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Complete Blood Count Parameters to Predict COVID-19 Severity in Pediatric Patients

Çocuk Hastalarda COVID-19 Şiddetini Öngörmede Tam Kan Sayımı Parametreleri

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Abstract

Objective: It is thought that hyperinflammation has an important role in the pathogenesis of severe COVID-19 and tests that determine the degree of inflammation can be used to predict the severity of the disease. From this point of view, we aimed to determine the hematological parameters that can predict the severity of COVID-19 in pediatric patients.

Material and Methods: Symptomatic and SARS-CoV-2-PCR test positive 105 children were included to study. Seventy-nine patients had mild, 26 had moderate to severe COVID-19 at admission. Data about their demographic characteristics, clinical and laboratory findings were collected from their medical records. Correlations between the hematological parameters and disease severity of patients were investigated by using univariate and multivariate regression analyses. Predictive value of different diagnostic markers was studied.

Results: Mean age was older (177 months vs. 70 months) and mean body mass index (BMI) was higher (18.8 kg/m^2 vs. 25.0 kg/m^2) in patients with severe COVID-19 than those with mild. Univariate analysis showed that mean leucocyte (WBC), lymphocyte, eosinophiles, and platelet counts were lower; mean platelet volume (MPV), neutrophil to lymphocyte ratio (NLR), and derived neutrophil to lymphocyte ratio (dNLR) were higher in severe COVID-19 group ($p< 0.05$). Multivariant analysis showed low lymphocyte (OR 0.072) and WBC count (OR 0.085), high dNLR (OR 2.14) and MPV (OR 2.35) indexes were the most valuable parameters to predict disease severity, ROC curve analysis revealed lymphocyte count has superior predictive value (<1.55 /mm^3 has 84.6% sensitivity, 70.9% specificity) than other CBC parameters have.

Öz

Giriş: Şiddetli COVID-19 patogenezinde hiperenflamasyonun önemli bir rolü olduğu ve enflamasyon derecesini belirleyen testlerin hastalık şiddetini tahmin etmede kullanılabileceği düşünülmektedir. Buradan yola çıkarak bu çalışmada çocuk hastalarda COVID-19 şiddetini öngörebilecek hematolojik parametreleri belirlemeyi amaçladık.

Gereç ve Yöntemler: SARS-CoV-2-PCR testi pozitif olan semptomatik 105 çocuk çalışmaya dahil edildi. Başvuru sırasında 79 hastada hafif, 26 hastada orta ila şiddetli COVID-19 vardı. Hastaların demografik özellikleri, başvurudaki klinik ve laboratuvar bulguları ile ilgili veriler tıbbi kayıtlardan elde edildi. Hastaların hematolojik parametreleri ile hastalık şiddeti arasındaki ilişki tek değişkenli ve çok değişkenli regresyon analizleri kullanılarak araştırıldı. Farklı tanısal belirteçlerin tahmin değeri çalışıldı.

Bulgular: Şiddetli COVID-19 hastalarında ortalama yaş hafif COVID-19 grubuna oranla daha büyük (177 aya karşı 70 ay) ve ortalama vücut kitle indeksleri (VKİ) daha yüksekti (18.8 kg/m^2'ye karşı 25.0 kg/m^2). Tek değişkenli analiz, şiddetli COVID-19 grubunda ortalama lökosit (WBC), lenfosit, eozinofil ve trombosit sayılarının daha düşük, ortalama trombosit hacmi (MPV), nötrofil lenfosit oranı (NLR) ve türetilmiş nötrofil lenfosit oranının (dNLR) daha yüksek olduğunu gösterdi ($p< 0.05$). Multivaryant analiz, düşük lenfosit (OR 0.072) ve WBC sayısı (OR 0.085), yüksek dNLR (OR 2.14) ve MPV (OR 2.35) indekslerinin hastalık şiddetini tahmin etmek için en değerli parametreler olduğunu gösterdi, ROC eğrisi analizi, lenfosit sayısının hastalığın ağırlığını öngörmede diğer Tam kan sayımı parametrelerine göre üstün prediktif değere sahip olduğunu gösterdi (<1.55 /mm^3, %84.6 duyarlılığa, %70.9 özgüllüğe sahipti).

