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Evaluation of three common scoring systems in COVID-19 patients: neutrophil-lymphocyte ratio (NLR), The Acute Physiology and Chronic Health Evaluation II (APACHE II), and C-reactive protein (CRP)

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Background: As SARS-CoV-2 becomes a major global health, the authors aimed to predict the severity of the disease, the length of hospitalization, and the death rate of COVID-19 patients based on The Acute Physiology and Chronic Health Evaluation II (APACHE II) criteria, neutrophil-lymphocyte ratio (NLR), and C-reactive protein (CRP) levels to prioritize, and use them for special care facilities.
Methods: In a retrospective study, 369 patients with COVID-19 hospitalized in the ICU from March 2021 to April 2022, were evaluated. In addition to the APACHE II score, several of laboratory factors, such as CRP and NLR, were measured.
Results: The values of CRP, NLR, and APACHE II scores were significantly higher in hospitalized and intubated patients, as well as those who died 1 month and 3 months after hospital discharge than those in surviving patients. The baseline NLR levels were the strongest factor that adversely affected death in the hospital, death 1 month and 3 months after discharge, and it was able to predict death, significantly.
Conclusion: CRP, NLR, and APACHE II were all linked to prognostic factors in COVID-19 patients. NLR was a better predictor of disease severity, the need for intubation, and death than the other two scoring tools.

Keywords: APACHE II, COVID-19, CRP, NLR

Introduction

Critically ill patients with COVID-19 have a mortality rate that ranges from 11 to 61%[1], depending on the severity of the illness. Several factors can be considered predictive of the severity of the disease, such as old age, underlying diseases (e.g. diabetes, cardiovascular diseases, chronic kidney and vein diseases)[2], and laboratory parameters (e.g. the number of white blood cells[3] and D-dimer levels[4]).

There are some haematologic biomarkers for COVID-19 patient's severity identification including WBC count, lymphocyte count, neutrophil count, neutrophil-lymphocyte ratio (NLR), platelet count, eosinophil count, and haemoglobin. Also, helper T cells and suppressor T cells below normal levels are associated with the severity of COVID-19. On the other hand, biochemical biomarkers included total bilirubin and CK, together with serum ferritin, white blood cell (WBC) count, and IL-6 reported in non-survivors compared to survivors. The thrombo-embolism, myocardial injury, D-dimer, and cardiac markers (cardiac troponin

HIGHLIGHTS

- There is a significant relationship between mortality and complications due to COVID-19, based on C-reactive protein and neutrophil-lymphocyte ratio (NLR) prediction tools, and the Acute Physiology and Chronic Health Evaluation II scoring system.
- The NLR is useful tool for mapping disease severity and mortality outcomes from COVID-19 based on the results of the present study.
- Increased NLR is associated with a significantly higher admission to the ICU, higher mortality in the ICU, and a more frequent need for mechanical ventilation in the ICU.

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levels) are associated with COVID-19 severity, too. Additionally, inflammatory biomarkers included C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), granulocyte/lymphocyte ratio, IL-6, IL-2, IL-7, tumour necrosis factor (TNF)-a, interferon-c inducible protein (IP)-10, monocyte chemoattractant protein (MCP)-1, macrophage inflammatory protein (MIP) 1-a, granulocyte-colony stimulating factor (G-CSF), CRP, procalcitonin (PCT), and ferritin reported associated with the disease severity[5–7].

The Acute Physiology and Chronic Health Evaluation II (APACHE II) is a system of classification of disease severity in acute patients based on their age, past medical history, and some physiological measurements[8]. The use of the APACHE II system can facilitate the assessment of treatment, the prognosis of patients, and decision-making to allocate hospital resources efficiently[9].

The NLR is one of the biomarkers that can be used to evaluate the outcomes related to COVID-19 disease as well as determine the extent of inflammation in the patient[10]. Several conditions are being investigated using NLR as a biomarker, including tumours, pancreatitis, chronic obstructive pulmonary disease (COPD), cardiovascular disease, and infectious diseases. It has also been used to determine the prognosis of infectious diseases, such as influenza virus infection, and respiratory syndromes like COVID-19[11].

CRP also plays an important role in the prognosis of COVID-19 as well as its severity. It has been reported that the CRP can serve as an early indicator of the severity of infectious diseases, and could prioritize patients' transfer to the ICU and treatment monitoring of patients with COVID-19[12].

