OTJHS
Online Turkish Journal of Health Sciences

e-ISSN: 2459-1467

OTSBD
Online Türk Sağlık Bilimleri Dergisi

Online Turkish Journal of Health Sciences 2023;8(1):127-133 *Online Türk Sağlık Bilimleri Dergisi 2023;8(1):127-133*

Can NLR, D-Dimer, and MPV Values Predict Mortality and Clinical Severity in Covid-19 Patients?

Kovid-19 Hastalarında NLR, D-Dimer ve MPV Değerleri Mortaliteyi ve Klinik Ciddiyeti Öngörebilir Mi?

[1]Hüseyin KARATAŞ, [2]Murat YÜCEL, [2]Murat GÜZEL, [2]Metin YADİGAROĞLU, [3]Hatice OĞUZ, [4]Emre ÖZGEN, [5]Muhammet Faruk AKYÜZ, [6]Nurçin ÖĞRETEN YADİGAROĞLU

[1]Samsun Gazi Public Hospital, Emergency Clinic, Samsun Türkiye
[2]Samsun University Faculty of Medicine, Department of Emergency Medicine, Samsun Türkiye
[3]Kulu Public Hospital, Emergency Clinic, Konya, Türkiye
[4]Samsun Provincial Directorate of Health, Samsun, Türkiye
[5]Çarşamba Public Hospital, Emergency Clinic, Samsun, Türkiye
[6]Samsun Education and Research Hospital, Department of Internal Medicine, Samsun, Türkiye

Hüseyin Karataş: https://orcid.org/0000-0003-3644-0510
Murat Yücel: https://orcid.org/0000-0003-0220-9230
Murat Güzel: https://orcid.org/0000-0003-0276-4576
Metin Yadigaroğlu: https://orcid.org/0000-0003-1771-5523
Hatice Oğuz: https://orcid.org/0000-0002-2047-7522
Emre Özgen: https://orcid.org/0000-0001-8153-4132
Muhammet Faruk Akyüz: https://orcid.org/0000-0002-5533-3617
Nurçin Öğreten Yadigaroğlu: https://orcid.org/0000-0002-2629-7346

ABSTRACT

Objective: In this study, we aim to determine the relationship between neutrophil/lymphocyte ratio (NLR), D-dimer, and mean platelet volume (MPV) parameters with mortality and clinical severity in Covid-19 patients.

Materials and Methods: This retrospectively planned study included Covid-19 patients admitted to the emergency department between March 2020 and September 2020. Sociodemographic characteristics, laboratory parameters, and imaging results of the patients were obtained. The patients were grouped according to the development of mortality and clinical follow-up.

Results: Seven hundred patients were included in the study and the mean age of the patients was 49.1±18.2 years. Mortality developed in 5.4% (n=38) of the patients. NLR, D-dimer, and MPV levels of patients who developed mortality were higher than those who survived (p<0.001; p <0.001 and p=0.035, respectively). In ROC analysis, >6 NLR levels, >8.45 MPV levels, and >0.57 D-dimer levels were found to be predictive for mortality (p<0.001; p=0.019; p <0.001, respectively).

Conclusions: The high NLR, D-dimer, and MPV levels obtained at the time of admission in Covid-19 patients can be used as an indicator of mortality. Elevated NLR and D-dimer levels are useful in determining the severity of the disease and clinical follow-up.

Keywords: Covid-19, D-dimer, mean platelet volume, mortality, neutrophil/lymphocyte ratio

ÖZ

Amaç: Bu çalışmada amacımız Kovid-19 hastalarında nötrofil/lenfosit oranı (NLR), D-dimer ve ortalama trombosit hacmi (MPV) parametrelerinin mortalite ve klinik ciddiyet ile olan ilişkisini tespit etmektir.

Materyal ve Metot: Retrospektif olarak planlanan bu çalışmaya Mart 2020 ile Eylül 2020 tarihleri arasında acil servise başvuran Kovid-19 hastaları dahil edildi. Hastaların sosyodemografik özellikleri, laboratuvar parametreleri ve görüntüleme sonuçları hastanenin elektronik kayıt sisteminden elde edildi. Hastalar mortalite gelişimine ve klinik takip şekline göre gruplandırıldı.

