# Prognostic Role of Inflammatory and Coagulation Factors in Severe COVID-19: A Descriptive Analysis From an Intensive Care Unit

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***Received:2025-05-24, Revised:2025-09-14, Accepted: 2025-09-24, Published:2025-09-30***

**Abstract**

***Background:*** Severe COVID-19 is often associated with systemic inflammation and coagulopathy, which may influence clinical outcomes. Identifying prognostic biomarkers at ICU admission can aid in risk stratification and management.

***Methods:*** In this retrospective study, 363 ICU-admitted patients with severe COVID-19 were evaluated. The primary outcome was in-hospital mortality; secondary outcomes included associations between inflammatory/coagulation biomarkers and mortality, and comparison of derived ratios with their individual components.

***Results:*** Mortality was 62.8%. Non-survivors had significantly higher D-dimer ($p = 0.047$), ferritin ($p = 0.057$), ESR ($p = 0.018$), and PCT ($p = 0.049$), with lower lymphocyte counts ($p = 0.058$) and vitamin D levels ($p = 0.002$). NLR was markedly elevated in non-survivors ($p = 0.037$) and showed the best predictive value (AUC = 0.66), outperforming neutrophil and lymphocyte counts individually. PLR provided limited discrimination. Diabetes and hypertension were also associated with increased mortality.

***Conclusion:*** Inflammatory and coagulation markers—particularly NLR, D-dimer, ferritin, ESR, PCT, lymphocyte count, and vitamin D—are useful predictors of mortality in critically ill COVID-19. Early recognition of these parameters may aid triage and optimize ICU resource allocation.

J Pharm Care 2025; 13(3): 180-187.

**Keywords:** COVID-19; Inflammation; Coagulopathy; Mortality; ICU; D-dimer; Ferritin; NLR; Lymphopenia

## Introduction

Since its emergence in December 2019, COVID-19 has posed an unprecedented challenge to global healthcare systems. While the majority of infected individuals exhibit mild symptoms, a significant proportion—particularly those with underlying comorbidities—progress to critical illness, often requiring intensive care support (1, 2).

Numerous studies have identified dysregulation of inflammatory and coagulation pathways as a pivotal factor in COVID-19 pathogenesis. Elevated levels of inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), ferritin, and interleukin-6 (IL-6), along with coagulopathy indicators such as D-dimer and fibrinogen, has been linked to disease severity and mortality (3–5).

Hematologic indices derived from complete blood count, such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), have also gained prominence

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as accessible prognostic tools. Moreover, lymphopenia has emerged as a hallmark of severe COVID-19, suggesting immune system exhaustion or viral cytotoxicity (6, 7).

This study investigates the prognostic value of inflammatory and coagulation biomarkers in ICU-admitted patients with severe COVID-19, aiming to identify laboratory indicators that may guide early therapeutic interventions.

## Methods

### *Study Design*

This retrospective, descriptive-analytical, cross-sectional study was conducted at Sina Hospital, a tertiary referral center affiliated with Tehran University of Medical Sciences (TUMS). The study focused on adult patients with confirmed COVID-19 who were admitted to the ICU between March 21, 2021, and March 20, 2022. The primary outcome was in-hospital mortality. Secondary outcomes included the association of admission inflammatory and coagulation biomarkers and derived ratios with in-hospital mortality, and the comparative predictive performance of composite ratios versus their individual components. The study design allowed the investigation of associations between initial laboratory parameters and in-hospital prognosis without introducing intervention-related biases.

### *Ethical Consideration*

Ethical approval was obtained from the institutional review board (ethics code: IR.TUMS.SINAHOSPITAL.REC.1401.016). The research adhered to the ethical principles outlined in the Declaration of Helsinki, and all data were anonymized to ensure patient confidentiality.

### *Inclusion and Exclusion Criteria*

The study included all adult patients (≥18 years old) with laboratory-confirmed SARS-CoV-2 infection by RT-PCR and compatible high-resolution chest computed tomography findings. Only patients admitted to the ICU with severe COVID-19 manifestations—defined by oxygen saturation <94% on room air, $PaO_2/FiO_2$ ratio <300 mmHg, respiratory rate >30 breaths/min, or extensive pulmonary infiltrates >50%—were eligible. Patients were excluded if essential data, such as laboratory tests, outcome status, or comorbidity profiles, were missing or incomplete in the hospital records.

