Correlation of Complete Blood Count Parameters and Ferritin Levels at the Time of Diagnosis with the Prognosis of Patients Hospitalized Due to Covid 19

Rafiye Çiftçiler[1], Ali Erdinc Ciftciler[1], and adnan batman[1]

[1]Aksaray Universitesi

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Abstract

Background and Aim:The novel coronavirus (SARS-CoV-2) that causes novel coronavirus pneumonia (COVID-19) is the third fatal coronavirus. The prognosis of disease varies depending on patient's specialties. The aim of this study was to evaluate the correlation of CBC parameters and ferritin levels at the time of diagnosis with the prognosis of patients hospitalized due to COVID 19. Materials and Methods: In this retrospective study, 1320 patients hospitalized at the Aksaray University Training and Research Hospital between July 2020 and December 2020 were evaluated. Results: All of the patients were hospitalized because of symptoms associated with COVID 19. There were 688 males and 632 females with a median age of 70 (19-98) at the time of hospitalization with COVID 19 symptoms. The median follow-up time was 7 (range, 1-57) days in hospital for all patients. Median age was significantly higher in patients who do not respond to treatment and have mortality ($p<0.001$). Most of the patients with mortality were males ($p=0.001$). There was a statistically significant difference in the parameters other than monocyte and basophil among the hemogram parameters checked at the time of presentation. Neutrophil / lymphocyte ratio was significantly higher in patients with mortality ($p<0.001$). Conclusion: In conclusion, this study indicates that by using the most simple and routine hematological tests at the time of COVID-19 diagnosis, it may be possible to predict a patient's prognosis. This will help patients receive early clinical care, reducing patient mortality and aiding in the control and prevention of the outbreak.

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Materials and Methods: In this retrospective study, 1320 patients hospitalized at the Aksaray University Training and Research Hospital between July 2020 and December 2020 were evaluated.

Results: All of the patients were hospitalized because of symptoms associated with COVID 19. There were 688 males and 632 females with a median age of 70 (19-98) at the time of hospitalization with COVID 19 symptoms. The median follow-up time was 7 (range, 1-57) days in hospital for all patients. Median age was significantly higher in patients who do not respond to treatment and have mortality ($p<0.001$). Most of the patients with mortality were males ($p=0.001$). There was a statistically significant difference in the parameters other than monocyte and basophil among the hemogram parameters checked at the time of presentation. Neutrophil / lymphocyte ratio was significantly higher in patients with mortality ($p<0.001$).

Conclusion: In conclusion, this study indicates that by using the most simple and routine hematological tests at the time of COVID-19 diagnosis, it may be possible to predict a patient's prognosis. This will help patients receive early clinical care, reducing patient mortality and aiding in the control and prevention of the outbreak.

Keywords: COVID-19, novel coronavirus, complete blood counts, ferritin, prognosis

What is already known about this topic?

*The prognosis of the disease varies depending on patient specialties.

*It has been shown that the total number of peripheral white blood cells is normal or the number of lymphocytes is decreased in patients in the early stage of COVID-19.

* Lymphocyte percent was inversely linked to patient severity and prognosis, and could be used to predict COVID-19 patient's severity and prognosis

What does this article add?

*The majority of patients who did not respond to treatment and had mortality were males. In patients who responded to the treatment and could be discharged, the duration of hospitalization was observed to be longer in women..

*Multiple laboratory parameters can be related to the severity and mortality of COVID-19 infection and should be screened and assessed on a regular basis as the pandemic progresses. WBC count, neutrophil, lymphocytes, NLR, eosinophil, platelet count, ferritin, ALT, urea, uric acid, CK, albumin, D-dimer, and LDH were among the parameters tested.