Bulgular: Çalışmaya 700 hasta alınmış olup hastaların yaş ortalaması 49,1±18,2 yıldı. Hastaların %5,4'ünde (n=38) mortalite gelişti. Mortalite gelişen hastaların NLR, D-dimer ve MPV düzeyleri sağ kalanlardan daha yüksekti (p<0,001; p<0,001 ve p=0,035 sırasıyla). ROC analizinde >6 NLR düzeylerinin ((%71,05 sensitivite ve %92,15 spesifite; AUC: 0,900 (%95 GA 0,858-0,941, p<0,001)), >8,45 MPV düzeylerinin (%68,4 sensitivite ve %53,9 spesifite; AUC: 0,601 (%95 GA 0,564-0,638, p=0,019)) ve >0,57 D-dimer düzeylerinin (%81,6 sensitivite ve %73,9 spesifite; AUC:0,841 (%95 GA 0,812-0,867 p<0,001)) mortalite için belirleyici olduğu görüldü.

Sonuç: Kovid-19 hastalarında başvuru anında alınan NLR, D-dimer ve MPV düzeylerindeki yükseklik mortalite için bir gösterge olarak kullanılabilir. NLR ve D-dimer düzeylerindeki yükseklikler hastalığın ciddiyetini ve klinik takip şeklini belirlemede kullanışlıdır.

Anahtar Kelimeler: D-dimer, kovid-19, mortalite, nötrofil/lenfosit oranı, ortalama trombosit hacmi

Sorumlu Yazar / Corresponding Author:
Metin Yadigaroğlu
Mevlana District Bornova Avenue Megacity Apartment No:81 Flat:28 Atakum/Samsun, Türkiye
Tel: +905367818888
E-mail: metin.yadigaroglu@samsun.edu.tr

Yayın Bilgisi / Article Info:
Gönderi Tarihi/ Received: 23/01/2023
Kabul Tarihi/ Accepted: 11/02/2023
Online Yayın Tarihi/ Published: 05/03/2023

Atıf / Cited: Karataş H and et al. Can NLR, D-Dimer, and MPV Values Predict Mortality and Clinical Severity in Covid-19 Patients?. *Online Türk Sağlık Bilimleri Dergisi* 2023;8(1):127-133. doi: 10.26453/otjhs.1240858

INTRODUCTION

At the end of 2019, a new coronavirus named 2019 novel coronavirus (Covid-19; SARS-nCoV-2) emerged in Wuhan, China, causing an unusual viral pneumonia epidemic. This novel coronavirus disease, also known as Covid-19, has spread rapidly worldwide as it is highly contagious.[1] The ongoing Covid-19 pandemic has posed an extraordinary threat to global public health.[2] Ultimately, on March 11, 2020, the World Health Organization (WHO) officially described the global Covid-19 outbreak as a pandemic.[3]

About 80% of infected individuals have mild to moderate symptoms. The remaining patients may be in a clinical condition severe enough to require hospitalization. Among the severely ill, the most serious complications are acute respiratory distress syndrome (ARDS)/diffuse alveolar damage.[4]

Neutrophil/Lymphocyte ratio (NLR) is a widely used marker to evaluate bacterial infections' severity, define the immune response to stress stimuli, and may have prognostic value in pneumonia and malignancies.[5] Recent studies have shown that changes in NLR may damage T lymphocytes caused by Covid-19, which may be responsible for disease worsening.[6] Platelet activation is linked to the pathophysiology of diseases prone to thrombosis and inflammation.

Studies suggest a relationship between the increase in mean platelet volume (MPV) and the risk of thrombosis. D-Dimer is a specific degradation product produced in the hydrolysis of fibrin.[7] It may reflect the effects of infection on coagulation in infectious diseases. Some studies have reported increased levels of D-Dimer in patients with pneumonia.[8] The level of D-Dimer in critically ill Covid-19 patients is significantly increased, with frequent coagulation disorders and microthrombotic formation in peripheral blood vessels.[9]

In this study, we aim to determine the relationship between NLR, D-dimer, and MPV parameters with mortality in Covid-19 patients.

