Research Article

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Early creatinine and e-GFR changes as prognostic predictors of COVID-19 patients

COVID-19 hastalarının prognostik belirleyicileri olarak erken dönem kreatinin ve eGFR değişiklikleri

Abstract

Objectives: We aimed to investigate the effects of the COVID-19 disease on kidney functions and early prognosis.

Methods: All cases were divided into those discharged and exitus cases. The patients were diagnosed with acute kidney injury (AKI) according to the KDIGO criteria.

Results: As a result of the ROC analysis, the patients with a creatinine value above 1.05 for day 1 and 0.975 for creatinine value on day 7 would be mortal (AUC values of 0.641 (0.569–0.714) and 0.757 (0.689–0.825), respectively). As a result of Univariate analysis; D-Dimer, Procalcitonin, BUN and creatinine values are risk factors and a one-unit increase in these values is 1.184; 1.105; It was determined that it would increase 1.024 and 1.304 times (p values 0.008; 0.007; <0.001; 0.002), respectively. Decreased in e-GFR value would increase the risk of death 1.026 (1/0.975) times (p<0.001).

Conclusions: We observed the high creatinine, D-dimer, procalcitonin, ferritin, and low e-GFR levels were risk factors for severity and mortality for COVID-19 disease. While physicians and all stakeholders focus on the prognosis and mortality of the disease of COVID-19 disease, it is necessary to be thorough about kidney involvement as much as respiratory system involvement.

Keywords: COVID-19 disease; early prognosis; kidney involvement; laboratory parameters; mortality.

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In this study, we aimed to investigate the effects of the COVID-19 on kidney functions and early prognosis.

Materials and methods

After our study was approved by the Clinical Research Board established for the COVID-19 pandemic from the Ministry of Health of the Republic of Turkey, the use of data was obtained from the Ordu Provincial Health Directorate Public Health unit and the local ethics committee approval was applied. To that end, with decision number 2020/98, ethical approval was obtained from Ordu University Clinical Research Ethics Committee. Patients hospitalized in the pandemic service and/or intensive care units of Training and Research Hospital of Ordu University between 15.03.2020 and 10.03.2021 and taking a definite diagnosis of COVID-19 in line with the COVID-19 scientific committee diagnostic guide of the Ministry of Health were included in our retrospective and single-center study.

The blood urea nitrogen (BUN), creatinine, estimated glomerular filtration rate (e-GFR), sodium, potassium, calcium, albumin, uric acid, procalcitonin, ferritin, D-dimer, CRP, hemoglobin, and blood gas values of 431 patients diagnosed with COVID-19 who were registered in the 'SARUS Software' system in our hospital were recorded from the 1st and 7th days of their hospitalization. The anti-hypertensive drug uses of the patients and the drugs they used for the treatment of COVID-19 were recorded.

In terms of kidney involvement and mortality of COVID-19, the laboratory parameters of the cases were evaluated whether if they were risk factors or not. All cases were divided into two as those who were discharged and exits. The diagnosis of acute kidney injury (AKI) was made according to KDIGO criteria. An increase of 0.3 mg/dl in serum creatinine in the last 48 hr or a 1.5-fold increase in 7 days was accepted as acute kidney injury. In patients who did not have baseline creatinine at the time of admission to the hospital, the e-GFR value was taken as 75% [7]. The Modification of Diet in Renal Disease (MDRD) study was used to measure e-GFR [8].

The criteria for inclusion in our study were as follows; in line with the COVID-19 diagnostic guide of the Ministry of Health, those who were diagnosed with COVID-19, over the age of 18, with sufficient data, all cases followed in both the pandemic wards and the intensive care unit were included. Cases under the age of 18, not diagnosed with COVID-19, and not having sufficient filed data were excluded from the study.