The objective of this study is to investigate the changes in the NLR, CRP, and APACHE II indexes during the COVID-19 and to predict the severity of the disease, the length of hospitalization, and the mortality status of patients suffering from COVID-19.

Materials and methods

In a retrospective study, we obtained the records of 369 hospitalized patients, from March 2021 to April 2022. Cases identified with COVID-19 disease were admitted to the ICU. They were diagnosed by clinical disease and/or RT-PCR test. In addition to demographic information, comorbidities, vital signs, and laboratory tests were recorded on the day of admission to the ICU. Also, other factors such as the length of ICU stay, the length of the hospital stay, and the need for ventilatory support were considered as possible factors that may affect the patient's outcome. As part of the management of COVID-19, routine laboratory tests were performed and the results were collected.

APACHE II score and approximate ICU mortality were calculated by taking into account the worsening values and vital signs associated with declining medical conditions in the first 24 hours. The average length of stay of the patients was calculated at 8.59 days, and the correlation between this index and the level of the NLR, the CRP, and the basic APACHE II score of the patients was determined using Pearson's correlation coefficient. After that, the patients were divided into two groups based on their survival status at the time of discharge: those who survived (with 277 people) and those who died (with 92 people). The demographic and clinical characteristics of the two groups were compared, as well as the factors affecting death in the hospital, using logistic regression for the NLR, CRP, and APACHE II scores.

Then, the relationship between haematological factors such as neutrophils, lymphocyte, lactic acid dehydrogenase, ferritin, PCT, mean platelet volume (MPV), and APACHE II score were investigated in all 369 patients.

We also made the same comparison based on the death status of the patients one month after their discharge and divided them into two groups of patients, those who survived (255 people) and those who died (22 people). Among the 255 patients who survived one month after discharge, 17 of them died within 3 months of discharge, and 237 of them survived longer than 3 months. The demographic and clinical characteristics of the patients, as well as the NLR, CRP, and APACHE II scores, were compared with each other. Logistic regression was used to analyze the data.

In addition to the mean and standard deviation for continuous variables with a normal distribution, descriptive statistics were presented as median, minimum, and maximum values for non-normally distributed continuous variables, as well as numbers and percentages for categorical variables, with a confidence interval of 95% CI for all variables. To compare the differences between the variables classified in the tables, Pearson's χ^2 test was used and for the discrimination of specificity and sensitivity, characteristic (ROC) curves were generated. All statistical analyses were performed using SPSS version 26.0. To be considered statistically significant, the *P* value had to be less than 0.05.

Table 1

Basic characteristics of COVID-19 patients (*n* = 369).

Characteristics	Variables	Values
Age (Y)	Mean ± SD (95% CI)	56.11 ± 17.21 (54.35–57.87)
Sex; *n* (%)	Male	203 (55)
	Female	166 (45)
Smoker	*n* (%)	87 (24)
BMI (kg/m^2)	Mean ± SD (95% CI)	26.33 ± 5.11 (25.81–26.85)
Comorbidity: *n* (%)	Diabetic	97 (26)
	Hypertension	53 (14)
	IHD/CHF	53 (14)
	COPD	43 (12)
	Asthma	39 (11)
	CKD	33 (9)
	Congestive heart failure	28 (8)
	CVA	28 (8)
	ILD	19 (5)
Laboratory indexes: Mean ± SD (95% CI)	NLR	3.20 ± 2.30 (2.96–3.43)
	PCT ng/ml	0.26 ± 0.08 (0.25–0.27)
	MPV (fl)	7.23 ± 1.23 (7.10–7.35)
	CRP mg/l	82.08 ± 42.96 (77.68–86.47)
	Ferritin (Per 100) μg/l	4.53 ± 3.30 (4.19–4.87)
	LDH (Per 100) U/l	5.27 ± 2.75 (4.99–5.55)

CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CVA, cerebrovascular accident; ILD, interstitial lung disease; IHD/CHF, ischaemic heart disease; LDH, lactate dehydrogenase; MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio; PCT, procalcitonin.

Table 2

Correlation of basic values of blood inflammatory factors and APACHE II with length of hospitalization in COVID-19 patients.