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Conclusion: Low lymphocyte and leukocyte count, high MPV and dNLR values have significant predictive value in predicting COVID-19 severity. In particular, lymphopenia appears to be a valuable parameter to identify patients at high risk for severe disease and initiate accurate treatment to prevent disease deterioration.

Keywords: COVID-19, pediatric, hematological, parameters

Sonuç: Düşük lenfosit ve lökosit sayısı, yüksek MPV ve dNLR indeksleri COVID-19 şiddetini öngörmede önemli değere sahiptir. Özellikle lenfopeni, ciddi hastalık açısından yüksek risk altındaki hastaları belirlemek ve hastalığın kötüleşmesini önlemek için doğru tedaviyi başlatmada değerli bir parametre olarak görünmektedir.

Anahtar Kelimeler: COVID-19, çocuk, hematolojik, parametreler

Introduction

At the end of 2019, a novel coronavirus was identified as the cause of acute respiratory distress syndrome in China (1). Subsequently at February 2020, World Health Organization (WHO) named the disease as Coronavirus Disease 2019 (COVID-19), and the virus was named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (2,3). Following to rapid spread of SARS-CoV-2 all around the world, the COVID-19 pandemic was declared by WHO on March 11, 2020 (4). About six-teen months after this declaration at 8 July, 2021, 184.820.132 confirmed cases and 4.002.209 deaths have been reported worldwide (5).

COVID-19 has the clinical course varying from asymptomatic disease to life threating conditions such as respiratory distress, shock, cardiac arrest, multiorgan failure. Children seems to have less serious disease than adults (6,7). Recently published pediatric series reported severe and critical disease as 3-12%, mortality rate as 0.03-0.17% (8,9). Early determination of the severity of COVID-19 can enable timely optimal treatment so prevent deterioration of disease.

It is thought to be hyperinflammation result from an intense immune response to the virus has important role in the pathogenesis of severe COVID-19 (10,11). From this point of view, biomarkers represent inflammation state can be used to predict disease severity. The complete blood count (CBC) is one of the easiest and inexpensive laboratory tests to determine state of inflammation. Several recent adult studies have found relations between some hematologic parameters and/or their combined ratio and the severity of COVID-19 (12-15). So far, there are no studies investigate predictive value of these parameters in pediatric patients with COVID-19. Here we investigated if CBC parameters are useful in the assessment of severity of COVID-19 in pediatric age.

Materials and Methods

This retrospective study was conducted with pediatric patients aged between one months to 18 years who hospitalized in pediatric clinic between October 2020 to June 2021. Both symptomatic and SARS-CoV-2 polymerase chain reaction (PCR) test positive patients were included to study. Data about their demographic characteristics, clinical laboratory and radiological findings at first day admission, treatment and outcomes were collected from medical records.

COVID-19 severity was classified as mild, moderate, severe and critical (Table 1) (16). Additionally, for study patients were classified in two groups; "mild group" was consisted of 79 patients with mild COVID-19 without organ involvement, including pneumonia and "severe group" was consisted of patients with moderate, severe, and critical COVID-19 with varying severity of pneumonia or any other organ involvement. Patients with SARS-CoV-2-PCR positivity showed clinical feature of "multisystem inflammatory syndrome in children" (MIS-C) were excluded from study.

Complete blood count (BC-6800, Mindray, Shenzhen, China), serum biochemistry (Cobas 6000 systems (c501 + e601), Roche Diagnostics Mannheim, Germany), coagulation tests (STA Compact Max, Stago, Asnieres-sur-Seine, France), and D-dimer test (BCSXP, Simens Healthcare Diagnostics, Marburg, Germany) were obtained from medical records. The CBC parameters including leucocyte (WBC), neutrophil, lymphocyte, eosinophil count, hemoglobin (Hg), red blood cell distribution width (RDW), platelet, mean platelet volume (MPV), and combined ratio of these parameters named as inflammatory indexes including neutrophil-to-lymphocyte ratio (NLR), derived neutrophil-to-lymphocyte ratio (dNLR, N/(WBC-N), platelet mass index (MPR, mean platelet volume divided by platelet

Table 1. Classification of coronavirus disease 2019 (COVID-19) severity in patients

