Original Article

Internal Medicine

DAHUDER Medical Journal
e-ISSN: 2791-9250

Relationship between platelet parameters and disease severity and coagulpathy in COVID 19

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ABSTRACT

Objectives: Coagulopathy plays an important role in the clinical course of Covid-19 disease. The aim of our study is to examine the factors affecting the severity of this disease and to examine whether there is a relationship between platelet parameters and disease severity and coagulopathy markers.

Methods: The study was planned single-center, retrospective, and cross-sectional. 189 patients diagnosed with Covid-19 were admitted to the Internal Medicine Department. Patients were divided into 3 clinical categories according to the severity of the disease. The relationship between mean platelet volume and other platelet parameters, and disease severity and coagulopathy parameters were statistically analyzed.

Results: The study included 189 patients.182 of whom were discharged and 7 of whom died. The average age of the patients was 54.13 ± 14.21. D-Dimer levels were compared between the groups and were found to be significantly higher in cases of severe pneumonia. The group with severe pneumonia group had a higher PDW level than other groups. MPV was detected over 10 fl in the severe pneumonia group, but no statistically significant difference was found with the other groups. PT and INR levels are higher in patients with upper respiratory tract infection (URTI) compared to patients with mild to moderate pneumonia. APTT levels were found to be higher in patients with URTI than in patients with severe pneumonia.

Conclusion: In our study, PDW height and MPV height were determined from the findings showing platelet activation in patients with severe pneumonia. If an increase in these parameters is detected in patients diagnosed with the Covid 19 disease, close follow-up should be performed in terms of the development of complications.
Keywords: Coronavirus, Covid-19, platelet parameters, prognostic markers.

The Coronavirus disease (Covid-19) was first detected in Wuhan, China in December 2019. The Covid-19 disease is a disease in which the new type of beta coronavirus (SARS-CoV2) from the coronavirus family is the causative pathogen. İt can cause respiratory tract infection, and can develop in acute respiratory distress syndrome (ARDS) in severe cases.[1] This disease, which has spread around the world in a short period of time, was declared a pandemic by the World Health Organization on March 11, 2020.[2] Asymptomatic, mild viral infection, pneumonia and ARDS are observed in the clinic. Cases that develop Pneumonia are divided into two groups: mild-moderate pneumonia and severe pneumonia.[3] As the pandemic process progresseds, it has been determined that the disease is not limited to the respiratory tract, but it

Received: *September 24, 2021;* ***Accepted:*** *April 29, 2022;* ***Published Online:*** *April 29, 2022*

How to cite this article: *Erarslan S, Kilit TP, Çeviker SA, Gümüşçü HH, Akıncı M, Gülcan A. Relationship between platelet parameters and disease severity and coagulpathy in covid 19. DAHUDER M J 2022, 2(2):48-52.*

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affects other systems, and various complications may develop. SARS-CoV2 enters the cell by binding to the angiotensin-converting enzyme 2(ACE2) receptor. These receptors are known to exist in many tissues in the body(alveoli, vascular endothelium, cardiac myocytes, endocrine cells, etc.).[4] In clinical studies, Covid-19 has been shown to display a predisposition to thrombosis and thromboembolic complications during the course of the disease.[5] Especially in severe cases, findings such as thrombocytopenia, increased fibrin destruction products, lactate dehydrogenase height, fibrinogen height and prothrombin time prolongation were found.[6]

Platelets are the cells responsible for primary hemostasis and thrombosis in the peripheral circulation. They also contain granules with many immune receptors on the cell surface and various immune mediators in the cytoplasm. For this reason, it is believed that platelets are part of the immune system and have a regulatory and activating role in the immune response. [7] It is likely that the immune response caused by uncontrolled platelet activation can cause uncontrolled thrombosis and other complications(microvascular angiopathy, embolism, disseminated intravascular coagulation). Mean platelet volume(MPV) can increase due to increased platelet production, and MPV high platelets are more reactive.[8] The Platelet distribution rate(PDW) is a quantitative indicator of platelet size and volume and increases in the presence of platelet anisocytosis.[9] Plateletcrit (PCT) refers to platelet percentage and platelet large cell ratio (P-LCR) refers to the ratio of circulating large-sized platelets to other platelets.

In this study, we aimed to investigate whether there is a relationship between platelet parameters and coagulopathy, differences in prognostic factors in Covid-19 disease and differences in development laboratory levels according to clinical categories.

METHODS

PatientReception

This cross-sectional study included 189 patients between the ages of 26 and 87 who were hospitalized with the diagnosis of Covid-19 between the periods of April 2020 June 2020, a single-center. Covid-19 was diagnosed by polymerase chain reaction (PCR) test (Rotor-Gene Q, Qiagen, Hilden, Germany).

