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Elevated Platelet Large Cell-Ratio Levels As A Demonstrative Biomarker Associated with Severe COVID-19

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Objective: To represent the effects of the severity of COVID-19 infection on platelet large cell ratio (PLC-R).

Materials and Methods: A hundred eleven patients diagnosed with COVID-19 were included in this study. Positive results for SARS-CoV-2 based on a typical RT-PCR test performed on nasopharyngeal swabs were included in the study Groups. Patients with COVID-19 were divided into three Groups according to their chest CT features. Group 1 (45 patients) was defined as mild, Group 2 (34 patients) as moderate and Group 3 (32 patients) as severe. Complete blood count parameters including platelet volume indices (PVI) values, CRP, D-dimer and lipid profiles were analyzed in all study participants. The correlation between COVID-19 patient Groups and PLC-R values were demonstrated using SPSS and ANFC methods.

Results: The significant impact of our study is that PLC-R was significantly higher in the severe COVID-19 patients than the moderate and mild patients. Spearman's rho correlation analysis showed that PLC-R and WBC levels increased, and Htc and Hb levels decreased with the severity of the disease. ROC analysis showed that PLC-R> 38.3% had 59.4% sensitivity and 68.4% specificity in predicting severe COVID-19 disease (AUC 0.672, %95 CI 0.560, 0.784; p=0.005, cut off=38.3). CRP, ferritin and D-dimer values of the patients in Group 3 were significantly higher than the patients in Group 1, and the iron values of the patients in Group 3 were significantly lower than the patients in Group 1.

Conclusion: PLC-R values are useful for anticipating acute thrombotic events. Based on the results of our study, PLC-R values can be used as appropriate biomarkers to describe the severity of COVID-19 infection.

Key Words: *COVID-19, SARS-CoV-2, platelet large cell-ratio, platelet volume indices*

Şiddetli COVID-19 Enfeksiyonunda Önemli Bir Biyomarker Olarak Artan Platelet Large Cell-Ratio Düzeyi

Amaç: Şiddetli COVID-19 enfeksiyonunun PLC-R düzeyleri üzerindeki etkilerini ortaya koymak amaçlandı.

Gereç ve Yöntem: COVID-19 tanısı konan 111 hasta çalışmaya dahil edildi. Nazofaringeal sürüntülerinde RT-PCR testleri ile SARS-CoV-2 pozitif tespit edilen hastalar çalışmaya dahil edildi. COVID-19 hastaları akciğer BT bulgularına göre üç gruba ayrıldı. Grup 1 (45 hasta) hafif, Grup 2 (34 hasta) orta ve Grup 3 (32 hasta) şiddetli olarak tanımlandı. Tüm hastaların PVI değerleri, CRP, D-dimer ve lipid profilleri dahil olmak üzere tam kan sayımı parametreleri analiz edildi. COVID-19 hasta grupları ile PLC-R değerleri arasındaki korelasyon SPSS programı ve ANFC yöntemleri kullanılarak gösterildi.

Bulgular: Bu çalışmanın en önemli bulgusu, şiddetli COVID-19 hastalarında PLC-R'nin orta ve hafif hastalara göre anlamlı derecede daha yüksek olmasıdır. Spearman's rho korelasyon analizi hastalığın şiddeti ile PLC-R ve WBC düzeylerinin arttığını, Htc ve Hb düzeylerinin ise azaldığını gösterdi. ROC analizi, PLC-R>%38.3'ün şiddetli COVID-19 hastalığını öngörmede %59.4 duyarlılığa ve %68,4 özgüllüğe sahip olduğunu gösterdi (AUC 0.672, %95 CI 0.560, 0.784; p=0.005, cut off=38.3). Grup 3'teki hastaların CRP, ferritin ve D-dimer değerlerinin Grup 1'deki hastalara göre anlamlı düzeyde yüksek olduğu, grup 3'teki hastaların demir değerlerinin ise grup 1'deki hastalara göre anlamlı düzeyde düşük olduğu görüldü.