Mild	Symptoms of acute upper respiratory tract infection including fever, headache, fatigue, muscle pain, sore throat, runny nose, sneezing, cough, and symptoms of gastrointestinal system including abdominal pain, nausea, vomiting, and diarrhea without pneumonia
Moderate	Pneumonia without hypoxemia
Severe	Respiratory distress with oxygen saturation< 92%
Critical	Acute respiratory distress syndrome (ARDS) or respiratory failure requiring ventilatory support. Shock, and/or organ dysfunction
Adapted from Dong et al. (30)	

count), systemic inflammatory index (SII, platelet *N/L) were compared between two patient groups in order to determine their value in predicting COVID-19 severity.

All continuous variables were expressed as median [interquartile range (IQR)]. Differences between patients with mild and severe COVID-19 were assessed using the Mann-Whitney U test, or the Chi-squared test, as appropriate. Univariate and multivariate logistic regression analyses were performed to identify independent correlates of severe COVID-19. With BMI, reciprocal transformation of the lymphocyte and leucocyte count (1/lymphocyte, 1/WBC), MPV, and dNLR, a receiver operating characteristic (ROC) curve was generated, and the area under the curve (AUC) was calculated to assess diagnostic value. All statistical analyses were performed using SPSS Version 23.0 (IBM Corp., Armonk, NY). P values less than or equal to 5% were considered significant.

The diagnostic values of parameters for mild and severe cases of COVID-19 patients were evaluated by ROC and area under the ROC curve (AUC).

Results

The median age of 105 children was 120 months (IQR24-186), of them 45 (42.9%) were female. Mild group consisted of 79 (75.2%) patients, severe group consisted of 26 patients of whom 12 had moderate, eight had severe and six had critical COVID-19. These two groups were compared according to their demographic, clinical, and laboratory findings (Table 1).

In the severe group the median age was older (177 month, IQR 148-200 months vs. 70 months, IQR 13-182 months; $p< 0.05$), mean body mass index (BMI) was higher (median 25, IQR= 19.5-32.5 vs. 18.8, IQR 16.0-22.6). Time of fever was longer in severe group (median 4 days, IQR 3-5 days vs. two days, IQR 1-2 days). Seven patients needed monitoring and treatment in pediatric intensive care unit (PICU), one of them, a girl with Down syndrome, died. The median hospitalization time was longer in severe group (median nine days, IQR 6-13 days vs. four days, IQR 3-7 days) On the other hand, there was no significant difference between the two groups in terms of gender and co-morbidity.

CBC parameters and inflammatory indexes of two groups were presented in Table 3. In severe group leucocyte, lymphocyte, eosinophil, platelet counts were significantly lower, RDW-SW, MPV, MPR, and NLR were higher than those in the mild group ($p< 0.05$). Additionally, other inflammatory biomarkers such as C-reactive protein (CRP), lactate dehydrogenase (LDH), ferritin and fibrinogen were higher, albumin level was lower in severe group.

Complete blood count parameters and inflammatory indexes which were significantly different between two groups, were examined using univariate and multivariate analyses to find predictive values for severe COVID-19 (Table 3). Univariate analysis identified older age, high BMI, low WBC, low lymphocyte, low eosinophil, and low platelet counts, high MPV, high NLR, and high dNLR as independent factors predicting severe COVID-19. Multivariate analysis revealed that high BMI, low WBC, low lymphocyte, high MPV, high dNLR had superior predictive value for severe COVID-19 (Table 2). To test the ability of CBC parameters to differentiate between patients with severe and mild disease ROC analyses were used. The AUC was higher for lymphocyte than for BMI, WBC, dNLR and MPV. The optimal cutoff values for lymphocyte, WBC, MPV and dNLR were calculated as 1.55, 6.05, 9.45, 1.64 with a sensitivity of 84.6%, 73.1%, 69.2%, 64.0% and a specificity of 70.9%, 72.2%, 65.5%, 63.3 respectively (Table 5).