The fallowing groups were excluded from this study; under the age of eighteen, patients whom could not use drugs that affect platelet function, patients with hematologic and oncologic malignancies, patients with immune thrombocytopenia, patients with the diagnosis of coagulopathy, severe vitamin B12 deficiency, bone marrow and other related pathologies(essential thrombocytosis, myelodysplastic syndrome, aplastic anemia, etc.), patients with other diseases of platelet number and function that are affected bye use of drugs; patients with the presence of liver cirrhosis, splenomegaly, renal disease, collagen, connective tissue disorders, immunosuppressive, rheumatologic diseases and lastly patients with immunomodulatory.

This study was evaluated and accepted by the Ethics Committee of the Faculty of Medicine of Kütahya University of Health Sciences (Approval number is 2020/13-19. Date: 19.08.2020).

Data Collection

Demographic data (age, gender), comorbidities (chronic obstructive pulmonary disease, diabetes mellitus, hypertension, cardiovascular disease), clinical findings and hospitalization laboratory levels of the patients hospitalized with the diagnosis of Covid-19 were recorded through the system. Among the hemogram parameters white blood cell count (WBC), lymphocyte count(LYM), hemoglobin(Hgb), red blood cell count(RBC), erythrocyte distribution width (RDW), mean erythrocyte volume (MCV), platelet count (PLT) percentage of platelets (PCT, %), mean platelet volume (MPV, fl), platelet distribution ratio (PDW%) and platelet-large cell ratio (P-LCR%) were recorded.

Biochemical parameters urea, creatinine,aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH) and D-Dimer levels were noted. Fibrinogen levels, prothrombin time (PT), INR and activated partial thromboplastin time (aPTT) were recorded as markers of coagulopathy.

Statistical Analysis

SPSS (Statistical Package for Social Science) version 22 program was used for the analysis of the data. The compliance of continuous variables to normal distribution was examined by Kolmogorov-Smirnov and Shapiro-Wilk tests. Normally distributed data was expressed as mean ± standard deviation, non-normally distributed data was expressed as median and interquartile range (25-75 percent), and categorical variables as percentages. Differences between independent groups were compared using Student's t test for normally distributed data and

Mann-Whitney U test for data not showing normal distribution. Categorical parameters were analyzed using the Chi-Square test. In correlation analysis, Pearson correlation test was used for variables with normal distribution, and Spearman correlation test was used for variables with abnormal distribution. *P* value of < 0.05 was considered statistically significant for all tests.

RESULTS

A total of 189 patients, 96 females and 93 males, participated in the study. 7 of the 19 patients with Covid-19 who were followed-up with inpatient treatment died. Sociodemographic characteristics and chronic diseases of our patients taken into the study are shown in Table 1. Mean age of the patients was 54.13 ± 14.21. The average day of hospitalization was 10.45 ± 5.99. Smoking rates, DM and HT incidence and mortality rates were significantly higher in patients with severe pneumonia than in other groups ($p < 0.005$).

Evaluation of laboratory parameters in clinical categories is shown in Table 2. Glucose levels in patients with upper respiratory tract infection (URTI) were lower than in patients with mild to moderate pneumonia and severe pneumonia ($p < 0.001$). Urea levels in patients with severe pneumonia were higher than in patients with URTI and mild to moderate pneumonia ($p < 0.05$). AST levels were higher in patients with severe pneumonia and in patients with mild to moderate pneumonia ($p < 0.001$). In patients with severe pneumonia, the PDW level is higher than in patients with URTI and mild to moderate pneumonia ($p < 0.05$). MPV was detected over 10 fl in the severe pneumonia group, but no statistically significant difference was found with the other groups ($p > 0.05$). PT (p: 0.024) and INR (p: 0.003) levels were higher in patients with URTI than patients with mild to moderate pneumonia. aPTT level was higher in patients with URTI than in patients with severe pneumonia (p: 0.033).

In severe pneumonia, the CRP level increases until the 3rd day, and a decrease began after the 3rd day. The CRP level of those with URTI decreased after the first day.CRP levels increased for up to 5 days in patients with mild to moderate pneumonia and. it decreased after the 5th day (Figures 1 and 2). Although there was a significant relationship between the groups in

Table 1. Sociodemographic characteristics and chronic diseases of the patients*

		URTI		Mild-Moderate Pneumonia		Severe Pneumonia		P
		n	%	n	%	n	%	
Gender	Male	19	(51.35)	49	(45.79)	25	(55.56)	0.524
	Female	18	(48.65)	58	(54.21)	20	(44.44)	
Cigarette	No	26	(70.27)	56	(52.34)	16	(35.56)	**0.038**
	Yes	9	(24.32)	37	(34.58)	22	(48.89)	
	Former	2	(5.41)	14	(13.08)	7	(15.56)	
DM	No	31	(83.78)	68	(63.55)	12	(26.67)	**< 0.001**
	Yes	6	(16.22)	39	(36.45)	33	(73.33)	
HT	No	29	(78.38)	73	(68.22)	23	(51.11)	**0.027**
	Yes	8	(21.62)	34	(31.78)	22	(48.89)	
HL	No	35	(94.59)	90	(84.11)	36	(80.00)	0.161
	Yes	2	(5.41)	17	(15.89)	9	(20.00)	
COPD	No	32	(86.49)	91	(85.05)	34	(75.56)	0.300
	Yes	5	(13.51)	16	(14.95)	11	(24.44)	
Chronic Heart Disease	No	34	(91.89)	99	(92.52)	42	(93.33)	0.969
	Yes	3	(8.11)	8	(7.48)	3	(6.67)	
Result	Discharge	37	(100.00)	107	(100.00)	38	(84.44)	**< 0.001**
	Exitus	0	(.00)	0	(.00)	7	(15.56)	