Sonuç: PLC-R değerleri, akut trombotik olayları öngörmede değerli bir parametredir. Bu çalışmanın sonuçlarına göre PLC-R değerleri, COVID-19 enfeksiyonunun şiddetini tanımlamak için uygun bir biyobelirteç olarak kullanılabilir.

Anahtar Kelimeler**:** *COVID-19, SARS-CoV-2, trombosit büyük hücre oranı, trombosit hacim indeksleri*

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Introduction

In December 2019, the World Health Organization reported a new beta-coronavirus named "SARS-CoV2" responsible for the COVID-19 outbreak (1). Since clinical symptoms and radiological findings are not specific for this disease, the diagnosis should be confirmed by nucleic acid-based polymerase chain reaction (PCR) (2). Individuals infected with SARS-CoV-2 present with different clinical pictures ranging from mild respiratory tract infection to acute respiratory distress syndrome, organ dysfunctions, and even death in critical cases (3). Timely clinical intervention and follow-

up of the diagnosed patients are essential in terms of prognosis (4). Severe COVID-19 patients have an increased risk of thrombosis, including pulmonary embolism, venous thrombosis, and ischemic stroke (5). The high incidence of venous thromboembolism and the importance of anticoagulant thromboprophylaxis are noted in the guidelines and supported by sequential autopsy findings (6).

It is known that platelets, which also have important roles in the immune response, play an important role in developing these thrombotic complications (7). Hematological tests used in diagnosing and treating many diseases, including COVID-19 infection, are used as the first choice in terms of low cost and ease of operation (8, 9). Platelet volume indices (PVI) are parameters that are checked in hematological tests. PVI can be considered an indicator of increased platelet activity. PVI parameters include PLC-R, platelet large cell count (PLCC), mean platelet volume (MPV), mean platelet volume-to-platelet count ratio (MPV/P), platelet distribution width (PDW) and platelet distribution width-to-platelet count ratio (PDW/P) (10).

PLC-R is a percentage-based measure of circulating larger platelets (>12 fL), measured by using the formula PLC-R=Large platelet cell counts (>12 fL)/Total platelet counts. It has been used to monitor platelet activity as well. The number of platelets greater than 12 fL is referred to as PLCC. Plt×PLC-R is multiplied to form PLCC (11).

In this study, we aimed to represent the effects of the severity of COVID-19 infection on PLC-R.

Materials and Methods

Research and Publication Ethics: The study was performed by Helsinki principles and approved by the local Ethics Committee (Presidency of T.C. Firat University Ethics Committee). Ethical approval number: 2021/07-37, date: 27.05.2021.

Study Participants: This cross-sectional study was conducted in the Elazığ Fethi Sekin City Hospital, designated as the coronavirus pandemic hospital in the province by the ministry of health. A total of 111 SARS-CoV-2 infected patients with lung involvement treated in the COVID-19 wards and intensive care units between November 2020 and April 2021 were included in the study. Patients with a prior diagnosis of chronic illness or atherosclerotic risk factors were excepted from the study. Positive results for SARS-CoV-2 based on a typical RT-PCR test Bio-Rad CFX96 Real-Time PCR Detection System (Bio-Rad Laboratories, Inc., Hercules, CA, USA) performed on nasopharyngeal swabs were included in the study Groups.

Patients with COVID-19 pneumonia were divided into three Groups according to their chest computed tomography (CT) features. Group 1 (45 patients) was defined as mild, Group 2 (34 patients) as moderate, Group 3 (32 patients) as severe. The distribution of ground-glass opacities and consolidations to the affected lung lobes was evaluated qualitatively and visually using CT images (12). Group 1 (mild): small, localized ground glass opacities beginning at the lung periphery (SpO_2 96%-98%). Group 2 (moderate): opacities in more lung lobule, diffused, reticular "crazy-paving" patterns, and arterial stiffening, with small consolidations possible (SpO_2 90%-95%). Group 3 (severe): heavy porous consolidations covering a large proportion of the lungs, with more noticeable septal thickenings (SpO_2 90%). Laboratory parameters of the patients at the time of admission were examined.