MATERIALS AND METHODS

Ethical Approval: By the Declaration of Helsinki, it was gotten after the tertiary Training and Research Hospital ethics committee approval (Dated: 13.01.2021, decision no: 2021/1/19).

Study Population: Patients older than 18 with a positive PCR test for Covid-19 and a lung computed tomography who came to the emergency department of a tertiary hospital between March 2020 and September 2020 were included in the study. Patients younger than 18 years of age, with pregnancy status, with a diagnosis of hematological disease, with a diagnosis of oncological disease, with a diagnosis of rheumatological disease, who received immunosuppressive therapy, and whose adequate clinical information, laboratory and imaging data could not be reached were excluded from the study.

Data Collection: Sociodemographic characteristics such as age, gender, comorbidity, laboratory values such as neutrophils, lymphocytes, D-dimer and MPV, and thorax CT images and comments of the patients included in the study were obtained from the electronic registry system of the hospital. The clinical course of the patients was analyzed from the electronic record system. Regarding follow-up, the patients were divided into three groups: outpatients (discharged from the emergency room), patients admitted to the service, and patients admitted to the intensive care unit. As an outcome measure, patients who developed mortality during the hospital stay and patients who did not were divided into two groups. Sociodemographic characteristics and laboratory parameters were compared between all groups.

Statistical Analysis: Obtained data were analyzed using IBM SPSS Statistics 25 and MedCalc statistical software (version 20; MedCalc Software, Ostend, Belgium) package programs. Categorical variables are expressed as frequency and percentage. The mean±standard deviation for the numerical variables that fit the normal distribution, the median (minimum-maximum) for the variables that did not include the normal distribution; Student's t-test was used to compare numerical data with normal distribution in pairwise group comparisons, the Mann-Whitney U test was used to compare data that did not fit. The Chi-square or Fisher's exact test was used to compare categorical data. Kruskal-Wallis's analysis of variance was used for multiple group comparisons. Receiver operating characteristics (ROC) analysis was performed to determine the best NLR, D-dimer, and MPV levels in evaluating the mortality. Optimal cut-off values and sensitivity and specificity values were determined for these measurements. The area under the curve (AUC) and 95% confidence intervals (CI) are indicated. All statistical tests were two-tailed, and the statistical significance level was accepted as $p<0.05$ for all analyses.

RESULTS

Between the specified dates, the data of 1154 patients were examined for the study, and a total of 700 patients were eligible for the study after the exclusion criteria were applied. The mean age of the patients was 49.1 ± 18.2 years. The female/male ratio was 1.2/1. There was at least one other disease in 39% (n=273) of the patients. Mortality developed in 5.4% (n=38) of the patients. Pneumonia was observed in 58.6% (n=410) of the patients on thorax CT (Table 1).

Table 1. Sociodemographic characteristics, laboratory results, and imaging results of the patients.

Characteristic		Value
Age (years)	Mean ± Sd	49.1 ± 18.2
Gender n (%)	Female	388 (55.4)
	Male	312 (44.6)
Comorbidity n (%)	Comorbidity (-)	427 (61.0)
	Comorbidity (+)	273 (39.0)
	Hypertension	232 (33.1)
	Asthma	55 (7.9)
	Diabetes mellitus	54 (7.7)
	COPD	22 (3.1)
	Chronic kidney disease	7 (1.0)
	Heart failure	5 (0.7)
	Cerebrovascular disease	4 (0.6)
	Coronary artery disease	4 (0.6)
	Other*	6 (0.8)
Mortality (+) n (%)		38 (5.4)
NLR Med (min-max)		2 (0-40)
MPV (fl) Ort ± SS		8.4 ± 1.0
D-dimer (µg/ml) Med (min-max)		0.34 (0.02-35)
Thorax CT n (%)	Pneumonia (-)	290 (41.4)
	Pneumonia (+)	410 (58.6)

* Other; 2 patients with hypothyroidism, 1 patient with pulmonary arterial hypertension, 1 patient with chronic HBV, 1 patient with HCV, 1 patient with arrhythmia; CT: computed tomography; MPV: Mean Platelet Volume; NLR: Neutrophil Lymphocyte Ratio; COPD: Chronic Obstructive Pulmonary Disease.