*Chi-Square Test

Table 2. Comparison of Laboratory Parameters in Clinical Groups*

	URTI			Mild-Moderate Pneumonia			Severe Pneumonia			*P*
	Mean	Sd	Median	Mean	Sd	Median	Mean	Sd	Median	
Glucose	114.30	± 36.68	100.00	135.58	± 54.66	119.00	154.36	± 71.01	138.00	**< 0.001**
Urea	35.55	± 28.03	26.00	34.50	± 23.36	31.00	43.91	± 29.98	36.00	**0.008**
Creatinine	1.12	± 1.31	.86	1.05	± .89	.91	1.16	± .88	.99	**0.059**
AST	24.81	± 18.91	22.00	29.18	± 17.94	24.00	36.31	± 16.73	34.00	**< 0.001**
ALT	23.08	± 19.13	20.00	24.34	± 18.46	18.00	26.71	± 14.19	23.00	0.235
WBC	5.61	± 2.08	5.18	5.29	± 1.94	4.76	6.03	± 2.66	5.35	0.242
Hgb	13.72	± 2.13	14.00	13.11	± 1.62	13.20	12.90	± 1.77	12.80	0.073
RBC	4.70	± .55	4.69	4.59	± .53	4.60	4.43	± .55	4.33	0.063
PLT	208.97	± 59.00	198.00	205.79	± 61.60	198.00	193.36	± 78.18	173.00	0.221
MPV	9.82	± 1.25	9.60	9.75	± 1.14	9.60	10.02	± 1.21	10.30	0.313
PDW	16.06	± .35	16.10	16.07	± .46	16.10	16.28	± .39	16.30	**0.013**
PCT	.20	± .05	.19	.20	± .06	.19	.19	± .06	.17	0.323
P-LCR	25.66	± 8.46	24.10	25.34	± 7.80	24.60	27.22	± 8.33	28.20	0.303
PT	11.65	± .83	11.50	11.23	± .70	11.20	11.54	± .98	11.40	**0.024**
INR	1.02	± .08	1.00	.97	± .07	1.00	1.01	± .10	1.00	**0.003**
APTT	24.74	± 3.23	24.55	23.42	± 2.23	23.50	23.92	± 4.64	23.00	**0.033**

