Original Article

# The Role of Hematological Parameters in Predicting the Death of Hospitalized Patients with COVID-19

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## Abstract

**Background:** The role of the hematologic indicators in the identification of severe or critical patients requires further investigation. In this study, we focused on predicting Covid-19 patients at risk of progression using blood parameters.

**Materials and Methods:** We performed a retrospective study including 444 patients with confirmed Covid-19. Hematological parameters were evaluated. The logistic regression analysis was performed with step-wise method with dependent variables such as intensive care units admission, partial pressure of oxygen saturation, and mortality. Also, independent variables such as hematological parameters, age and sex to assess variables that are likely to predict patients at risk of progression.

**Results:** Patients in intensive care units had significantly higher mean absolute neutrophil count than outpatients ($P < 0.001$). There was a statistically significant difference in the mean absolute lymphocyte count between dead and survived patients ($P = 0.015$). Multivariate analysis confirmed the positive association of the white blood cells ($P < 0.001$), absolute neutrophil count ($P < 0.004$), red cell distribution width ($P < 0.001$), and lactate dehydrogenase ($P = 0.007$) to be positively associated with the admission of Covid-19 patients in the intensive care units and the absolute monocyte count ($P = 0.012$, Odds ratios = 0.100, CI95% = 0.066-0.605) to be negatively associated with mortality.

**Conclusion:** Based on the results of our study, it is recommended to use hematological data to make clinical decisions and evaluate the patient's prognosis.

**Keywords:** COVID-19, monocytes, neutrophils, novel coronavirus

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## Introduction

On 11 February 2020, the World Health Organization announced the official name of the disease caused by the 2019 novel coronavirus, Covid-19, short for "coronavirus disease 2019".[1] On the same day, the International Committee on Taxonomy of Viruses changed the temporarily named 2019-nCoV to "severe acute respiratory syndrome coronavirus 2" as the reason for Covid-19.[2] Coronaviruses are a large group of enveloped viruses with a single-stranded RNA and a crown on their surface. Covid-19 has a wide range of presentations ranging from asymptomatic patients to septic shock.[3] Severe patients often present dyspnea with or without hypoxemia which ultimately develops into acute respiratory distress syndrome, septic shock, coagulation dysfunction, incurable metabolic acidosis, and multiple organ failure.[4,5] Covid-19 can be classified into four types, mild, moderate, severe, and critical based on the severity of the presentation.[3,6] An exploratory analysis of the 72,314 cases of Covid-19 reported

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that about 81% of reported cases are mild and 13.8% severe. In addition, 4.7% of confirmed cases are critical the mortality rate is more noteworthy among critical cases at 49%, and no deaths have been reported in patients with mild symptoms.[7] In addition, critical infection was scarce among pediatrics.[8] According to achievements in china, about 26.1% to 32% of infected cases deteriorate into a severe or critical infection.[9] This signifies, the early need for diagnosis and identification of severe or critical patients. Therefore, sufficient healthcare and reduction of mortality rate highly depend on early diagnosis of deteriorating patients.

Patients with COVID-19 present with multiple hematological abnormalities. It has been determined that lactate dehydrogenase, didimer level and ferritin concentration are correlated with disease severity and prognosis. Reduced leucocyte and platelet counts are frequent.[10] There are few reports on the prognostic role of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio.

The routine hematologic test is the most accessible, efficient, and cost-benefit test done in infected patients. The role of the hematologic indicators in the identification of severe or critical patients requires further investigation. In this study, we are going to focus on creating an effective model for predicting COVID-19 patients at risk of progression using hematological parameters.

## Materials and Methods

In a single-center retrospective study from February 2020 to May 2020, All patients with COVID-19 referred to the Khansari Hospital, Arak, Iran, were included. A total of 859 patients were included in the study. We obtained the primary information of patients such as demographic and clinical details, laboratory findings, outcomes, and comorbidities from the admission records and during hospitalization. We confirmed the diagnosis of COVID-19 via reverse transcriptase-polymerase chain reaction (RT-PCR) assays performed on nasopharyngeal swab specimens and used standard automated laboratory methods to obtain the hematological parameters. All the nasopharynx samples were collected and placed in a sterile tube. To determine the severe COVID-19 group at least one of these three criteria should be filled: (1) the saturated $PO_2$ (resting status) ≤95%, (2) the status of the patient who died due to COVID-19 (3) patients who were hospitalized in intensive care units (ICU).