### *Data Collection and Variables*

Data were extracted retrospectively from the hospital's Health Information System. A structured data extraction form was used to collect the following: demographic data (age, sex, and body mass index), comorbidities (hypertension, diabetes, chronic kidney disease, malignancies, cardiovascular disease, etc.), clinical scores (APACHE II and SOFA at ICU admission), and outcomes (death/discharge, ICU length of stay).

Laboratory data collected at the time of ICU admission included WBC count, neutrophil and lymphocyte percentages, hemoglobin, platelet count, prothrombin time, activated partial thromboplastin time, international normalized ratio, ferritin, D-dimer, fibrinogen, CRP, ESR, procalcitonin (PCT), ALT, AST, LDH, bilirubin (total/direct), serum albumin, BUN, creatinine, troponin, triglycerides, vitamin D, and uric acid.

### *Inflammatory and Coagulation Ratios*

To assess the predictive significance of hematologic markers, various ratios were derived using admission laboratory values:

1) Neutrophil-to-lymphocyte ratio (NLR): the absolute neutrophil count (ANC) divided by the absolute lymphocyte count (ALC), 2) Platelet-to-lymphocyte ratio (PLR): the platelet count divided by ALC, 3) Absolute lymphocyte count (ALC): the total white blood cell count multiplied by the lymphocyte percentage, 4) Absolute neutrophil count (ANC): the total white blood cell count multiplied by the neutrophil percentage.

### *Statistical analysis*

Statistical analyses were performed using IBM SPSS Statistics version 16.0. Continuous variables were described as mean ± standard deviation (SD) or medians with interquartile ranges, depending on the distribution assessed via the Shapiro–Wilk test. Categorical variables were summarized as frequencies and percentages. For group comparisons between survivors and non-survivors, an independent-samples T-test or Mann–Whitney U test was used for continuous variables, and a Chi-square test or Fisher's exact test for categorical variables. A two-sided p-value less than 0.05 was considered statistically significant. In addition to univariate group comparisons, we compared the predictive performance of composite ratios (e.g., NLR, PLR) versus their individual components (neutrophil %, lymphocyte %, platelet count) using receiver-operating characteristic (ROC) curve analysis and area under the curve (AUC) comparison. Variables with $p < 0.10$ in univariate analysis were entered into a multivariable logistic regression model (adjusting for age, sex, BMI, need for mechanical ventilation, APACHE II/SOFA where available, and major comorbidities) to

identify independent predictors of in-hospital mortality. A two-sided $p < 0.05$ was considered statistically significant.

## Results

### *Baseline Demographics and Clinical Characteristics*

A total of 363 patients were included, of whom 228 (62.8%) did not survive and 135 (37.2%) survived. Baseline characteristics are summarized in Table 1. The mean (SD) age of the non-survivors was slightly higher than that of the survivors (68.1 (8) vs. 66.5 (4) years), and this difference reached statistical significance (P = 0.013). However, the absolute difference of 1.6 years is unlikely to be clinically meaningful. The groups were comparable regarding sex distribution (male proportion: 56.6% vs. 54.1%, P = 0.60) and BMI (mean (SD): 22.8 (4.80 vs. 23.5 (4.9) kg/m², P = 0.35).

In contrast, ventilatory support requirements differed markedly between the groups. The non-survivors required invasive mechanical ventilation far more frequently than the survivors (94.3% vs. 73.3%, P < 0.001). Conversely, the need for BiPAP support was significantly higher among the survivors (26.7% vs. 5.7%, P < 0.001). The use of oxygen via nasal cannula was observed only in two survivors, not in the non-survivors (p = 0.15).