*Kruskal-Wallis Test

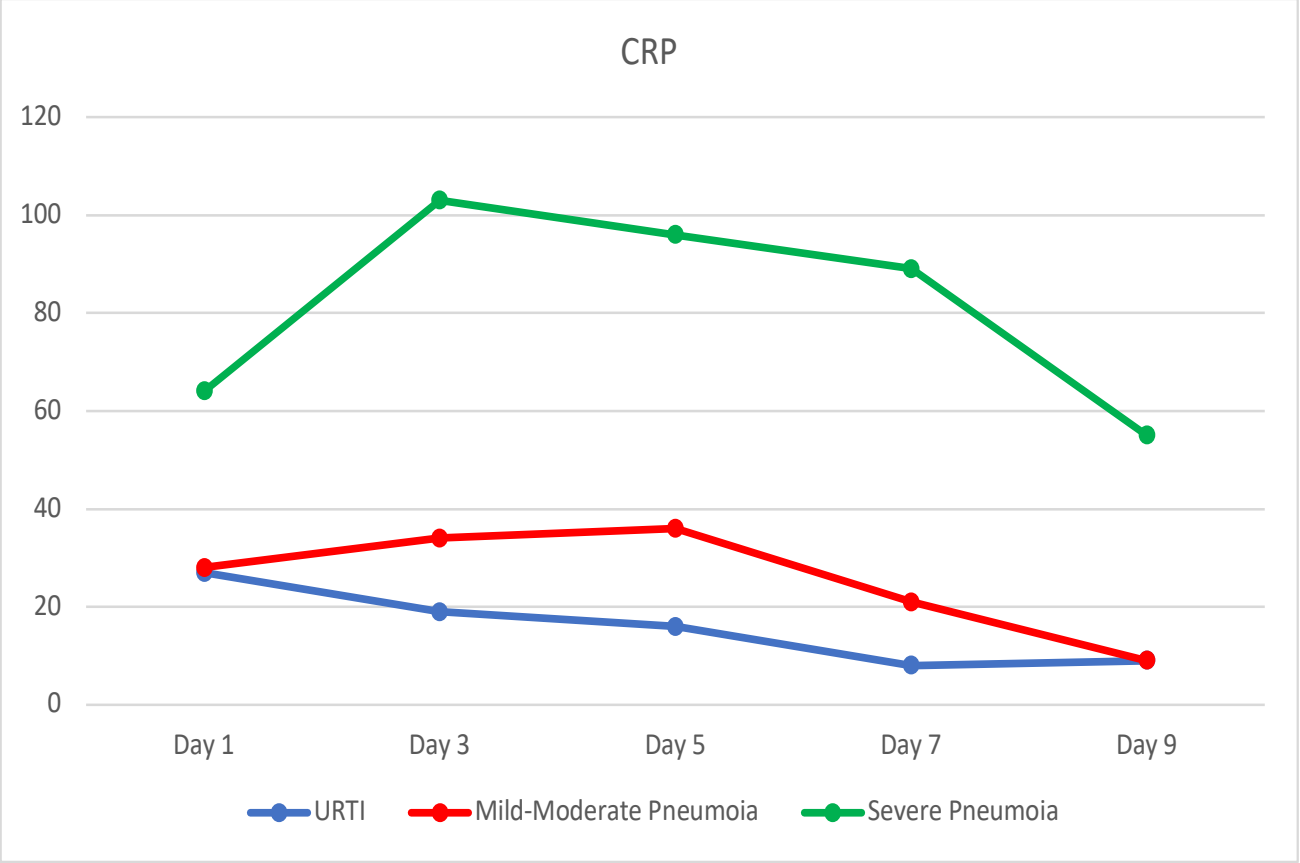

Figure 1. Change of CRP In Follow Up

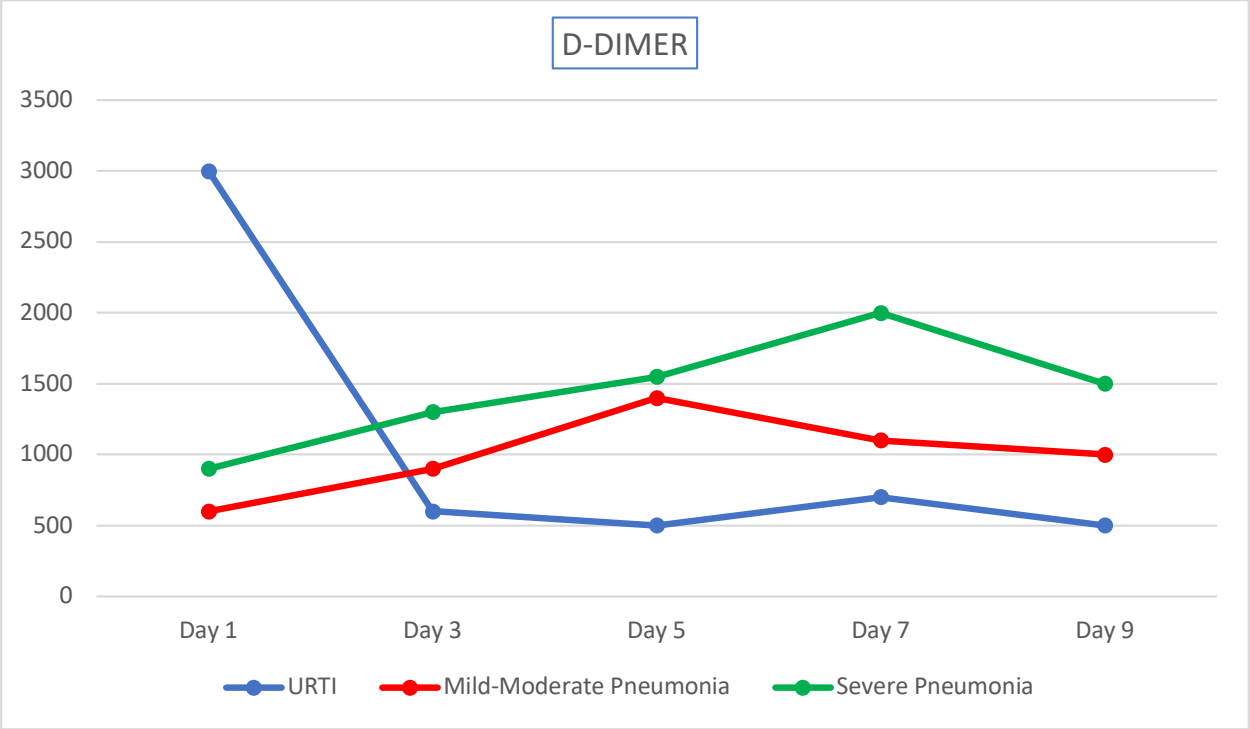

Figure 2. Change of D-DIMER In Follow Up

terms of the change in D-Dimer levels, no significant relationship was found in the post hoc analysis (Table 3). Figure 1 and Figure 2 demonsrate daily changes in CRP and D-Dimerlevels between groups. According to the results of PLT, patients were grouped and the groups and changes in CRP, ferritin, D-Dimer, lymphocyte, lactate, LDH, fibrinogen and troponin levels were examined and it was determined that no significant differences were found (Table 4). When the platelet parameters and coagulopathy markers and coagulation parameters were compared, the same direct correlation was found between aPTT and MPV and P-LCR, and an inverse correlation with PLT was found (Table 5)

DISCUSSION

With the Covid-19 disease, advanced age, smoking and the presence of additional comorbid diseases have been shown to cause an increase in the severity of the disease and a poorer prognosis.