This study was approved by the Ethics Committee of Arak University of Medical Sciences (ethical committee code number: IR.ARAKMU.REC.1400.149).

### *Laboratory methods*

1. Hematological parameters include white blood cells (WBCs), absolute neutrophil count (ANC), absolute lymphocyte count (ALC), absolute monocyte count (AMC), red cell distribution width-coefficient variation (RDW-CV), mean platelet volume (MPV), mean corpuscular volume (MCV), lactate dehydrogenase (LDH), platelet (PLT) count, hemoglobin (Hb), prothrombin time (PT), partial thromboplastin time (PTT), the international normalized ratio (INR), erythrocyte sedimentation rate (ESR), and c-reactive protein (CRP) were collected from the electronic medical records and reviewed by physicians. We also calculated NLR (Neutrophil-Lymphocyte Ratio) and PLR (Platelet-Lymphocyte Ratio). All the parameters were collected within standard laboratory methods. Complete Blood Count was carried out on Sysmex KX-21N (Sysmex Corporation Kobe, Japan), LDH was carried out on Roche analyzer (Roche Cobas 6000 c501, Roche, Mannheim, Germany) while coagulation tests were performed on Sysmex CA-560 (Kobe, Japan). PT and PTT using specific kits (Moshake Biotechnology Company, Wuhan, China) according to the instructions (With ISI = 1.2). CRP qualitative test by using protocol in the Latex kit for C-Reactive protein (RECKON DIAGNOSTICS, INDIA). ESR test was performed on Sedi-System Automation. Oxygen saturation was estimated via pulse oximetry (Nellcor N-600, Nellcor Inc., Hayward, CA).

### *Statistical analysis*

To summarize the gathered data, mean ±SD (standard deviation), as well as count (percent), were used. Two independent sample tests and the Mann-Whitney test were used to compare the interested variables based on the outcome's status such as ICU admission, saturated $PO_2$ ($SPO_2$), and mortality.

Univariate analysis was by the Mann–Whitney rank-sum test for means. Odds ratios (OR) and 95% confidence intervals (CI) were determined by multivariate regression analysis. The multivariate logistic regression analysis was performed to assess variables that are likely to predict patients at risk of progression. The dependent variables were qualitative, ICU admission (yes or no), $PO_2$ saturation (>95% or <95%), and mortality. The predictors included WBCs, ANC, ALC, AMC, RDW, MPV, MCV, LDH, PLT, Hb, PT, PTT, INR, NLR, and PLR. All analyses were done using Stata software version 13 (Stata Corp, College Station, TX, USA). The level of significance for all statistical tests was $P < 0.05$.

## Results

### *Demographic and clinical characteristics of COVID-19 patients*

A total of 859 patients were assessed in our center and tested positive for COVID-19. Four hundred and fifteen patients were excluded from the study due to a lack of clinical and laboratory data. Among all 444 patients, 387 (87.16%) patients had been discharged and 57 (12.83%) of them died during our study see Table 1]. Of the 444 patients, 223 (52.48%) patients were male and 211 (47.52%) were females with a mean age (±SD) of 56.13 ± 17.78 years (range 3-99 years) [see Table 2]. There were 37 (8.33%) patients who had a history of close contact