**Table 1. Demographic and baseline clinical characteristics of the study population**

| Variables | Total N=363 | Survivors N= 135 (37.19%) | Non-survivors N= 228 (62.81%) | P value |
|---|---|---|---|---|
| **Demographics** | | | | |
| Age (year), Mean (SD) | 67.87(3) | 66.53(4) | 68.11(8) | 0.013 |
| Sex (male), N (%) | 202 (55.64) | 73 (54.07) | 129 (56.58) | 0.35 |
| BMI (kg/m2), Mean (SD) | 22.98 (3.13) | 23.45(4.9) | 22.81(4.8) | 0.6 |
| **Ventilation Assessment** | | | | |
| Required Invasive Mechanical Ventilation, N (%) | 314 (86.50) | 99 (73.33) | 215 (94.29) | <0.001 |
| Required BiPAP Support, N (%) | 47 (12.94) | 36 (26.66) | 13 (5.75) | <0.001 |
| Required O2 nasal cannula, N (%) | 2 (0.55) | 2 (100) | 0 | 0.15 |

SD: Standard Deviation, BMI: Body Mass Index, BiPAP: Bilevel Positive Airway Pressure

### *Comorbidities and Their Association with Mortality*

Analysis showed that patients with diabetes mellitus and hypertension had significantly higher mortality rates (P = 0.043 and P < 0.01, respectively). The proportion of patients without any comorbidity was higher among the survivors (54.07%) compared to the non-survivors (24.56%) (Table 2).

**Table 2. Association between comorbidities and mortality outcomes**

| Comorbidities, N (%) | Total N=363 | Non-survivors N= 228 (62.81%) | Survivors N= 135 (37.19%) | P value |
|---|---|---|---|---|
| **Smoking** | 66 (18.18) | 40 (17.54) | 26 (19.26) | 0.68 |
| **DM** | 96 (26.45) | 63 (27.63) | 33 (24.44) | 0.043 |
| **HTN** | 64 (17.63) | 48 (21.05) | 16 (11.85) | <0.01 |
| **CKD** | 10 (2.75) | 8 (3.51) | 2 (1.48) | 0.751 |
| **IHD** | 41 (11.29) | 34 (14.91) | 7 (5.19) | 0.99 |
| **Cancer** | 15 (4.13) | 15 (6.58) | 0 (0) | 0.976 |
| **COPD** | 9 (2.47) | 7(3.07) | 2(1.48) | 0.493 |
| **HLP** | 4 (1.10) | 1 (0.44) | 3 (2.22) | 0.843 |
| **HF** | 4 (1.10) | 3 (1.32) | 1 (0.74) | 0.5 |
| **Without PMH** | 129 (35.54) | 56 (24.56) | 73 (54.07) | 0.083 |

DM: Diabetes Mellitus, HTN: Hypertension, CKD: Chronic Kidney Disease, IHD: Ischemic Heart Disease, COPD: Chronic Obstructive Pulmonary Disease, HLP: Hyperlipidemia, HF: Heart Failure, PMH: Past Medical History

### *Clinical Outcomes*

The mean (SD) hospital stay was 13.14 (11) days. Overall mortality was 62.8%, representing patients who died during hospitalization (non-survivor group). The mean (SD) computed tomography severity score was significantly higher in the deceased group (18.32(4.57)) compared to the recovered group (15.57 (15.72)) (P = 0.042) (Table 3).

**Table 3. Comparison of clinical outcomes between non-survivors and survivors**

| Outcome parameters | Non-survivors N= 228 (62.81) | Survivors N= 135 (37.19) | P value |
|---|---|---|---|
| **Length of hospital stay (day), Mean (SD)** | 13.08 (10.96) | 15.28 (22.64) | 0.631 |
| **Mortality, N (%)** | 228 (62.80) | 135 (37.2) | 0.013 |
| **CT score (out of 25), Mean (SD)** | 18.32 (4.57) | 15.57 (15.72) | 0.042 |

SD: Standard Deviation, CT: Computed Tomography

### *Laboratory Parameters at Admission*

Among the inflammatory markers, ESR, PCT, ferritin, and D-dimer were significantly higher in the deceased group. CRP and IL-6 levels were also elevated but not statistically significant. The lymphocyte percentage was lower in the non-survivor group (mean (SD): 8.97 (9.40) vs. 14.5 (8.46); P = 0.058) (Table 4).