In our study, we aimed to compare the chronic diseases, prognostic factors and platelet parameters in hospitalized patients with Covid-19. As a result of the study, we found that the RDW and MPV values of the platelet parameters in Covid 19 patients were high in cases of severe disease.

Platelet parameters vary according to the activation state of platelets and turnover rate. Young platelets are larger and more active.[8] MPV increase may happen due to cell activation or increase in production.[10] MPV has been shown to be significant as a prognostic marker in cardiovascular diseases and atherosclerosis. Chu *et al*. demonsrated in their study that MPV could be used as a cardiovascular disease risk marker.[11] In the study conducted by Zhang Y *et al*, it was found that in critical patients in intensive care, the RDW level of platelet parameters may again increase depending on the activation state (number of PLT, MPV, PCT, PDW). They found that there are independent risk factors for mortality.[12] The result of the study conducted by Zhang *et al*, revealed that PLT indices are an important marker in evaluating clinical indicators and assessing disease severity. Abnormally low PLT, high MPV levels and high PDW levels were found to be associated with more severe diseases. Again, high PDW has been shown in various studies to be a poor prognostic criterion in sleep apnea syndrome, chronic obstructive pulmonary disease and myocardial infarction.[13, 14] In this study that we conducted with Covid-19 patients, we revealed that PDW, one of the PLT indices, increased in a statistically significant way in severe disease with severe pneumonia ($p < 0.005$). MPV value was found over 10 fl in severe pneumonia and below 10 fl in other groups. However, no statistically significant difference was found with the other groups. No statistically significant relationship

Table 3. Relationship between clinical groups and bad prognostic factors*

	URTI			Mild-Moderate Pneumonia			Severe Pneumonia			*P*
	Mean	Sd	Median	Mean	Sd	Median	Mean	Sd	Median	
CRP (1st day)	15.65	± 45.44	3.77	21.33	± 31.29	11.54	64.08	± 57.79	46.50	**0.034**
CRP (3rd day)	12.84	± 41.96	2.97	27.93	± 37.78	10.82	102.89	± 91.70	72.04	
CRP (5th day)	10.65	± 21.33	2.65	27.47	± 37.13	10.62	93.56	± 76.92	83.34	
CRP (7th day)	9.19	± 21.78	1.00	21.20	± 29.36	9.85	88.86	± 116.23	35.73	
CRP (9th day)	8.00	± 19.93	1.42	8.61	± 14.58	3.48	50.21	± 86.12	8.56	
Ferritin (1st day)	120.83	± 250.21	73.00	134.70	± 177.03	95.00	271.52	± 305.59	188.50	0.133
Ferritin (3rd day)	146.88	± 290.34	72.50	148.76	± 184.81	108.00	343.79	± 362.49	225.50	
Ferritin (5th day)	133.26	± 177.86	67.00	163.91	± 189.21	110.00	370.77	± 357.46	291.00	
Ferritin (7th day)	161.50	± 144.33	97.00	163.10	± 205.88	114.00	390.10	± 391.35	243.00	
Ferritin (9th day)	103.36	± 90.90	91.50	136.14	± 192.75	91.00	287.64	± 274.62	206.00	
D-Dimer (1st day)	1678.03	± 5849.97	378.00	568.68	± 506.45	458.00	870.47	± 757.53	687.00	**0.008**
D-Dimer (3rd day)	542.50	± 431.65	352.50	904.69	± 1239.74	517.50	1204.00	± 929.95	935.50	
D-Dimer (5th day)	620.53	± 1051.49	390.50	1095.99	± 1774.76	546.00	1471.95	± 1396.94	769.00	
D-Dimer (7th day)	636.65	± 696.54	402.00	977.05	± 1560.84	507.00	1997.90	± 2797.49	1011.00	
D-Dimer (9th day)	481.21	± 329.82	369.50	875.16	± 1439.28	470.00	1386.27	± 1312.17	848.00	
LYM (1st day)	1.77	± .64	1.70	1.51	± .61	1.43	1.19	± .50	1.13	0.065
LYM (3rd day)	1.96	± .69	1.86	1.56	± .61	1.45	1.16	± .57	1.03	
LYM (5th day)	2.06	± .83	1.85	1.74	± .68	1.67	1.19	± .69	1.05	
LYM (7th day)	2.10	± .63	2.11	1.86	± .78	1.70	1.36	± .73	1.19	
LYM (9th day)	2.21	± .67	2.20	1.94	± .71	1.81	1.72	± 1.19	1.48	
Lactate (1st day)	2.37	± 1.13	2.20	1.99	± .89	1.80	1.87	± .77	1.70	0.476
Lactate (3rd day)	1.59	± .65	1.60	1.92	± .70	1.90	1.98	± 1.04	1.60	
Lactate (5th day)	1.93	± .66	2.00	2.08	± .73	2.10	2.44	± 1.00	2.10	
Lactate (7th day)	2.11	± .52	1.90	2.31	± 1.56	2.00	2.26	± .87	2.00	
Lactate (9th day)	2.09	± .73	1.95	2.43	± .83	2.30	2.38	± 1.40	2.10	
LDH (1st day)	224.40	± 84.28	198.00	260.02	± 96.04	236.00	300.87	± 106.80	290.00	0.747
LDH (3rd day)	235.27	± 138.60	178.50	256.45	± 77.77	241.00	322.49	± 114.56	314.00	
LDH (5th day)	240.78	± 110.05	215.00	264.99	± 84.29	241.00	354.98	± 104.15	356.50	
LDH (7th day)	269.00	± 118.69	233.00	293.21	± 104.22	263.50	366.33	± 139.95	326.00	
LDH (9th day)	233.52	± 63.52	225.00	273.77	± 187.27	236.00	303.83	± 136.52	273.50	
Fibrinogen (1st day)	356.29	± 113.11	334.50	425.73	± 110.60	414.50	516.02	± 110.06	514.00	0.797
Fibrinogen (3rd day)	383.78	± 118.93	362.50	445.84	± 113.45	449.20	540.40	± 155.74	510.40	
Fibrinogen (5th day)	379.15	± 142.68	316.30	442.95	± 116.53	434.10	550.17	± 123.19	568.10	
Fibrinogen (7th day)	398.55	± 164.11	426.00	431.89	± 123.90	412.00	520.28	± 155.09	537.00	
Fibrinogen (9th day)	339.09	± 100.45	333.50	368.47	± 123.43	341.00	471.47	± 165.23	439.00	
TROP (1st day)	4.78	± 6.33	3.00	4.98	± 7.46	3.20	13.26	± 23.35	5.70	0.706
TROP (3rd day)	5.24	± 6.12	3.30	5.45	± 8.24	3.20	12.86	± 21.81	4.70	
TROP (5th day)	3.85	± 3.75	2.55	4.86	± 6.76	3.20	66.58	± 315.64	4.70	
TROP (7th day)	5.52	± 4.95	3.90	825.12	± 6401.14	3.10	70.22	± 320.90	3.60	
TROP (9th day)	3.88	± 4.65	2.30	429.02	± 3425.20	2.90	10.86	± 17.57	3.40	

