

## Determination of Plateletcrit, Mean Platelet Volume in Patients with COVID-19 Pneumonia

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### Abstract

**Background:** Plateletcrit (PCT), Mean platelet volume (MPV), MPV/Platelet ratio, and other parameters of complete blood count have been used as predictive indicators in many inflammatory diseases. By considering COVID-19 pneumonia as an inflammatory process depending on similarity to ARDS, we can state that platelet indices might be a predictor of clinical course. This study aims to investigate the role of plateletcrit (PCT) mean platelet volume (MPV), MPV/PLT ratio, and other parameters of complete blood count in predicting prognosis on patients with COVID-19 pneumonia.

**Materials and methods:** We retrospectively recruited 150 patients who were admitted to our institute, a tertiary center, between March 2020 and May 2020 to our research. Demographic data, comorbidities (hypertension, diabetes, cardiovascular disease etc), clinical manifestations, and laboratory findings (PCT, MPV, MPV/PLT ratio, PLT) were collected from retrospectively from medical resources and electronic database. The patients divided into three groups. The ones who diagnosed COVID-19 pneumonia in the ward (n=50) considered as mild clinical course (mild group), and the ones in the intensive care unit (n=50) considered as severe clinical course (severe group). There was an additional ICU patient who are not diagnosed COVID-19 as a control group (n=50 Control group).

**Results:** Even though platelet count, MPV and MPV/PLT ratio were statistically similar, PCT was significantly lower in COVID-19 diagnosed groups. PCT showed no significant statistical difference between severe (0,2346±0,17218) and mild group (0,2148±0,9296) (p>0.05), but comparing the covid diagnosed groups (0,2148±0,9296) with control group (0,2334±0,0653), PCT was significantly lower in the covid diagnosed groups (p<0,05).

**Conclusion:** Our research showed an association between platelet indices (especially PCT) and clinical course of COVID-19 pneumonia. PCT may be a predictor in the prognosis of patients with COVID-19 patients. Early detection of prognosis might be possible with monitoring PCT, but further clinical and basic research are necessary.

**Key words:** Platelet indices, coronavirus 19, plateletcrit

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## Introduction

Platelets have a significant role in hemostasis and thrombosis. Furthermore, they are involved in the inflammatory process, wound healing, angiogenesis, and remodeling (1,2). Platelets also mediate leukocyte movement from the bloodstream through the vessel wall to tissues (3). Pulmonary vascular leakage, disseminated intravascular coagulation and intravascular thrombosis may occur during COVID-19 related by abnormal coagulation. Thrombocytopenia is also a common clinical manifestation associated with poor outcome in patients with community acquired pneumonia (4,5). Coagulation disorders are frequently encountered among COVID-19 patients, especially among those with severe disease (6). Although many cases of thrombocytopenia have been reported in patients with severe viral pneumonia. It is suggested that this is a clinical characteristic of COVID-19. The association between changes in platelets, platelet indices and adverse COVID-19 outcome remains unclear (7). It is still not possible to guess the clinical course of COVID-19 at admission of hospital. Thrombocytopenia or changes of thrombocyte indices may predict the clinical progress of disease. So, we can decide about the clinical course of COVID-19 pneumonia by evaluating the simple test hemogram which is done at admission to hospital.

Based on this, we suggest that platelet indices (plateletcrit (PCT), mean platelet volume (MPV) and platelet distribution width (PDW) as derivative platelet parameters may have prognostic value in COVID-19 pneumonia. In our study we tried to identify if platelet indices can give an opinion about COVID-19 pneumonia clinical progress from the hemogram at admission of hospital.

## Materials and Methods

### *Study population*

We retrospectively recruited 150 patients who were admitted to our institute-a tertiary center- between March 2020 and May 2020 to our research. The study protocol was approved by the local ethical committee (69-12.05.2020) and conducted according to the declaration of Helsinki. The study was registered in the Clinical Trials Registry (NCT04408378) on October 8, 2020. The patients over 18 years old who were diagnosed with COVID-19 pneumonia at the emergency department and who were interned either to intensive care or ward were included in the study. Patients with hemolytic diseases and under 18 years were exclusion criteria.

### *Data collection and outcome measurements*

Demographic data (gender and age), comorbidities (chronic obstructive pulmonary disease, hypertension, cardiovascular disease, cerebrovascular disease, diabetes, and chronic kidney disease), clinical manifestations, and laboratory findings (PCT, MPV, MPV/PLT ratio, PLT) were collected retrospectively from medical resources and electronic database. Hemogram test is a simple method to evaluate patients' status and applied to every patient in the emergency department in our hospital. Platelet count, MPV and PCT counts were recorded from the hemogram (Mindray BC 6800 Haematology Analyzer) at admission to hospital.