The mean age of patients who developed mortality (75.6 ± 10.5) was significantly higher than that of survivors (47.5 ± 17.4) (p<0.001). It was observed that patients who developed mortality had a higher rate of another disease than those who did not (p<0.001). The median NLR value of patients who developed mortality was 8.5, while 2 in patients who did not (p<0.001). The median D-dimer level of patients who developed mortality was 1.16, while it was 0.32 in patients who did not (p<0.001). The median MPV level of patients who developed mortality was 8.6, while it was 8.4 in patients who did not (p=0.035). All three parameters were statistically higher in patients who developed mortality than in those who did not (Table 2).

Table 2. Comparison of demographic, clinical, and laboratory results of groups with and without mortality.

		Mortality (+) (n=38)	Mortality (-) (n=662)	p
Age (years)	Mean ± Sd	75.6 ± 10.5	47.5 ± 17.4	0.001†
Gender n (%)	Kadın	17 (44.7)	371 (56.0)	0.173††
	Erkek	21 (55.3)	291 (44.0)	
Comorbidity n (%)	Comorbidity (-)	6 (15.8)	421 (63.6)	0.001††
	Comorbidity (+)	32 (84.2)	241 (36.4)	
ICU (+) n (%)		35 (92.1)	23 (3.5)	0.001††
NLR Med (min-max)		8.5 (2-36)	2 (0-40)	0.001*
MPV (fl) Med (min-max)		8.6 (7.2-10.6)	8.4 (0.16-12.40)	0.035*
D-dimer (µg/ml) Med (min-max)		1.16 (0.2-35.0)	0.32 (0.02-9.7)	0.001*
Thorax CT n (%)	Pneumonia (-)	2 (5.3)	288 (43.5)	0.001††
	Pneumonia (+)	36 (94.7)	374 (56.5)	

†Independent samples t test; ††Chi-square test; *Mann Whitney U test; ICU: intensive care unit; CT: computed tomography; MPV: Mean Platelet Volume; NLR: Neutrophil Lymphocyte Ratio.

When outpatients (discharged from the emergency room) and inpatients were compared; The mean age of the patients hospitalized in the ICU was among the patients hospitalized in the ward; The mean age of patients hospitalized in the community was also higher than the mean age of patients discharged from the emergency department (p<0.001; for both). The comorbidities of the patients admitted to the ICU were more common than those admitted to the service and discharged from the emergency department (Table 3). NLR levels of the patients hospitalized in the ICU were higher than the patients hospitalized in the service (p<0.001); NLR levels of hospitalized patients were also higher than those discharged (p<0.001). It was determined that MPV levels were higher in those who were followed up in the ICU than those who were discharged (p=0.049) and were similar among the other groups. Patients admitted to the ICU had higher D-dimer levels than those released and disclosed to the ward (p<0.001; for each). The D-dimer levels of the patients who were

Table 3. Comparison of demographic, clinical, and laboratory results according to the follow-up type of patients.