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Introduction

The novel coronavirus (SARS-CoV-2) that causes novel coronavirus pneumonia (COVID-19) is the third fatal coronavirus. It first emerged in December 2019 in China(1). The most common symptoms are fever, dry cough, and exhaustion. Dyspnea and/or hypoxemia are common 1 week after the onset of symptoms in severe patients. Acute respiratory distress syndrome (ARDS), septic shock, difficult-to-correct metabolic acidosis, coagulation deficiency, and multiple organ failure can all occur rapidly in serious cases (2, 3). Patients with mild clinical manifestations do not require hospitalization at first, but they may develop respiratory symptoms by the second week, so all patients should be closely monitored(4). According to the World Health Organization (WHO), approximately 80 percent of sick people have mild to moderate infections (including those with or without pneumonia), 13.8 percent have serious infections, and 6.1 percent have critical illness (4). The prognosis of the disease varies depending on patient specialties. As a result, identifying and diagnosing serious or critical patients is important. Hematological analysis is the most commonly conducted procedure in clinics, and complete blood count (CBC) findings are the first things that physicians want to see in nearly all labs, outpatient and inpatient clinics. In the current novel coronavirus pandemic, it would be very helpful for clinicians to make a rational allocation of medical resources if the most routine and affordable laboratory tests can be used to provide clinicians with convenient assistance in assessing the patient's condition. Early clinical intervention is expected to minimize patient mortality(4). It has been shown that the total number of peripheral white blood cells is normal or the number of lymphocytes is decreased in patients in the early stage of COVID-19. Tan et al. reported that Lymphocyte percent was inversely linked to patient severity and prognosis, and could be used to predict COVID-19 patient's severity and prognosis (5). This means that patients with SARS-CoV-2 infections will experience changes in their peripheral blood. These adjustments can hold clues or provide guidance for COVID-19 patients' diagnosis, care, and prognosis. The aim of this study was to correlate CBC parameters and ferritin levels at the time of diagnosis with the prognosis of patients hospitalized due to Covid-19.

Materials and Methods

Patients

In this retrospective study, 1320 patients hospitalized at the Aksaray University Training and Research Hospital between July 2020 and December 2020 were evaluated. Recommended criteria established by the Scientific Committee of the Ministry of Health were used in the selection of definite COVID-19 patients (6). The diagnosis of COVID-19 was made according to the guidelines of Ministry of Health of Turkey and confirmed by real time polymerase chain reactions (RT-PCR) performed on respiratory samples of the patient(6). All of the cases included in the study were patients with moderate and severe symptoms and in need of hospitalization. Patients who had acute respiratory tract infection in the last 14 days were hospitalized and followed up in case of severe infection, fever, cough, dyspnea, tachypnea, hypoxemia, hypotension, diffuse radiological findings on lung imaging or change in consciousness (6). Patients who had missing hematological results, transfers to other medical facilities with uncertain outcomes, and patients under 18 years of age were excluded from the study.

Data collection

The date of admission, demographic data of the patients, clinical status and hematological findings at the time of admission, and clinical course of the patients were obtained from the patient files and hospital database. As a result of application standards of the hospitals of Aksaray University Training and Research Hospital, it has been recognized from the patient records that all of the studied patients had given informed consents at the time of hospitalization and before the administration of relevant diagnostic/therapeutic standards of care. Patients gave informed consent for the procedure. Permission of the study was obtained from T.C. Ministry of Health General Directorate of Health Services with the number of 2020-08-27T14_49_14.

Statistical analyses

Statistical analyses were performed using the SPSS software version 25. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorow-Simirnov/Shapiro-Wilk's test) to determine whether they are normally distributed or not. Descriptive analyses were presented using means and standard deviations for normally distributed variables. Comparisons were made using the t test, chi-square test, Fisher's exact test, and analysis of variance. Variables that are found to be significant ($p < 0.05$) in univariate analysis were tested in multivariate analysis, which was performed using a stepwise logistic regression model. Values of $p < 0.05$ were considered statistically significant. Survival analyses were made using Kaplan-Meier test.

Results

General Characteristics of hospitalized COVID-19 Patients

A total of 1320 patients who were hospitalized between July 2020 and December 2020 were included in the study. All of the patients were hospitalized because of symptoms associated with COVID 19. There were 632 (52.1%) males and 688 (47.9%) females with a median age of 70 (19-98) at the time of hospitalization because of COVID 19 symptoms. The median follow-up time was 7 (range, 1-57) days in hospital for all patients (Figure 1). 1054 patients (79.8%) were followed-up in COVID 19 clinics. 1035 of these patients (78.4%) were discharged from the service after their treatment in the service was finished and recovered. Nineteen of these patients (1.4%) died while being followed in the service. Two-hundred sixty-six patients (20.2%) needed follow-up in intensive care unit at the time of admission or follow-up. Patients who needed intensive care unit during treatment period were referred to the intensive care unit at a median of 3 (0-21) days. Seventy-five of these patients (5.7%) needed an intensive care unit on the day which they admitted to the hospital. Mortality was observed in 270 (20.5%) of all these patients who were hospitalized and followed up. Median time for admission o intensive care unit was 3 (0-21) days for patients who needed intensive care follow-up.