Laboratory Measurements: Each blood sample (6 mL for complete biochemistry, 5 mL for complete blood count) was drawn from the antecubital vein. Samples were collected and analyzed in vacuum tubes, including 15% K3-ethylenediaminetetraacetic acid anticoagulation tubes (Sarstedt, Essen, Belgium). Complete blood count (CBC) parameters were measured using a Sysmex XN-550 hematology analysis tool (Sysmex Europe GmbH, Sysmex Corporation, Hamburg, Germany). A 3 mL sample of venous blood obtained in diamine tetraacetic acid-containing anticoagulation tubes were used to assess PVI. After half an hour of bloodletting, the blood samples of two Groups by using an electronic blood counter were analyzed. Platelet shape changes were allowed to stabilize during the half-hour waiting period. The levels of *D*-dimer, glucose, urea, creatinine, total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol (LDL-c) were tested using the chemiluminescence method on a Beckman Coulter AU5800 (Beckman Coulter, USA) auto-analyzer. C-reactive protein (CRP) levels were measured by using a nephelometric method (image 800, Beckman Coulter, USA).

Statistical Analysis: Power analysis was applied with the G*Power program to determine the adequacy of the sample size for PLC-R value comparison in COVID-19 patients. The sample size was found to be 58 patients in total, 29 patients for each Group (d: 0.879 ve Actual Power:0.951).

Statistical analyses were performed using SPSS software, version 26.0 (SPSS Inc., Chicago, IL, USA) for Windows. The Kolmogorov-Smirnov test was used to evaluate whether the variables were normally distributed. Platelet, glucose, triglycerides, urea, creatinine, CRP, iron, transferrin saturation (TSAT), ferritin, and D-dimer didn't show normal distribution. These variables were analyzed by the Kruskal Wallis test and were presented as medians with 25^{th}–75^{th} percentiles. Tamhane's T2 test was used for post hoc comparisons. Other continuous variables were analyzed by one-way ANOVA and were presented as means with standard deviations (SD). Bonferronni test was used for post hoc comparisons. Correlation analyses were performed using Spearman's rho correlation test. Receiver operating characteristics (ROC) analysis was performed to evaluate the specificity and sensitivity of PLC-R levels in detecting severe COVID-19 disease. All P-values were two-tailed, and values <0.05 were considered to indicate statistical significance.

In addition, all parameters were analyzed in detail with the adaptive neuro-fuzzy classifier (ANFC) method. ANFC systems can be used in pattern recognition, decision making, and many other fields. These systems depend on linguistic rules, which are ensured by experts or the rules, and are removed from a given training dataset by various clustering methods (13).

Results

This study performed laboratory analyses, among 111 SARS-CoV-2 infected patients, including 45 mild, 34 moderates, and 32 severe cases. Comparison of PLC-R average value comparison between mild, moderate, and severe Groups are demonstrated (Figure 1). It was observed that PLC-R values increased significantly in severe SARS CoV-2 patients (33.24%±6.24%, 35.73%±6.98% and 38.92%±7.64% in three Groups, respectively, p=0.003) (Table 1). There was no statistically significant difference in other PVI values between the three Groups (MPV (p=0.290), PDW (p=0.493), PLCC (p=0.080), total platelet counts (p=0.073) (Table 1). White blood cell (WBC), LDL-c, hemoglobin and hematocrit results showed significant values between Groups (p=0.002, p=0.002, p=0.018, p=0.007, respectively) (Table 1).

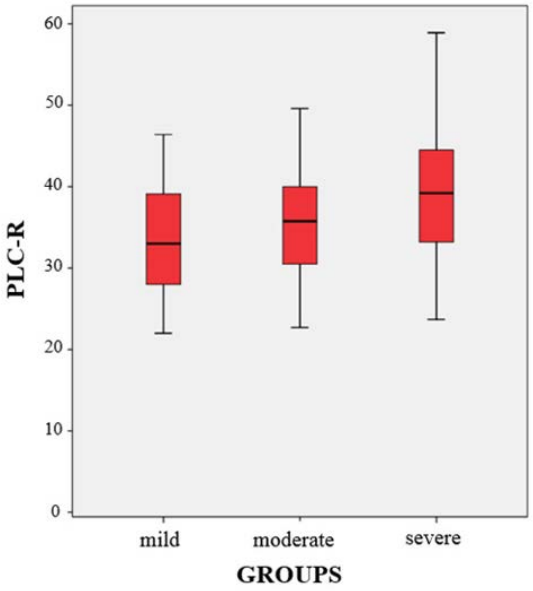

Figure 1. Comparison of average PLC-R value between Groups.