Statistical analysis

Data were analyzed with IBM SPSS V23. Conformity to normal distribution was evaluated with the Kolmogorov-Smirnov test. Correlations between quantitative data were assessed using the Spearman test. Chi-square and Fisher’s Exact tests were used to compare categorical variables according to groups. The Mann-Whitney U test was used to compare non-normally distributed data according to paired groups, and the independent two-sample t-test was used to compare normally

Introduction

Twenty seven cases of clinical symptoms of dry cough, shortness of breath, fever, and bilateral lung infiltrate presenting with pneumonia of unknown etiology were identified in Wuhan City (Hubei Province, China) in December 2019 [1]. The disease was called COVID-19 by the World Health Organization (WHO) in February 2020 [2]. Thus far, most of the patients infected with COVID-19 have developed mild symptoms such as dry cough, sore throat, and fever. Most cases healed spontaneously, but some developed various fatal complications such as organ failure, septic shock, pulmonary edema, severe pneumonia, and acute respiratory distress syndrome [3].

Viral infection-related kidney diseases are an emerging public health problem in both developing and developed countries. Many novel viruses have emerged with new paradigms of kidney injury, either directly through their cytopathic effects or indirectly through immune-mediated glomerulopathy, tubulointerstitial disease, and acute kidney injury as part of multi-organ failure. It shows that viruses infect the kidneys by making anatomical and functional changes and sometimes continue as chronic kidney infections [4, 5]. After the infection in the lung, the COVID-19 virus can transmit into the blood, accumulate in the kidney and damage the settled kidney cells. Indeed, COVID-19 RNA was found in the plasma of 15% of patients by real-time polymerase chain reaction [6]. In previous outbreaks of the coronavirus family (Coronaviridae), acute kidney injury (AKI) was observed in 6.7% of SARS patients and the mortality of those with AKI was reported to be 91.7%. In other words, AKI is rare in SARS but carries a high mortality. AKI is mostly seen in patients with acute respiratory distress syndrome (ARDS) or multi-organ failure [6].
distributed data. Wilcoxon test was used to compare the data that was not normally distributed according to time within the group, and paired two-sample t-test was used to compare the normally distributed data. ROC analysis was used to determine the cutoff values of the exitus state. Risk factors affecting mortality were evaluated with binary logistic regression analysis. Analysis results for quantitative data mean ± standard deviation and median (minimum – maximum) and categorical data were presented as frequency (percentage). Significance level was taken as p<0.050.

## Results

Demographic data of drug use history of inpatients in the pandemic service and intensive care units in our hospital between March 15, 2020, and March 10, 2021, are presented in Table 1.

Statistically, there is a significant difference between the distributions of pneumonia status between those who were discharged and exitus (p=0.007). Pneumonia was detected in 92.6% of those who were discharged and 100% of those who were exitus. Statistically, there is a significant difference between the distributions of the departments according to those who were discharged and exitus (p<0.001). 63.4% of those who were discharged were in the pandemic department and 82.7% of those who were exitus were in the ICU department. Statistically, there is no significant difference between the distributions of other conditions according to the groups (p>0.050).

The average age of the patients is listed in Table 2.

The comparison of the 1st day and 7th day laboratory values of the cases was presented in Table 3.

The medians of D-dimer; procalcitonine; BUN; creatinine; e-GFR values on the 1st day and 7th day differ from those with externe and exitus (p<0.001, p<0.001, p<0.002, p<0.001, p<0.001, p<0.001, p<0.001, p<0.001).