Factor	n	Correlation coefficient	P
NLR	369	– 0.150	0.004***
PCT ng/ml	369	0.087	0.096*
MPV (fl)	369	– 0.071	0.176*
CRP mg/l	369	– 0.107	0.040**
Ferritin μg/l	369	– 0.025	0.637*
LDH U/l	369	– 0.021	0.683*
APACHE II	369	– 0.144	0.006***

APACHE II, The Acute Physiology and Chronic Health Evaluation II; CRP, C-reactive protein; LDH, lactate dehydrogenase; MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio; PCT, procalcitonin.
*Spearman was used for analyzing bivariate correlation.
**Correlation is significant at the 0.05 level.
***Correlation is significant at the 0.01 level.

Results

A total of 369 hospitalized patients with COVID-19 were investigated in this study, males constituted 55% ($n = 203$) while 45% ($n = 166$) were females. The average age of patients was 56.11 ± 17.21 years (95% CI: 57.87–54.35). A significant percentage of patients with co-morbid conditions had diabetes (26%; $n = 97$), hypertension, IHD/CHF (14%; $n = 53$ for each condition), and COPD (12%; $n = 43$), which together with the average baseline laboratory indicators and clinical measurements are listed in Table 1.

Among the patients, the average length of hospitalization was 8.59 days (95% CI: 7.96–9.22); Pearson's correlation coefficient was used to examine the relationship between this hospitalization duration index and the patient's baseline NLR levels, finding that the length of hospitalization decreased as the patient's baseline NLR increased ($P = 0.004$ and $r = -0.150$). In addition, the APACHE II score increased (Table 2).

Meanwhile, when the length of hospitalization of patients was investigated using generalized linear models in which both the inflammatory factors, NLR and CRP, and APACHE II scores were simultaneously investigated and the main effects of the variables were entered into the model, the results did not show any significant correlation between any of the inflammatory factors and the APACHE II score.

Based on the presented data, it has been found that higher levels of NLR, CRP, and APACHE II have been associated with more severe disease outcomes, such as the need for intubation and the duration of intubation. As a result, patients with higher NLR, CRP, and APACHE II levels are likely to have longer hospitalizations or will die sooner as a result. Even though some patients died in the hospital, they still had a higher baseline level of NLR, CRP, and APACHE II ($P < 0.001$ for each). Furthermore, the intubation rates were significantly higher in these patients than in surviving patients. Further, it has been demonstrated that patients who died in the hospital did not have a significantly shorter hospital stay ($P = 0.228$) than patients who survived during their hospital stay (Table 3 and Fig. 1).

Using logistic regression techniques to investigate the factors that affect death in the hospital, the results showed that all three of the factors, NLR, CRP, and APACHE II, were significant. The ROC analysis also showed a significant difference between the cut-off values of the studied prognostic parameters, and the NLR factor had a higher AUC value than the other two parameters. As a result of having the information on all three factors mentioned above, the basic NLR level appears to be very strong, and the hospitalization factor was the most important factor contributing to death. (Fig. 2).

Among the 277 patients who were discharged, 22 (8%) died within one month of discharge; the average NLR level of these patients was equal to 3.64 ± 1.72 (95% CI: 2.88–4.40), a significantly different level from those who were able to survive this period 2.22 ± 1.50 (95% CI; 2.04–2.41). In addition, it was found that the average levels of CRP and APACHE II of patients who died within one month after discharge were significantly higher than those of patients who survived during this period (P values equal to 0.30 and 0.001, respectively) (Table 4 and Fig. 3).

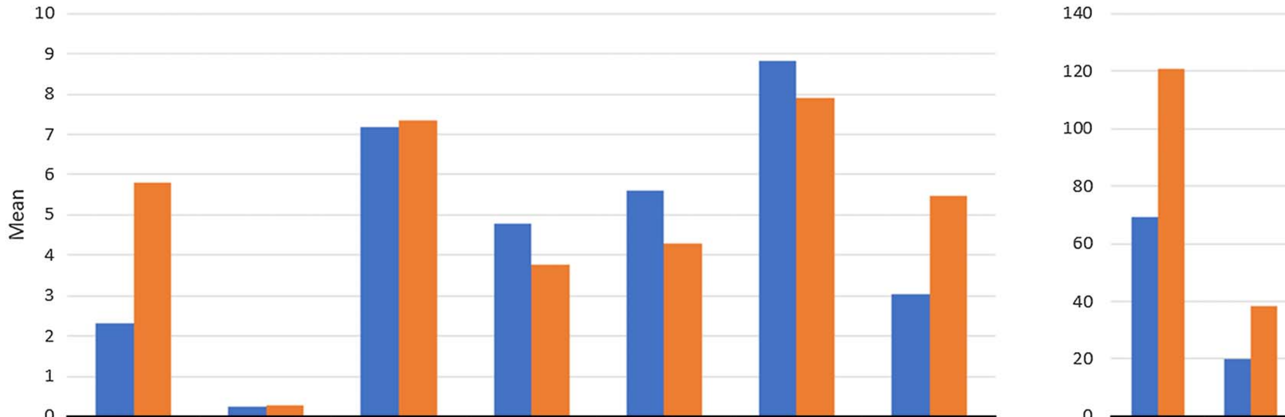
The comparison of demographic and clinical characteristics of patients according to the status of death one month after discharge is presented in Table 4, as shown in the following section: Because, in terms of basic characteristics, there was no significant difference between the two groups of patients who died and who survived within one month of being discharged from the hospital, it was not necessary to repeat the above examinations in a revised manner. The average NLR level was 3.70 ± 1.59 (95% CI: 2.88–4.52) for 255 patients who survived the first month of