**Table 1: Demographic characteristics of patients with COVID-19**

| Variables | Frequency | Percentage |
|---|---|---|
| Gender | | |
| Male | 233 | 52.4 |
| Female | 211 | 47.5 |
| Ward; | | |
| Isolated | 21 | 4.7 |
| Usual care | 402 | 90.5 |
| ICU | 21 | 4.7 |
| Contact; | | |
| Yes | 37 | 8.3 |
| No | 407 | 91.6 |
| Clinical manifestations | | |
| Fever | 219 | 49.3 |
| Cough | 167 | 37.6 |
| Myalgia | 76 | 17.1 |
| Respiratory distress | 95 | 21.4 |
| Loss of consciousness | 21 | 4.7 |
| Headache | 296 | 66.6 |
| Weakness | 163 | 36.7 |
| Chest pain | 146 | 32.8 |
| Skin lesions | 80 | 18.0 |
| Abdominal pain | 48 | 10.8 |
| Nausea | 82 | 18.4 |
| Vomiting | 66 | 14.8 |
| Dyspnea | 31 | 6.9 |
| Diarrhea | 126 | 28.3 |
| Anorexia | 240 | 54.0 |
| Comorbidities | | |
| Cardiovascular disease | 17 | 3.8 |
| Diabetes | 38 | 8.5 |
| Chronic disease | 41 | 9.2 |
| Outcome | | |
| Survived | 387 | 87.1 |
| Death | 57 | 12.8 |
| $PO_2$ | | |
| >93% | 409 | 92.1 |
| <93% | 35 | 7.8 |
| ICUs | 21 | 4.7 |
| Yes | 423 | 95.2 |
| No | | |
| CRP | | |
| Neg | 175 | 39.4 |
| Weakly pos. | 108 | 24.3 |
| 1+ | 84 | 18.9 |
| 2+ | 45 | 10.1 |
| 3+ | 32 | 7.2 |

$PO_2$; (Partial pressure of oxygen), ICUs; Intensive care units, CRP; C-Reactive Protein, Pos; positive

with COVID-19 patients. Among all 444 patients, 21 (4.73%) cases were admitted to ICU, 21 (4.73%) in the isolated ward and 402 (90.54%) cases were in the usual care ward.

As shown in Table 1, 296 (66.67%), 240 (54.05%), 219 (49.32%) patients had headaches, anorexia, and fever, respectively. Other clinical findings in order of prevalence were as follows: cough, weakness, chest pain, diarrhea, respiratory distress, and myalgia. Of the 444 patients, 38 (8.56%), 17 (3.83%), and 41 (9.23%) patients had diabetes, cardiovascular disease (CVD), and other chronic diseases, respectively.

**Table 2: Clinical laboratory data of patients with COVID-19**

| Variables | Mean±SD | Min | Max |
|---|---|---|---|
| Age | 56.1±17.7 | 3.0 | 99.0 |
| WBC (×10⁹/L) | 6.2±3.7 | 1.4 | 35.0 |
| ANC (×10⁹/L) | 4.3±3.0 | 0.8 | 26.4 |
| ALC (×10⁹/L) | 1.3±2.1 | 0.1 | 30.0 |
| NLR | 5.4±6.9 | 0.1 | 73.5 |
| AMC (×10⁹/L) | 0.6±2.1 | 0.0 | 38.0 |
| Hb (g/dL) | 13.5±1.8 | 7.9 | 18.1 |
| Plt count (×10⁹/L) | 191.0±76.7 | 17.0 | 543.0 |
| PLR | 209.2±157.9 | 4.5 | 1187.5 |
| RDW-SD (fL) | 42.5±18.6 | 33.3 | 354.0 |
| MPV (fL) | 10.5±0.9 | 8.4 | 13.8 |
| LDH (U/L) | 457.9±280.6 | 82.8 | 289 |
| PT (sec) | 14.2±2.2 | 11.7 | 35.5 |
| PTT (sec) | 39.0±9.7 | 25.0 | 90.0 |
| INR | 1.2±0.3 | 1.0 | 5.0 |
| MCV (fL) | 85.7±6.0 | 55.1 | 111.0 |
| ESR (mm/h) | 33.6±21.7 | 4.0 | 96.0 |

The full description of the abbreviation of variables is given in the materials and methods section, sec; Second.