Table 1. Comparison of laboratory data between three Groups.

Variables	Group 1 (mild, n=45)	Group 2 (moderate, and=34)	Group 3 (severe, n=32)	P values
Age (year)	66.08±18.48	69.58±13.04	68.81±9.89	0.541
Platelet* (10^3/mm^3)	263.0(155.0-334.0)	314.5(188.7-384.5)	192.5(142.2-343.5)	0.073
Mean platelet volume (fL)	11.24±1.34	11.49±0.98	11.66±1.14	0.290
PDW (fL)	14.98±2.93	14.64±2.78	15.45±2.58	0.493
PLC-R (%)	33.24±6.24	35.73±6.98	38.92±7.64	0.003
PLCC (10^3/mm^3)	84.60±40.14	104.97±37.43	89.70±42.91	0.080
Glucose* (mg/dL)	127.0(103.5-180.5)	146.5(114.7-220.0)	166.0(132.0-229.7)	0.041
Triglycerides* (mg/dL)	150.0(101.5-210.0)	151.0(115.0-221.5)	197.5(145.5-238.2)	0.328
Low density lipoprotein cholesterol(mg/dL)	113.60±35.46	92.91±31.91	85.34±37.73	0.002
High density lipoprotein cholesterol(mg/dL)	41.37±13.01	37.17±12.17	35.00±14.46	0.101
Hemoglobin (g/dL)	13.45±1.99	12.85±2.29	12.05±2.01	0.018
Hematocrit (%)	43.33±5.84	42.02±7.65	38.44±6.44	0.007
White blood cell (10^3/mm^3)	9.85±4.50	12.96±5.13	13.77±5.13	0.002
Urea* (mg/dL)	37.0(30.0-57.8)	49.4(32.6-74.0)	75.65(44.7-114.9)	0.002
Creatinine* (mg/dL)	0.9(0.6-1.0)	0.7(0.6-1.2)	0.7(0.5-1.5)	0.242
Sodium (mmol/L)	136.46±5.59	138.38±6.79	140.78±6.95	0.016
Potassium (mg/L)	4.36±0.51	4.47±0.91	4.48±0.69	0.689
Calcium (mg/dL)	8.82±0.59	8.40±0.67	7.85±0.95	<0.001
Total cholesterol (mg/dL)	189.42±41.43	159.79±41.96	158.84±48.81	0.003
CRP* (mg/L)	97.8(39.1-160.0)	135.5(94.8-295.7)	241.0(122.5-344.5)	<0.001
Iron* (µg/dL)	40.0(18.5-76.0)	33.0(20.0-54.0)	20.0(14.2-35.7)	0.031
TSAT* (%)	28.3(9.2-36.2)	17.4(11.0-32.2)	10.5(7.4-35.5)	0.399
Ferritin* (µg/L)	425.0(183.5-697.0)	633.0(392.2-1071.5)	857.5(658.7-1403.5)	0.003
D-dimer* (µg/mL)	1.1(0.8-3.6)	3.0(1.7-7.0)	5.6(2.5-9.2)	<0.001

PDW: Platelet distribution width, PLC-R: Platelet large cell-ratio, PLCC: Platelet large cell count, TSAT: Transferrin saturation. Data are shown as mean±SD or n (%) prevalence and analyzed using the One-way ANOVA test. *Non-normally distributed variables were presented with median and 25^{th}–75^{th} percentiles (Q1-Q3) and analyzed using the Kruskal Wallis test.