### Table 1: Comparison of categorical variables by groups.

|                | Discharged | Exitus | Total | Test statistic | p-Value |
|----------------|------------|--------|-------|----------------|---------|
| Gender         |            |        |       |                |         |
| Female         | 142 (40.6) | 35 (43.2) | 177 (41.1) | χ²=0.189 | 0.664  |
| Male           | 208 (59.4) | 46 (56.8) | 254 (58.9) |           |         |
| Drugs          |            |        |       |                |         |
| Not using      | 280 (80)   | 66 (81.5) | 346 (80.3) | χ²=0.863 | 0.834  |
| ACE inhibitors | 42 (12)    | 8 (9.9)  | 50 (11.6)  |           |         |
| ARBs           | 8 (2.3)    | 3 (3.7)  | 11 (2.6)   |           |         |
| Others         | 20 (5.7)   | 4 (4.9)  | 24 (5.6)   |           |         |
| Drug           |            |        |       |                |         |
| No drug        | 3 (0.9)    | 1 (1.2)  | 4 (0.9)    | χ²=2.992 | 0.393  |
| Hydroxychloroquine | 11 (3.1) | 1 (1.2)  | 12 (2.8)   |           |         |
| Favipiravir    | 291 (83.1) | 73 (90.1) | 364 (84.5) |           |         |
| Hydroxychloroquine + favipiravir | 45 (12.9) | 6 (7.4)  | 51 (11.8)  |           |         |
| Diagnosis      |            |        |       |                |         |
| PCR positive   | 330 (94.3) | 80 (98.8) | 410 (95.1) | –          | 0.147f |
| Compatible CT findings | 20 (5.7) | 1 (1.2)  | 21 (4.9)   |           |         |
| Pneumonia      |            |        |       |                |         |
| Absent         | 26 (7.4)   | 0 (0)   | 26 (6)    | –          | 0.007f |
| Present        | 324 (92.6) | 81 (100) | 405 (94)  |           |         |
| Department     |            |        |       |                |         |
| Pandemic department | 222 (63.4) | 14 (17.3) | 236 (54.8) | χ²=56.536 | <0.001 |
| ICU            | 128 (36.6) | 67 (82.7) | 195 (45.2) |           |         |

χ², Chi-square test statistic; F, Fisher’s Exact test; ICU, Intensive Care Unit; ACE inhibitors, angiotensin-converting enzyme inhibitors; ARBs, angiotensin II receptor blockers.

### Table 2: Comparison of the mean age of the patients according to the groups.

| Outcome | Mean ± s. deviation | Median (min.–max.) | Test statistic | p-Value |
|---------|---------------------|--------------------|----------------|---------|
| Discharged | 62.97 ± 16.30 | 65.00 (18.00–94.00) | U=6,888.0 | <0.001 |
| Exitus   | 77.21 ± 11.31 | 78.00 (52.00–101.00) |             |         |
| Total    | 65.65 ± 16.44 | 67.00 (18.00–101.00) |             |         |

U, Mann-Whitney U test statistic.
Table 3: Comparison of laboratory parameters between and within groups.

| Parameter                  | Exteme | Exitus   | p-Value* |
|----------------------------|--------|----------|----------|
| Ddimer_{1st day}           | 0.38   | 0.72     | <0.001   |
| Ddimer_{7th day}           | 0.48   | 2.07     | <0.001   |
| p                          | 0.663^b| <0.001^b|          |
| Procalcitonine_{1st day}   | 0.09   | 0.31     | <0.001   |
| Procalcitonine_{7th day}   | 0.07   | 0.56     | <0.001   |
| p                          | <0.001^b| 0.002^c|          |
| BUN_{1st day}              | 16.90  | 26.30    | <0.001   |
| BUN_{7th day}              | 19.60  | 49.50    | <0.001   |
| p                          | <0.001^b| <0.001^b|          |
| Creatinine_{1st day}       | 0.92   | 1.25     | <0.001   |
| Creatinine_{7th day}       | 0.79   | 1.68     | <0.001   |
| p                          | <0.001^b| 0.026^c|          |
| EGFR_{1st day}             | 80.26  | 51.07    | <0.001   |
| EGFR_{7th day}             | 90.61  | 39.76    | <0.001   |
| p                          | <0.001^b| 0.038^d|          |
| CRP_{1st day}              | 4.58   | 6.34     | 0.008^a  |
| CRP_{7th day}              | 1.41   | 10.32    | <0.001^a |
| p                          | <0.001^b| 0.022^e|          |
| Albumin_{1st day}          | 3.62 ± 0.58 | 3.09 ± 0.57 | <0.001^c |
| Albumin_{7th day}          | 3.42 ± 0.58 | 2.64 ± 0.66 | <0.001^c |
| p                          | 0.022^f| <0.001^f|          |
| WBC_{1st day}              | 6,980.00 (1,640.00–33,580.00) | 6910.00 (450.00–80,820.00) | 0.588 |
| WBC_{7th day}              | 8,505.00 (2,010.00–29,430.00) | 13,260.00 (1,020.00–83,470.00) | <0.001 |
| p                          | <0.001^f| <0.001^f|          |
| Neutrophil_{1st day}       | 4.63 (1.26–26.74) | 4.58 (0.13–38.62) | 0.994 |
| Neutrophil_{7th day}       | 6.28 (1.28–28.61) | 12.07 (0.34–58.44) | <0.001 |
| p                          | <0.001^f| <0.001^f|          |
| Lymphocyte_{1st day}       | 1.25 (0.16–8.54) | 0.95 (0.17–10.11) | 0.007 |
| Lymphocyte_{7th day}       | 1.35 (0.16–16.90) | 0.56 (0.03–9.61) | <0.001 |
| p                          | 0.117^g| 0.001^h|          |
| NLR_{1st day}              | 3.93 (0.60–38.19) | 4.10 (0.36–51.61) | 0.713 |
| NLR_{7th day}              | 5.06 (0.65–86.17) | 17.77 (0.06–98.72) | <0.001 |
| p                          | 0.001^h| <0.001^h|          |
| Ferritin_{1st day}         | 235.00 (3.41–7,469.00) | 418.00 (13.60–29,237.00) | 0.002 |
| Ferritin_{7th day}         | 326.00 (12.40–7,469.00) | 921.50 (23.65–100,000.00) | <0.001 |
| p                          | 0.003^h| <0.001^i|          |

