# **Research Article**,

# Neutrophil Lymphocyte Rate: A Marker of Mortality and Prognosis for Covid-19?

Selda Tekin<sup>1</sup>, Erman Şen<sup>2</sup>, Esra Adıyeke<sup>3</sup>, Nilüfer Coşkun<sup>4</sup>, Özgün Topçuoğlu Sarı<sup>5</sup>, Nurten Bakan<sup>6</sup>

Sancaktepe Martyr Prof.dr. İlhan Varank Training and Research Hospital Email Address: esasaladiyeke@gmail.com

#### **Summary:**

**Objective:** In recent years, the neutrophil-to-lymphocyte ratio (NLR) has become a parameter sought in the prediction of aggressive prognosis or mortality in many studies including sepsis, infectious diseases, and malignancies. There are publications studying the correlation between the high values of this parameter, which can be interpreted as an indirect indicator of the host's immune response, in the COVID-19 infection with mortality. The primary objective of our study is to evaluate the correlation between the height of NLR values in the patients followed up in our intensive care units (ICU) with the final diagnosis of COVID-19 infection (PCR(+)), the continuation of such high values throughout the treatment and mortality, and finally obtain a cut-off value in predicting the prognosis.

**Method:** The case files with final diagnosis of COVID-19 infection followed up and treated in our 3rd Level Intensive Care Unit from 21 March 2020 to 1 July 2020 were screened retrospectively and included in the study. These cases were examined in two groups: exitus (n=113) and survivors (n=70). The demographics of the cases such as age, gender, comorbid diseases as well as their vital signs and clinical and laboratory features were screened from the Hospital Operating System (HOS) and archive files, and recorded. The correlation among the data obtained as well as the correlation between such data and mortality were analyzed.

**Findings:** In the study conducted on 183 cases, the ages, APACHE II scores, admission NLR values, study endpoint NLR values, neutrophil, procalcitonin, D-dimer, PT and INR levels, and MV (Mechanical Ventilation) durations of the exitus cases were found statistically significantly higher than the survivor cases. In the exitus cases, the cut-off point found for the admission NLR was >7.82. During the course of treatment, the patients with high NLR level had poor prognosis. The patients' NLR values at the study endpoint were analyzed. The conclusion is that >6 as the cut-off point value is significant from the viewpoint of mortality. In addition, it was observed that a NLR level over 6 despite the treatment increased the mortality rate by 15.6 times.

**Conclusion:** We have found out that old age, long MV duration, prolonged high levels of D-dimer, neutrophil, PT, INR and NLR levels increase the mortality rate. Being able to predict the course of prognosis and using early warning systems will increase the survival rate. In this regards, we consider closer monitoring of the patients with high NLR level, particularly in the intensive care units even if they do not have respiratory distress, will decrease mortality significantly. NLR can help identifying the COVID-19 patients with high risk level. High NLR level during the intensive care monitoring process may be regarded as insufficient immune response, and thus correlated with mortality and aggressive prognosis.