Table 3

Comparing blood and physiological characteristics of COVID-19 patients by in-hospital death.

Variables	Value	Alive ($n = 277$)	Expired ($n = 92$)	P
NLR	Mean ± SD (95% CI)	2.33 ± 1.57 (2.15, 2.52)	5.80 ± 2.22 (5.34, 6.26)	< 0.001*
PCT ng/ml	Mean ± SD (95% CI)	0.26 ± 0.08 (0.25, 0.27)	0.27 ± 0.08 (0.25, 0.28)	0.562*
MPV (fl)	Mean ± SD (95% CI)	7.18 ± 1.21 (7.04, 7.33)	7.35 ± 1.29 (7.09, 7.62)	0.271*
CRP mg/l	Mean ± SD (95% CI)	69.27 ± 32.57 (65.42, 73.13)	120.63 ± 47.36 (110.82, 130.44)	< 0.001*
Ferritin (Per 100) μg/L	Mean ± SD (95% CI)	4.78 ± 3.43 (4.38, 5.19)	3.77 ± 2.73 (3.20, 4.33)	0.010*
LDH (Per 100) U/L	Mean ± SD (95% CI)	5.60 ± 2.77 (5.27, 5.93)	4.29 ± 2.43 (3.78, 4.79)	< 0.001*
APACHE II	Mean ± SD (95% CI)	19.18 ± 9.69 (18.03, 20.33)	38.61 ± 17.05 (35.08, 42.15)	< 0.001*
Length of hospitalization (day)	Mean ± SD (95% CI)	8.82 ± 6.46 (8.05, 9.58)	7.90 ± 5 (6.87, 8.94)	0.228*
With intubation	*n* (%)	69 (25)	64 (70)	< 0.001**
length of intubation (day)	Mean ± SD (95% CI)	3.04 ± 3.44 (2.21, 3.87)	5.46 ± 4.08 (4.44, 6.48)	< 0.001*

APACHE II, The Acute Physiology and Chronic Health Evaluation II; CRP, C-reactive protein; LDH, lactate dehydrogenase; MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio; PCT, procalcitonin.
*Mann–Whitney test was used for comparison.
**Chi-square test was used for comparison.



	NLR	PCT	MPV	Ferritin	LDH	length of hospitalization	length of intubation
Alive	2.33	0.26	7.18	4.78	5.6	8.82	3.04
Death	5.8	0.27	7.35	3.77	4.29	7.9	5.46

	CRP	APACHE II
Alive	69.27	19.8
Death	120.63	38.61

Figure 1. Mean of some variables of COVID-19 patients alive and died cases. 1 m, 1 month; 3 m, 3 months.

discharge but expired within the next three months ($n = 17$; 7%). In comparison, the average NLR level of patients who survived during the three month was significantly different from that of those who died during this period 2.12 ± 1.45 (95% CI: 1.93–2.30). So, the average levels of CRP and APACHE II in patients who died within a month of being discharged from the