Bold values indicate statistically significant (p < 0.05). *Mann-Whitney U test statistic, ^Wilcoxon test statistic, mean (min – max), ^two independent samples t-test statistics, ^paired two sample t-test statistics.

ROC analysis results of the exitus group were presented in Table 4.

ROC analysis technique was used for the power of laboratory findings to diagnose mortality. As a result of the analysis, it was determined that the patients with a D-Dimer value above 0.52 on the 1st day and above 0.93 for the D-Dimer value on the 7th day would be mortal (AUC values of 0.636 (0.571–0.701) and 0.789 (0.734–0.845) respectively. As a result of the analysis, it was determined that the patients with a Procalcitonin value above 0.1735 on the 1st day and above 0.18 on the 7th day Procalcitonin value would be mortal (AUC values of 0.752 (0.691–0.813) and 0.852 (0.803–0.901) respectively). Mortality was observed in patients with a Ferritin value above 327.5 for the 1st day Ferritin value and above 556.5 for the 7th day Ferritin value (AUC values of 0.612 (0.538–0.685) and 0.783 (0.723–0.844), respectively). Mortality was determined in patients with a creatinine value above 1.05 for day 1 and 0.975 for creatinine value on day 7 (AUC values of 0.641 (0.569–0.714) and 0.757 (0.689–0.825), respectively). Mortality was found in patients with an e-GFR value below 69.375 for day 1 and e-GFR for day 7 below 66.87 (AUC values of 0.711 (0.652–0.77) and 0.812 (0.759–0.865), respectively.

ROC curves of creatinine, e-GFR, ferritin, D-dimer and procalcitonin were presented in Figure 1.
Table 4: ROC analysis results of the exitus group.

