Original Investigation / *Özgün Araştırma*

DOI: 10.5578/ced.20229802 • *J Pediatr Inf 2022;16(2):e69-e76*

Evaluation of the Relationship Between Clinical Findings and Neutrophil-Lymphocyte Ratio and Mean Platelet Volume in COVID-19 PCR-Positive Children

COVID-19 PCR Pozitif Çocuklarda Nötrofil Lenfosit Oranının ve Ortalama Trombosit Hacminin Klinik Bulguları ile İlişkisinin Değerlendirilmesi

Zeynep Betül Türkoğlu(İD), Meltem Erol(İD), Özlem Bostan Gayret(İD), Abdulrahman Özel(İD)

Clinic of Pediatrics, Health Sciences University Bağcılar Training and Research Hospital, İstanbul, Türkiye

Cite this article as: Türkoğlu ZB, Erol M, Bostan Gayret Ö, Özel A. Evaluation of the relationship between clinical findings and neutrophil-lymphocyte ratio and mean platelet volume in COVID-19 pcr-positive children. J Pediatr Inf 2022;16(2):e69-e76.

Abstract

Objective: In this study, we aimed to evaluate the importance of predicting the severity of the disease by measuring the hematological parameters such as the neutrophil-lymphocyte ratio and mean platelet volume, are positively correlated or not. We used COVID-19 PCR positive children who applied to the pediatrics outpatient clinic of our hospital for measurement.

Material and Methods: Our study was designed retrospectively and included 136 children aged 6-18 years who applied to the pediatrics outpatient clinic of our hospital between 29 March 2020 and 31 November 2020. Sixty-eight of these children were found to be healthy and COVID-19 negative, while the other 68 were positive. COVID-19 PCR-positive patients were divided into four groups, each consisting of 17 patients, as asymptomatic infection, acute upper respiratory tract infection, mild pneumonia and severe pneumonia.

Results: The three most common clinical findings in COVID-19 PCR positive patients are; cough was present in 44 (64.7%), fever in 37 (54.4%), and tachypnea in 17 (25%). Neutrophil count, neutrophil-lymphocyte ratio and mean platelet volume were found to be statistically significantly higher in COVID-19 PCR positive children compared to negative ones ($p< 0.05$). The lymphocyte count was found to be significantly lower in COVID-19 PCR positive children ($p< 0.05$). When the subgroups of COVID-19 PCR positive patients are evaluated; as the clinical severity increased between the groups, a significant increase was found in neutrophil count and neutrophil-lymphocyte ratio ($p< 0.05$). A significant decrease was observed in the lymphocyte count with the increase in

Öz

Giriş: Bu çalışmada; hastanemiz çocuk sağlığı ve hastalıkları kliniğine başvuran COVID-19 PCR pozitif çocuklarda hematolojik parametreler olan nötrofil-lenfosit oranının ve ortalama trombosit hacminin klinik veriler ile pozitif korelasyonu olup olmadığının ölçülerek, hastalık şiddetini öngörmede öneminin değerlendirilmesi amaçlanmaktadır.

Gereç ve Yöntemler: Çalışmamıza 29 Mart 2020 ile 31 Kasım 2020 tarihleri arasında hastanemiz çocuk sağlığı ve hastalıkları kliniğine başvurmuş COVID-19 PCR pozitif saptanan 6-18 yaş aralığındaki 68 çocuk ile 6-18 yaş aralığındaki sağlıklı 68 çocuk dahil edildi. COVID-19 PCR pozitif hastalar klinik şiddetine göre asemptomatik enfeksiyon, akut üst solunum yolu enfeksiyonu, hafif pnömoni ve şiddetli pnömoni olarak her biri 17 hastadan oluşan dört gruba ayrıldı.

Bulgular: Çalışmamıza dahil edilen 6-18 yaş aralığında olan toplam 136 çocuğun yaş ortalaması 12.1 (± 3) olup 54 erkek (%40) ve 82 kız (%60) cinsiyetten oluşmaktadır. COVID-19 PCR pozitif hastaların yaş ortalaması 11.8 (± 3.4) olup 28 (%41.2) erkek ve 40 (%58.8) kızdan oluşmaktadır. COVID-19 PCR negatif grubun yaş ortalaması 12.5 (± 2.5) olup 26 (%38.2) erkek ve 42 (%61.8) kız olmak üzere 68 sağlıklı çocuktan oluşmaktadır. Gruplar arasında yaş ve cinsiyet açısından istatistiksel bir fark bulunmamıştır ($p> 0.05$). COVID-19 PCR pozitif hastalarda saptanan en sık üç klinik bulgu; 44'ünde öksürük (%64.7), 37'sinde ateş (%54.4), 17'sinde takipneydi (%25). COVID-19 PCR pozitif ve negatif çocuklar arasında; nötrofil sayısı, nötrofil-lenfosit oranının ve ortalama trombosit hacminin, COVID-19 PCR pozitif çocuklarda istatistiksel anlamlı olarak yüksek bulunmuştur ($p< 0.05$). Lenfosit sayısı ise COVID-19 PCR pozitif çocuklarda