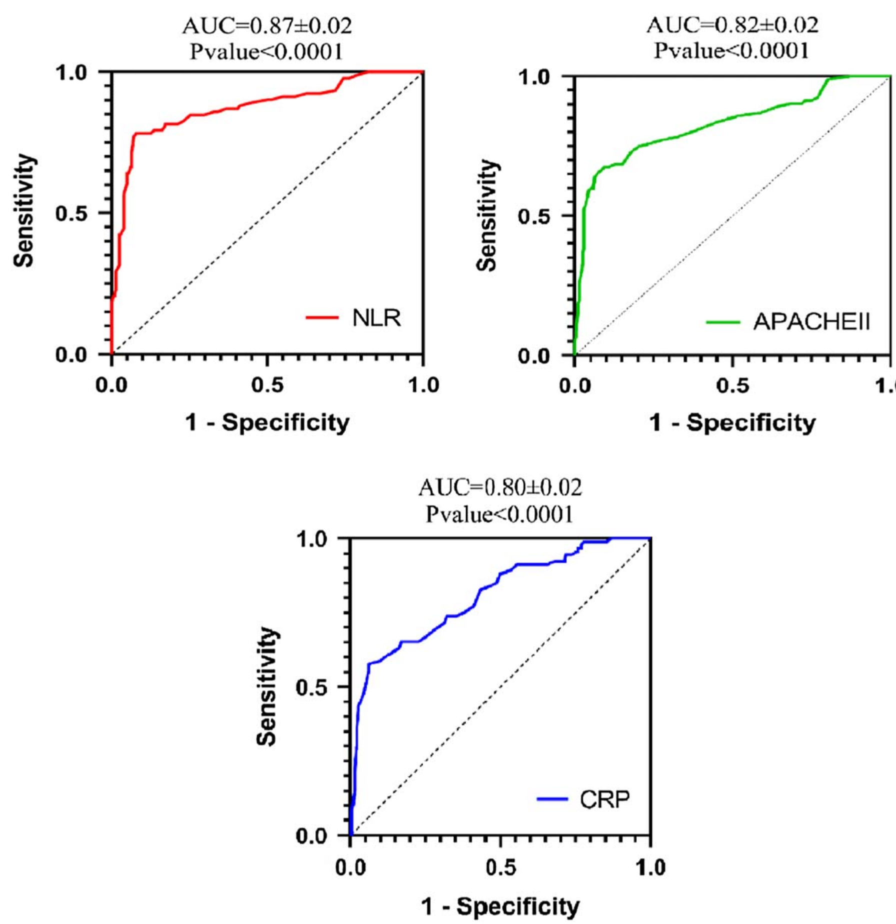


Figure 2. Receiving operating characteristic analysis for three parameters NLR, CRP, APACHE II in predicting hospital mortality in COVID-19 patients. APACHE II, The Acute Physiology and Chronic Health Evaluation II; CRP, C-reactive protein; NLR, neutrophil-lymphocyte ratio; PCT, procalcitonin.

Table 4

Comparing basic values of blood inflammatory factors and APACHE II of discharged patients by 1 month mortality[a] and 3 months mortality[a].

	1 month mortality			3 months mortality		
Variables	Alive $n=255$	Expired $n=22$	*P*	Alive $n=238$	Expired $n=17$	*P*
NLR	2.22 ± 1.50 (2.04–2.41)[b]	3.64 ± 1.72 (2.88–4.40)	< 0.001	2.12 ± 1.45 (1.93–2.30)	3.70 ± 1.59 (2.88–4.52)	< 0.001
PCT ng/ml	0.26 ± 0.08 (0.25–0.27)	0.26 ± 0.07 (0.23–0.29)	0.971	0.26 ± 0.08 (0.25–0.27)	0.27 ± 0.08 (0.22–0.31)	0.534
MPV (fl)	7.17 ± 1.22 (7.02–7.32)	7.31 ± 1.12 (6.81–7.81)	0.453	7.15 ± 1.21 (7–7.31)	7.41 ± 1.32 (6.73–8.09)	0.402
CRP mg/l	69.69 ± 30.50 (63.93–71.45)	87.59 ± 48.10 (66.26–108.92)	0.030	69.42 ± 30.57 (62.52–70.33)	85.47 ± 23.78 (73.24–97.69)	0.002
Ferritin μg/l	4.82 ± 3.47 (4.40–5.25)	4.33 ± 3.04 (2.98–5.68)	0.580	4.84 ± 3.46 (4.39–5.28)	4.65 ± 3.62 (2.79–6.51)	0.652
LDH U/l	5.62 ± 2.80 (5.27–5.96)	5.42 ± 2.45 (4.33–6.50)	0.903	5.63 ± 2.81 (5.27–5.99)	5.37 ± 2.71 (3.98–6.77)	0.663
APACHE II	18.56 ± 9.09 (17.44–19.68)	26.36 ± 13.31 (20.46–32.26)	0.001	18.05 ± 9.01 (16.90–19.20)	25.70 ± 7.20 (22–29.40)	< 0.001

APACHE II, The Acute Physiology and Chronic Health Evaluation II; CRP, C-reactive protein; LDH, lactate dehydrogenase; MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio; PCT, procalcitonin.
[a]Mann–Whitney test was used for comparison.
[b]Mean ± SD (95% CI).

hospital were significantly higher than in those who lived (*P* values of 0.002 and < 0.001, respectively) (Table 4).