### *Hematology findings of COVID-19 patients*

Looking at the hematologic parameters, total leukocyte count was significantly higher in patients admitted to ICU than in outpatients (P = 0.002). In addition, patients in ICU had significantly higher mean ANC than other patients (P < 0.001). However, there was a statistically significant difference in the mean ALC between dead and survived patients. (1.8 ± 2.3 vs 0.9 ± 0.5, *P* = 0.015). NLR was not associated with the possibility of ICU admission, $PO_2$ saturation, and case fatality rate (P = 1.000, *P* = 0.436, *P* = 0.083, respectively). On the other hand, patients who died had a significantly higher mean AMC compared to those who survived (0.8 ± 2.3 vs. 0.4 ± 0.2, *P* = 0.009). There was a significant relationship between MCV and the possibility of ICU admission (P = 0.031). PLR was higher among ICU patients than outpatients, although the difference was not significant (256.1 ± 141.5 vs. 206.8 ± 158.6, *P* = 0.06). The mean level of LDH was significantly higher in patients admitted to ICU than in outpatients (P = 0.002). However, mean LDH did not significantly correlate with the mortality rate and $SPO_2$ (P = 0.591 and *P* = 0.281, respectively). Among coagulation parameters, mean PT and the INR were higher in ICU admissions than in outpatients (P = 0.005 and *P* = 0.003, respectively) [Table 3].

Univariate analysis identified the WBC, ANC, ALC, RDW, LDH, and MCV to be positively associated with the admission of Covid-19 patients to the ICU [see Table 4]. The univariate analysis also showed that the ANC was positively associated & the PTT to be negatively associated with PO2 saturation >95% [see

Table 5]. As shown in Table 6, AMC to be negatively associated with mortality (P = 0.014, OR = 0.105, CI95% = 0.017-0.638). Multivariate analysis confirmed the positive association of the WBC (P < 0.001, OR = 1.166, CI95% = 1.064-1.277), ANC (P < 0.004, OR = 1.196, CI95% = 1.051-1.352), RDW (P < 0.001, OR = 1.172, CI95% = 1.072-1.281), and LDH (P = 0.007, OR = 1.002, CI95% = 1.000-1.005) to be positively associated with the admission of Covid-19 patients in the ICU, the PTT (P = 0.039, OR = 0.883, CI95% = 0.784-0.993) to be negatively associated with $PO_2$ saturation >95%, & the AMC (P = 0.012, OR = 0.100, CI95% = 0.066-0.605) to be negatively associated with mortality after adjustment for the confounding variables: age, sex, hospitalization duration [Tables 4-6].

## Discussion

Our study showed that patients admitted to the ICU had higher levels of WBC, ANC, ALC, PLR LDH, PT, INR, and MCV in the evaluation of peripheral blood samples. A higher PTT was associated with increased $PO_2$ saturation. Our study also showed that patients who died from Covid-19 had a lower mean of AMC in peripheral blood samples caused by the recruitment of monocytes to inflammatory tissues.[11] This finding indicates that there is a significant relationship between monocytopenia and increased mortality.

So far, several studies have examined the relationship between hematological parameters and the severity of Covid-19 disease and reported different results.[12,13] Similar results were reported by Pakos *et al.* in patients with Covid-19. In the study of

**Table 3: Comparison of hematologic findings with consideration of admission status in ICU, $PO_2$ saturation, and outcome**