		Discharged (n=342)	Service admission (n=300)	ICU admission (n=58)	p
Age[abc]	Mean ± Sd	40.5[a] ± 14.1	54.1[b] ± 17.2	73.5[c] ± 12.2	0.001[†]
Gender n (%)	Kadın	186 (54.4)	175 (58.3)	27 (46.6)	0.220[††]
	Erkek	156 (45.6)	125 (41.7)	31 (53.4)	
Comorbidity n (%)	Comorbidity (-)	278 (81.3)	140 (46.7)	9 (15.5)	0.001[††]
	Comorbidity (+)	64 (18.7)	160 (55.3)	49 (84.5)	
****NLR[abc]**		2 (0-26)[a]	2 (0-28)[b]	8 (2-40)[c]	0.001[*]
****MPV[abc] (fl)**		8.4 (0.16-12)[a]	8.3 (6.5-11.3)[b]	8.6 (6.8-12.4)[c]	0.045[*]
****D-dimer[abc] (µg/ml)**		0.28 (0.02-8.07)[a]	0.36 (0.04-9.29)[b]	0.93(0.2-35)[c]	0.001[*]
Thorax CT n (%)	Pneumonia (-)	225 (65.8)	62 (20.7)	3 (5.2)	0.001[††]
	Pneumonia (+)	117 (34.2)	238 (79.3)	55 (94.8)	

[†]One Way ANOVA test; [††]Chi-square test; *Kruskal Wallis test; **Median (minimum-maximum); CT: computed tomography; MPV: Mean Platelet Volume; NLR: Neutrophil Lymphocyte Ratio; ICU: intensive care unit; Age[a-b]:p<0.001; Age[a-c]: p<0.001; Age[b-c]: p<0.001; NLR[a-b]: p<0.001; NLR[a-c]: p<0.001; NLR[b-c]: p<0.001; MPV[a-b]: p=0.996; MPV[a-c]: p=0.049; MPV[b-c]: p=0.052; D-dimer[a-b]: p=0.003; D-dimer[a-c]: p<0.001; D-dimer[b-c]: p<0.001.

followed up in the community were also higher than those who were discharged (p=0.003) (Table 3).

In ROC analysis, it was observed that NLR (p<0.001), D-dimer (p<0.001), and MPV levels (p=0.035), respectively, were the only determinants of mortality. Accordingly, NLR levels >6 were an indicator for mortality with a sensitivity of 71.05% and a specificity of 92.15% (AUC: 0.900 (95% CI 0.858-0.941, p<0.001)); MPV levels >8.45 were an indicator for mortality with 68.4% sensitivity and 53.9% specificity (AUC: 0.601 (95% CI 0.564-0.638, p=0.019)), and >0.57 D-dimer levels 81%, It was found to be an indicator for mortality (AUC:0.841 (95% CI 0.812-0.867 p<0.001)) with a

Table 4. Diagnostic performance of NLR, MPV and D-dimer on mortality.

	AUC	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	p
NLR	0.900	>6.0	71.05	92.15	20.1	98.7	0.001
MPV (fl)	0.601	>8.45	68.4	53.9	7.8	96.7	0.019
D-dimer (µg/ml)	0.841	>0.57	81.6	73.9	15.2	98.6	0.001

AUC: Area Under the Curve; PPD: positive predictive value; NPD: negative predictive value; MPV: Mean Platelet Volume; NLR: Neutrophil Lymphocyte Ratio.

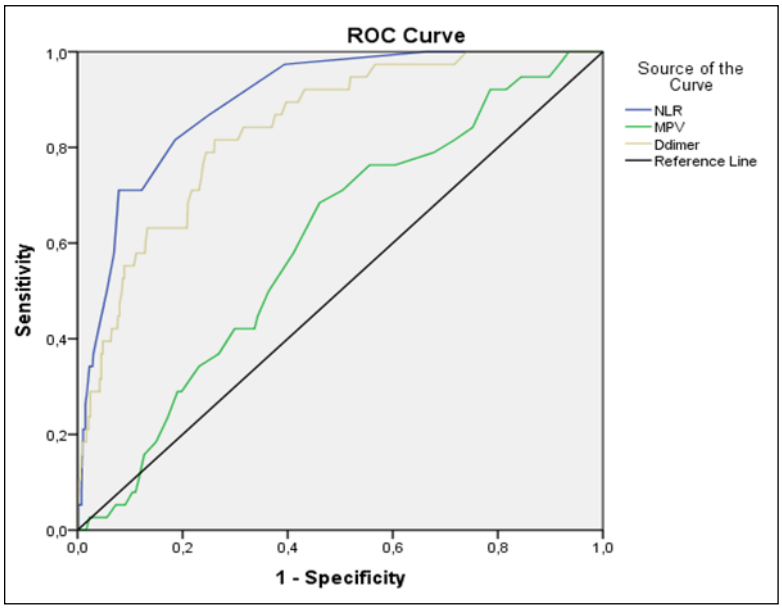

Figure 1. ROC curve for NLR, MPV, and D-dimer - mortality association.

sensitivity of 6 and a specificity of 73.9% (Table 4). The corresponding ROC curve is shown in Figure 1.