**Table 4. Laboratory parameters and inflammation markers in survivors and non-survivors**

| Parameter | | Non-survivors N= 228 | Survivors N= 135 | P value |
|---|---|---|---|---|
| **WBC,** ×10⁹/L | Mean (SD) | 10.1 (5.51) | 10.2 (6.00) | 0.703 |
| | Median [Min, Max] | 8.80 [1.40, 25.6] | 6.80 [4.70, 19.0] | |
| **Platelet,** ×10⁹/L | Mean (SD) | 199 (82.2) | 280 (203) | 0.587 |
| | Median [Min, Max] | 185 [62.0, 401] | 219 [120, 719] | |
| **Neutrophil,** % | Mean (SD) | 89.2 (11.3) | 83.3 (11.2) | 0.061 |
| | Median [Min, Max] | 93.4 [26.0, 96.0] | 81.1 [64.4, 100] | |
| **Lymphocyte,** % | Mean (SD) | 8.97 (9.40) | 14.5 (8.46) | 0.058 |
| | Median [Min, Max] | 7.70 [0.300, 71.0] | 14.5 [4.10, 29.3] | |
| **IL6,** ng/mL | Mean (SD) | 361 (853) | NA (NA) | NA |
| | Median [Min, Max] | 22.8 [3.30, 2550] | NA [NA, NA] | |
| **CRP,** mg/L | Mean (SD) | 92.2 (41.9) | 103 (73.5) | 0.978 |
| | Median [Min, Max] | 102 [3.50, 251] | 96.0 [12.0, 245] | |
| **ESR,** mm/hr | Mean (SD) | 69.4 (23.1) | 54.1 (29.0) | 0.018 |
| | Median [Min, Max] | 61.0 [43.0, 96.0] | 51.0 [7.00, 125] | |
| **Procalcitonin**, ng/mL | Mean (SD) | 3.42 (5.70) | 1.72 (3.23) | 0.049 |
| | Median [Min, Max] | 0.200 [0.0500, 10.0] | 0.245 [0.0100, 10.0] | |
| **LDH**, U/L | Mean (SD) | 982 (468) | 897 (347) | 0.277 |
| | Median [Min, Max] | 905 [0, 2440] | 886 [408, 1390] | |
| **Albumin**, g/dL | Mean (SD) | 3.01 (0.691) | 3.22 (0.110) | 0.821 |
| | Median [Min, Max] | 3.20 [0.900, 4.30] | 3.20 [3.10, 3.40] | |
| **Vitamin D**, ng/mL | Mean (SD) | 27.3 (12.0) | 39.5 (20.3) | 0.002 |
| | Median [Min, Max] | 23.0 [16.2, 47.4] | 36.5 [4.20, 78.0] | |
| **Uric acid**, mg/dL | Mean (SD) | 7.76 (2.91) | 5.23 (3.53) | 0.784 |
| | Median [Min, Max] | 7.55 [3.00, 12.1] | 4.50 [1.90, 10.0] | |
| **PT**, s | Mean (SD) | 15.1 (3.89) | 14.3 (2.14) | 0.248 |
| | Median [Min, Max] | 14.0 [11.7, 33.2] | 13.4 [12.0, 18.0] | |
| **INR,** ratio | Mean (SD) | 1.19 (0.300) | 1.12 (0.169) | 0.132 |
| | Median [Min, Max] | 1.10 [1.00, 2.79] | 1.00 [1.00, 1.40] | |
| **PTT**, s | Mean (SD) | 35.3 (21.9) | 31.3 (9.48) | 0.145 |
| | Median [Min, Max] | 28.9 [22.0, 173] | 28.0 [25.0, 52.0] | |
| **Ferritin**, ng/mL | Mean (SD) | 927 (1690) | 470 (52.2) | 0.057 |
| | Median [Min, Max] | 759 [0, 10700] | 500 [710, 800] | |
| **D-Dimer**, ng/mL | Mean (SD) | 1820 (2570) | 965 (1060) | 0.047 |
| | Median [Min, Max] | 829 [14.3, 11600] | 659 [331, 3330] | |
| **Fibrinogen**, g/L | Mean (SD) | 1.25 (2.23) | NA (NA) | NA |
| | Median [Min, Max] | 0 [0, 5.46] | NA [NA, NA] | |