Discussion

Several recent studies investigated role of hematologic parameters to predict COVID-19 severity in adult. Among these Wang et al. found combined parameters of NLR and RDW-SD were the most valuable, Lin et al. found NLR to have superior predictive value, Fois et al. found SII to be the most valuable in predicting COVID-19 severity (12-14). Here is the first study to assess predictive value of CBC parameters in pediatric patients with COVID-19. It revealed that patients with severe COVID-19 had low WBC, low lymphocyte, low eosinophil, low platelet counts, and had high MPV, high NLR and high dNLR values. Multivariant analysis revealed low lymphocyte, low WBC, high MPV and high dNLR has superior predicting value for severe COVID-19. Receiver operating characteristic analysis showed lymphocyte to have the highest area under curve (AUC) among other parameters.

Decrease in lymphocyte count is common in many infectious diseases. Also, alteration in the number of B and T cells and change in T-cell subsets can occur during infections (17). In adult patients, lymphopenia (especially decrease in CD4+ and CD+8 T lymphocytes) have been related to severity of COVID-19 (18). In a meta-analysis of 66 studies that included 9335 children reported lymphopenia in 19% of children with COVID-19 (19). Even elevated inflammatory markers and lymphocytopenia are noted as characteristic of MIS-C, our findings reveal relation between lymphopenia and severity of acute COVID-19 (20). On the other hand, adult patients and children with MIS-C had high WBC counts mainly due to neutrophilia, in our study children with severe COVID-19 inversely had leucopenia. Thus, we suggest that the main problem in acute SARS-CoV-2 infection may not be only severe inflammation like in MIS-C, but that the decreased lymphocyte level may be related to disease progression.

Table 2. Demographic and clinical characteristics of hospitalized children with COVID-19

Characteristics	Global cohort (n= 105)	Mild COVID-19 group without pneumonia (n= 79)	Severe COVID-19 group with varying severity of pneumonia (n= 26)	p
Demographic features				
Age, months	120 (24-186)	70 (13-182)	177 (148-200)	<0.0001
Gender (F/M)	45/60	31/48	14/12	0.282
BMI (kg/m^2)	**20.0 (17.0-25.8)**	**18.8 (16.0-22.6)**	**25 (19.5-32.5)**	<0.0001
COVID-19 severity				
Mild (No/Yes)	**26/79**	**0/79**	**26/0**	
Moderate (No/Yes))	**93/12**	**79/0**	**14/12**	
Severe (No/Yes)	**97/8**	**79/0**	**18/8**	
Critical (No/Yes)	**99/6**	**79/0**	**20/6**	
Comorbidity (No/Yes)	74/34	54/25	17/9	0.969
Chronic pulmonary disease (No/Yes)	97/8	72/7	25/1	0.676
Neurological disease (No/Yes)	98/7	74/5	24/2	1.000
Hematological disease (No/Yes)	103/2	78/1	25/1	0.436
Diabetes mellitus (No/Yes)	103/2	78/1	25/1	0.436
Renal disease (No/Yes)	101/4	75/4	26/0	0.570
Rheumatological disease (No/Yes)	103/2	78/1	25/1	0.436
Endocrinologic disease (No/Yes))	103/2	77/2	26/0	1.000
Metabolic Disease (No/Yes)	103/2	77/2	26/0	1.000
Down (No/Yes) Others	103/2 102/3	79/0 77/2	24/2 25/1	0.060 0.400
First degree family member died or need intensive care	**99/6**	**77/2**	**22/4**	**0.072**
Symptoms and signs				
Symptoms days at admission	**2 (1-4)**	**2 (1-3)**	**5 (3-6)**	**<0.0001**
Fever (No/Yes)	24/81	22/57	2/24	0.064
Febrile days before admission, n	**2 (1-4)**	**2 (1-2)**	**4 (3-5)**	**<0.0001**
Cough (No/Yes)	**40/65**	**38/41**	**2/24**	**<0.0001**
Shortness of breath (No/Yes)	81/24	65/14	16/10	0.055
Chest pain (No/Yes)	97/8	73/6	24/2	1.000
Rhinitis (No/Yes)	97/8	71/8	26/0	0.196
Nasal congestion (No/Yes)	100/5	74/5	26/0	0.329
Sneezing (No/Yes)	102/3	77/2	25/1	1.000
Throat pain (No/Yes)	98/7	73/6	25/1	0.678
Headache (No/Yes)	98/7	73/6	25/1	0.678
Abdominal pain (No/Yes)	101/4	76/3	25/1	1.000
Diarrhea (No/Yes)	89/16	67/12	22/4	1.000
Vomiting (No/Yes)	80/25	58/21	22/4	0.370
Tachypnea/dyspnea (No/Yes)	92/13	72/7	20/6	0.083
Rhonchus, ral (No/Yes)	**81/24**	**70/9**	**11/15**	**<0.0001**