DISCUSSION AND CONCLUSION

Due to the rapid spread of the Covid-19 pandemic, there has been a need to define markers that can be used in diagnosing the disease, in the follow-up of its clinical course, and in determining the prognosis. Because tags that can show disease progression and severity can enable the identification of high-risk individuals and the optimal use of resources. However, the sensitivity of frequently used markers in clinical practice, such as platelet, hemoglobin, lactate dehydrogenase, prothrombin time, and transaminases, the diagnosis and severity of Covid-19 needs to be revised.[10-13] Therefore, the need to define easily accessible and widely used laboratory parameters arose to predict the disease's severity and outcome. Therefore, our study aimed to determine the NLR, D-dimer, and MPV values in the prognosis and severity of Covid-19.

The mortality rate of the patients included in our study was 5.4%. Although this rate is consistent with the literature data, it can be seen as relatively low since patients in the good clinical condition who are scheduled to be discharged are also included in the study. Patients planned for discharge were almost half of the patients in the study (48.8%). Although the patients with and without mortality in our study were similar in terms of gender, it was seen that the mean age and the rate of having other diseases were higher in patients who developed mortality following the literature data (Table 1). The relationship between age, gender, and comorbidity variables with the way of follow-up of the patients (discharge, hospitalization, and admission to the intensive care unit) was similar to the relationship with mortality (Table 2). As in other diseases, sociodemographic characteristics are insufficient for managing the disease, and there is a need to benefit from rapidly accessible and frequently used laboratory parameters. In this context, we evaluated the NLR, D-dimer, and MPV parameters we looked at among the groups we formed among the patients in our study.

In our study, NLR levels were higher in patients who developed mortality than in those who did not. We even found that an NLR level of >6 indicates mortality, with a sensitivity of 71.05% and a specificity of 92.15%. In a retrospective study of 681 clinically severe Covid-19 patients by Chen et al., it was reported that the mortality rate was 15.3%, and NLR levels >6.66 could be a strong indicator of mortality if myocardial damage is also present.[14] In our study, D-dimer levels were an important prognostic and clinical severity indicator in patients with Covid-19. However, many factors or diseases affect D-dimer levels, and the clinician should be kept in mind for the follow-up of patients with Covid-19.

In a prospective study of 61 patients by Liu et al., it was shown that NLR levels >3.13 were an independent factor in predicting critical illness, with a sensitivity of 87.5% and a specificity of 71.7%.[6] In our retrospective study, which we conducted with a more significant number of patients compared to this study, we found that high NLR levels were a determining parameter in the follow-up of patients (Table 3). In a prospective cohort study by Zeng et al. with 352 hospitalized and followed-up patients, NLR levels were reported to indicate clinical worsening.[15] In our study, blood parameters taken at the time of application were evaluated following the emergency service practice, but results similar to those of Zeng et al.'s study on NLR were obtained. In a compilation of 32 studies by Alkhatip et al., more than 7500 patients were evaluated. It was stated that the NLR level was higher in those with high disease severity among Covid-19 patients.[16] In light of all these data, NLR levels are a useful parameter in determining critically ill patients, regardless of study design and the number of patients.