#### Keywords: COVID-19, NLR, mortality

#### **Introduction:**

On December 31, 2019, China Country Office of the World Health Organization (WHO) reported pneumonia cases of unknown etiology in Wuhan city in China's Hubei province. On January 7, 2020, the causative agent was identified as a new coronavirus "2019-nCoV". Later, the virus was named as "SARS-CoV-2" and the disease it has caused as "COVID-19". Transmitted from human to human via respiratory droplets, the infection has spread over the world before long, and was declared pandemic by the WHO (World Health Organization).(1) The disease may have an asymptomatic course, but it may also follow a wide range of clinical courses ranging from light upper respiratory tract infection progressing with the symptoms like fatigue, fever, joint pain, diminished taste and smell perception to acute pneumonia that causes respiratory failure, sepsis, septic shock, multiple organ dysfunction, and death. One-sided or two-sided ground-glass opacity (GGO) shows up on the pulmonary CT scans of the patients with lung involvement frequently; and prevalent involvement indicates poor prognosis.(2) The studies on COVID-19 have examined, and continue to examine, numerous parameters like old age, existence of the systemic diseases like comorbid chronic obstructive pulmonary disease, hypertension, cardiac disease, the high NLR and D-dimer levels and low albumin levels as potential mortality predictors.(3) In recent years, the neutrophil-tolymphocyte ratio (NLR) has become a parameter sought in the prediction of aggressive prognosis or mortality in many studies including sepsis, infectious diseases, and malignancies. There are publications indicating that this parameter, which can be interpreted as an indirect indicator of the host's immune response, has increased in the COVID-19 infection as well.(4) At this point, a parameter that ensures early prediction of mortality will allow the patients to be taken into intensive care earlier, followed up closely, and thus increase the survival. The primary objective of our study is to evaluate the correlation between the high NLR values and mortality in the patients followed up in our intensive care units with the final diagnosis of COVID-19 infection and, differently from the other studies, obtain a cut-off value in predicting the prognosis. Our secondary objective is to determine the other independent risk factors affecting the mortality rates of the patients followed up in the intensive care units.

# Method and material:

In the study planned as a retrospective clinical study and approved by the local ethics committee, the patients with the final diagnosis of COVID-19 infection (PCR(+)) followed up and treated in 3rd level intensive care units of Martyr Prof. Dr. Ilhan Varank E.A.H and additional service building Cekmekov D. H. between the dates of 21 March were 2020 and 1 July 2020 screened retrospectively and included in the study. The demographics of the cases such as age, gender, comorbid diseases as well as their vital signs

(fever, oxygen saturation, pulse, blood pressure, respiration rate per minute) and clinical and laboratory features were screened from the Hospital Operating System (HOS) and archive files, and recorded in the hospital. The correlation among the data obtained as well as the correlation between such data and mortality were analyzed.

Totally 183 patients' data were screened. The ICU patients over 18 years of age diagnosed to have COVID-19 definitively with PCR test were included in the study. These cases were examined in two groups: exitus (n=113) and survivors (n=70).

In addition to the COVID-19 PCR, Hemogram (WBC, neutrophil level, lymphocyte level, NLR), CRP, procalcitonin, D-dimer, LDH, ferritin, fibrinogen, creatinine kinase, PT, APTT, and INR levels, the age, gender, comorbid diseases, APACHE II, duration of ICU, and the need for and duration of mechanical ventilation were recorded. For the patients who met the potential COVID-19 case definition, the COVID-19 PCR tests on the respiratory tract samples were made in the General Directorate of Public Health (GDPH) Microbiology Reference Laboratory, while the other tests were made in the Central Microbiology and Biochemistry Laboratories of the hospitals.

During evaluation of the findings of the study, IBM SPSS Statistics 22 (IBM SPSS, Turkey) program was used for the statistical analyses. During evaluation of the study data, the Kolmogorov-Smirnov and Shapiro Wilks tests were used to assess the compliance of the parameters with normal distribution. During evaluation of the study data, the Mann Whitney U test was used to compare quantitative data in addition to the descriptive statistical methods (mean, standard deviation, frequency). The Chi-Square test was used to compare qualitative data. The optimum cut-off point was selected on the basis of the ROC curve analysis. The logistic analysis was used for the multivariate analysis. The significance level was assessed as p < 0.05.

# Findings:

The study was conducted on 183 cases in total, i.e. 112 males (61.2%) and 71 females (38.8%), between the ages of 20 and 96 ( $64.93\pm17.60$ , median=69). The duration of ICU was ranging from 1 to 123 days ( $15.04\pm16.61$ , median=10). Of the cases, 54.6% were above 65 years of age. The duration of MV was ranging from 0 to 123 days ( $8.26\pm15.30$ , median=2). The APACHE II score was ranging between 10 and 90 ( $41.38\pm12.51$ ,

median=40). Of the cases, 61.7% were exitus (n=113), 37.2% discharged (n=70), and 1.1% referred to other hospitals (due to the need for ECMO). Of the cases, 32.8% had no comorbid

disease at all in comparison with one for 24.6% and two or more for 42.6%. The demographics of the cases are given in Table 1.