|                     | Cut-off | AUC (95%CI) | p-Value | Sensitivity (95% CI) | Specificity (95% CI) |
|---------------------|---------|-------------|---------|----------------------|----------------------|
| D-dimer 1st day, mg/L | >0.52   | 0.636 (0.571–0.701) | <0.001 | 0.608 (0.5–0.716)    | 0.6 (0.548–0.652)    |
| D-dimer 7th day, mg/L | >0.935  | 0.789 (0.734–0.845)  | <0.001 | 0.709 (0.609–0.809)  | 0.728 (0.681–0.775)  |
| Procalcitonin 1st day, ng/mL | >0.1735 | 0.752 (0.691–0.813)  | <0.001 | 0.726 (0.624–0.828)  | 0.696 (0.64–0.752)   |
| Procalcitonin 7th day, ng/mL | >0.18   | 0.852 (0.803–0.901)  | <0.001 | 0.767 (0.67–0.864)   | 0.776 (0.726–0.826)  |
| Ferritin 1st day, ng/mL | >337.5  | 0.612 (0.538–0.685)  | <0.002 | 0.566 (0.455–0.677)  | 0.601 (0.549–0.653)  |
| Ferritin 7th day, ng/mL | >556.5  | 0.783 (0.723–0.844)  | <0.001 | 0.724 (0.623–0.825)  | 0.714 (0.666–0.762)  |
| Creatinine 1st day, mg/dL | >1.055  | 0.641 (0.569–0.714)  | <0.001 | 0.617 (0.511–0.723)  | 0.649 (0.599–0.699)  |
| Creatinine 7th day, mg/dL | >0.975  | 0.757 (0.689–0.825)  | <0.001 | 0.716 (0.618–0.814)  | 0.734 (0.688–0.78)   |
| EGFR 1st day, mL/min/1.73 m² | <69.375 | 0.711 (0.652–0.77)   | <0.001 | 0.642 (0.538–0.746)  | 0.666 (0.596–0.696)  |
| EGFR 7th day, mL/min/1.73 m² | <66.87  | 0.812 (0.759–0.865)  | <0.001 | 0.753 (0.659–0.847)  | 0.769 (0.725–0.813)  |

Figure 1: ROC curves of creatinine, e-GFR, ferritin, D-dimer and procalcitonin.

Binary logistic regression analysis was performed for the factors affecting mortality, D-dimer, procalcitonin, BUN, creatinine, e-GFR, WBC, platelet, and NLR. Binary logistic regression analysis results are presented in Table 5.

As a result of univariate analysis, it was found that the values of D-dimer, procalcitonin, BUN and creatinine are a risk factor, and a one-unit increase in these values will increase the risk of death by 1,184; 1,105; 1,024 and 1,304 times, respectively (p values, respectively 0.008; 0.007; <0.001; 0.002).

It has been determined that a decrease in the e-GFR value will increase the risk of death by 1,026 (1/0.975) times and, similarly, a decrease in the platelet value will increase the risk of death by 1,007 (1/0.993) times (p<0.001, p<0.001) It was determined that the WBC value did not pose a risk of death (p=0.186). An increase in the NLR value increases the risk of death by 1,030 times (p=0.024).

As a result of multivariate analysis, only an increase in creatinine, a decrease in the values of e-GFR and platelets were determined as independent risk factors. In this context, the increase in creatinine, the decrease in e-GFR and platelet values increase the risk of death.

A heat map correlation matrix is shown in Tables 6, 7.

In our correlation analysis; as creatinine increases, our D-dimer, procalcitonin, ferritin, NLR and CRP values increase. This proves that the increase in creatinine in COVID-19 cases is strongly correlated with mortality. As a result of the correlation analysis we conducted, we can say that we have proved once again that the frequency of renal involvement in COVID-19 cases is quite high (Tables 6, 7)

The correlation matrix of the first-day variables is presented in Table 6.

The correlation matrix of the seventh-day variables is presented in Table 7.

**Discussion**

In our study, we found out that the kidney function values of COVID-19 patients who were exitus were worse than those who were discharged. The creatinine values of those who were exitus were found to be quite higher when compared to those who were discharged. In the advanced analysis methods, we observed that the increase in creatinine values contributed significantly to mortality. We detected that the increase in the creatinine value alone can be used as a predictor of mortality in COVID-19 cases. Similarly, we detected a very high decrease in e-GFR in COVID-19 cases. In other words, decreases in e-GFR, that is, disruption of kidney functions, contribute significantly to mortality in COVID-19 cases. Kidney involvement is very
common in COVID-19 disease and can be fatal. Clinicians, with a rough view, may speculate that COVID-19 patients died due to respiratory complications. However, in COVID-19 cases, the development of acute kidney injury is highly possible to occur as well as respiratory complications. It is increasingly recognized that AKI is associated with hospital mortality for COVID-19 patients, similar to all forms of sepsis. In other words, mortality is reported to be much lower risk in COVID-19 patients without AKI [9]. AKI in patients with COVID-19, especially in the critically ill group admitted to intensive care unit, is considered an important predictor of disease severity and an adverse prognostic factor for survival, is affecting approximately 20–40% of patients [10, 11]. In the study conducted by Jamie S. Hirsch et al., it was shown that AKI developed in 1,993 of 5,449 patients (36.6%) presenting with COVID-19 [12]. In our study, the AKI was found to be high in our patients as well.