CRP, ferritin, iron and D-dimer values differ significantly between Group 3 and Group 1 (p<0.001, p=0.003, p=0.031 and p<0.001, respectively). It was observed that the CRP, ferritin and D-dimer values of the patients in Group 3 were significantly higher than the patients in Group 1, and the iron values of the patients in Group 3 were significantly lower than the patients in Group 1. There was no significant difference between Groups in TSAT levels (p=0.399) (Table 1).

According to Spearman's rho correlation analysis results, PLC-R levels (r=0.299, p=0.001) and WBC levels (r=0.332, p<0.001) were positively correlated with COVID-19 severity. Ht levels (r=-0.276, p=0.003) and Hb levels (r=-0.273, p=0.004) were negatively correlated with COVID-19 severity.

The ROC curve analysis showed that PLC-R> 38.3% had 59.4% sensitivity and 68.4% specificity in predicting severe COVID-19 disease (AUC 0.672, %95 CI 0.560, 0.784; p=0.005, cut off=38.3) (Figure 2). There was no statistically significant difference between the Groups regarding age and other investigated laboratory parameters (Table 1).

As shown in Table 2, the increase in the p-value calculated by the ANFC method detects an increasing disease association. Thus, the relationship between PLC-R and COVID-19 is proven in Table 3. It makes sense if the correlation coefficient is positive and significant. For this reason, it is understood that PLC-R is an effective finding parameter among COVID-19 patients. In the meantime, we made two separate calculations of total linguistic hedge values and correlation coefficient with the ANFC method. The PLC-R value was found to be the only platelet parameter that significantly correlated with these two calculations (Figure 3 and 4).

With many different analysis results, the PLC-R value has been an essential parameter for COVID-19 patients. Also schematic representation of pathogenic inflammatory cytokine response and clot formation with large platelets in SARS-CoV-2 infections are demonstrated in Figure 5.

Table 2. The representation of linguistic hedge (P) values

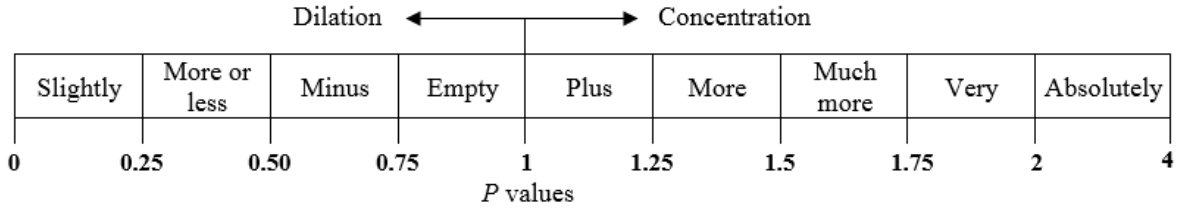

Table 3. The representation of *p* and correlation Coefficient values oth the ANFC method

Variables	Feature	Linguistic Hedge (p) value	Correlation Coefficient
BT	1	1	0.117
Age (year)	2	0.466	0.083
Platelet (10^3/mm^3)	3	1.261	-0.022
Mean platelet volume (fL)	4	0.212	0.150
PDW (fL)	5	0	0.061
PLC-R (%)	6	2.635	0.323
PLCC (10^3/mm^3)	7	0.860	0.071
Glucose (mg/dL)	8	0	0.232
Triglycerides (mg/dL)	9	0	0.143
Low density lipoprotein cholesterol (mg/dL)	10	1.612	-0.325
High density lipoprotein cholesterol (mg/dL)	11	0	-0.201
Hemoglobin (g/dL)	12	0	-0.267
Hematocrit (%)	13	0.321	-0.288
White blood cell (10^3/mm^3)	14	0.955	0.312
Urea (mg/dL)	15	0.621	0.332
Creatinine (mg/dL)	16	0.046	0.159
Sodium (mmol/L)	17	2.637	0.270
Potassium (mg/L)	18	0	0.077
Calcium (mg/dL)	19	2.696	-0.479
Total cholesterol (mg/dL)	20	1.601	-0.290
CRP (mg/L)	21	1.424	0.449
Iron (µg/dL)	22	0.168	-0.245
Ferritin (µg/L)	23	0.887	0.321
TSAT (%)	24	0	-0.113
D-dimer (µg/mL)	25	1.954	0.357