SD: Standard Deviation, IL6: Interleukin 6, CRP: C-Reactive Protein, ESR: Erythrocyte Sedimentation Rate, LDH: Lactate Dehydrogenase, PT: Prothrombin Time, INR: International Normalized Ratio, PTT: Partial Thromboplastin Time

### *Inflammatory/Coagulation Ratios and Mortality*

Derived indices were compared between the groups. NLR was significantly higher in the non-survivors (mean (SD): 20.1 (39.6) vs. 9.85 (8.17); P = 0.037). ALC was significantly lower in the non-survivors (P = 0.046). PLR did not differ significantly between the groups (P = 0.061) (Table 5).

**Table 5. Inflammatory/coagulation ratios associated with outcome**

| Parameter | | Non-survivors N= 228 | Survivors N= 135 | P value |
|---|---|---|---|---|
| **ANC** | Mean (SD) | 867 (527) | 899 (634) | 0.074 |
| | Median [Min, Max] | 771 [105, 2410] | 551 [375, 1820] | |
| **ALC** | Mean (SD) | 93.9 (158) | 105 (38.1) | 0.046 |
| | Median [Min, Max] | 65.1 [2.94, 1280] | 89.9 [63.5, 179] | |
| **NLR** | Mean (SD) | 20.1 (39.6) | 9.85 (8.17) | 0.037 |
| | Median [Min, Max] | 9.26 [0.366, 307] | 5.90 [2.20, 22.7] | |
| **PLR** | Mean (SD) | 44.0 (72.9) | 40.2 (60.9) | 0.061 |
| | Median [Min, Max] | 18.6 [2.70, 507] | 15.3 [9.45, 175] | |

SD: Standard Deviation, ANC: Absolute Neutrophil Count, ALC: Absolute Lymphocyte Count, NLR = ANC ÷ ALC (Neutrophil-To-Lymphocyte Ratio), PLR= Platelet ÷ ALC (Platelet-To-Lymphocyte Ratio)

ROC analysis (Table 6, Figure 1) was used to compare the predictive ability of single parameters to that of derived ratios. The lymphocyte percentage achieved an AUC of 0.64 (95% CI 0.58–0.70), whereas the neutrophil percentage provided an AUC of 0.62 (95% CI 0.55–0.68). Absolute counts provided limited information. ALC (AUC 0.56, 95% CI 0.49–0.63) and ANC (AUC 0.52, 95% CI 0.45–0.59) showed limited discriminatory power. Conversely, NLR had the highest predictive accuracy (AUC 0.66, 95% CI 0.61–0.72), surpassing its individual components. PLR demonstrated inadequate discriminative capacity (AUC 0.51, 95% CI 0.45–0.58). Overall, these findings indicate that composite indices, particularly NLR, capture prognostic information more effectively than single leukocyte parameters.

**Table 6. Receiver-operating characteristic (ROC) analysis comparing predictive performance of single parameters and derived ratios for in-hospital mortality**

| Marker | AUC | 95% CI (approximate) |
|---|---|---|
| **Lymphocyte %** | 0.64 | 0.58 – 0.70 |
| **Neutrophil %** | 0.62 | 0.55 – 0.68 |
| **ALC** | 0.56 | 0.49 – 0.63 |
| **ANC** | 0.52 | 0.45 – 0.59 |
| **NLR** | 0.66 | 0.61 – 0.72 |
| **PLR** | 0.51 | 0.45 – 0.58 |

AUC: Area Under the ROC Curve, ALC: Absolute Lymphocyte Count, ANC: Absolute Neutrophil Count, NLR: Neutrophil-to-Lymphocyte Ratio, PLR: Platelet-to-Lymphocyte Ratio