As a result of the logistic regression analysis of the simultaneous effects of NLR, CRP, and APACHE II on death within 1 month after discharge, the results showed that only NLR had a significant effect on death within one month after discharge. Accordingly, the basic NLR level of the patients was the single most significant factor in determining whether or not they died within one month of discharge from the hospital, regarding the information available for all three factors. In other words, with each 1-unit increase in a patient's NLR, the chances that a patient will die within one month after discharge will increase by 1.54 times (95% CI: 1.23, 1.93).

In a logistic regression analysis of the simultaneous effects of NLR, CRP, and APACHE II on death within three months of discharge, only NLR was significant; therefore, it could be concluded that based on the information of all three factors above, a patient's basic NLR levels presents as the most effective indicator of death within 3 months of discharge when analyzed together. This means that for every unit increase in a patient's NLR, the chance that the patient will die within 3 months of discharge will increase by 1.63 times (95% CI: 1.26, 2.10) (Table 5).

Discussion

The records of a total of 369 hospitalized patients with COVID-19 were investigated in the current study. There were some patients with underlying diseases, such as diabetes (26%; $n=97$), hypertension, IHD/CHF (14%; $n=53$ for each), and COPD (12%; $n=43$). It has been found that as patients' baseline NLR increased, not only did the duration of hospitalization decrease, but that also higher levels of NLR, CRP and APACHE II resulted in intubation and longer intubation times. In the present study, the basic NLR level was found to be the strongest factor associated with mortality

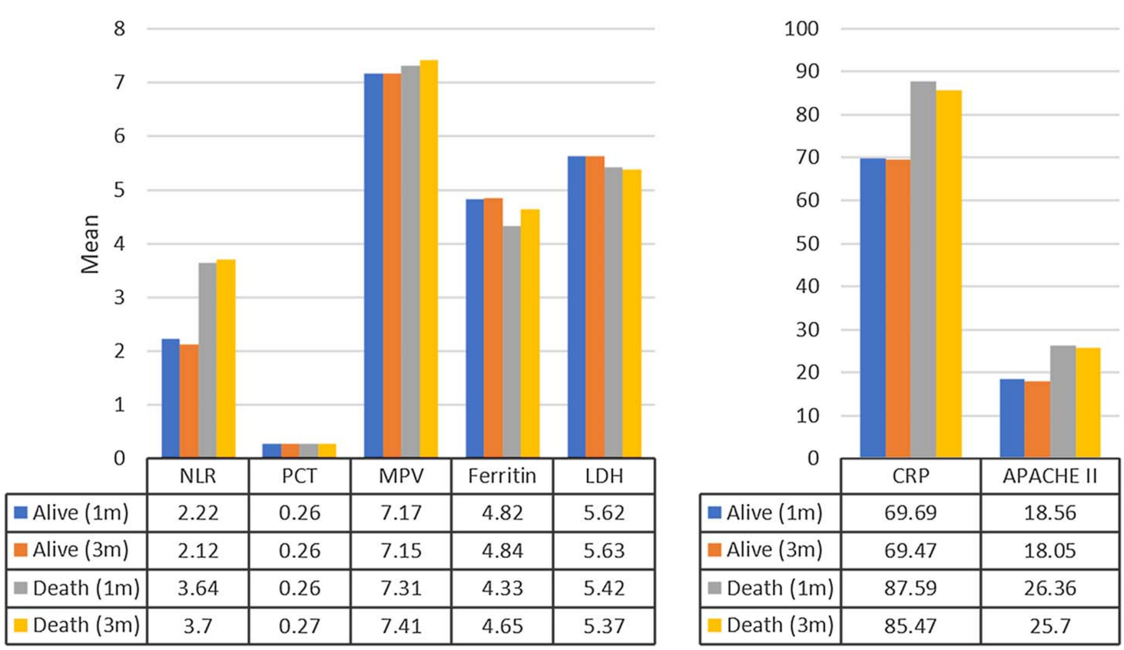


Figure 3. Comparison of blood inflammatory factors and APACHE II in discharged patients by 1 and 3 months follow-ups. 1 m, 1 month; 3 m, 3 months; APACHE II, The Acute Physiology and Chronic Health Evaluation II; CRP, C-reactive protein; LDH, lactate dehydrogenase; MPV, mean platelet volume; NLR, neutrophil-lymphocyte ratio.