#### **Table 1: Demographics table**

	Min-Max	Mean±SD (median)	
Age	20-96	64.93±17.60 (69)	
Duration of ICU (day)	1-123	15.04±16.61 (10)	
Duration of MV (day)	0-123	8.26±15.30 (2)	
APACHE II	10-90	41.38±12.51 (40)	
	n	% p	
Gender			
Male	112	61.2 <sup>1</sup> 0.793	
Female	71	38.8	
Age			
≤65	83	45.4 <sup>1</sup> 0.000*	
>65	100	54.6	
Result			
Exitus	113	61.7	
Discharged	68	37.2	
Referral	2	1.1	
Comorbid diseases			
None	60	32.8	
1	45	24.6	
2 and more	78	42.6	

Of the male cases, 62.5% were exitus in comparison with 60.6% of the female cases, indicating no statistically significant difference (p>0.05).

The exitus percentage for the cases over 65 years of age (75%) was statistically significantly higher (p<0.05) than the exitus percentage for the cases at and under 65 years of age (45.8%) (Figure 1).

In contrast to nonexistence of significant difference between the exitus cases and the surviving cases in terms of comorbid disease and duration of ICU (p>0.05), the duration of MV and the APACHE II scores were significantly higher for the exitus cases (p<0.05) (Table 2)(Figure 2).





#### Table 2: Evaluation of demographics by mortality

		Mortality			
		Survivor	Exitus	Total	
		n (%)	n (%)	n (%)	р
Gender	Male	42 (37.5%)	70 (62.5%)	112 (61.2%)	<sup>1</sup> 0.793
	Female	28 (39.4%)	43 (60.6%)	71 (38.8%)	
Age	≤65	45 (54.2%)	38 (45.8%)	83 (45.4%)	10.000*
	>65	25 (25%)	75 (75%)	100 (54.6%)	
Comorbid	None	29 (48.3%)	31 (51.7%)	60 (32.8%)	<sup>1</sup> 0.136
diseases					
	1	16 (35.6%)	29 (64.4%)	45 (24.6%)	
	2 and more	25 (32.1%)	53 (67.9%)	78 (42.6%)	
Duration of ICU (day) Mean±SD		15.68±14.14 (12)	14.65±18.02 (9)	15.04±16.61 (10)	<sup>2</sup> 0.099
(median)					
Duration of MV (day) Mean±SD		3.43±7.87 (0)	11.25±17.86 (6)	8.26±15.30 (2)	$^{2}0.000*$
(median)					
APACHE II Mean±SD (median)		38.5±11.70 (40)	43.17±12.71 (44)	41.38±12.51 (40)	<sup>2</sup> 0.013*



Figure 2: Chart of MV duration and APACHE II score by mortality (p<0.05)

The admission and study endpoint NLR levels of the exitus cases were statistically significantly higher than the same of the surviving cases (p<0.05) (Table 3) (Figure 3). There was no statistically significant difference regarding the admission WBC and CRP levels by mortality (p>0.05) (Table 3).

The admission procalcitonin levels of the exitus cases were statistically significantly higher than the same of the surviving cases (p<0.05) (Table 3) (Figure 4).

	Mortality			
	Survivor	Exitus	Total	р
	Mean±SD (median)	Mean±SD (median)	Mean±SD (median)	
NLR admission	11.43±12.73 (7.3)	13.93±10.79 (11.7)	12.98±11.6 (10.1)	0.010*
NLR endpoint	4.92±4.31 (3.7)	14.83±11.65 (11.9)	10.77±10.55 (7.2)	0.000*
WBC	12.49±10.2 (10.3)	12.43±5.9 (11.2)	12.45±7.8 (11)	0.305
CRP	12.58±8.3 (13)	12.15±7.9 (11.8)	12.31±8.04 (12.6)	0.852
Proc	3.05±12.25 (0.2)	5.18±21.5 (0.4)	4.37±18.5 (0.3)	0.001*