| Variables | ICU admission | | | $PO_2$ saturation | | | Outcome | | |
|---|---|---|---|---|---|---|---|---|---|
| | Yes | No | *P* | >95% | <95% | *P* | Survived | Death | *P* |
| WBC (×10⁹/L) | 11.4±9.2 | 5.9±2.9 | 0.002 | 6.1±3.5 | 7.4±5.2 | 0.058 | 6.3±3.8 | 6.0±2.7 | 0.703 |
| ANC (×10⁹/L) | 8.0±6.3 | 4.1±2.6 | 0.000 | 4.2±2.7 | 5.8±5.2 | 0.044 | 4.3±3.1 | 4.7±2.8 | 0.342 |
| ALC (×10⁹/L) | 2.8±7.7 | 1.2±1.3 | 0.043 | 1.3±2.2 | 1.3±1.0 | 0.817 | 1.8±2.3 | 0.9±0.5 | 0.015 |
| NLR | 5.8±11.9 | 5.0±6.4 | 1.000 | 5.2±6.5 | 7.7±11.0 | 0.436 | 5.2±5.9 | 7.6±12.3 | 0.083 |
| AMC (×10⁹/L) | 0.5±0.3 | 0.6±2.2 | 0.446 | 0.65±2.2 | 0.5±0.2 | 0.867 | 0.8±2.3 | 0.4±0.2 | 0.009 |
| Hb (g/dL) | 12.9±2.1 | 13.5±1.7 | 0.277 | 13.5±1.8 | 13.0±1.7 | 0.145 | 13.4±1.8 | 13.6±1.2 | 0.624 |
| PLT count (×10⁹/L) | 179.4±51.3 | 191.5±77.7 | 0.697 | 191.0±77.4 | 189.9±66.8 | 0.766 | 191.6±75.5 | 180.5±91.8 | 0.137 |
| PLR | 256.1±141.5 | 206.8±158.6 | 0.06 | 210.0±160.7 | 198.1±115.8 | 0.928 | 208.9±154.5 | 225.7±197.8 | 0.769 |
| RDW-SD (fL) | 47.7±6.1 | 42.3±18.9 | 1.000 | 41.3±4.5 | 43.2±7.4 | 0.522 | 41.4±4.9 | 41.4±3.9 | 0.661 |
| MPV (fL) | 10.4±1.0 | 10.5±0.9 | 0.601 | 10.5±1.1 | 10.5±0.8 | 0.929 | 10.5±1.0 | 10.6±1.0 | 0.367 |
| LDH (U/L) | 929.8±779.9 | 433.9±206.6 | 0.002 | 454.1±282.1 | 500.2±266.9 | 0.281 | 465.6±287.9 | 487.3±258.1 | 0.591 |
| PT (Sec to clot) | 15.6±2.5 | 14.1±2.2 | 0.005 | 14.2±2.2 | 14.8±2.2 | 0.375 | 14.2±2.3 | 14.5±1.7 | 0.235 |
| PTT (Sec to clot) | 43.7±16.9 | 38.7±9.0 | 0.525 | 39.4±9.9 | 34.4±5.4 | 0.01 | 38.6±9.1 | 40.3±10.5 | 0.411 |
| INR | 1.41±0.3 | 1.2±0.3 | 0.003 | 1.2±0.3 | 1.2±0.3 | 0.498 | 1.2±0.3 | 1.2±0.2 | 0.427 |
| MCV (fL) | 89.2±6.3 | 81.5±6.0 | 0.031 | 85.7±6.0 | 85.5±6.5 | 0.851 | 85.7±5.9 | 84.9±7.5 | 0.835 |

Data are reported as mean±SD. The full description of the abbreviation of variables is given in the materials and methods section, sec; Second

**Table 4: Multivariate logistic regression showing variables associated with the admission of COVID-19 patients in the ICU including blood parameters**