*Analysis Of Repetitive Measurements

was found between other platelet parameters (PCT, P-LCR) and disease severity.

Uncontrolled activation of thrombocytes may play a role in the pathogenesis of coagulopathy and thromboembolic complications in Covid-19. These findings showing thrombocyte activation in patients with severe pneumonia (PDW elevation, MPV above 10 fl) may have developed secondary to severe inflammationand may also have caused the development of severe pneumonia as the platelet activation exacerbates the inflammation. When the relationship between platelet parameters and coagulation tests and coagulopathy markers was examined, a positive significant relationship was found between aPTT and MPV and P-LCR, and a negative relationship was found with PLT.

Table 4. Relationship between PLT levels and bad prognostic factors*

		PLT Group												
		< 100			100-149			150-199			> 200			*P*
		Mean	Sd	Median	Mean	Sd	Median	Mean	Sd	Median	Mean	Sd	Median	
CRP	1st day	24.84	± 32.97	6.52	27.05	± 35.30	16.48	28.92	± 51.23	7.60	32.97	± 46.04	12.95	0.485
	3rd day	28.58	± 37.81	10.39	45.79	± 59.91	16.34	49.88	± 72.31	9.61	40.28	± 66.25	13.66	
	5th day	60.56	± 77.99	60.56	49.82	± 59.12	20.28	47.65	± 66.97	9.64	32.97	± 48.74	12.57	
	7th day	37.39	± 47.72	37.39	41.45	± 65.00	12.15	57.97	± 110.63	14.17	28.57	± 49.25	8.36	
	9th day	6.28	± 5.88	6.28	27.11	± 51.76	3.48	24.22	± 63.56	2.72	15.90	± 42.65	5.11	
Ferritin	1st day	315.33	± 316.50	222.00	195.68	± 322.67	98.50	187.89	± 277.64	100.00	130.92	± 136.10	97.50	0.390
	3rd day	286.33	± 286.31	178.00	242.00	± 370.45	99.00	276.07	± 345.23	128.00	136.74	± 136.99	104.50	
	5th day	571.50	± 727.61	571.50	255.34	± 295.30	170.50	272.43	± 334.34	152.00	154.99	± 144.60	110.00	
	7th day	540.00	± 697.21	540.00	264.34	± 353.33	148.00	270.59	± 333.15	170.00	176.09	± 174.00	114.50	
	9th day	500.50	± 651.25	500.50	160.11	± 156.41	118.00	216.77	± 280.83	115.00	143.95	± 165.83	93.00	
D-Dimer	1st day	1092.67	± 890.65	660.00	1485.51	± 5847.01	454.00	750.21	± 1316.51	448.10	679.48	± 581.66	521.00	0.228
	3rd day	1510.33	± 1907.68	430.00	756.39	± 571.08	607.00	783.04	± 761.65	528.00	1061.30	± 1355.81	561.00	
	5th day	1156.00	± 551.54	1156.00	909.72	± 678.10	692.00	989.98	± 1319.65	499.00	1264.28	± 1972.89	540.00	
	7th day	1560.00	± 1343.50	1560.00	926.27	± 1006.15	629.50	1689.47	± 3090.07	658.50	1120.28	± 1513.99	574.00	
	9th day	1380.50	± 1137.73	1380.50	811.48	± 859.24	554.00	870.77	± 1087.74	500.00	1066.23	± 1601.52	553.00	
LYM	1st day	1.20	± .59	.94	1.36	± .65	1.11	1.49	± .57	1.41	1.54	± .65	1.52	0.504
	3rd day	1.20	± .59	1.43	1.34	± .64	1.31	1.46	± .64	1.36	1.69	± .67	1.61	
	5th day	.99	± .30	.91	1.36	± .67	1.30	1.59	± .73	1.50	1.85	± .79	1.72	
	7th day	.82	± .35	.82	1.55	± .79	1.34	1.68	± .68	1.58	1.91	± .82	1.81	
	9th day	1.17	± .36	1.17	1.59	± .71	1.42	1.85	± .60	1.67	2.15	± 1.06	1.99	