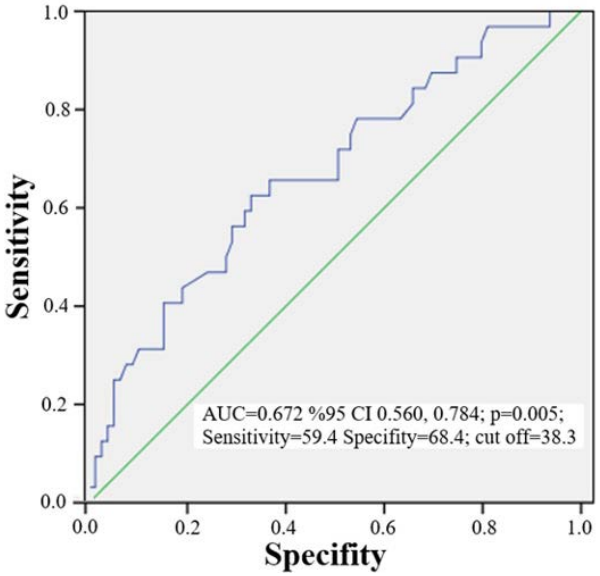

Figure 2. ROC analysis for PLC-R cut-off predicting severe COVID-19 disease. AUC: Area under the curve; *CI*: Confidence interval; ROC: Receiver operating characteristics.

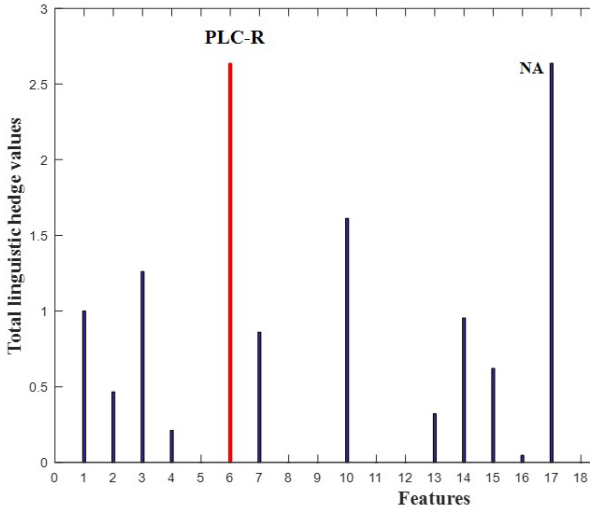

Figure 3. Feature selection criteria with total linguistic hedge values for the sensitivity of 25 features in the ANFC method.

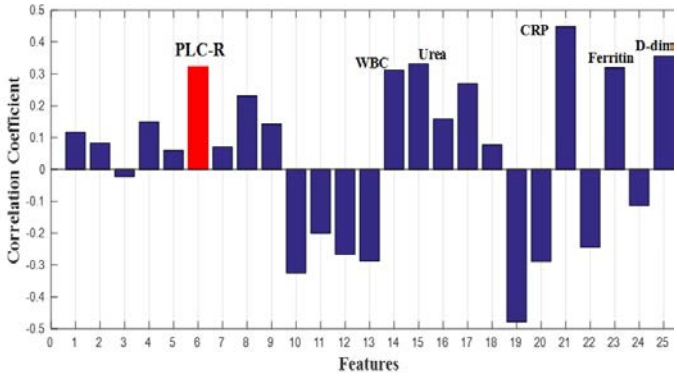

Figure 4. Feature selection criteria with a correlation coefficient values for the sensitivity of 25 features in the ANFC method.