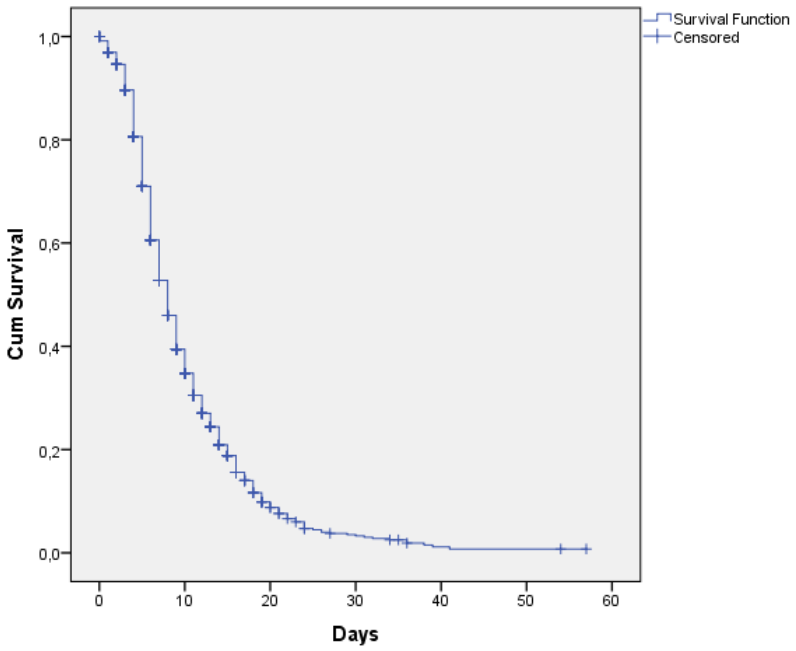

Figure 1. Follow-up time for all hospitalized patients (day)

Hematological findings of COVID-19 patients at the time of admission

The comparison of hematological parameters at the time of admission of patients who respond to treatment and can be discharged and patients who do not respond to treatment and have mortality were depicted in table 1. Median age was significantly higher in patients who do not respond to treatment and have mortality ($p<0.001$). Most of the patients with mortality were males ($p=0.001$). There was a statistically significant difference in the parameters other than monocyte and basophil among the hemogram parameters checked at the time of presentation. Neutrophil / lymphocyte ratio was significantly higher in patients with mortality ($p<0.001$). In addition, when we evaluated ferritin ($p<0.001$), D-dimer ($p<0.001$) and lactate dehydrogenase (LDH) ($p<0.001$), among other parameters, mortality was found to be significantly higher in both parameters at the time of admission to hospital. Among the other biochemical parameters of the patients, alanine aminotransferase (ALT), creatine kinase (CK), urea and uric acid were found to be statistically significantly higher at the time of admission to the hospital in patients with mortality, while albumin was found to be statistically significantly lower ($p<0.001$).

Table 1. The comparison of laboratory parameters at the time of admission for all hospitalized patients

Parameters	Normal range	Patients who respond to treatment and can be discharged	Pa
Number		1050 (79.5%)	270
Age (median, range)		71 (19-98)	75
Gender (male/female)		478/572 (45.5%/54.5%)	154
Hemoglobin, (gr/dl)	11-16gr/dl	12.7 (6.5-19.7)	12.
Mean corpuscular volume (femtolitre, fL)	80-100	87.3 (63.3-104.9)	90.
Platelet count, $\times 10^9$/L	100-400	263(45-834)	187
Mean platelet volume, (femtolitre, fL)	6.5-12	9.7 (6.6-14.7)	11
Leukocyte count, $\times 10^9$/L	4-10	7.2(1.2-85.8)	13.