Mann Whitney U Test \*p < 0.05; when surviving and exitus cases compared



Figure 3: Chart of admission and endpoint NLR levels by mortality (p<0.05)



Figure 5: ROC curve for admission NLR

# Determination of cut-off point for admission NLR

In the exitus cases, the ROC curve was drawn for the admission NLR level. The field under the curve was 0.614, with a standard deviation of 0.05. The field under the ROC curve was significantly higher than 0.5 (p:0.011; p<0.05). In the exitus cases, the cut-off point found for the admission NLR was >7.82. The sensitivity of this value was 66.7%, while its specificity was 55.9%, positive predictive value was 71.2%, and negative predictive value was 50.7% (Figure 5).

#### Determination of cut-off point for study endpoint NLR

The ROC curve was drawn for the NLR value at the study endpoint. The field under the curve was 0.825, with a standard deviation of 0.03. The field under the ROC curve was significantly higher than 0.5 (p:0.001; p<0.05). The cut-off point found for the endpoint NLR value was >6. The sensitivity of this value was 78.7%, while its specificity was 80%, positive predictive value was 85.1%, and negative predictive value was 72.2% (Figure 6).





Figure 6: ROC curve for endpoint NLR

When the admission NLR values of the cases were compared relative to the cut-off value (>7.82), there was no significant difference (p>0.05) in terms of gender, age, comorbid disease, duration of ICU, and APACHE II score. The admission NLR level was higher than 7.82 for 62.4% of the male cases and 51.5% of the female cases. The admission NLR level was higher than 7.82 for 51.9% of the cases at and under 65 years of age and 63% of the cases over 65 years of age. The only significant difference was in the MV durations. The MV durations of the cases whose admission NLR levels were over 7.82 were statistically significantly longer than the MV durations of the cases whose admission NLR levels were below 7.82 (p < 0.05) (Table 4).

The admission neutrophil, D-dimer, PT, and INR levels of the exitus cases were statistically significantly higher than the same of the surviving cases (p<0.05). There was no significant difference between the admission lymphocyte, LDH, ferritin, fibrinogen, CK, and APTT levels of the two groups of cases by mortality (p>0.05) (Table 5).

		Admission NLR		
		<7.82	>7.82	
		n (%)	n (%)	р
Gender	Male	41 (37.6%)	68 (62.4%)	<sup>1</sup> 0.147
	Female	34 (48.6%)	36 (51.4%)	
Age	≤65	38 (48.1%)	41 (51.9%)	<sup>1</sup> 0.135
	>65	37 (37.0%)	63 (63.0%)	
Comorbid diseases	None	31 (53.4%)	27 (46.6%)	<sup>1</sup> 0.063
	1	18 (41.9%)	25 (58.1%)	
	2 and more	26 (33.3%)	52 (66.7%)	
Duration of ICU (day) Mean±SD (median)		13.64±16.25 (9)	16.21±17.09 (11)	<sup>2</sup> 0.159
Duration of MV (day) <sub>Mean±SD (median)</sub>		5.07±11.42 (1)	10.74±17.47 (4)	$^{2}0.000*$
APACHE II Mean±SD (median)		40.48±13.79 (40)	42.18±11.55 (42)	<sup>2</sup> 0.284
<sup>1</sup> Chi-Square Test		<sup>2</sup> Mann Whitney U Test	*	<i>v</i> <0.05