Table 2. Demographic and clinical characteristics of hospitalized children with COVID-19 (continue)

Characteristics	Global cohort (n= 105)	Mild COVID-19 group without pneumonia (n= 79)	Severe COVID-19 group with varying severity of pneumonia (n= 26)	p
Treatment and Prognosis				
PICU admission (No/Yes)	**98/7**	**79/0**	**19/7**	**<0.0001**
Intubation (No/Yes)	104/1	79/0	25/1	0.248
NIMV (No/Yes)	103/2	79/0	24/2	0.060
HFO (No/Yes)	**100/5**	**79/0**	**21/5**	**0.001**
Steroid usage				
Dexamethasone (No/Yes)	**80/25**	**76/3**	**4/22**	**<0.0001**
Methyl prednisolone (No/Yes)	100/5	76/3	24/2	0.595
Duration of hospitalization (day)	**5 (3-8)**	**4 (3-7)**	**9 (6-13)**	**<0.0001**

* F: Female; M: Male; BMI: Body mass index, PICU: Pediatric intensive care unit, NIMV: Non-invasive mechanical ventilation, HFO: Hih flow nasal oxygen therapy. All continuous variables were expressed as median [interquartile range (IQR)], values less than or equal to 0.05% were considered significant. All statistically significant value shown in bold.

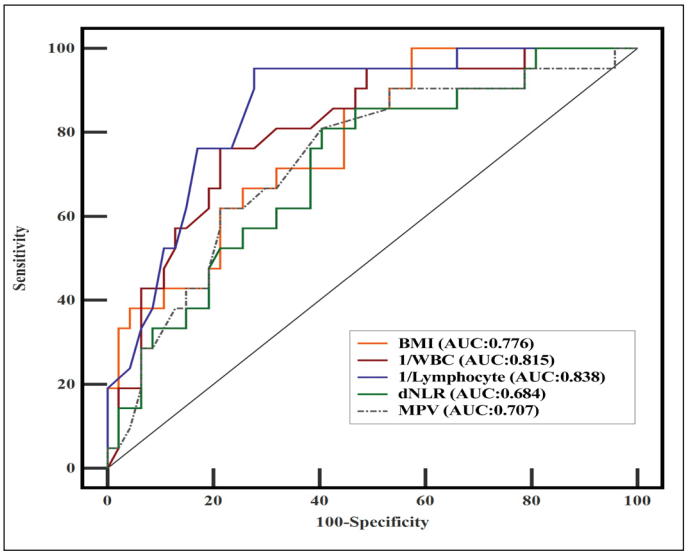

Figure 1. ROC analysis reveals diagnostic value of BMI and CBC parameters for prediction of COVID-19 severity.

Elevated NLR and dNLR are other markers of inflammation, their elevation may result from lymphopenia, neutrophilia or a combination of both. In this study NLR and dNLR values were higher in severe group than in mild group and predictive value of dNLR was superior to that of NLR. Similarly, Yang et al. analyzed these inflammatory markers in adult patients with COVID-19 and found that both were significantly higher in severe group, they also reported elevated NLR as independent prognostic markers influencing pneumonia progression in severe COVID-19 (21).

Another finding of study is that eosinopenia had association with severe COVID-19. As known eosinopenia generally correlate with severity of infections, and its presence may suggest poor prognosis (17). Tanni et al. reported that persistent eosinopenia is associated with disease severity and low recovery rate (22). The pathophysiology of eosinopenia in COVID-19 is unclear; it may be due to blocking of eosinophil production, inhibition of eosinophil influx from the bone marrow, eosinophil apoptosis caused by interferons released during acute infection and/or it may be result of redistribution of circulating eosinophils due to the chemotactic effects of increased cytokines (23,24).