Lactate	1st day	1.85	± .07	1.85	1.74	± .74	1.60	2.07	± .79	2.10	2.09	± 1.02	1.80	0.820
	3rd day	1.85	± .64	1.85	1.96	± .97	1.80	1.79	± .60	1.80	1.95	± .97	1.80	
	5th day	1.95	± .21	1.95	2.17	± 1.08	1.80	2.12	± .69	2.00	2.26	± .86	2.20	
	7th day	2.30	± .42	2.30	2.08	± .63	1.90	2.33	± 1.18	2.00	2.28	± 1.34	1.90	
	9th day	2.55	± .78	2.55	2.25	± 1.31	2.00	2.41	± 1.45	2.20	2.35	± .79	2.20	
LDH	1st day	262.00	± 122.34	199.00	260.42	± 92.40	239.00	233.39	± 83.05	202.00	285.20	± 108.01	259.00	0.754
	3rd day	276.50	± 173.24	276.50	279.54	± 139.97	244.00	271.00	± 92.26	241.00	269.07	± 98.54	257.00	
	5th day	331.00	± .00	331.00	307.04	± 142.58	262.50	290.67	± 92.53	285.00	277.73	± 96.03	257.50	
	7th day	218.50	± 48.79	218.50	305.11	± 98.59	289.50	353.83	± 162.36	306.50	299.48	± 99.19	278.00	
	9th day	181.50	± 27.58	181.50	279.28	± 105.94	244.00	260.97	± 119.94	233.00	290.89	± 201.34	244.00	
Fibrinogen	1st day	324.90	± 66.37	353.70	419.87	± 95.86	424.00	425.71	± 138.94	381.00	458.25	± 118.86	456.50	0.335
	3rd day	356.65	± 58.90	356.65	458.26	± 114.24	439.25	487.80	± 178.33	458.00	453.70	± 117.99	452.00	
	5th day	361.15	± 14.35	361.15	454.83	± 125.57	439.00	482.07	± 164.11	520.00	459.02	± 122.94	460.00	
	7th day	368.85	± 28.07	368.85	413.52	± 118.46	393.45	498.61	± 178.84	491.90	454.57	± 128.19	456.50	
	9th day	190.25	± 133.29	190.25	374.21	± 118.95	331.60	405.28	± 186.91	366.00	418.24	± 112.94	408.35	
TROP	1st day	4.93	± .71	4.80	8.54	± 14.02	5.10	6.77	± 10.98	3.45	6.52	± 15.09	3.20	0.664
	3rd day	3.50	± .71	3.50	9.00	± 9.39	5.05	10.58	± 21.13	3.95	5.03	± 7.95	3.30	
	5th day	5.50	± 3.96	5.50	7.24	± 7.09	4.90	53.63	± 293.09	3.60	6.49	± 17.95	3.20	
	7th day	3.45	± 3.46	3.45	9.10	± 12.98	5.20	68.99	± 330.17	3.65	987.70	± 7000.37	3.00	
	9th day	3.50	± .42	3.50	4.34	± 4.22	3.15	7.10	± 12.68	2.80	606.22	± 4071.34	2.75	

*Analysis Of Repetitive Measurements

Thrombocytopenia may be an indicator of the poor prognosis in infectious diseases. Development of thrombocytopenia in community-acquired pneumonia is associated with poor clinical outcomes.[15] In Severe Acute Respiratory Syndrome (SARS), thrombocytopenia has been detected at a rate of 50% and it is known to be an important marker of poor prognosis.[16] Thrombocytopenia may develop in Covid-19, as in the SARS epidemic.[17] Liu Y *et al*., in his study found that, Covid-19 patients with thrombocytopenia had 3 times more mortality compared to patients without thrombocytopenia, and the platelet count was shown to be an independent risk factor for mortality.[18] In a meta-analysis, it was shown that severe Covid-19 infection is three times higher in the presence of thrombocytopenia.[19] Ourstudy was conducted in internal medicine clinic and no significant relationship was found between the platelet count and disease severity.Again,the patients were grouped according to the platelet count (< 100 thousand, 100-