#### Table 4: Evaluation of demographics by admission NLR level

 Table 5: Evaluation of laboratory findings by mortality

	Mortality			
	Survivor	Exitus	Total	р
	Mean±SD (median)	Mean±SD (median)	Mean±SD (median)	
Neutrophil	9.82±9.66 (8.2)	10.69±5.67 (9.8)	10.36±7.44 (9)	0.046*
Lymphocytes	1.87±3.12 (0.9)	1.25±1.59 (0.8)	1.48±2.31 (0.8)	0.065
D-Dimer	2.99±3.54 (1.8)	7.63±19.86 (3.7)	5.83±15.82 (2.8)	0.000*
LDH	529.93±682.32 (391)	528.83±514.13 (391)	529.25±582.61 (391)	0.558
Ferritin	791.61±904.54 (481.1)	1135.91±1303.92 (704)	986.07±1155.23 (536)	0.216
Fibrin	626.52±223.36 (609)	592.86±233.94 (609.5)	606.03±229.74 (609)	0.438
СК	849.74±3268.51 (130)	263.33±540.99 (109.5)	497.17±2116.3 (121)	0.054
РТ	14.99±2.15 (14.6)	19.28±14.56 (16)	17.58±11.57 (15.4)	0.000*
APTT	28.4±5.08 (27.9)	28.61±6.57 (27.6)	28.53±6.02 (27.6)	0.887
INR	1.12±0.16 (1.1)	1.45±1.19 (1.2)	1.32±0.94 (1.2)	0.000*

Mann Whitney U \*p<0.05

When we evaluated the effects of the parameters affecting mortality significantly such as age, duration of MV, APACHE II score, NLR admission, NLR endpoint, procalcitonin, neutrophil, D-dimer, PT, and INR by backward stepwise logistic regression analysis, we saw that the model was significant (p:0.001; p<0.05), the Nagelkerke R-square value was 0.640, and the exploratory factor of the model was at good level (83.7%). The effects of the parameters of age, duration of MV, NLR endpoint, D-dimer, and PT on the model were found statistically significant (p<0.05). It was seen that the age over 65 increased mortality by 4.3 times, the duration of MV by 1.1 times, the endpoint NLR level over 6 by 15.6 times, the D-dimer level by 1.1 times, and the PT level by 1.3 times. The effect of the neutrophil level on the model was not statistically significant (p>0.05).(Table 6)

		95% C.I.for OR		
Step 5a	OR	Lower	Upper	р
Age (>65)	4.3	1.502	12.197	0.007*
Duration of MV	1.1	1.048	1.184	0.001*
NLR endpoint (>6)	15.6	5.41	44.916	0.000*
Neutrophil	0.9	0.823	1.003	0.059
D-Dimer	1.1	1.012	1.296	0.031*
РТ	1.3	1.001	1.604	0.049*

 Table 6: Evaluation of parameters affecting mortality significantly by logistic regression analysis

\*Variable(s) entered on step 1: Age, MV, APACHE II, NLR admission, NLR endpoint, Proc, Neutrophil, D-Dimer, PT, INR.

#### **Discussion:**

The simplest and the most effective strategy against the COVID-19 pandemic that has become a serious health problem for the whole world, and for which a definitive treatment is yet to be found, is early detection, early diagnosis, early isolation and early treatment. The primary objective of the clinicians working on this matter all over the world is to decrease and prevent the mortality.(5) Likewise, the primary objective of our study is to reveal the independent mortality markers affecting the mortality, take the necessary measures accordingly, and finalize the principles of definitive treatment to that end. In consequence of our study, we have not only found out that NLR is an important marker in predicting mortality but also determined the cut-off value, which is the outcome that separates our study from the others. Besides, we have also found out that the old age, procalcitonin, neutrophil, PT, D-dimer, and INR could be used as early markers in the prediction of mortality, and that the old age, the duration of MV, high NLR level despite the supportive treatment, PT, and D-dimer level all have positive effects on mortality. Recently, it has been proven that the NLR level is a useful marker providing guidance on numerous diseases and their prognosis. It is a biomarker detected to be rising in numerous diseases like tumoral diseases. autoimmune diseases, bacterial pneumonia, sepsis, peptic ulcer. It has been exhibited that NLR is superior to certain other inflammation-based scores in predicting mortality of pneumonia patients. (6,7,8,9) High NLR level indicates low lymphocyte count accompanied by increased neutrophil count. While the increase in neutrophil count is due to inflammation, the decrease in lymphocyte count may be due to immune-induced destruction, apoptosis, lymphocyte or sequestration in the lung. In the COVID-19