Plateletcrit which calculated according to the formula  $PCT = \text{platelet count} \times MPV / 10,000$  was our primer outcome parameter. The normal range for PCT is 0.22–0.24% (8–10). Platelet count, mean platelet volume, values recorded and MPV/PLT ratio calculated by dividing mean platelet volume into platelet count as seconder outcome parameters. The

patients divided into three groups. The ones in the ward (n=50) considered as mild clinical course (mild group), and the ones in the intensive care unit (n=50) considered as severe clinical course (severe group). There was an additional ICU patient who are not diagnosed COVID-19 as a control group (n=50). ICU admission criteria were acut severe respiratory failure, hemodynamic instability, multiorgan failure and neurological impairment in our study. Patients with mild symptoms (cough, headache, fatigue, fever etc.) but need medical or supplemental support were the patients in the wards.

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## Results

A total of 150 patients from ICU, wards and covid negative control group were examined retrospectively due to admission hemograms. There was a statistical difference regarding gender between the groups ( $p < 0,05$ ). There was 38% female, 62% male in the severe group; 36% female, 64% male mild group, although the control group was 66% female and 34% male. There was not any statistical difference in each 3 groups regarding age and gender as shown in the Table 1.

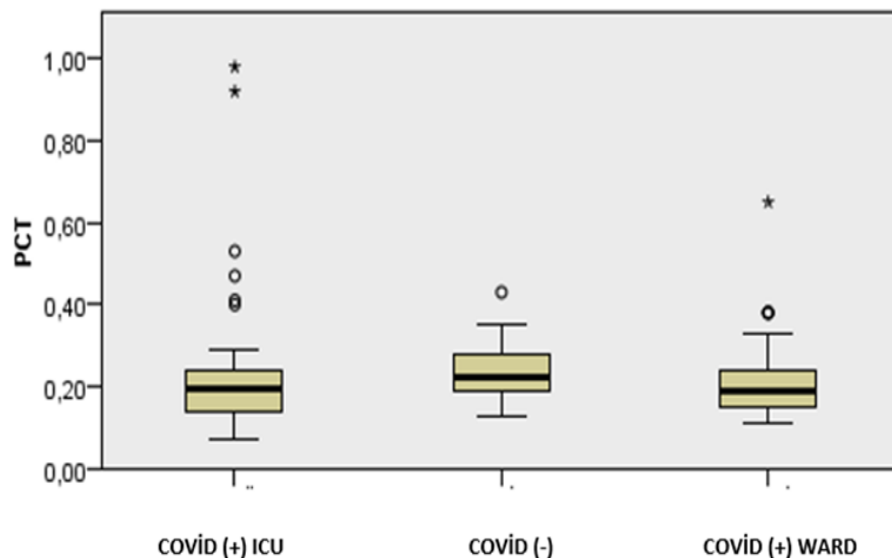
Comparing the groups regarding to comorbidities; diabetes mellitus (DM), hypertension (HT), coronary artery disease (CAD), chronic renal failure (CRF), lung cancer (Lung CA) statistically significant difference determined ( $p < 0,05$ ). In the Covid positive groups DM, HT, CAD and CRF incidence was higher. Between the COVID-19 diagnosed groups, patients with CRF had a mild clinical course and were interned mostly in the ward. Three patients accompanying lung CA were in the severe group and charged in ICU. Differences among the groups regarding to comorbidity shown in Table 1.

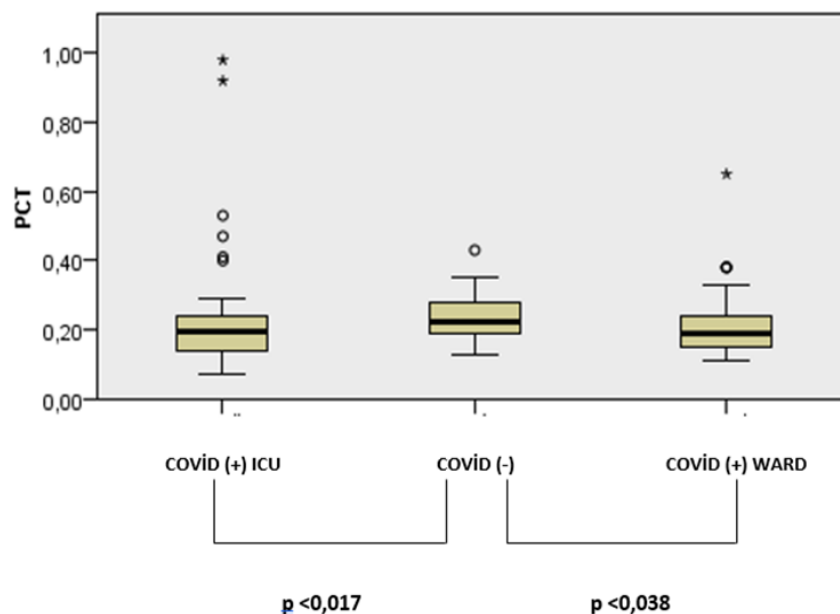
**Table 1.** Distribution of gender, age and comorbidities in three groups.

