unit: results of a prospective multicenter study. Intensive Care Med 2013;39:1460-8.
16. Levi M, Opal SM. Coagulation abnormalities in critically ill patients. Crit Care. 2006; 10(4): 222.
17. Shalansky S, Verma AK, Levine M, Spinelli JJ, Dodek PM. Risk markers for thrombocytopenia in critically ill patients: a prospective analysis. Pharmacotherapy. 2002;22:803-13
18. Crowther MA, Cook DJ, Meade MO et al. Thrombocytopeniain medical-surgical critically illpatients: prevalence, incidence, and risk factors. J Crit Care. 2005;20:348-53.
19. Akca S, at al Time course of platelet counts in critically ill patients Crit Care Med 2002 Apr;30(4):753-6