Table 5

Effect of basic values of NLR, CRP and APACHE II of discharged patients on 1 month and 3 months mortality in COVID-19 patients.

	1 month mortality			3-month mortality		
Factor*	***n***	**OR (95% CI)**	***P***	***n***	**OR (95% CI)**	***P***
NLR	277	1.54 (1.23–1.93)	< 0.001*	255	1.63 (1.26–2.10)	< 0.001*
CRP mg/l	277	0.99 (0.97–1)	0.646	255	0.99 (0.97–1.01)	0.422
APACHE II	277	1.09 (0.96–1.24)	0.183	255	1.07 (0.92–1.25)	0.345

APACHE II, The Acute Physiology and Chronic Health Evaluation II; CRP, C-reactive protein; NLR, neutrophil to lymphocyte ratio.
Logistic regression (backward stepwise model) was used for comparison.
*Correlation is significant at the 0.01 level.

while in the hospital compared with CRP, and APACHE II. The average NLR level of 22 patients who died one month after discharge was 3.64, which was significantly higher ($P < 0.001$) than the level of patients who survived (2.22 ± 1.50) during this period. In addition to the NLR, the mean CRP and APACHE II levels were significantly higher in the 1-month survival. Based on an analysis of the effects of NLR, CRP, and APACHE II, the baseline NLR levels of patients were found to be the best predictor of death within one month and within 3 months after discharge from the hospital. This correlates to the chance of death increasing with every unit increase in the patients' NLR.

Since the COVID-19 pandemic, it has been difficult for healthcare systems to predict death or how sick COVID-19 patients will be[9]. To evaluate and classify patients with serious diseases, the APACHE II score is a reliable and feasible scoring method that can be used to predictably score and classify patients. If a patient's APACHE II score is over 17, it means that aggressive treatment is likely to help, if the treatment is based on the APACHE II score[13]. Zou *et al.*[14] found that APACHE II was a better predictor of in-hospital mortality than other variables like sequential organ failure assessment SOFA in a study they conducted. In addition to the COVID-19 prognosis, NLR levels have been studied for a long time about death rates in intensive care units and have yielded many positive results. Salciccioli *et al.*[15] found a significant association between high levels of NLR and mortality in intensive care units in an observational cohort study. According to the findings of the study of Ham *et al.*[16], the level of NLR in an intensive care unit was associated with a significant relationship to 1-year ICU mortality. Hwang *et al.*[17] conducted a study on sepsis and septic shock patients in the intensive care unit in which a significant relationship was found between the admission NLR levels and the 28-day mortality rate for patients with sepsis or septic shock. Similarly, Curbelo *et al.*[18] found that the NLR of patients with pneumonia had a significant relationship with the mortality rate of the patients at 30 days and 90 days after the onset of the disease. The results of Zhou's study also demonstrated that there is a positive correlation between NLR levels and ICU admission among patients who have recovered[19]. Thus, there was a significant association between increased NLR values and mortality in this study[20]. According to Parthasarathi and colleagues, the lower NLR means the lower the risk of death due to COVID-19, and the NLR is an effective and reliable assessment tool for expressing how severe the disease is and how significant the mortality rate is due to the disease. The NLR can be used to quickly figure out what is wrong and how dangerous is, so that treatment can start as soon as possible[11]. Sun and colleagues did a study that showed NLR can predict Non-invasive ventilation (NIV) failure in acute respiratory distress syndrome (ARDS) patients with pneumonia. This means that carefully looking at these markers can help avoid intubation delays[21]. Yong *et al.*, in their study, found that patients with high NLR values during hospitalization in the intensive care unit were more likely to require intubation during the hospitalization as well as have poorer clinical outcomes[22]. According to Zhu and colleagues, a multicenter retrospective study of 428 patients showed no significant difference in NLR levels between survivors and non-survivors. They concluded that NLR is not as good a marker as APACHE II, procalcitonin, and CRP levels. According to Basile-Filho and colleagues, APACHE II scores were more effective at predicting mortality than CRP (CRP, a positive acute-phase protein) to albumin (a negative acute-phase protein) ratio (CAR) scores. It was reported by Shenyurt and colleagues that parameters of the complete blood count, such as the NLR, had a greater predictive value than APACHE II scores when it came to predicting mortality. Additionally, these parameters together have a much more significant impact on prognosis than their individual effects. A study by Usta and colleagues found that they were significantly related to Red Cell Distribution Width (RDW), NLR, CRP, and APACHE II scores[9].