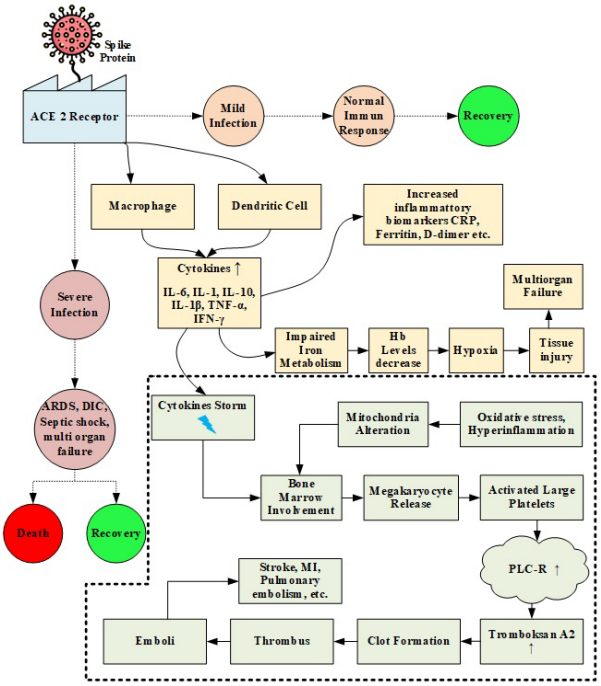

Figure 5. Schematic representation of pathogenic inflammatory cytokine response and clot formation with large platelets in SARS-CoV-2 infections.

Discussion

The critical result of our study is that PLC-R was remarkably higher in the severe COVID-19 patients. According to different types of correlation analysis results, PLC-R levels were positively correlated with COVID-19 severity.

Inflammation caused by viral infections can cause dyslipidemia in patients. A previous study reported that the LDL-c levels of COVID-19 patients decreased (14). SARS-CoV-2 can damage, liver function and reduce LDL-c biosynthesis. SARS-CoV-2 causes acute inflammation by causing an increase in proinflammatory cytokine levels. It can disrupt the efflux and transport of lipids by changing liver functions in cytokines. Free radicals occurring in the host cell in viral infection can also disrupt lipid metabolism (15). SARS-CoV-2 infection can cause cholesterol molecules to leak into tissues such as alveolar spaces to form exudate by increasing vascular permeability. This causes the lipid level in the plasma to decrease (16). This study observed that LDL-c levels decreased in the severe Group of COVID-19 patients.

The literature studies found severe impairment occurred in kidney function tests and blood electrolyte levels in severe COVID-19 patients. Acute kidney damage due to cell and tissue damage from SARS-CoV-2 and lack of oral intake of patients reveasl these pathological findings (17). According to our data, as the severity of COVID-19 infection increased, urea, Na, Ca levels increased meaningfully.

An increase in non-specific inflammatory biomarkers such as CRP, *D*-dimer, and ferritin is observed in COVID-19 patients. A study of 653 COVID-19 patients reported that serum ferritin values in patients with severe COVID-19 infection were higher than patients with mild COVID-19 infection (18). Shah *et al*. reported no significant difference in serum ferritin levels and transferrin saturation between patients with non-severe and severe hypoxemia, but serum iron levels were significantly lower (19). In our study, in the Group with severe COVID-19 infection, it was observed that CRP and ferritin levels increased statistically, and iron levels were statistically decreased. There was no significant difference in transferrin saturation. High ferritin levels may indicate a robust inflammatory response, with SARS-CoV-2 entry into the human body and its effect on iron metabolism (20). Iron is an essential micronutrient for both humans and pathogens (21). During infection, humans' innate immune system response limits the amount of iron to deprive it of the pathogen, leading to anemia (22). Anemia reduces oxygen delivery to tissues and causes multi-organ failure. Studies show that Hb levels decrease in COVID-19 infection (23). We also obtained findings that support previous studies. Inflammatory changes caused by COVID-19 infection can affect erythropoiesis and cause a decrease in hemoglobin. SARS-CoV-2 binds to the beta chains of hemoglobin *via* surface glycoproteins, inhibiting both metabolism and hemoglobin denaturation. Hemoglobinopathy and iron dysmetabolism together with hypoxia can seriously compromise the O_2 carrying capacity of erythrocytes and induce tissue changes due to hyperferritinemia (24). For these reasons, decreased hemoglobin levels for COVID-19 may be an indicator of disease progression.