Thrombocytopenia can be seen in septicemia in the absence of disseminated intravascular coagulopathy (DIC), and in more than two third of bacteremia cases. This may be related to suppression of platelet production, increased platelet utilization, and/or destruction due to immune reactions (17). In this study thrombocyte number was significantly lower and MPV was higher in severe COVID-19 group than in mild group. Mean platelet volume value increases when the bone marrow produces immature platelets as response to increased destruction of platelets. The recent few studies in adults indicated that increase in the MPV level is associated with the severity of the COVID-19. For this reason, MPV is also should be followed beside platelet count for better prognosis of the patient (25).

Study has some limitations, first of all data were obtained retrospectively from a single center. The study has a small sample size, to demonstrate the strength of these parameters' studies with a large number of patients are required.

Conclusion

Older age, high BMI, low lymphocyte, leukocyte, eosinophil and platelet counts high MPV, NLR, dNLR values were found to be associated with severe COVID-19. On the other hand, high BMI, low lymphocyte and leukocyte counts, high MPV and dNLR values are parameters have best predictive

Table 3. Complete blood count (CBC) parameters. derived inflammation indexes and some inflammatory markers in children with COVID-19

Parameters	Global cohort (n= 105)	Mild COVID-19 group without pneumonia (n= 79)	Severe COVID-19 group with varying severity of pneumonia (n= 26)	p
WBC (mm^3)	**6.6 (4.7-9.1)**	**7.5 (5.8-9.6)**	**4.3 (3.4-6.1)**	**<0.0001**
Neutrophil (mm^3)	3.6 (2.2-5.4)	4.1 (2.23-6.01)	2.75 (2.2-4.3)	0.079
Lymphocytes (mm^3)	**1.8 (1.3-2.7)**	**2.2 (1.5-3.5)**	**1.2 (0.8-1.5)**	**<0.0001**
Eosinophil (mm^3)	**0.04 (0.01-0.10)**	**0.05 (0.01-0.17)**	**0.00 (0.00-0.05)**	**<0.0001**
Hg	12.9 (11.8-13.9)	12.9 (11.7-13.9)	12.9 (12.2-14.0)	0.699
RDW-SD	**40 (38-42)**	**40.0 (37.0-41.0)**	**41 (39-43)**	**0.010**
PLT	**240 (184-302)**	**266.5 (200-335)**	**181 (140-232)**	**<0.0001**
MPV	**9.2 (8.7-10.0)**	**9.0 (8.6-9.7)**	**9.8 (9.2-11.0)**	**0.002**
MPR (MPV/PLT)	**0.04 (0.03-0.05)**	**0.03 (0.03-0.05)**	**0.06 (0.04-0.08)**	**<0.0001**
NLR (N/R)	**1.96 (1.04-4.00)**	**1.61 (0.90-3.29)**	**2.86 (1.5-5.98)**	**0.027**
SII [(N/L) X PLT. NLPR]	442.86 (189.21-839.85)	447.89 (181.64-824.63)	426.5 (259.87-1498.25)	0.417
dNLR [N/(WBC-N)]	**1.39 (0.80-2.55)**	**1.17 (0.74-2.27)**	**2.29 (1.19-3.94)**	**0.006**
AST	30 (21-41)	29 (19-41)	31 (24-38)	0.448
ALT	17 (11-29)	16 (10-25)	24 (13-36)	0.079
Indirect Bilirubin	0.15 (0.10-0.24)	0.15 (0.10-0.23)	0.15 (0.10-0.26)	0.727
Direct Bilirubin	0.14 (0.10-0.19)	0.14 (0.11-0.19)	0.12 (0.09-0.17)	0.154
Creatinine	**0.58 (0.42-0.77)**	**0.51 (0.41-0.71)**	**0.66 (0.54-0.80)**	**0.023**
Urea	21 (17-28)	21 (17-28)	21 (16-25)	0.540
Na	137 (135-138)	137 (134-138)	137 (136-139)	0.491
K	**4.3 (4.1-4.6)**	**4.4 (4.1-4.7)**	**4.2 (3.9-4.4)**	**0.032**
Albumin	**43.5 (40.7-45.5)**	**44 (41.6-45.9)**	**40.6 (37.8-43.5)**	**0.001**
Total Protein	69.7 (63.7-75.3)	69.8 (63-75.3)	69 (65.7-73.7)	0.954
Ck	90 (60-134.5)	88 (61-133)	92.5 (57.0-249.0)	0.344
LDH	**276 (216-348)**	**254.5 (202.5-322.5)**	**345 (268-410)**	**0.002**
CRP (mg/L)	**5.2 (1.0-22.3)**	**3.4 (1.0-12.0)**	**27.2 (5.1-42.2)**	**<0.0001**
Procalcitonin	0.098 (0.04-0.135)	0.1 (0.04-0.14)	0.095 (0.05-0.12)	0.790
Ferritin	**161 (64-275)**	**74 (36.9-209)**	**255 (132-351)**	**0.021**
D-Dimer	**0.59 (0.27-1.0)**	**0.52 (0.26-0.84)**	**0.86 (0.5-1.7)**	**0.044**
Fibrinogen	**380 (324-454)**	**344 (306-354)**	**425 (369-461)**	**0.001**