The uncertainty of the initial phase of the Covid-19 disease and the information supported by the studies have directed clinicians to study D-dimer examination from patients even in the early stages of the pandemic. As a matter of fact, in the study of Santotoribio et al., it was reported that D-dimer levels are a valuable parameter even at the diagnosis stage in Covid-19 patients.[17] In our study, D-dimer levels were evaluated in terms of the prognosis and clinical severity of the disease, and we found that D-dimer levels were higher in patients with mortality than those who did not (Table 2). It can be thought that age and comorbidity also contributed to the higher D -dimer in the mortality group. This situation can be considered as a limitation of the study. Besides we found that D-dimer levels had 81.6% sensitivity and 73.9% specificity for values >0.57. In addition, we found that D-dimer elevation was determinant in the clinical follow-up of the disease (discharge, service admission, and admission to the intensive care unit) (Table 3). In a study by Emin et al., it was reported that D-dimer levels increased as the disease severity increased.[18] In a study of 248 patients by Yao et al., it was reported that high D-dimer levels were an indicator of mortality.[19] Although our study supports all these literature data, it should be kept in mind that there may be variability in various hemostasis parameters, including D-dimer, prothrombin time, and thrombocytopenia, due to the presence of both hyperinflammation and coagulopathy in Covid-19 disease.[20,21] In our study, D-dimer levels were found to be an important prognostic and clinical severity indicator in patients with Covid-19. However, we think that many factors or diseases affect D-dimer

levels, and the clinician should be kept in mind for the follow-up of patients with Covid-19.

Among the indicators of the inflammatory response, MPV is a strong candidate, and many studies have evaluated the relationship between inflammation and MPV.[22] Therefore, in our study, we evaluated the clinical significance of MPV in patients with Covid-19. Our study found that MPV levels were higher in the mortality group than in the non-developing group (p=0.035). However, MPV levels are not a valuable parameter for the clinical follow-up of the disease (Table 3). A study by Aydınyılmaz et al. reported that MPV levels of >10.45 were an indicator of mortality.[23] In our study, MPV >8.45 fl had a sensitivity of 68.4% and a specificity of 53.9% for mortality.

In conclusion, the high NLR, D-dimer, and MPV levels obtained at the time of admission in Covid-19 patients can be used as an indicator of mortality. Elevated NLR and D-dimer levels are useful in determining the severity of the disease and clinical follow-up.

Ethics Committee Approval: Our study was approved by the University of Health Science Samsun Education and Research Hospital Ethics Committee (Date: 13.01.2021, decision no: 2021/1/19). The study was carried out following the international declaration, guidelines, and the study was conducted following the international declaration, guidelines.

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

Author Contributions: Concept-HK, MY; Supervision-HK, MY, MG, MY; Materials-HK, EÖ, MY, MG; Data Collection and/or Processing-HK, HO, MFA; Analysis and/or Interpretation-MY, MG, MY, NÖY; Writing-HK, MY, NÖY.

Peer-review: Externally peer-reviewed.

Other Information: Congress presentation: The University of Health Science 1st International Emergency Medicine Congress (28-31 October Bodrum, Türkiye). This article has been produced from a specialization thesis