		Severe	Ccontrol	Mild	p value
<b>Age</b>		63,56±15,111	60,62±16,456	63,84±16,457	
<b>Sex</b>	M	31 (%62)	17 (%34)	32 (%64)	
	F	19 (%38)	33 (%66)	18 (%36)	
<b>DM</b>		11 (%22)	48 (%96)	38 (%76)	0,013
<b>HT</b>		33 (%66)	47 (%94)	32 (%64)	0,001
<b>CAD</b>		43 (%86)	49 (%98)	42 (%84)	0,049
<b>CRF</b>		46 (%92)	48 (%96)	40 (%80)	0,26
<b>LUNG</b>					
<b>CA</b>		47 (%94)	50 (%100)	50 (100)	0,047

DM : Diabetes Mellitus, HT : Hypertension, CAD : Coronary Artery Disease, CRF : Chronic Renal Failure, Lung CA : Lung Cancer.

PCT showed no significant statistical difference between severe ( $0,2346 \pm 0,17218$ ) and mild group ( $0,2148 \pm 0,9296$ ) ( $p > 0,05$ ), but comparing the covid positive diagnosed groups ( $0,2148 \pm 0,9296$ ) with control group ( $0,2334 \pm 0,0653$ ), PCT was significantly lower in the covid positive diagnosed groups ( $p < 0,05$ ) as shown in Figure 1-2.

**Figure 1.** Comparison PCT values among severe, mild and control groups.



**Figure 2.** Comparison PCT values among severe, mild and control groups.

The averages of PCT, MPV, MPV/PLT and PLT values of our participants are presented in table 2. Platelet count was statistically insignificant among groups. Similarly, there were not any statistically difference in MPV and MPV/PLT ratio comparing 3 groups ( $p > 0,05$ ).

**Table 2.** PLT, MPV, PCT values and MPV/PLT ratio data are presented as mean  $\pm$  standard deviation.

Groups		PLT ( $\times 10^3/\mu\text{l}$ )	MPV (fL)	MPV/PLT Ratio	PCT (%)
<b>Severe</b>	Minimum	86	7,6	0,018	0,07
	Maximum	525	12,2	0,099	0,98
	Mean + SD	219,38 $\pm$ 97,792	9,776 $\pm$ 1,0901	0,05258 $\pm$ 0,02155	0,2346 $\pm$ 0,17218
<b>Control</b>	Minimum	150	7,2	0,015	0,13
	Maximum	487	13,3	0,072	0,43
	Mean + SD	244,9 $\pm$ 76,718	9,768 $\pm$ 1,2293	0,04358 $\pm$ 0,013319	0,2334 $\pm$ 0,0653
<b>Mild</b>	Minimum	107	7,8	0,01	0,11
	Maximum	800	12	0,104	0,65
	Mean + SD	230,66 $\pm$ 119,663	9,642 $\pm$ 1,0668	0,0505 $\pm$ 0,021459	0,2148 $\pm$ 0,9296

PCT: Plateletcrit, MPV: Mean platelet volume.

## Discussion

Platelet count, MPV and MPV/PLT ratios have similar insignificant statistical data, but PCT has an important role in evaluating the severity of COVID-19 pneumonia according to our study. Our findings also demonstrate that COVID-19 is more frequent in male gender and accompanying diseases may influence COVID-19 pneumonia clinical course.

Abnormal coagulation results, especially obviously elevated D-dimer levels and fibrin degradation products are common in severe findings in COVID-19 pneumonia patients. Thrombocytopenia is one of the most common findings in COVID-19 patients. Pathophysiological processes include direct attack of hematopoietic stem/progenitor cells and lung damage by autoantibodies and immune complexes by coronavirus. Decreased thrombopoietin production, increased platelet clearance and platelet consumption, dysfunctional bone marrow microenvironment, lung damage, and antiviral drugs may develop thrombocytopenia in patients with COVID-19 (11,12). Plateletcrit, one of the platelet indices, were revealed to have a predictive role in the correlation between thrombocyte function and clinical course of COVID-19 pneumonia based on our findings. Among many platelet indices, PCT, MPV/PLT ratio and MPV are mentioned in many studies claiming that platelet indices can be used in diagnosis, and as a predictability marker in prognosis several diseases (sepsis, ARDS, COPD, septic shock) (13-15). Even though there is not any connection between the prognosis, MPV, MPV/PLT, and thrombocyte count are opposite to previous studies.