* All continuous variables were expressed as median [interquartile range (IQR)], values less than or equal to 0.05% were considered significant. All statistically significant value shown in bold.

ratio for disease severity, and can be used to identify patients with high risk at admission. Initiation of timely accurate treatment will prevent disease deterioration and decrease morbidity and mortality.

Ethics Committe Approval: This study was approved by the decision of İstanbul Medeniyet University Göztepe Education and Research Ethics Committee (Decision no: 2021/0309, Date: 16.06.2021).
Informed Consent: The informed consent was not applicable, because the study was conducted retrospectively and the patients' routine tests were screened.

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Table 4. Hematological parameters and inflammatory indexes predicting severe COVID-19

Parameters	Univariate		Multivariate*	
	OR (%95 GA)	p	OR (%95 GA)	p
Age (month)	**1.017 (1.008-1.025)**	**<0.0001**	1.023 (0.997-1.050)	0.089
BMI (kg/m²)	**1.184 (1.076-1.303)**	**0.001**	**1.317 (1.036-1.675)**	**0.025**
Gender				
Female	**Reference**	-		
Male	0.554 (0.227-1.353)	0.195		
WBC (mm³)	**0.572 (0.433-0.756)**	**<0.0001**	**0.085 (0.015-0.471)**	**0.005**
Neutrophil (mm³)	0.829 (0.677-1.015)	0.069		
Lymphocyte (mm³)	**0.161 (0.064-0.410)**	**<0.0001**	**0.072 (0.006-0.929)**	**0.044**
Eosinophil (mm³)	**0.001 (0.000-0.013)**	**0.006**		
Hg	1.063 (0.787-1.435)	0.691		
RDW-SD	1.095 (0.989-1.212)	0.080		
PLT	**0.985 (0.977-0.993)**	**<0.0001**		
MPV	**1.839 (1.223-2.764)**	**0.003**	**2.347 (1.426-7.000)**	**0.013**
N/L (NLR)	**1.163 (1.012-1.337)**	**0.034**		
dNLR	**1.336 (1.056-1.689)**	**0.016**	**2.142 (1.240-8.119)**	**0.007**
SII	1.001 (1.000-1.002)	0.073		
MPV/PLT (MPR)	1.100 (0.700-1.397)	0.089		

* Backward stepwise (Wald).

Table 5. ROC analysis for significant hematological parameters

Parameters	AUC	SE*	Cut-off value	Sensitivity	Specificity	p	AUC (%95 CI)	
							LL	UL
WBC (mm³)	**0.815**	**0.047**	**6.05**	**73.1**	**72.2**	**<0.0001**	**0.723**	**0.906**
Lympocyte (mm³)	**0.838**	**0.041**	**1.55**	**84.6**	**70.9**	**<0.0001**	**0.757**	**0.918**
dNLR	**0.684**	**0.061**	**1.643**	**64.0**	**63.3**	**0.006**	**0.565**	**0.803**
MPV	**0.707**	**0.061**	**9.45**	**69.2**	**65.8**	**0.002**	**0.587**	**0.826**

AUC: Area under curve, SE*: Standart error, LL: Lower limit, UL: Upper limit, CI: Confidence interval.

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