REFERENCES

1. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modeling study. Lancet. 2020;395(10225):689-697. doi:10.1016/S0140-6736(20)30260-9
2. Deng SQ, Peng HJ. Characteristics of and Public Health Responses to the Coronavirus Disease 2019 Outbreak in China. J Clin Med. 2020;9 (2):575. doi:10.3390/jcm9020575
3. WHO. Coronavirus disease (COVID-2019) situation reports. Situation report–51. 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200311-sitrep-51-Covid-19 .pdf?sfvrsn=1ba62e57_10. Accessed March 11, 2020.
4. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054-1062. doi:10.1016/S0140-6736(20)30566-3
5. Yoon NB, Son C, Um SJ. Role of the neutrophil-lymphocyte count ratio in the differential diagnosis between pulmonary tuberculosis and bacterial community-acquired pneumonia. Ann Lab Med. 2013;33(2):105-110. doi:10.3343/alm.2013.33.2.105
6. Liu J, Liu Y, Xiang P, et al.Neutrophil-to-lymphocyte ratio predicts critical illness patients with 2019 coronavirus disease in the early stage. J Transl Med. 2020 May 20;18(1):206. doi:10.1186/s12967-020-02374-0
7. Gorjipour F, Totonchi Z, Gholampour Dehaki M, et al. Serum levels of interleukin-6, interleukin-8, interleukin-10, and tumor necrosis factor-α, renal function biochemical parameters and clinical outcomes in pediatric cardiopulmonary bypass surgery. Perfusion. 2019;34(8):651-659. doi:10.1177/0267659119842470
8. Inoue Arita Y, Akutsu K, Yamamoto T, et al. A fever in acute aortic dissection is caused by endogenous mediators that influence the extrinsic coagulation pathway and do not elevate procalcitonin. Intern Med. 2016;55(14):1845-1852. doi:10.2169/internalmedicine.55.5924
9. Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Mil Med Res. 2020;7 (1):4. doi:10.1186/s40779-020-0233-6
10. Ciaccio M, Agnello L. Biochemical biomarkers alterations in Coronavirus Disease 2019 (COVID -19). Diagnosis (Berl). 2020;7(4):365-372. doi:10.1515/dx-2020-0057
11. Henry BM, De Oliveira MHS, Benoit S, et al. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med. 2020;58(7):1021–1028. doi:10.1515/cclm-2020-0369
12. Ponti G, Maccaferri M, Ruini C, et al. Biomarkers associated with COVID-19 disease progression. Crit Rev Clin Lab Sci. 2020;57(6):389-399. doi:10.1080/10408363.2020.1770685
13. Huang C, Wang Y, Li X and et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15;395 (10223):497-506. doi:10.1016/S0140-6736(20)

30183-5
14. Chen FF, Zhong M, Liu Y, et al. The characteristics and outcomes of 681 severe cases with COVID-19 in China. J Crit Care. 2020;60:32-37. doi:10.1016/j.jcrc.2020.07.003
15. Zeng ZY, Feng SD, Chen GP, Wu JN. Predictive value of the neutrophil to lymphocyte ratio for disease deterioration and serious adverse outcomes in patients with COVID-19: a prospective cohort study. BMC Infect Dis. 2021;21(1):80. doi:10.1186/s12879-021-05796-3
16. Alkhatip AAAMM, Kamel MG, Hamza MK, et al. The diagnostic and prognostic role of neutrophil-to-lymphocyte ratio in COVID-19: a systematic review and meta-analysis. Expert Rev Mol Diagn. 2021;21(5):505-514. doi:10.1080/14737159.2021.1915773
17. Santotoribio JD, Nuñez-Jurado D, Lepe-Balsalobre E. Evaluation of routine blood tests for diagnosis of suspected coronavirus disease 2019. Clin Lab. 2020;66(9). doi:10.7754/Clin.Lab.2020.200522
18. Düz ME, Balcı A, Menekşe E. D-dimer levels and COVİD-19 severity: systematic review and meta-analysis. Tuberk Toraks. 2020;68(4):353-360. doi:10.5578/tt.70351
19. Yao Y, Cao J, Wang Q, et al. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. J Intensive Care. 2020;8:49. doi:10.1186/s40560-020-00466-z
20. Miesbach W, Makris M. COVID-19: coagulopathy, risk of thrombosis, and the rationale for anticoagulation. Clin Appl Thromb Hemost. 2020; 26: 1076029620938149. doi:10.1177/1076029620938149
21. Thachil J, Srivastava A. SARS-2 coronavirus associated hemostatic lung abnormality in COVID-19: is it pulmonary thrombosis or pulmonary embolism?. Semin Thromb Hemost. 2020; 46: 777-780. doi:10.1055/s-0040-1712155
22. Aktas A, Sener K, Yılmaz N, Tunc M, Yolcu S. Is mean platelet volume useful for predicting the prognosis of COVID-19 diagnosed patients?. IJSR. 2020;5(7):8-11.
23. Aydınyılmaz F, Aksakal E, Pamukcu HE, et al. Significance of MPV, RDW and PDW with the severity and mortality of COVID-19 and effects of acetylsalicylic acid use. Clin Appl Thromb Hemost. 2021;27:10760296211048808. doi:10.1177/10760296211048808