Viral and bacterial infections are generally associated with thrombocytopenia and changes in platelet morphology. Platelets are involved in hemostasis, coagulation, immune, and inflammatory responses (25). SARS-CoV-2 uses the spike protein to enter host cells by binding to angiotensin-converting enzyme 2 in the host cell membrane. Spike protein enhances thrombus formation. Coagulation factors are released, inflammatory cytokines are secreted, and leukocyte platelet clusters are formed (26). Fibrin deposition with coagulation activation and subsequent fibrinolysis increase *D*-dimer level, an essential intravascular coagulation indicator. Studies have proven that high *D*-dimer values at admission to the hospital are associated with poor prognosis (27). According to the results of our research, it was observed that *D*-dimer values increased statistically significantly in severe COVID-19 infection. Continued inflammation can rapidly lead to the development of cytokine storm and macrophage activation syndrome and hyperinflammatory response. Cytokine storm is a syndrome that releases proinflammatory cytokines that cause acute respiratory distress syndrome and multiple organ dysfunction syndromes in case of infection (28). Macrophage activation syndrome is a proinflammatory cascade associated with a high rate of thrombosis and death in sepsis (29). In COVID-19 disease, increasing cytokine levels and inflammation initiate platelet destruction by causing bone marrow involvement. Accumulation in the lungs causes more platelet consumption. The decrease in the platelet count leads to an increase in the production of young and immature platelets that are functionally more active and larger sized (30). Larger platelets have more granules and receptors, and they are metabolically and enzymatically more active than small platelets, produce more thromboxane A2, and tend to clot more quickly (31). Since the destruction in the bone marrow will be more significant in severe COVID-19 infection, the number of large platelets released into the circulation will increase with the release of more megakaryocytes (32). Mitophagy impairment occurs in patients with COVID-19 due to oxidative stress and hyperinflammation. Mitophagy protects platelets from oxidative stress and mitochondrial destruction by removing damaged mitochondria to prevent platelet apoptosis in healthy individuals. However, mitochondrial dysfunction in platelets in COVID-19 infection may affect platelet survival and apoptosis, potentially increasing the risk of thrombus formation. Studies have shown that apoptotic platelets can induce clotting ≥50 times faster than normal platelets (33). In the studies, patients with myocardial infection have reported that larger platelets contribute to the prothrombotic state (34). Microvascular and macrovascular thromboembolic complications in the lung, spleen, brain, intestine and peripheral vessels have been reported in COVID-19 (35). It has been reported that stroke has been detected in young patients with covid-19, even without underlying coagulopathy before the infection (36). Large platelets may be one of the causes of these thrombotic events seen in COVID-19 infection.

Platelet activity should be evaluated with PVI parameter values, not platelet counts. PVI parameters are measurements calculated by devices and can be easily detected in blood tests, typically as part of the CBC, not requiring advanced or expensive technology (11).

The MPV and PDW parameters are widely and routinely used in clinics around the world. When platelet production decreases, young platelets grow, their volume increases, and they become more active. As a result, MPV and PDW levels increase (37). It has been reported that MPV and PDW values increase to higher levels in patients with sepsis, and PDW is a poor prognostic factor in severe sepsis (38). In a study by Güçlü et al., it was reported that mortality increased in parallel with the increase in MPV value in COVID-19 infection (39). However, we found that PLC-R was significantly higher in severe COVID-19 disease, although we did not see an increase in these values. In the meantime, a comprehensive calculation was made with the ANFC method, while PLC-R findings were found as a constant factor parameter, and it was brought to the literature.

PVI in patients with COVID-19 infection is a simple, effortless, and economical test that should be used to predict the probability of acute thrombotic events. Larger platelets can easily be identified during routine complete

blood count analysis, and such patients can benefit from preventive treatment. According to our data, it has been proven by many analysis methods that the PLC-R value can be used as a suitable biomarker that can describe the severity of COVID-19 infection.

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