infection, the neutrophil count increasing in the complete blood count due to severe inflammation is conspicuous. As lymphopenia deepens, it can be predicted that the immune response to infection is insufficient. Therefore, this rate also gives an idea to clinicians about the severity of the disease. In the study conducted by Ai-Ping Yang et al. on 93 patients, 24 of whom had a severe course, it was concluded that the progress of infection was severe in patients with NLR value > 3.3, aged 49.5 and over, and NLR was an independent risk disease in COVID-19 factor for severe patients.(10) In another study conducted on 102 patients, it was concluded that the NLR value was higher in the inpatients.(11) The study conducted by Yuwei Liu et al. concluded that high NLR level was a predictor of in-hospital mortality(12), while the meta-analysis conducted by Xudong et al., which included 4911 patients in a total of 29 studies, showed that high NLR levels were proportional to the increase in disease severity, and concluded that the NLR level could be an mortality in COVID-19 early marker of patients.(13) In our own study, we concluded that the admission and endpoint NLR levels of the exitus cases were significantly higher than the same of the surviving cases (p<0.05). In our study, we drew the ROC curves of the admission and endpoint NLR levels for both groups, and the field below the curve was significantly higher than 0.5 for both groups. The cut-off point found for the admission NLR was >7.82; and the cut-off point found for the endpoint NLR was >6. When we evaluated our findings with the logistic regression analysis, we found that the model was significant, and having an endpoint NLR value above 6 increased mortality by 15.6 times. We concluded that the NLR level that does not drop despite supportive treatment as well as the high NLR level at the time of diagnosis is correlated with mortality. In addition to NLR, another indicator of severe inflammation is the procalcitonin level, which is basically secreted from the parafollicular C cells of the thyroid tissue, but also known to be secreted from the non-thyroid tissues in case of bacteremia, sepsis. The studies conducted with COVID-19 patients revealed an increase in the procalcitonin levels, which was correlated with the severity of the disease.(14) In our study, as a positive acute phase reactant, the procalcitonin level was significantly higher in the exitus patients than the surviving patients. We think that the secondary bacterial infections entering the picture frequently during the COVID-19 infection suppressing the immunity severely are responsible for this situation and contributing to the poor prognosis. We did not find a significant difference in the CRP and WBC levels we monitored together with procalcitonin during the infection follow-up between the two groups in terms of mortality. Other than inflammation. the hematological system pathology is another factor that causes mortality in COVID-19 infection. The pathophysiology of hematological system changes, which can be seen on a wide scale from thrombosis disseminated to intravascular coagulation (DIC), is not yet clearly understood. However, it is clear that they cause multiple organ dysfunction, even death. The risk of thrombosis increases due to endothelial damage, activation of the coagulation system, and intravascular fibrin storage. Arterial and venous thrombosis can be seen during the disease. While arterial thrombosis often causes cerebral and myocardial infarctions, we encounter the venous thrombosis as deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE).(15) At this point, the increased D-dimer levels resulting from the breakdown of stabilized fibrin polymers in the blood by plasmin emerge as an important biomarker for diagnosing thrombosis. Since thromboembolism poses a severe risk for mortality, the high level of D-dimer in this patient group can also be used as an early mortality marker. The standard or prolonged levels of PT and aPTT, which are effective mediators in the coagulation cascade, increase or decrease in thrombocyte count, and increase or decrease in fibrinogen levels are frequently used laboratory parameters in mortality studies.(16) Ning Tang et al. monitored the PT, aPTT, fibrinogen and Ddimer levels in a retrospective study of 183 patients followed up with coronavirus pneumonia,

and found a significant increase in the D-dimer and fibrinogen levels as well as prolonged PT levels in the exitus patients.(17)

Zhang L. et al. concluded in their study conducted on 313 patients that the D-dimer level was correlated with the hospital mortality, and that a level above 2.0 mcg/ml could be used as a mortality marker with 92.3% sensitivity and 83.3% specificity rates.(18) In our study, the Ddimer in the exitus group was 7.63±19.86.