| Variables | Univariate | | | | Multivariate | | | |
|---|---|---|---|---|---|---|---|---|
| | $Z_{score}$ | SE | *P* | OR (95%CI) | $Z_{score}$ | SE | *P* | OR (95%CI)¶ |
| WBC | 3.92 | 0.05 | 0.000 | 1.196 (1.094-1.301) | 3.29 | 0.54 | 0.001 | 1.166 (1.064-1.277) |
| ANC | 3.74 | 0.72 | 0.000 | 1.244 (1.109-1.395) | 2.88 | 0.74 | 0.004 | 1.196 (1.051-1.352) |
| ALC | 1.98 | 0.65 | 0.047 | 1.122 (1.001-1.260) | 1.95 | 0.67 | 0.051 | 1.125 (0.999-1.265) |
| NLR | -0.10 | 0.10 | 0.897 | 0.704 (0.536-0.987) | -0.10 | 0.20 | 0.974 | 0.698 (0.557-1.002) |
| AMC | -0.11 | 0.16 | 0.909 | 0.980 (0.700-1.373) | -0.11 | 0.24 | 0.914 | 0.972 (0.588-1.607) |
| Hb | -1.33 | 0.11 | 0.183 | 0.826 (0.624-1.093) | -0.53 | 0.15 | 0.593 | 0.915 (0.662-1.265) |
| Plt | -0.60 | 0.00 | 0.550 | 0.997 (0.990-1.005) | -0.027 | 0.00 | 0.789 | 0.998 (0.990-1.006) |
| RDW | 4.36 | 0.48 | 0.000 | 1.194 (1.103-1.293) | 3.48 | 0.53 | 0.000 | 1.172 (1.072-1.281) |
| MPV | -0.17 | 0.25 | 0.866 | 0.955 (0.563-1.620) | -0.40 | 0.25 | 0.688 | 0.890 (0.503-1.572) |
| LDH | 3.18 | 0.00 | 0.001 | 1.004 (1.001-1.005) | 2.71 | 0.00 | 0.007 | 1.002 (1.000-1.005) |
| PT | 1.92 | 0.94 | 0.055 | 1.166 (0.966-1.366) | 1.36 | 0.91 | 0.174 | 1.117 (0.952-1.310) |
| PTT | 1.74 | 0.20 | 0.081 | 1.035 (0.955-1.075) | 1.14 | 0.21 | 0.255 | 1.023 (0.983-1.065) |
| INR | 1.68 | 1.05 | 0.094 | 2.220 (0.873-5.641) | 1.21 | 0.90 | 0.228 | 1.817 (0.688-4.796) |
| MCV | 2.44 | 0.51 | 0.015 | 1.120 (1.022-1.225) | 1.96 | 0.51 | 0.050 | 1.096 (1.000-1.201) |

¶aOR; adjusted odds ratios (adjusted for age, sex, hospitalization duration), OR: Odds ratio; CI: Confidence interval, SE, standard error

**Table 5: Multivariate logistic regression showing variables associated with $PO_2$ saturation <93% including blood parameters**

| Variables | Univariate | | | | Multivariate | | | |
|---|---|---|---|---|---|---|---|---|
| | $Z_{score}$ | SE | *P* | OR (95%CI) | $Z_{score}$ | SE | *P* | OR (95%CI)¶ |
| WBC | 1.07 | 0.04 | 0.123 | 1.069 (0.982-1.163) | 1.33 | 0.04 | 0.182 | 1.060 (0.972-1.156) |
| ANC | 2.15 | 0.06 | 0.032 | 1.120 (1.009-1.242) | 1.91 | 0.06 | 0.056 | 1.111 (0.997-1.238) |
| ALC | -0.04 | 0.11 | 0.964 | 0.995 (0.800-1.236) | -0.02 | 0.10 | 0.982 | 0.997 (0.817-1.217) |
| NLR | -0.11 | 0.21 | 0.701 | 0.665 (0.847-0.908) | -0.10 | 0.22 | 0.921 | 0.717 (0.638-0.957) |
| AMC | -0.19 | 0.56 | 0.846 | 0.882 (0.249-3.120) | -0.24 | 0.67 | 0.813 | 0.823 (0.165-4.104) |
| Hb | -1.21 | 0.10 | 0.225 | 0.861 (0.677-1.096) | -1.12 | 0.11 | 0.262 | 0.861 (0.664-1.177) |
| Plt | -0.07 | 0.00 | 0.948 | 0.999 (0.993-1.005) | 0.03 | 0.00 | 0.979 | 1.000 (0.994-1.005) |
| RDW | 1.69 | 0.04 | 0.090 | 1.067 (0.989-1.152) | 1.44 | 0.04 | 0.149 | 1.059 (0.979-1.147) |
| MPV | -0.08 | 0.22 | 0.933 | 0.981 (0.626-1.536) | -0.09 | 0.22 | 0.932 | 0.980 (0.624-1.539) |
| LDH | 0.64 | 0.00 | 0.521 | 1.000 (0.999-1.001) | 0.23 | 0.00 | 0.817 | 1.000 (0.998-1.001) |
| PT | 0.98 | 0.09 | 0.327 | 1.086 (0.920-1.283) | 1.07 | 0.92 | 0.283 | 1.095 (0.927-1.293) |
| PTT | -02.10 | 0.05 | 0.036 | 0.882 (0.785-0.991) | -2.06 | 0.05 | 0.039 | 0.883 (0.784-0.993) |
| INR | 0.58 | 0.78 | 0.559 | 1.391 (0.459-4.210) | 0.66 | 0.79 | 0.508 | 1.438 (0.489-4.230) |
| MCV | -0.09 | 0.03 | 0.927 | 0.996 (0.927-1.071) | -0.19 | 0.03 | 0.850 | 0.993 (0.924-1.066) |