Correspondence Address/Yazışma Adresi

Zeynep Betül Türkoğlu

Sağlık Bilimleri Üniversitesi,
Bağcılar Eğitim ve Araştırma Hastanesi,
Çocuk Sağlığı ve Hastalıkları Kliniği,
İstanbul-Türkiye

E-mail: zbetultasdemir@hotmail.com

Received: 08.09.2021 **Accepted:** 09.12.2021 **Available Online Date:** 30.06.2022

clinical severity (p< 0.05). There was no significant difference between subgroups in the mean platelet volume of COVID-19 patients, consistent with clinical severity (p> 0.05).

Conclusion: In our study, increased neutrophil count and neutrophil-lymphocyte ratio and decreased lymphocyte count were found to be associated with the clinical severity of COVID-19 disease. It is thought that these parameters can be used as good markers to predict the severity of COVID-19 disease. Although mean platelet volume was found to be significantly higher in COVID-19 PCR positive cases, it was not significantly associated with the clinical severity of the disease. Therefore, it was concluded that mean platelet volume is not a good prognostic predictor of the clinical course of the disease.

Keywords: SARS-CoV-2, COVID-19 PCR, neutrophil-lymphocyte ratio, mean platelet volume

anlamlı olarak düşük bulunmuştur (p< 0.05). COVID-19 PCR pozitif hastaların alt grupları değerlendirildiğinde ise; gruplar arasında klinik şiddet arttıkça nötrofil sayısı ve nötrofil-lenfosit oranının değerinde anlamlı artış saptanmıştır (p< 0.05). Lenfosit sayısında ise klinik şiddet artışı ile beraber anlamlı azalma görülmüştür (p< 0.05). COVID-19 hastalarının ortalama trombosit hacminin alt gruplar arasında klinik şiddet ile uyumlu olarak anlamlı farklılık bulunmamıştır (p> 0.05).

Sonuç: Çalışmamızda artmış nötrofil sayısı ve nötrofil-lenfosit oranıyla azalmış lenfosit sayısı hastalığın klinik şiddetiyle ilişkili bulundu. Bu parametrelerin COVID-19 hastalığının ciddiyetini öngörmede iyi birer belirteç olarak kullanılabileceği düşünülmektedir. Ortalama trombosit hacminin ise COVID-19 PCR pozitif vakalarda anlamlı olarak yüksek bulunmuş olsa da hastalığın klinik şiddeti ile anlamlı ilişkisi bulunmadı. Bu nedenle ortalama trombosit hacminin, hastalığın klinik seyri ile ilgili iyi bir prognostik prediktör olmadığı sonucuna ulaşıldı.

Anahtar Kelimeler: SARS-CoV-2, COVID-19 PCR, nötrofil-lenfosit oranı, ortalama trombosit hacmi

Introduction

In December 2019, cases of pneumonia with unknown etiology in the city of Wuhan in the Hubei state of China were reported by the World Health Organization (WHO) China office. On 7 January 2020, it was determined to be a novel type of coronavirus (2019-nCoV) with an agent previously undetected in humans. Later, this virus was referred to as SARS-CoV-2 due to its similarity with the SARS-CoV, the coronavirus associated with the Severe Acute Respiratory Failure Syndrome, and the disease it caused was called the "Coronavirus Disease-2019 (COVID-19)" (1).

COVID-19, which spread rapidly in China since the very first cases, has spread to more than 100 countries by March 2020. Therefore, COVID-19 was declared a pandemic by the WHO on 11 March 2020 (2). The first case in Turkey was detected on 11 March 2020 (3).

SARS-CoV-2 was shown to be transmitted through droplets or when people who come into contact with the surfaces contaminated with the droplets dispersed by the coughing and sneezing of the infected individuals touch the mucous membranes of their mouth, nose, or eyes (4). The most common symptoms are fever, cough, loss of taste and smell, fatigue, muscle pain, and shortness of breath. It manifests with a broad clinical spectrum, from a mild respiratory infection to pneumonia, acute respiratory distress syndrome (ARDS), and death (5). Children, on the other hand, have milder symptoms and fewer hospitalizations compared to adults (6).