In patients with severe pneumonia, CRP is a significant indicator for the diagnosis and evaluation of serious pulmonary infectious diseases, including COVID-19. In addition to showing the usefulness of CRP levels in severe pneumonia, Matsumoto's study also found that CRP levels are positively related to the diameter of the largest lung lesion and that these levels tend to increase with the progression of the disease[23]. It has been shown in another study in the same direction that there is a positive correlation between a high CRP level and lung lesions[12]. An individual's CRP level can be a reliable indicator of the severity of a disease and should be used as one of the key indicators to monitor the disease[12]. Sharifpour and colleagues demonstrated that the CRP level of patients who died was significantly higher than that of those who survived, and the average CRP value was associated with the severity of COVID-19, so it could be considered an independent predictor of mortality. Also, a rise in CRP levels during the first seven days of hospitalization can be considered a tool to predict disease progression and the need for early transfer to an intensive care unit (ICU)[24]. There is a positive correlation between plasma CRP level and CT grading in the retrospective study by Chen and colleagues, which can be used to identify moderate to severe levels of COVID-19 disease based on this correlation. As a result, they found that higher levels of CRP are associated with longer hospital stays. Also, these levels can improve the prognosis and treatment for people with diseases that are more serious[25].

MPV (mean platelat volume) is considered in both proinflammatory and prothrombotic conditions. It seems that our study could not find a significant relationship between MPV and disease outcome such as another study done by Aktaş *et al.*[26]. The reason may be the existence of confounding factors in two groups in which by their elimination, MPV could be associated with the progression of COVID-19[27].

In the present study, there was a significant correlation in the data between the severity and mortality caused by COVID-19 disease. CRP and NLR scoring tools, can be easily studied using routine, inexpensive, and practical blood tests and, be used to develop appropriate treatment strategies. They would be helpful in decreasing the death rate, especially in developing countries where medical resources may be limited.

There were some limitations to our study as well. As a first point, this was a retrospective study that was conducted at a single centre. Secondly, as a result of the small sample size in the group of patients who died within 3 months after discharge, the analysis related to this outcome may be affected by random error and have insufficient statistical power. Consequently, it is necessary to evaluate the delayed consequences of COVID-19 that have been examined in the present study in other studies with sufficient samples and taking into account related confounding factors that have been investigated. Third, we did not analyze data on any other biomarkers in the fields of inflammation, haematology, and clinical factors that may have effects on COVID-19 disease diagnosis, treatment, and mortality.

Conclusion

There was a significant relationship between mortality and complications due to COVID-19, CRP, and NLR prediction tools, and the APACHE II scoring system. Scoring systems can be performed with routine, inexpensive, and practical blood tests. In addition, the NLR is another useful tool for mapping disease severity and mortality outcomes from COVID-19 based on the results of the present study. As a result of our study, we observed that increased NLR was associated with a significantly higher likelihood of admission to the intensive care unit, higher mortality in the ICU, and a more frequent need for mechanical ventilation in the ICU. Despite this, more studies are needed to arrive at a definitive value that could potentially improve clinical outcomes and reduce the overall mortality associated with COVID-19.

Ethic approval

Ethics was approved by the ethical commitee of Iran University of Medical Sciences, Tehran, Iran (code: IR.IUMS.FMD.REC.1400.278).

Consent

Written consent signed and obtained from each participants.

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Iran University of Medical Sciences, Tehran, Iran.

Author contribution

N.R.: conceptualization, methodology, software. M.M.N., F.S.T., A.A.: data curation, writing—original draft preparation. M.M.N., P.D.: visualization, investigation. A.A., P.D.: supervision. N.A., F.S.T.: software, validation. M.H.K.N., D.P., M.A.: writing—reviewing and editing

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

None.

Guarantor

Neda Rahimian, Mohammad Hadi Karbalaie Niya.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author, [N.R.].

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