Parameters	Normal range	Patients who respond to treatment and can be discharged	Pa
Neutrophil count, $\times 10^9$/L	2-7	5.47 (0.74-31.2)	12.
Lymphocyte count, $\times 10^9$/L	0.80-4	1.16(0.17-77.2)	0.5
Neutrophil-to-lymphocyte ratio		4.6 (0.09-94.6)	23.
Monocyte count, x10^9/L	0.12-1.20	0.48 (0.02-1.46)	0.4
Eosinophil count, x10^9/L	0.02-0.50	0.02 (0-1.43)	0.0
Basophile count, x10^9/L	0-0.10	0.01(0-0.13)	0(0
Alanine aminotransferase (ALT) (U/L)	0-50	27.8 (1.7-1866)	28.
Urea (mg/dl)	12-43	44 (9-276)	125
Uric acid (mg/dl)	2.6-6.5	5.1 (1.40-12.8)	7.1
Creatinine kinase (U/L)	0-170	34 (1-2491)	95
Albumin (g/L)	35-52	31.6 (11.5-46.0)	24.
D-dimer(ng/ml)	<500	821 (138-64700)	362
Ferritin level(ng/mL)	23-336	249(7.9-2105)	958
Lactate dehydrogenase level (U/L)	0-248	278 (110-12444)	564

Clinical Course of COVID-19 Patients according to hematological findings

A total of 1050 (79.5%) patients recovered during follow-up and were discharged. Median follow-up time was 7 (1-41) days for those patients in hospital. Five hundred and five (48.1%) of these patients were able to be discharged in less than 7 days. Five hundred and forty-five patients (51.9%) were followed up in the hospital for 7 or more days and were discharged after a maximum of 41 days. Median age was statistically significantly higher in patients who stayed longer in the hospital (p=0.001). The majority of the patients who were hospitalized for shorter periods consisted of women, while the proportions of both sexes were almost equal in longer hospitalization periods. The hemoglobin and thrombocyte level at the time of admission were statistically significantly higher in patients who were discharged in <7 days than in patients who were discharged in [?]7 days. The leukocyte, neutrophil, monocyte, eosinophile, basophile and ferritin values at the time of admission were statistically significantly lower in patients who were discharged in <7 days than in patients who were discharged in [?]7 days (Table 2).

After univariate analysis, among the factors that had p value <0.05 were taken to multivariate analysis. In multivariate analysis, age (p<0.001) and platelet counts (p=0.001) at the admission time were found to be independent factors related with hospitalization for a longer period of time.

Table 2. The comparison of hematological parameters of patients at the time of admission according to hospitalization time

Parameters	Normal range	Patients who were discharged <7 days	Patients who were disc
Number		505 (48.1%)	545 (51.9%)
Age (median, range)		70 (19-98)	71 (30-96)
Gender (male/female)		209/296 (41.4%/58.6%)	269/276 (49.4%/50.6%
Hemoglobin, (gr/dl)	11-16gr/dl	12.9 (7.2-17.5)	12.5 (6.5-19.7)
Mean corpuscular volume (femtolitre, fL)	80-100	87 (64-103)	87.7 (63.7-104.9)
Platelet count, $\times 10^9$/L	100-400	247 (55-763)	179 (48-834)
Mean platelet volume, (femtolitre, fL)	6.5-12	9.9 (6.6-14.7)	9.7 (7.3-13.1)
Leukocyte count, $\times 10^9$/L	4-10	6.7 (1.9-37.6)	7.7 (1.2-85.8)
Neutrophil count, $\times 10^9$/L	2-7	4.8 (1.1-31.2)	5.9 (0.74-21.5)
Lymphocyte count, $\times 10^9$/L	0.80-4	1.1 (0.2-28.9)	1.1 (0.17-77.2)
Neutrophil-to-lymphocyte ratio		4.1 (0.28-94.6)	5 (0.09-73.2)
Monocyte count, x10^9/L	0.12-1.20	0.46 (0.05-1.32)	0.51 (0.02-1.46)
Eosinophil count, x10^9/L	0.02-0.50	0.01 (0-1.43)	0.03 (0-0.75)

Parameters	Normal range	Patients who were discharged <7 days	Patients who were disc
Basophile count, x10^9/L	0-0.10	0.01 (0-0.1)	0.01 (0-0.13)
Ferritin level (ng/mL)	23-336	217.9 (7.9-2105)	273 (8.9-1500)

Discussion

In the last one year, the prevalence of COVID-19 infection has increased on a daily basis among all over the world. As a result, determining the severity and mortality of the disease is necessary in order to minimize the pandemic's spread. Many studies have identified clinical features of COVID-19 patients, including epidemiological, clinical, laboratory, radiological, and treatment results. Laboratory findings at the time of admission to hospital were shown as important differences between severe and non-severe patients. In addition, the role of several laboratory parameters in the evaluation of the disease severity of COVID-19 in hospitalization has been revealed in some previous studies. (3, 7-9). In this study, our aim was to evaluate whether hematological parameters and ferritin level predicted the mortality of patients and whether they had an effect on the duration of hospitalization in patients treated by hospitalization.