It is known that an increase in neutrophil-lymphocyte ratio (NLR) and mean platelet volume (MPV), which are hematological parameters, occur in many inflammatory diseases. It is thought that these two parameters can also be used as markers in COVID-19 disease, which causes an inflammatory response, and may help predict the clinical severity of the disease. In many studies on COVID-19 cases, whether NLR and MPV can be the predictive markers for the clinical severity is investigated (7,8).

Our study aimed to evaluate whether neutrophil-lymphocyte ratio (NLR) and mean platelet volume (MPV) can be used as parameters to predict the disease severity and facilitate early treatment, by assessing if the NLR and MPV calculated from complete blood count at the time of diagnosis in COVID-19 PCR-positive children admitted to our hospital's pediatrics clinic were positively correlated with the clinical findings.

Materials and Methods

This randomized controlled retrospective study was performed in "University of Health Sciences Türkiye, İstanbul Bağcılar Training and Research Hospital" Pediatrics Clinic between 1 May 2021 and 1 June 2021. Ethics committee approval (04/04/2021, 2021/43) was obtained for the study. Study participants and/or their parents provided written informed consent.

Sixty-eight children, aged between 6-18 years, who were COVID-19 PCR-positive and followed up as outpatients or inpatients in our hospital's pediatrics clinic between 29 March 2020 and 31 November 2020, were included in the study. The clinical, laboratory and radiologic data of the patients were gathered from official medical reports with a standardized data collection form. NLR and MPV were calculated based on their hemogram parameters and whether these values were correlated with the severity of clinical findings was evaluated.

When grouping the patients by clinical severity, the classification in one of the frequently used recommendation guides for the clinical classification of pediatric COVID-19 patients, "Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement" by Shen et al. was used (9). Sixty-eight patients included in

the study were divided into four groups, the first group with asymptomatic infection, the second group with acute upper respiratory tract infection, the third group with mild pneumonia, and the fourth group with severe pneumonia. Each group consisted of 17 patients. Since no patients were meeting the criteria of critical cases in the study group, a fifth group could not be formed.

The control group included 68 children, aged between 6-18 years, who had no chronic diseases and were COVID-19 PCR-negative, admitted to our hospital's pediatrics clinic for routine control, and had no complaints, between 29 March 2020 and 31 November 2020. The clinical, laboratory and radiologic data of the control group were gathered from official medical reports with a standardized data collection form. NLR and MPV were calculated according to the hemogram parameters and results were compared with the NLR and MPV values of COVID-19 PCR-positive children.

Statistical Analysis

In this study, when the power (power of the test) was set at 0.80 and Type I error at 5%, it was found that each group should have 68 participants. Whether the continuous variables in the study were normally distributed was determined using Shapiro-Wilk (n< 50) and Skewness-Kurtosis tests, and since the variables were non-normally distributed, parametric tests were carried out. Descriptive statistics for continuous variables were expressed as mean, standard deviation, minimum, maximum; and the descriptive statistics for categorical variables were expressed as number (n) and percentage (%). When comparing the measurements by groups, "idependent t-test" and "one-way analysis of variance (ANOVA)" were used. To determine intervariable relationships, Pearson correlation coefficients were calculated. To determine the relationships between the groups and categorical variables, the Chi-square test was used. In calculations, statistical significance level (α) was set at 5% and SPSS (IBM SPSS for Windows, ver.24) statistics software package was used for analysis.

Results

A total of 136 children were included in our study. The mean age of the study group was 11.8 (± 3.4) years, comprising a total of 68 COVID-19 PCR-positive children, 28 of which were boys (41.2%) and 40 of which were girls (58.8%). When the subgroups of the study group were analyzed, the first subgroup is the asymptomatic group and comprising five boys (29.4%) and 12 girls (70.6%), had a mean age of 11.9 (± 3.3) years; the second subgroup is the acute upper respiratory tract infection group and comprising eight boys (47.1%) and nine girls (52.9%), had a mean age of 12.1 (± 3.6) years; the third subgroup is the mild pneumonia group and comprising six boys (35.3%) and 11 girls (64.7%), had a mean age of 12.4 (± 3.5) years; and the fourth subgroup is the severe pneumonia group and comprising nine boys (52.9%) and eight girls (47.1%), had a mean age of 10.7 (± 3.1) years. There was no statistically significant difference between the subgroups in terms of age and sex (p> 0.05). The control group comprised 68 healthy children, 26 boys (38.2%) and 42 girls (61.8%), with a mean age of 12.5 (± 2.5) years. There was no statistically significant difference between the study group and control group in terms of age and sex (p> 0.05).