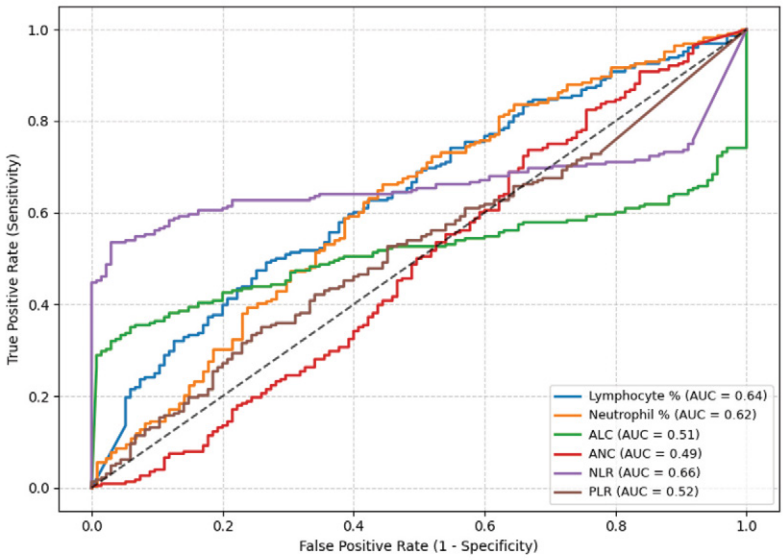


**Figure 1. Receiver-operating characteristic (ROC) curves for inflammatory and coagulation-related parameters in predicting in-hospital mortality among ICU patients with severe COVID-19**

## Discussion

The present study investigated the relationship between inflammatory and coagulation biomarkers and mortality outcomes in patients with severe COVID-19 admitted to the ICU. The results revealed significant differences between the survivors and non-survivors in a number of key parameters. These included elevated levels of D-dimer, ESR, PCT, ferritin, and an increased NLR, all of which were associated with poor outcomes. Conversely, lower lymphocyte counts and vitamin D levels were associated with survival, emphasizing the prognostic role of both immune suppression and nutritional status.

COVID-19 is known to induce a hyperinflammatory response, often described as a "cytokine storm," which contributes to disease severity and organ damage (1). Markers such as ESR and CRP are classic indicators of systemic inflammation. Our finding of a significantly elevated ESR in the non-survivors aligns with earlier research by Kaya et al., who showed that ESR values above 52.5 mm/hr were predictive of disease severity and mortality (2). Although ESR is a nonspecific marker, when considered in combination with other markers, its prognostic value increases substantially.

PCT is a biomarker traditionally used to detect bacterial infection. However, several studies have demonstrated that PCT can also rise in severe viral infections, likely reflecting systemic inflammation and potential superimposed bacterial infections (3, 4). In our study, PCT was significantly higher in the death group, consistent with the meta-analysis by Lippi and Plebani, which showed that elevated PCT was associated with COVID-19 severity (5).

Elevated D-dimer levels are well documented in critically ill COVID-19 patients. This fibrin degradation product is a marker of thrombus formation and breakdown, reflecting hypercoagulability (6, 7). Zhou et al. reported that D-dimer >1 μg/mL was strongly associated with in-hospital death in their cohort of 191 patients (8). Similarly, our results support incorporating D-dimer as part of the routine prognostic assessment in ICU-admitted COVID-19 patients.

Ferritin, an acute-phase reactant, reflects the intensity of inflammation. It has been proposed that severe COVID-19 triggers a macrophage activation-like syndrome, resulting in markedly elevated ferritin levels (9, 10). In our study, ferritin was significantly higher in the death group, consistent with reports by Vargas-Vargas and colleagues, who linked hyperferritinemia to cytokine storm and increased mortality (11). Furthermore, hyperferritinemia has been considered one of the defining laboratory abnormalities in the proposed "hyperferritinemic syndrome" associated with COVID-19 (12).

Lymphopenia is widely recognized as one of the most consistent laboratory abnormalities in COVID-19. In our study, lymphocyte percentage was markedly lower among the non-survivors. This finding is in line with multiple prior studies that proposed SARS-CoV-2 may directly infect lymphocytes or induce apoptosis via elevated cytokines (13, 14). Tan et al. suggested that lymphocyte count may serve as a reliable early indicator of disease severity (15). Low lymphocyte count reflects impaired adaptive immunity and has been linked to longer hospital stay, increased ICU need, and higher mortality.