¶aOR; adjusted odds ratios (adjusted for age, sex, hospitalization duration), OR: Odds ratio; CI: Confidence interval, SE, standard error

**Table 6: Multivariate logistic regression showing variables associated with mortality including blood parameters**

| Variables | Univariate | | | | Multivariate | | | |
|---|---|---|---|---|---|---|---|---|
| | $Z_{score}$ | SE | *P* | OR (95%CI) | $Z_{score}$ | SE | *P* | OR (95%CI)¶ |
| WBC | -0.49 | 0.05 | 0.649 | 0.976 (0.882-1.081) | -0.59 | 0.51 | 0.558 | 0.969 (0.872-1.076) |
| ANC | 0.72 | 0.05 | 0.473 | 1.037 (0.937-1.148) | 0.53 | 0.05 | 0.599 | 1.028 (0.926-1.142) |
| ALC | -1.16 | 0.21 | 0.246 | 0.707 (0.393-1.270) | -1.08 | 0.21 | 0.280 | 0.719 (0.396-1.306) |
| NLR | 0.30 | 0.08 | 0.579 | 0.765 (0.676-0.931) | 0.21 | 0.08 | 0.831 | 0.653 (0.707-1.022) |
| AMC | -2.45 | 0.09 | 0.014 | 0.105 (0.017-0.638) | -2.51 | 0.09 | 0.012 | 0.100 (0.066-0.605) |
| Hb | -1.21 | 0.10 | 0.225 | 0.861 (0.677-1.096) | -1.12 | 0.11 | 0.262 | 0.861 (0.664-1.177) |
| Plt | -0.82 | 0.00 | 0.411 | 0.998 (0.993-1.002) | -0.95 | 0.00 | 0.341 | 0.997 (0.992-1.002) |
| RDW | -0.02 | 0.03 | 0.983 | 0.999 (0.928-1.075) | -0.28 | 0.03 | 0.776 | 0.988 (0.916-1.067) |
| MPV | 0.88 | 0.20 | 0.380 | 1.168 (0.825-1.653) | 0.85 | 0.20 | 0.396 | 1.163 (0.819-1.651) |
| LDH | 0.38 | 0.00 | 0.707 | 1.000 (0.998-1.001) | 0.22 | 0.00 | 0.829 | 1.000 (0.998-1.001) |
| PT | 0.54 | 0.08 | 0.586 | 1.045 (0.891-1.224) | 0.34 | 0.08 | 0.734 | 1.028 (0.874-1.213) |
| PTT | 0.83 | 0.02 | 0.408 | 1.017 (0.977-1.058) | 0.76 | 0.02 | 0.447 | 1.015 (0.975-1.057) |
| INR | 0.21 | 0.61 | 0.836 | 1.120 (0.380-3.305) | 0.02 | 0.58 | 0.987 | 1.009 (0.321-3.170) |
| MCV | -0.74 | 0.02 | 0.461 | 0.979 (0.928-1.034) | -0.78 | 0.02 | 0.434 | 0.978 (0.927-1.032) |

¶aOR; adjusted odds ratios (adjusted for age, sex, hospitalization duration), OR: Odds ratio; CI: Confidence interval, SE, standard error

Pakos *et al*.[12] an inverse relationship was observed between the mean AMC and mortality in patients who died due to Covid-19. However, in contrast to our result, Qin *et al*.[14] in a recently published study reported that there was no statistically significant relationship between AMC and disease severity. One of the reasons for the differences in the reported results is due to ethnic differences.