The clinical signs and symptoms of patients in the study group at the time of admission were shown in Table 1. Clinical signs and symptoms detected in 68 patients were as follows according to their order of prevalence: cough in 44 patients (64.7%), fever in 37 patients (54.4%), tachypnea in 17 patients (25%), decreased oral intake in 12 patients (17.6%), listlessness in eight patients (11.8%), myalgia in eight patients (11.8%), intercostal-subcostal retraction (IC-SC retraction) in eight patients (11.8%), and sore throat in three patients (4.4%). In addition to the respiratory system signs, loss of taste-smell was detected in three patients (4.4%), diarrhea in one patient (1.5%), headache in one patient (1.5%), nausea in one patient (1.5%), and vomiting in two patients (2.9%).

Of patients with respiratory symptoms, pneumonia was not detected in the acute upper respiratory tract infection group, whereas pneumonia was detected in all of the 17 patients in each of the third and fourth subgroups. The first and second study subgroups were followed-up at-home quarantine, whereas the third and fourth study subgroups were followed up and treated after hospitalization.

The mean neutrophil count was 5.31 (± 2.7) in the study group and 4.09 (± 1.7) in the control group. Based on this data, neutrophil count is higher in the study group and the difference between the two groups is statistically significant (p< 0.05).

The mean lymphocyte count was found to be 2.78 (± 0.84) in the control group and this value was found to be higher than that in the study group, whose mean lymphocyte count was 2.05 (± 0.97). Here, the difference between the mean lymphocyte counts of the two groups was statistically significant (p< 0.05) (Table 2).

NLR was 3.2 (± 2.6) in the study group and 1.4 (± 0.65) in the control group. According to these results, NLR was higher in the study group. The difference between the control and study groups in terms of NLR was statistically significant (p< 0.05) (Table 2).

MPV in the study group was 10.1 (± 1.06), which was higher than that in the control group, whose MPV was 8.8 (± 2.02). Thus, the difference between the control and study groups in

Table 1. Clinical signs and symptoms of study subgroups

	Asymptomatic			Acute upper respiratory tract infection			Mild pneumonia			Severe pneumonia			Total		
	n	Row %	Column %	n	Row %	Column %	n	Row %	Column %	n	Row %	Column %	n	Row %	Column %
Cough	0	0.0	0.0	10	22.7	58.8	17	38.6	100.0	17	38.6	100.0	44	100.0	64.7
Fever	0	0.0	0.0	10	27.0	58.8	11	29.7	64.7	16	43.2	94.1	37	100.0	54.4
Diarrhea	0	0.0	0.0	1	100.0	5.9	0	0.0	0.0	0	0.0	0.0	1	100.0	1.5
Listlessness	0	0.0	0.0	5	62.5	29.4	2	25.0	11.8	1	12.5	5.9	8	100.0	11.8
Tachypnea	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	17	100.0	100.0	17	100.0	25.0
Retractions	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	8	100.0	47.1	8	100.0	11.8
Decreased oral intake	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	12	100.0	70.6	12	100.0	17.6
Headache	0	0.0	0.0	1	100.0	5.9	0	0.0	0.0	0	0.0	0.0	1	100.0	1.5
Sore throat	0	0.0	0.0	1	33.3	5.9	2	66.7	11.8	0	0.0	0.0	3	100.0	4.4
Loss of taste-smell	0	0.0	0.0	2	66.7	11.8	0	0.0	0.0	1	33.3	5.9	3	100.0	4.4
Nausea	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	1	100.0	5.9	1	100.0	1.5
Vomiting	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	2	100.0	11.8	2	100.0	2.9
Myalgia	0	0.0	0.0	3	37.5	17.6	2	25.0	11.8	3	37.5	17.6	8	100.0	11.8

terms of MPV value was statistically significant ($p< 0.05$) (Table 2).

When the mean neutrophil counts of the subgroups of the study groups were analyzed, it was found that the mean neutrophil count was 3.7 (± 1.6) in the first subgroup, 3.8 (± 1.6) in the second subgroup, 5.5 (± 2.4) in the third subgroup and 8.01 (± 3) in the fourth subgroup. The results of these measurements indicate that the mean neutrophil count was higher in the fourth subgroup than in the other subgroups. In the third subgroup, the mean neutrophil count was higher than the first and second subgroups but lower than the fourth subgroup. The first and second subgroups were similar in terms of their mean neutrophil counts. Based on these results, a statistically significant difference was detected between the subgroups of the study group in terms of their mean neutrophil counts ($p< 0.05$) (Table 3).