Another clinical course of hematological system pathologies is the DIC. DIC is a systemic event with thrombosis and bleeding. It causes ischemic tissue damage and severe bleeding due to diffuse intravascular coagulation and microangiopathic hemolytic anemia. In this mortal table, the increase in the D-dimer level is important as a diagnostic biomarker. Besides, fibrinogen decrease, high INR, PT prolongation, and thrombocytopenia are potential pathological laboratory results.(19)

In the autopsy series, both hematological profiles appeared in the patients who became exitus due to COVID-19 (thrombosis & DIC).(20) Therefore, we believe that monitoring patients' hematological parameters closely and making the necessary treatment changes accordingly without loss of time will decrease mortality. In our study, we concluded that the D-dimer and INR levels were significantly higher, and the PT levels were longer in the exitus patients compared to survivors. In this regard, we believe that routine studies of Ddimer, fibrinogen, coagulation tests in COVID-19 patients, appropriate and early initiation of anticoagulant therapy, close laboratory follow-up, and changing the treatment as per the analyses without delay will have a positive effect on survival. Another issue that should be kept in mind is that immobility will increase the risk of mortality in terms of complications such as stroke and embolism due to stasis during the period of hospitalization or intensive care of severe cases.

COVID-19 is an RNA virus infection that is transmitted from human to human rapidly, but has a relatively low mortality rate. Although it is observed rarely, the disease shows generally an asymptomatic prognosis in the children. It shows poor progression in the presence of comorbid diseases that are often severe in the elderly group of adults. As for clinical findings, in addition to the other non-specific viral infection symptoms like fever, cough, muscle pain, headache, nasal flow, nausea, and diarrhea, it may emerge with respiratory system involvement like pneumonia, pulmonary edema, ARDS, or multiple organ dysfunction, and even cause death in severe cases.(21, 22) In our study, in accordance with the literature, the median age of the patients we followed up in the intensive care unit was 69, and the rate of death was higher in patients over 65 compared to survival. As predicted, we found that the APACHE II scores were significantly higher in the exitus patients than the surviving patients. We did not see any statistically significant difference between comorbidities and mortality rates of the patients with DM, HT, COPD as comorbid diseases.

# **Conclusion:**

Since the beginning of the COVID-19 pandemic, immunological, hematological, inflammatory markers have been studied and continue to be studied to guide the diagnosis of infection, provide optimum treatment, and evaluate the response to treatment. In our study, we concluded that a high NLR value during admission to intensive care and not decreasing of this level during the course of treatment predicted poor prognosis and mortality. We think that this which is low-cost parameter. and easilv accessible, must be studied in COVID-19 patients from an early stage, and the ones with high levels of this parameter must be hospitalized, followed up closely, and treated.

# **Conflict of interest and funding:**

The authors received no funding for this study and report no conflicts of interest.

# **References:**

- [1] World Health Organization. Novel Corona virus situation report-1 (Date accessed: May 16, 2020) https://www.who.int/docs/defaultsource/cor onaviruse/situation reports/20200121-sitrep-1-2019-ncov.pdf.
- [2] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054–62.
- [3] Lian J, Jin C, Hao S, Zhang X, Yang M, Jin X, Lu Y, Hu J, Zhang S, Zheng L, et al. High neutrophil-to-lymphocyte ratio associated with progression to critical illness

in older patients with COVID-19: a multicenter retrospective study. Aging (Albany NY). 2020;12(14):13849–59.