Table 5. Relationship between PLT parameters and coagulopathy markers*

		PCT	MPV	PDW	P-LCR	PLT
D-Dimer mean	r	-0.011	-0.035	0.120	-0.036	0.016
	p	0.911	0.714	0.209	0.705	0.869
LDH mean	r	-0.033	0.046	0.115	0.016	-0.048
	p	0.776	0.690	0.321	0.890	0.675
Fibrinogen mean	r	0.095	-0.084	0.098	-0.059	0.158
	p	0.397	0.455	0.386	0.603	0.159
PT	r	-0.080	0.060	0.068	0.082	-0.104
	p	0.280	0.413	0.353	0.268	0.159
APTT	r	-0.076	**0.147**	0.141	**0.163**	**-0.151**
	p	0.306	**0.046**	0.055	**0.027**	**0.041**
INR	r	-0.024	0.056	0.039	0.072	-0.057
	p	0.749	0.450	0.600	0.326	0.442

*Spearman Correlation Test

150 thousand, 150-200 thousand, > 200 thousand) and their relationship with poor prognostic factors was evaluated using repetitive measurement analysis, and no significant difference was found in bad prognostic factor levels according to platelet count.

Covid-associated coagulopathy is related to the severity of the disease, and factors such as increased inflammation, immobility, platelet activation, and endothelial damage are thought to be effective in its pathogenesis.20D-Dimer is a fibrin degradation product and can be detected high in blood due to fibrinolysis.[21] LDH can be detected high due to cell damage (especially lung and endothelial cell damage) and fibrinogen can be detected high due to inflammation in Covid-19. These markers rise in relation to disease severity in the right direction.[22, 23]In a study, D-Dimer levels were found to be higher in Covid-19 patients who died compared to those who survived.[24] In another study, it was observed that the mortality rate was high in those with D-Dimer levels above 1 µg / dl.[25] In light of these studies, it is suggested that D-Dimer level can be used as a marker of poor prognosis in the early period.[26] In our study, the D-Dimer level was found to be high in all patient groups, and it was found to be higher in the group with severe pneumonia in clinical follow-ups compared to the other groups. İn addition, fibrinogen and LDH were found to be high compared to normal, and no significant differences were found between the study groups.

PT-INR, aPTT levels were found to be high in intensive care patients developing disseminated intravascular motility (DIC).[27] In our study, the PT-INR level was found to be significantly higher in the group with URTI compared to the group with mild-moderate pneumonia, and also significantly higher in the group with URTI than the group with severe pneumonia. As the severity of the disease increases, the severity of inflammation increases and consequently the increase in thrombosis susceptibility may explain this finding.

In individuals diagnosed with Covid-19, poor prognostic factors (ferritin, C-reactive protein (CRP), fibrinogen, D-Dimer, lactate dehydrogenase (LDH), lactate and troponin) are used in clinical follow-up to evaluate the severity of the disease and response to treatment. CRP, an acute phase reactant, has been shown to be associated with the severity of the disease. A study found that CRP levels were significantly higher in severe covid-19 patients than in non-severe ones.[28] In another study, CRP level was determined above 41.8 mg/dl in severe patients.[29] In our study, CRP level was significantly higher in the group with severe pneumonia than in other groups. It was also observed that the CRP response to treatment varies according to the disease severity.

Our study has some limitations. The first is that coagulopathy was defined by laboratory findings and radiological scanning was not performed. Second, the intensive care patient group who developed ARDS was not included in the study

CONCLUSION

In our study, high PDW and high MPV were

detected among these findings indicating thrombocyte activation in patients with severe pneumonia. This situation supports the role of uncontrolled activation of platelets in the pathogenesis of coagulopathy and thromboembolic complications in Covid-19. PLT indices can be measured simply and quickly. There may be a relationship between the severity of inflammation and platelet activation in the disease. High detection of these parameters, which are platelet activation markers, may predict the risk of severe disease and coagulopathy, and these patients may need to be followed up more closely.

More comprehensive studies are needed to fully demonstrate the role platelet activation plays in the pathogenesis of Covid-19.

Authors' Contribution

Study Conception: SE, TPK, SAÇ, HHG, MA, AG,; Study Design: SE, TPK, SAÇ, HHG, MA, AG,; Supervision: SE, TPK, SAÇ, HHG, MA, AG,; Materials: SE, TPK, SAÇ, HHG, MA, AG,; Data Collection and/or Processing: SE, TPK, SAÇ, HHG, MA, AG,; Statistical Analysis and/or Data Interpretation: SE, TPK, SAÇ, HHG, MA, AG,; Manuscript Preparation: SE, TPK, SAÇ, HHG, MA, AG

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