When the mean lymphocyte counts of the subgroups of the study group were analyzed, it was found that the mean lymphocyte count was 2.6 (± 0.8) in the first subgroup, 2.3 (± 0.9) in the second subgroup, 2 (± 0.8) in the third subgroup, and 1.2 (± 0.6) in the fourth subgroup. The results of these measurements indicate that the mean lymphocyte count was higher in the first subgroup than in the other subgroups. The mean lymphocyte count in the second subgroup was higher than the third and fourth subgroups. The mean lymphocyte count of the third subgroup was higher than the fourth subgroup, which had the lowest mean lymphocyte count. A statistically significant difference was detected between the subgroups of the study group in terms of their mean lymphocyte counts ($p< 0.05$) (Table 3).

When the mean NLR values of the subgroups of the study group were analyzed, it was found that the mean NLR was 1.4 (± 0.4) in the first subgroup, 1.6 (± 0.2) in the second subgroup, 2.8 (± 0.5) in the third subgroup, and 7.1 (± 2.3) in the fourth subgroup. Based on these measurements, the mean NLR value was higher in the fourth subgroup than the other subgroups. The mean NLR in the third subgroup was higher than the first and second subgroups, and lower than the fourth subgroup. The first and second subgroups had similar NLR values. In light of these results, a statistically significant difference was detected between the subgroups of the study group in terms of the mean NLR value ($p< 0.05$) (Table 3).

When the mean MPV values of the subgroups of the study group were analysed, it was found that the mean MPV value was 9.9 (± 0.9) in the first subgroup, 10.1 (± 1) in the second subgroup, 10.4 (± 1.2) in the third subgroup, and 9.9 (± 1) in the fourth subgroup. When these values were compared, a statistically significant difference could not be detected between the subgroups of the study group in terms of the mean MPV values ($p> 0.05$). (Table 3)

Table 2. Laboratory parameters of study and control groups

		n	Mean	Std. Dev.	Min.	Max.	*p.
Neutrophil	Control	68	4.0957	1.70204	1.69	10.09	***.003***
	Study	68	5.3159	2.78962	1.71	12.66	
	Total	136	4.7058	2.38220	1.69	12.66	
Lymphopcyte	Control	68	2.7865	.84410	1.08	5.27	***.001***
	Study	68	2.0571	.97094	.46	4.36	
	Total	136	2.4218	.97749	.46	5.27	
MPV	Control	68	8.8118	2.02619	4.40	14.80	***.001***
	Study	68	10.1309	1.06928	8.20	13.40	
	Total	136	9.4713	1.74448	4.40	14.80	
NLR	Control	68	1.4945	.65544	.03	3.53	***.001***
	Study	68	3.2491	2.60554	.74	11.30	
	Total	136	2.3718	2.08754	.03	11.30	

* Significance levels according to independent t test results.

Table 3. Laboratory parameters of study subgroups

		n	Mean	Std. Dev.	Min.	Max.	*p.
Neutrophil	Asymptomatic	17	3.7759	1.61007	1.71	6.53	***.001***
	Acute upper respiratory tract infection	17	3.8888	1.63540	2.04	7.74	
	Mild pneumonia	17	5.5876	2.40835	2.81	11.85	
	Severe pneumonia	17	8.0112	3.00654	3.56	12.66	
	Total	68	5.3159	2.78962	1.71	12.66	
Lymphopcyte	Asymptomatic	17	2.6382	.80920	1.06	4.30	***.001***
	Acute upper respiratory tract infection	17	2.3776	.95572	1.32	4.36	
	Mild pneumonia	17	2.0088	.85972	.88	4.11	
	Severe pneumonia	17	1.2035	.62907	.46	2.80	
	Total	68	2.0571	.97094	.46	4.36	
MPV	Asymptomatic	17	9.9765	.93710	8.40	11.30	***.617***
	Acute upper respiratory tract infection	17	10.1471	1.06367	8.30	12.20	
	Mild pneumonia	17	10.4118	1.24694	8.20	13.40	
	Severe pneumonia	17	9.9882	1.04516	8.50	11.90	
	Total	68	10.1309	1.06928	8.20	13.40	
NLR	Asymptomatic	17	1.4429	.44303	.74	2.26	***.001***
	Acute upper respiratory tract infection	17	1.6012	.22226	1.16	1.98	
	Mild pneumonia	17	2.8524	.53502	2.03	3.71	
	Severe pneumonia	17	7.1000	2.37092	3.38	11.30	
	Total	68	3.2491	2.60554	.74	11.30	

* Significance levels according to one-way ANOVA test results.