- [4] Fu J, Kong J, Wang W, Wu M, Yao L, Wang Z, Jin J, Wu D, Yu X. 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.
- [5] Wang FS, Zhang C. What to do next to control the 2019-nCoV epidemic? Lancet. 2020 Feb 8;395(10222):391-393. doi: 10.1016/S0140-6736(20)30300-7. PMID: 32035533; PMCID: PMC7138017.
- [6] Yuichiro, Shimoyama, Osamu, et al., The neutrophil to lymphocyte ratio is superior to other inflammation-based prognostic scores in predicting the mortality of patients with pneumonia, Acta Med. Okayama (2018).
- [7] A.U. Uslu, A. Küçük, A. Şahin, Y. Ugan, R. Yılmaz, T. Güngör, et al., Two new inflammatory markers associated with Disease Activity Score-28 in patients with rheumatoid arthritis: neutrophil-lymphocyte ratio and platelet-lymphocyte ratio, Int. J. Rheum. Dis. (2015) n/a–n/a.
- [8] H.Q. Ying, Q.W. Deng, B.S. He, et al., The prognostic value of preoperative NLR, dNLR, PLR and LMR for predicting clinical outcome in surgical colorectal cancer patients, Med. Oncol. 31 (12) (2014) 305.
- [9] Adıyeke E, Adıyeke L. Neutrophil to lymphocyte ratio and mean platelet volume may predict the development of the pressure ulcers. J Surg Med. 2020; 4(7): 578-581.
- [10] 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 Jul;84:106504. doi: 10.1016/j.intimp.2020.106504. Epub 2020 Apr 13. PMID: 32304994; PMCID: PMC7152924.
- [11] Samir Allahverdiyev, Alaa Quisi, Hazar Harbalıoğlu, Gökhan Alıcı, Ömer Genç, Abdullah Yıldırım, İbrahim Halil Kurt. 2020. The Neutrophil to Lymphocyte Ratio and In-Hospital All-Cause Mortality in Patients with COVID-19. European Journal of Therapeutics

- [12] Liu Y, Du X, Chen J, et al. Neutrophil-tolymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. J infect 2020;81:6-12. https://doi.org/10,1016/jinf.2020.04.002
- [13] Feng X, Li S, Sun Q, Zhu J, Chen B, Xiong M. Immune-Inflammatory Cao G. Parameters in COVID-19 Cases: A Systematic Review and Meta-Analysis. Front Med (Lausanne). 2020 Jun 9:7:301. doi: 10.3389/fmed.2020.00301. PMID: 32582743; PMCID: PMC7295898.
- [14] Hu R, Han C, Pei S, Yin M, Chen X. Procalcitonin levels in COVID-19 patients. Int J Antimicrob Agents. 2020 Aug;56(2):106051. doi: 10.1016/j.ijantimicag.2020.106051. Epub 2020 Jun 10. PMID: 32534186; PMCID: PMC7286278.
- [15] Asakura, H., Ogawa, H. COVID-19associated coagulopathy and disseminated intravascular coagulation. Int J Hematol 113, 45–57 (2021). https://doi.org/10.1007/s12185-020-03029-y
- [16] Panigada M, Bottino N, Tagliabue P, Grasselli G, Novembrino C, Chantarangkul V et al. Hypercoagulability of COVID-419 patients in intensive care unit: A report of thromboelastography finding and other parameters of hemostasis. J Thromb Haemost 2020;18:1738.
- [17] Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020 Apr;18(4):844-847. doi: 10.1111/jth.14768. Epub 2020 Mar 13. PMID: 32073213; PMCID: PMC7166509.
- [18] Zhang L, Yan X, Fan Q, Liu H, Liu X, Liu Z, Zhang Z. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost. 2020 Jun;18(6):1324-1329. doi: 10.1111/jth.14859. PMID: 32306492; PMCID: PMC7264730.
- [19] Jin X, Duan Y, Bao T, et al. The values of coagulation function in COVID-19 patients. PLoS One. 2020;15(10):e0241329. Published 2020 Oct 29. doi:10.1371/journal.pone.0241329.

- [20] Fox SE, Akmatbekov A, Harbert JL, Li G, Quincy Brown J, Vander Heide RS. Pulmonary and cardiac pathology in African American patients with COVID-19:an autopsy series from New Orleans. Lancet Respir Med.2020;8(7):681-6.
- [21] Q. Li, X. Guan, P. Wu, X. Wang, L. Zhou, Y. Tong, R. Ren, K.S.M. Leung, E.H.Y. Lau, J.Y. Wong, et al., Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia, N. Engl. J. Med. (2020) 10–1056.)
- [22] Y. Yin, R.G. Wunderink, MERS, SARS and other coronaviruses as causes of pneumonia, Respirology (Carlton, Vic.) 23 (2) (2018) 130–137.