The mean platelet volume (MPV) is a specific measurement of platelet dimension, calculated by hematological analyzers according to the volume distribution during routine hemogram test. MPV range is between 7.5 and 12.0 fl and large platelets should be 0.2-5.0% of the whole platelet amount (16). Korniluk et al (17) claims that there must be a MPV cut-off value indicating the intensity of inflammatory process, presence of disease, increased risk of disease development, increased risk of thrombotic complications, increased risk of death, and patient's response to applied treatment. Because MPV increases in some diseases and decreases in others. But in contrast to what our study stated, there was not an association between clinical course and basal MPV level. Zhao et al. (18) concluded that higher MPV and PDW are associated with increased risk of death, and the decrease in plateletcrit is associated with increased poor prognose risk in critical patients. Their research in a large cohort of critically ill patients also claims that there is a connection between platelet indices and clinical outcome. They thought that their results were not appropriate due to the diversity of patients in ICU. Conformably the same handicap exists in our study. They investigated the association of platelet indices with mortality in unselected ICU patients. In our study we identified the association of platelet indices with clinical outcome in COVID-19 pneumonia patients. According to our results, MPV/PLT ratio, MPV and platelet count were not significantly different, but a remarkable statistical difference was found in PCT. Our results confirmed the correlation of PCT with clinical outcome. PCT is thought to give a more specific opinion about prognosis than PLT count and MPV because it is determined by the combination of platelet count (PC) and MPV (PCxMPV).

PCT is a measurement derived from the platelet count and the mean platelet volume. In infectious conditions, increased or decreased PCT percentages were reported in several research. An example of them is tuberculosis in which increased PCT percentages were reported (19). In one of these studies, patients who died in intensive care probably due to sepsis presented decreased PCT, and in the other one, lowered PCT was found in neonates who had invasive fungal infection and bacterial sepsis (20,21). Like sepsis patients, PCT was lower in severe COVID-19 pneumonia patients.

In a study, Gao Y et al. (22) revealed an association between prognosis and baseline platelets in a hospital-based cohort study among 383 confirmed patients with COVID-19.



Hence, monitoring platelets during hospitalization may be important in the prognosis of patients COVID-19. Even though age, gender, pre-existing diseases, CD3+ CD8+T cells and cardiac troponin I are predictors of clinical course in covid pneumonia patients, there is not a predictive factor of prognosis yet (23). In our study, we confirmed that a simple measurement of PCT gained from routine complete blood counts (allowing us to assess platelet indices easily) at admission to hospital might be a simple inexpensive, simple predictor of clinical course of COVID-19 pneumonia. In contrast to this study, platelet count at admission was not correlated with prognosis in our study, we did not evaluate mortality.

During the coronavirus outbreak hypertension, diabetes mellitus and cardiovascular disease incidence were higher and correlated with severity of illness. Also, age was appointed as a prognostic factor of COVID-19 pneumonia (24). According to our results, age was irrelevant, but comorbidities differed among groups. Age and accompanying diseases both have different effects on hemogram parameters. Increased MPV was observed in cardiovascular diseases, cerebral stroke, respiratory diseases, chronic renal failure, intestine diseases, rheumatoid diseases, diabetes, and various cancers. Decreased MPV was noted in tuberculosis during disease exacerbation, ulcerative colitis, SLE in adults, and different neoplastic diseases (17). PCT has been supposed as a biomarker in several conditions, it has also been associated with pulmonary tuberculosis, Crohn's disease, coronary artery disease, deep vein thrombosis, endotoxemia, gastritis, and myocardial infarction (25-28). In this study, comorbidity incidence was higher in COVID-19 diagnosed groups and like previous studies PCT was lower in this group.

Limitations in our study are secondary infections, some therapeutic drugs including antibiotics and other baseline parameters like gender and age. They might have had an impact on the platelet indices and could have affected our results. And the current study was a retrospective analysis with limited numbers of unselected patients. Thus, a more thorough investigation in a larger series of patients is necessary to confirm the results.

## Conclusion

Lower PCT level may be a predictor in poor prognosis of patients with COVID-19 pneumonia. Examining the changes of PCT may be a factor to expose prognosis of COVID-19 pneumonia earlier. It is important to emphasize that low PCT levels are related to worse clinical courses of patients, but further clinical and basic research are necessary to clarify this issue.

**Ethics Committee Approval:** Yes

**Informed Consent:** NA

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

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

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