Discussion

In a meta-analysis that evaluated a total of 22 studies, 21 from China and one from Singapore, which analysed many laboratory parameters of mildly and severely ill COVID-19 PCR-positive patients, it was found that the lymphocyte count was lower and neutrophil count and NLR value were significantly higher in severely ill patients than the mildly ill patients. This suggested that NLR parameter can be an early predictor that can be used to determine the disease prognosis (10). Similarly, in another study on 63 adult COVID-19 patients, Xia

et al. divided the patients into two clinical groups, as moderately and severely ill. They found that NLR values of severely ill cases were significantly higher than those of moderately ill cases (11). In the Chinese study by Jianhong Fu et al., 75 adult COVID-19 PCR-positive patients were divided into two groups according to their clinical signs, as mildly/moderately ill and severely ill. It was found that the NLR value of the severely ill patients was significantly higher than that of the mildly/moderately ill patients (12). In the study by Yang et al. in 93 adult COVID-19 patients, lymphopenia was detected in 80.6% and neutrophilia was detected in 51.6% of the laboratory findings of the patients. However, NLR values of patients with severe COVID-19 were found to be significantly higher than patients who were not severely ill. It was suggested that an NLR of 3.3 and above can be used as an indicator of the change in the disease status from mild to severe (13). According to the data in the study by Asan et al., a lower lymphocyte count was detected in severe COVID-19 cases than the mild or moderate cases, whereas the neutrophil-lymphocyte ratio was higher. According to these results, it was found that NLR can be useful to clinicians in determining the disease severity at the early stage (14).

Studies show that the clinical course of COVID-19 in children is milder than the adults and the need for hospitalization is less (6). Although the asymptomatic course is more common in children than in adults, the number of severe cases is considerable. However, laboratory parameters that will enable the clinical course in children are as important as those in adults. While there is not a sufficient number of studies in children, studies on parameters that may help in predicting clinical severity continue.

In the study by Bari et al., which is one of the studies which investigated the clinical severity in pediatric COVID-19, there was a total of 83 children, 60 of which were COVID-19 patients, and 23 of which were diagnosed with the multisystem inflammatory syndrome in children (MIS-C) or Kawasaki disease after having COVID-19. The mean age of these 83 children was seven (± 4.3) years and male sex dominated with 61%. In the same study, 60 children who were COVID-19 patients were divided into two groups, and the NLR value of the severely critically ill group was significantly higher than that of the mildly-moderately ill group (15). In the study by Ötiken Arıkan et al. in 353 COVID-19 PCR-positive children, the sex of patients was mainly male, with 52.1%, and the mean age was nine years. The patients were divided into four groups according to their clinical conditions. When these groups were compared in terms of their NLR values, it was found that the NLR values of the severely critically ill patients were statistically significantly higher than the asymptomatic, mildly ill and moderately ill groups (16). Similarly, in the study by Huang et al. in 415 COVID-19 patients in the pediatric and adult age group, the male sex was dominant with 52.3% and the patients were divided into two groups according to their clinical condition. It was found that the NLR values of the severely ill group were higher than the group that was not severely ill (17).

In line with the literature, in our study, the mean NLR value was found to be higher in the severe pneumonia group than in the other groups. In the third subgroup, the NLR value was higher than the first and second subgroups and lower than the fourth subgroup. In conclusion, in our study, as the clinical severity increased, the mean NLR value increased significantly. The literature demonstrates that the NLR value can be a meaningful parameter in evaluating the severity of the clinical course of COVID-19 in both adult and pediatric patient groups.

In the study by Guan et al., the most commonly observed clinical findings in 1099 adult COVID-19 patients were fever (88.7%) and cough (67.8%). These were followed by fatigue (38.1%), expectoration (33.7%), and shortness of breath (18.7%) (18). Similarly; according to the results of a review which evaluated 38 studies in children with COVID-19 and included 1117 cases, the two most common findings in patients were fever (47.5%) and cough (41.5%), followed by nasal symptoms (11.2%), diarrhea (8.1%), nausea-vomiting (7.1%) (19). In our study, in concordance with these studies in the literature, the two most common clinical findings detected at the time of admission of 68 COVID-19 PCR-positive patients were cough (64.7%) and fever (54.4%), followed respectively by tachypnea (25%), decreased oral intake (17.6%), and listlessness (16.2%).

MPV, which is the marker of platelet function and activation together with the platelet count, can vary in diseases in which inflammation is triggered (20,21). MPV value is one of the parameters that is thought that can be used to predict the clinical course of COVID-19 and investigated in many studies. Although the mean platelet volume (MPV)/platelet count ratio is considered an important marker of inflammatory and infectious diseases, the role of MPV in predicting the clinical course of COVID-19 remains unclear.