The mechanisms of renal injury during COVID-19 are difficult to study due to the interference of several coexisting factors, such as polypharmacy, hypoxia, and cytokine storm [10]. There is an interaction between COVID-19 and kidney. Infection with COVID-19 can not only cause new kidney damage but also increase the difficulty of treatment and care for people with underlying kidney disease and increase mortality. Therefore, given the role of

| Mortality | Univariate | Multivariate |
|-----------|------------|--------------|
| Absent (n=350) | Present (n=81) | OR (95% CI) p-Value | OR (95% CI) p-Value |
| D-dimer | 0.38 (0.21–0.99) | 0.72 (0.35–1.85) | 1.184 (1.045–1.341) | 0.008 | 1.02 (0.857–1.213) | 0.827 |
| Procalcitonin | 0.09 (0.05–0.23) | 0.31 (0.13–0.99) | 1.105 (1.027–1.188) | 0.007 | 1.077 (0.999–1.161) | 0.052 |
| BUN | 16.9 (12.08–23.63) | 26.3 (17.5–40.7) | 1.024 (1.013–1.034) | <0.001 | 1.01 (0.99–1.031) | 0.314 |
| Creatinine | 0.92 (0.75–1.16) | 1.25 (0.79–1.85) | 1.304 (1.102–1.543) | 0.002 | 0.548 (0.355–0.846) | 0.007 |
| e-GFR | 80.26 (56.64–96.87) | 51.07 (32.16–79.99) | 0.975 (0.967–0.984) | <0.001 | 0.966 (0.95–0.982) | <0.001 |
| WBC | 6,980 (5,360–9,112.5) | 6,910 (4,300–10,435) | 1.000 (1.00–1.000) | 0.186 | 1.000 (1.00–1.000) | 0.943 |
| Platelet | 202.5 (159.75–253) | 173 (115–222) | 0.993 (0.989–0.996) | <0.001 | 0.992 (0.988–0.996) | <0.001 |
| NLR | 3.93 (2.26–7.45) | 4.1 (2.11–10.17) | 1.030 (1.004–1.057) | 0.024 | 1.025 (0.979–1.072) | 0.296 |

Table 5: Risk factors affecting mortality.

Table 6: Correlation analysis of day 1st variables of cases with mortality (Heat map correlation matrix between biochemical markers).

Table 7: Correlation analysis of 7th day variables of cases with mortality (Heat map correlation matrix between biochemical markers).
AKI as a fatal comorbidity for COVID-19, and the frequent presence of renal signs in the early phase of the infection, recommend early monitoring of renal involvement in these patients [10]. Our study results; It has been shown that kidney involvement is very common in COVID-19 disease and significantly increases mortality. To reduce patient mortality the diagnosis and treatment of COVID-19 must involve paying close attention to kidney complications. Renal functions should be strictly monitored if it is desired to reduce mortality in COVID-19 cases. Because we have proven many times in our study that an increase in creatinine increases mortality.

The role of the age factor on morbidity and mortality in patients with COVID-19 and developing AKI is controversial. In the study of JS Hirsch et al., the mean age of COVID-19 patients who developed AKI was 69, while it was 61 in patients who did not develop AKI [12]. In a retrospective cohort study conducted by Zhou F et al., they presented that advanced age was associated with mortality in COVID-19 patients [13]. Xiao G et al. showed that COVID-19 patients who developed AKI were older than those who did not develop AKI [14]. In the study of Guangchang Pei et al., it was displayed that age was not significant between the groups with and without AKI in COVID-19 patients [15]. In our study, we found that advanced age was a risk factor for mortality in parallel with the studies of JS Hirsch, Zhou F, Xiao G, et al.