Another important ratio, NLR, was significantly elevated in the non-survivors in our cohort. NLR combines two distinct immune pathways neutrophil-driven inflammation and lymphocyte-mediated immune response and has been validated in numerous studies as a prognostic biomarker in COVID-19 (16–18). Qin et al. showed that elevated NLR was associated with poor outcomes, and our results reinforce this finding (19). In addition, ROC analysis confirmed that NLR outperformed its individual components (lymphocyte % and neutrophil %), with the highest AUC (0.66) among all tested indices, highlighting its superior discriminative ability.

Although coagulation tests such as prothrombin time, international normalized ratio, and activated partial thromboplastin time did not show statistically significant differences between the groups in our cohort, they tended to be higher in the non-survivors. This trend mirrors findings from Tang et al., who observed that COVID-19-associated coagulopathy frequently preceded poor outcomes (20). It is likely that serial monitoring rather than a single measurement may provide better prognostic insight.

Vitamin D deficiency is another emerging risk factor in COVID-19 severity. Vitamin D plays an important role in modulating both innate and adaptive immunity and has anti-inflammatory properties (21). In our study, lower serum vitamin D levels were significantly associated with mortality. This supports the observations made by Meltzer et al. and Ahmad et al., who found a strong association between low vitamin D status and poor COVID-19

outcomes (22, 23).

Other derived ratios, such as PLR, ALC, and ANC, exhibited negligible discriminative capability in ROC analysis (AUCs ~0.49–0.56), further emphasizing that not all composite indices have the same prognostic significance. This indicates that the biological plausibility and equilibrium of immune pathways represented in NLR may explain its superior predictive efficacy relative to PLR or individual cell counts.

Unlike prior reports that separately examined inflammatory or coagulation pathways (24, 25), our study simultaneously assessed both and directly compared the predictive performance of derived ratios versus their individual parameters. This integrated evaluation, especially highlighting NLR superiority, adds novelty to the literature.

The strengths of our study include a relatively large ICU cohort, detailed laboratory evaluation at admission, and the inclusion of several prognostic biomarkers. However, limitations must be acknowledged. First, this was a single-center retrospective analysis, which limits generalizability. Second, IL-6 and serial measurements of markers were not consistently available due to technical constraints. Third, the study did not include multivariate analysis to adjust for confounders. Lastly, ROC results relied on estimated distributions from summary statistics instead of raw patient data, which could make AUC calculations less accurate.

Future research should focus on longitudinal trends in biomarkers, integration of multiple indicators into risk scores, and prospective multicenter validation. Moreover, exploring the mechanistic role of vitamin D supplementation, anticoagulant strategies based on D-dimer levels, and NLR-guided treatment stratification may yield clinically actionable insights.

In summary, our findings support the use of NLR, ferritin, D-dimer, ESR, PCT, and vitamin D as simple, accessible, and reliable predictors of poor prognosis in critically ill COVID-19 patients. ROC analysis reinforced the utility of NLR as the most robust marker among those tested, while other ratios such as PLR, ALC, and ANC added limited prognostic value. These parameters may help clinicians identify high-risk patients early, personalize treatment, and allocate ICU resources more efficiently.

## Conflict of Interest

There is no conflict of interest to declare.

## Acknowledgments

Our gratitude to the healthcare providers, including nurses and medical students, who dedicated their time in the ICU during the COVID-19 pandemic. This article, as a part of Dr. Pourfallah's Critical Care Medicine subspecialty thesis, was supported by Tehran University of Medical Sciences, Tehran, Iran. QuillBot® language tool was used to assist in grammar correction and to improve the clarity and readability of the manuscript. No content was generated or interpreted by AI, and all scientific interpretations and conclusions were made by the authors.

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**PLEASE CITE THIS PAPER AS:**

Pourfallah R, Badrbani M, Azadmehr B, Jahangirifard B, Mourtami R, Shariat Moharari R, et al. Prognostic Role of Inflammatory and Coagulation Factors in Severe COVID-19: A Descriptive Analysis From an Intensive Care Unit. J Pharm Care. 2025;13(3): 180-187.
DOI: 10.18502/jpc.v13i3.20321