In the study by Yun et al. in adult patients, it was found that the MPV value of the COVID-19 PCR-positive group was significantly higher than the healthy group (22). In the study by Zhong and Peng, MPV was studied in COVID-19 PCR-positive patients and was found to be significantly high in patients with severe pneumonia. This demonstrated that MPV can be used as a marker to predict especially whether severe pneumonia will develop in COVID-19 (8). Also, in the study by Güçlü et al. in 215 patients hospitalized due to COVID-19, the patients were divided into two groups, moderately and severely ill. A significant increase in MPV value was detected among these groups. The authors found that this increase was associated with disease severity and an increase in mortality (23).

In the study by Gümüş et al. in 58 COVID-19 PCR-positive asymptomatic children and 60 healthy children, MPV value was found significantly higher in children infected with SARS-CoV-2 despite the asymptomaticity, revealing that MPV value can be used as a predictor in COVID-19, which is an inflammatory disease (24). In another study by Güner Özenen et al. in 251 pediatric confirmed COVID-19 cases, the patients were divided into five groups as asymptomatic, mildly ill, moderately ill, severely ill, and critically ill, and the groups were compared. A significant difference was not observed between these groups in terms of their MPV values. Thus, the authors demonstrated that MPV values were not useful in predicting the severity of COVID-19 in pediatric patients (25). In concordance with the study by Güner Özenen et al., in our study, although MPV value was higher in COVID-19 PCR-positive children than COVID-19 PCR-negative children, it was found that MPV value did not increase with the clinical severity. In this context, higher MPV values observed in cases diagnosed with COVID-19, which is an inflammatory disease, than the healthy children, demonstrates that MPV can be used as an inflammatory marker but is not a guide to the clinical course as it does not always increase in correlation with the disease severity.

Although the relationship between MPV and COVID-19 was detected in adult patients, this relationship is not observed in pediatric patients. While more comprehensive studies are required in this subject, this issue suggests that the absence of this relationship can be attributed to the fact that COVID-19 infection has less severity and creates a less inflammatory response in children.

The limitation of our study was that it was conducted in a single center and therefore the number of confirmed cases was limited. Since our study is compatible with other studies, we believe that our results are contributing to the literature, even though the number of confirmed cases is low.

Conclusion

Increasing recognition of the hematological parameters NLR and MPV as inexpensive, easily attainable, and clinically significant in recent studies makes these parameters more valuable and usable in routine practice. In light of the findings obtained in our study; a significant increase was observed in the neutrophil count, NLR, and MPV values, and a significant decrease was detected in the lymphocyte count. Increased neutrophil count and NLR and decreased lymphocyte count were found to be associated with the clinical severity of COVID-19. Each of these parameters is believed to be a good biomarker in predicting COVID-19 disease severity. Although MPV was found to be significantly high in COVID-19 PCR-positive cases, no significant relationship was detected between MPV and the clinical severity of the disease. Therefore, it was concluded that MPV is not a good prognostic predictor for the clinical course of the disease.

Ethics Committe Approval: This study was approved by Health Sciences University, Hamidiye Clinical Research Ethics Commitee (Decision no: 1, Date: 04.04.2021).
Informed Consent: Patient consent was obtained.
Peer-review: Externally peer-reviewed.
Author Contributions: Concept- ZBT, AÖ; Design- ZBT, ME; Supervision- ÖBG, ME; Resource- AÖ, ME; Data Collection and/or Processing- ZBT, AÖ; Analysis and/or Interpretation- ZBT, ÖBG; Literature Search - ZBT, AÖ, Writing- ZBT, ME; Critical Review- ME, ÖBG, AÖ.
Conflict of Interest: All authors declare that they have no conflicts of interest or funding to disclose.
Financial Disclosure: The authors declared that this study has received no financial support.