Liao *et al*.[15] reported that mononuclear phagocytes were found in large quantities in the severely damaged lungs of patients with severe forms of the disease, indicating that they migrated from the peripheral blood to the damaged tissues.

Urbano *et al*.[16] proposed that patients with WBCs elevation, neutrophil elevation, lymphocyte decrease or platelet count increase during the hospital stay are more likely to end up in the ICU. In one study it was shown that 24.2% and 35.6% of patients with Covid-19 had leukopenia and lymphopenia, respectively. Their study also showed that 13.4% and 22.8% of patients had lower than normal range platelet counts and neutrophil counts, respectively.[13] In another study by Qin *et al*.[14] patients with severe Covid-19 had higher total WBCs counts and a higher percentage of neutrophils in line with our study but a lower percentage of monocytes at the same time consistent with our study findings. Another study from Einstein Medical Center Philadelphia, Pennsylvania by Pakos *et al*.[12] showed that patients with Covid-19 who died had lower levels of AMC and platelets in peripheral blood samples, which was the same as our study. Their study also showed that a higher NLR was associated with increased mortality. Yang X *et al*. also reported that a higher NLR was associated with a higher risk of mortality.[17]

Similarly, in our study, a higher tendency for NLR was evident in dead patients. Severe activation of the primary immune

system, especially neutrophils, can trigger an inflammatory response that is potentially associated with a poor prognosis.

A higher mean ALC was observed in patients admitted to the ICU, while there was a significant difference in the mean ALC values of dead and survived patients in this study so that the dead patients had lymphopenia relative to the surviving patients at the time of death caused by necrosis of lymphocytes in the spleen and lymph nodes due to IL6 production by virus-stimulated macrophages.[11] In a study, Feng *et al*.[11] reported that the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus and the spike protein, can trigger macrophages to secrete IL-6, which may accelerate lymphopenia. Other causes of lymphocytopenia in dead patients include the recruitment of lymphocytes to inflammatory tissues and severe lymphocyte apoptosis.[11] Similarly, Pakos *et al*.[12] reported that dead patients with Covid-19 had lymphocytopenia.

The current study revealed that headache (66.6%), and anorexia (54.0%) was the most common symptoms, whereas loss of consciousness (4.7%), and abdominal pain (10.8) were rare. In a study, Yang *et al*.[13] reported that fever (76.5%), cough (58.4%), and expectoration (32.2%) were the most common symptoms compared with 49.3% and 37.6% in our study, respectively, whereas vomiting (1.3%), and dyspnea (1.3%) were rare compared with 14.8% and 6.9% in our study, respectively.

Fifty-one patients (11.5%) had thrombocytopenia in this study, which was somewhat similar to that of Yang *et al*.[13] In this study, there was no significant difference in platelet count of dead and recovered patients, but Yang *et al*.[17] reported a significant association between thrombocytopenia and increased mortality, while another study showed a negative correlation between platelet count and mortality.[18] Yang *et al*.[17] also showed that 55.6% of patients had higher than normal range CRP compared with 60.5% in our study.

In summary, identifying risk factors associated with increased patient admission to the ICU as well as mortality is one of the most important aspects of Covid-19 disease management in medical centers. Severe activation of the primary immune system, especially neutrophils, in ICU patients is likely to elicit a severe inflammatory response, followed by the migration of monocytes and lymphocytes to the site of inflammation, leading to lymphopenia and monocytopenia in dead patients. Due to the increase in the number of patients referred to medical centers at the peak of the disease, the lack of hospital beds, and the importance of oxygen therapy in patients, it is very important to predict the progression of the disease. Based on the results of our study, it is recommended to use hematological data to make clinical decisions and evaluate the patient's prognosis.

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### Conflicts of interest

There are no conflicts of interest.

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