Li et al. observed that 31% of 193 COVID-19 patients had elevated BUN and 22% of them had increased IV creatinine drip [16]. In the study of Yichun Cheng et al., IV creatinine drip and BUN increased in 14.6% and 13.1% of patients, respectively, at hospital admission. In addition, the e-GFR level was reported as under 60 mL/min in 13.1% of patients [11]. In our study, we found out that the patients who were exitus had high BUN and creatinine levels, and significantly lower e-GFR levels following the literature. Our study is in line with the literature in this respect.

Significant changes are observed in hematological parameters in the course of COVID-19 infection. In many studies conducted upon COVID-19 patients, leukocytosis, increased neutrophil count (due to bacterial super-infection), decreased lymphocyte count (defective host response), and thrombocytopenia was detected [6, 17, 18]. Lymphopenia was found to be the most common characteristic with a rate of 35–75% in patients who died from COVID-19 infection in a meta-analysis conducted by Lippi G et al. [18]. Similar to the literature, we found in our study that leukocytosis, lymphopenia, and thrombocytopenia in patients who were exitus were significantly different from those who were discharged.

NLR is an indicator of a systematic inflammatory response [19]. In the study of Ai-Ping Yang et al., it was represented that the rate of NLR is high in severe COVID-19 cases [20]. It was shown in the study of Javanmard SH et al., that the probability of severity of the disease increased 5 times in COVID-19 patients [21]. In our study, the NLR value was found to be significantly higher in the patients who were exitus than in the patients discharged. We consider that NLR is an effective, easy, and inexpensive test for prognosis in COVID-19 patients.

It is reported that C-reactive protein, which is known as an acute-phase reactant produced by the liver and increases in inflammation, increases by 73–93%, especially in severe COVID-19 cases [18]. CRP levels were found to be high in studies conducted in patients with COVID-19 in different regions. In the study conducted by Guan WJ et al., in China, it was found that high CRP levels were associated with disease severity [22]. It was shown in the study of Young BE et al., in Singapore that there was a significant CRP increase in COVID-19 patients who needed O2 [23]. In our study, CRP was significantly higher in the patients who were exitus compared to those discharged.

Procalcitonin is a biomarker that increases in bacterial septic conditions and indicates the severity of the infection (25). Studies on COVID-19 have shown that procalcitonin levels were high in cases of severe disease, the need for intensive care, and mortality [18, 24]. In our study, we found that procalcitonin levels were high in patients who were exitus, as shown in the following analysis. In this respect, our study was found to be compatible with the literature.

High serum ferritin values have emerged as poor prognostic factors in the course of COVID-19 disease. In the study performed by Wu C et al., High serum ferritin values was associated with the development of ARDS, but it was not found to be significantly associated with survival [25]. High ferritin levels were associated with high mortality rates in the study of Zhou F et al. [26]. It was observed in the study of Tural Onur S et al., that high ferritin levels were determinant of mortality [27]. In our study, it was detected that high ferritin levels indicated mortality.

Coagulation disorders are important prognostic determinants, especially in severe COVID-19 patients [28]. In the study conducted by Guan WJ et al., it was presented that D-dimer levels were high in cases with severe disease [22]. Lippi et al. showed that D-dimer values were higher in severe COVID-19 patients than in patients with milder forms of it [18]. In our study, we found that D-dimer levels were significant between the groups, and it was an independent risk factor for mortality in the following analysis.
Studies have shown that albumin levels were low in the course of severe disease during COVID-19 disease [3, 15, 29]. We also found in our study that albumin levels were significantly lower in patients who were exitus compared to those who survived. However, low albumin level was not seen as an independent factor on mortality in the following analysis.

Our study has some limitations. First of all, due to the retrospective design of this study, past laboratory data of the cases could not be reached. Secondly, we did not have information about the follow-up values of our patients after discharge, especially their kidney function indicators in terms of prognosis.

Conclusions

In conclusion, in this study, we observed that high creatinine, D-dimer, procalcitonin, ferritin, and low e-GFR levels were risk factors for disease severity and mortality in COVID-19 disease. While physicians and all stakeholders focus on the prognosis and mortality of the disease in COVID-19 disease, it is necessary to be thorough about kidney involvement as much as respiratory system involvement. We believe that our study will be a guide for multi-center and prospective studies on this subject.

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