References

1. *Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395(10223):497-506. [CrossRef]*
2. *Cucinotta D, Vanelli M. WHO Declares COVID-19 a pandemic. Acta Biomed 2020;91(1):157-60.*
3. *T.C. Sağlık Bakanlığı. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü-COVID-19 (SARS-CoV-2 Enfeksiyonu) Genel Bilgiler, Epidemiyoloji ve Tanı. Ankara: T.C. Sağlık Bakanlığı HSGM Available from: https://covid19.saglik.gov.tr/TR- 66337/genel-bilgiler-epidemiyoloji-ve-tani.html (Accessed date: 30 Kasım 2020).*
4. *WHO, Novel Coronavirus (2019-nCoV) 22 January 2020. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200122-sitrep-2-2019-ncov.pdf?sfvrsn=4d5bcbca_2*
5. *Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun 2020;109:102433. [CrossRef]*
6. *Wang E, Brar K. COVID-19 in children: An epidemiology study from China. J Allergy Clin Immunol Pract 2020;8(6):2118-20. [CrossRef]*
7. *Wu H, Zhu H, Yuan C, Yao C, Luo W, Shen X, et al. Clinical and immune features of hospitalized pediatric patients with Coronavirus disease 2019 (COVID-19) in Wuhan, China. JAMA Netw Open 2020;3(6):e2010895. [CrossRef]*
8. *Zhong Q, Peng J, Mean platelet volume/platelet count ratio predicts severe pneumonia of COVID-19. J Clin Lab Anal 2021;35(1):e23607. [CrossRef]*
9. *Shen, K, Yang, Y, Wang, T, Zhao, D, Jiang, Y, Jin, R, et al. Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement. World J Pediatr 2020;16(3):223-31. [CrossRef]*
10. *Ghahramani S, Tabrizi R, Lankarani KB, Kashani SMA, Rezaei S, Zeidi N, et al. Laboratory features of severe vs. non-severe COVID-19 patients in Asian populations: a systematic review and meta-analysis. Eur J Med Res 2020;25(1):30. [CrossRef]*
11. *Xia X, Wen M, Zhan S, He J, Chen W. An increased neutrophil/lymphocyte ratio is an early warning signal of severe COVID-19. 2020 Mar 30;40(3):333-6.*

12. *Fu J, Kong J, Wang W, Wu M, Yao L, Wang Z, et al. The clinical implication of dynamic neutrophil to lymphocyte ratio and D-dimer in COVID-19: A retrospective study in Suzhou China. Thromb Res 2020;192:3-8.* **[CrossRef]**
13. *Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. Int Immunopharmacol 2020;84:106504.* **[CrossRef]**
14. *Asan A, Üstündağ Y, Koca N, Şimşek A, Sayan HE, Parildar H, et al. Do initial hematologic indices predict the severity of COVID-19 patients? Turk J Med Sci 2021;51:39-44.* **[CrossRef]**
15. *Bari A, Ch A, Bano I, Saqlain N. Is leukopenia and lymphopenia a characteristic feature of COVID-19 in children? Pak J Med Sci 2021;37(3):869-73.* **[CrossRef]**
16. *Ötiken Arıkan K, Şahinkaya Ş, Böncüoğlu E, Kıymet E, Cem E, Akaslan Kara A, et al. Can hematological findings of COVID-19 in pediatric patients guide physicians about clinical severity? Turk J Haematol 2021;38(3):243-5.* **[CrossRef]**
17. *Huang S, Liu M, Li X, Shang Z, Zhang T, Lu H. Significance of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio for predicting clinical outcomes in COVID-19, medRxiv 2020;05:04.20090431.* **[CrossRef]**
18. *Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708-20.* **[CrossRef]**
19. *Souza TH, Nadal J, Nogueira RJN, Pereira RM, Brandao MB. Clinical manifestations of children with COVID-19: A systematic rewiew. Pediatr Pulmonol 2020;55(8):1892-9.* **[CrossRef]**
20. *Catal F, Tayman C, Tonbul A, Akça H, Kara S, Tatlı MM, et al. Mean platelet volume (MPV) may simply predict the severity of sepsis in preterm infants. Clin Lab 2014;60:1193-200.* **[CrossRef]**
21. *Kitazawa T, Yoshino Y, Tatsuno K, Ota Y, Yotsuyanagi H. Changes in the mean platelet volume levels after bloodstream infection have prognostic value. Intern Med 2013;52:1487-93.* **[CrossRef]**
22. *Yun H, Sun Z, Wu J, Tang A, Hu M, Xiang Z. Laboratory data analysis of novel coronavirus (COVID-19) screening in 2510 patients. Clin Chim Acta 2020;507(94):97.* **[CrossRef]**
23. *Güçlü E, Kocayiğit H, Okan HD, Erkorkmaz U, Yürümez Y, Yaylacı S, et al. Effect of COVID-19 on platelet count and its indices. Rev Assoc Med Bras 2020;66(8):1122-7.* **[CrossRef]**
24. *Gumus H, Demir A, Yükkaldıran A. Is mean platelet volume a predictive marker for the diagnosis of COVID-19 in children? Int J Clin Pract 2021;75(4):e13892.* **[CrossRef]**
25. *Guner Ozenen G, Sahbudak Bal Z, Umit Z, Bilen NM, Yildirim Arslan S, Yurtseven A, et al. Demographic, clinical, and laboratory features of COVID-19 in children: The role of mean platelet volume in predicting hospitalization and severity. J Med Virol 2021;93(5):3227-37.* **[CrossRef]**