It has been stated that as the age of infected patients rises, so does the mortality rate, with the crude mortality rate in people over 80 years old being 21.9 percent (4). Multivariate analysis showed that old age and high concentration of LDH were independent predictors of poor prognosis in a retrospective study (10). As a consequence, identifying and diagnosing serious or critical patients is vital. This study showed that the patients' median age was 70 years, with a range of 19 to 98 years. In a study comparing moderate and severe patient groups, no significant difference was found in terms of gender (4). It was observed that the number of female patients hospitalized was higher than the number of male patients in this study. However, the majority of patients who did not respond to treatment and had mortality were males. In patients who responded to the treatment and could be discharged, the duration of hospitalization was observed to be longer in women.

According to a meta-analysis report, COVID-19 severity is associated with higher WBC counts and lower lymphocyte, CD4+ T cell, and CD8+ T cell counts in COVID-19 patients. (11). The decrease in lymphocyte count appears to be directly proportional to the severity of COVID-19 infection. Wang et al. reported that leukocyte, neutrophil, NLR, platelet-to-lymphocyte ratio in the severe group were significantly higher than those in the moderate group; additionally the study reported that lymphocyte, eosinophile, and hemoglobin in the severe group were significantly lower than those in the moderate group (4). In our study, leukocyte, neutrophil and NLR levels were found to be statistically significantly higher in patients with mortality. At the same time, hemoglobin, lymphocyte, eosinophil and albumin levels were found to be statistically significantly lower in patients with mortality. This may be due to long-term infection and hypoxia, which allows the bone marrow to compensate by producing more granulocytes. SARS-CoV-2 can continue to invade more lymphocytes, proliferate, and cause lymphocytes to die or become exhausted when they enter the spleen and other immune organs, resulting in severe lymphopenia in patients with mortality (4). Fan et al. reported that mild thrombocytopenia and leukopenia were found in some COVID-19 positive patients at first admission. Additionally, they showed that on admission; older age, lymphopenia and raised LDH were associated with intensive care unit admissions (12). In previous years Xu et al. reported that thrombocyte counts are substantially low in pneumonia patients, and this drop is directly proportional to the patients' clinical status(13).

Henry et al. reported that both serious and fatal COVID-19 patients had elevated biomarkers of cardiac and muscle damage. Patients who deceased due to disease had substantially elevated cardiac troponin levels at the time of diagnosis. When these results are coupled with substantial elevations in liver enzymes (alanine aminotransferase and aspartate aminotransferase), renal biomarkers (blood urea nitrogen, creatinine), and coagulation steps, an image of multiorgan failure appears in patients who experience the extreme type of the disease. In one study, increased serum ferritin levels were reported among patients who did not survive compared with patients who survived(14). This important result was also observed in another meta-analysis

study among severe and non-survival patients with COVID-19 infection(15). Similarly, in our study, ferritin values were found to be significantly higher in patients with mortality on admission to the hospital. Among other biochemical parameters evaluated during hospital admission, ALT, urea, uric acid, CK, D-dimer and LDH were found to be statistically significantly higher in patients with mortality. On the other hand, it was observed that the albumin value at admission in these patients was statistically significantly lower than the patients who were discharged.

Our study had some limitations. First, this study was retrospective. Second all patients included in the study consisted of patients who were hospitalized due to their symptoms. Outpatients with mild symptoms were not included in the study and blood values were not known at the time of diagnosis. However, in this study, it has seen that it is important to associate the onset of symptoms (days of illness) with hematological parameters. In conclusion, multiple laboratory parameters can be related to the severity and mortality of COVID-19 infection and should be screened and assessed on a regular basis as the pandemic progresses. WBC count, neutrophil, lymphocytes, NLR, eosinophil, platelet count, ferritin, ALT, urea, uric acid, CK, albumin, D-dimer, and LDH were among the parameters tested. This study indicates that by using the most simple and routine hematological tests at the time of COVID-19 diagnosis, it may be possible to predict a patient's prognosis. This will help patients receive early clinical care, reducing patient mortality and aiding in the control and prevention of the outbreak.

Conflict of Interests

The authors of this paper have no conflict of interests, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Role of the funding source

None.

Informed consent statement

Informed consent for the procedure was obtained from blood donors for this study.

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