Effectiveness of Laboratory Parameters as Morbidity and Mortality Indicators in Patients with Coronavirus Disease-2019 Admitted to the Intensive Care Unit

Korunavirüs Hastalığı-2019 Tanısıyla Yoğun Bakıma Alınan Hastalarda Morbidite ve Mortalitenin Belirteçleri Olarak Laboratuvar Parametrelerinin Etkinliği

ABSTRACT

Objective: Laboratory parameters may predict the severity and mortality of coronavirus disease 2019 (COVID-19). We investigated the relationship of laboratory findings obtained at admission and 72nd hour and mortality and morbidity of patients with pneumonia who were treated in two intensive care units.

Materials and Methods: Chart data of 75 patients (March–May 2020) were retrospectively analysed. Patient characteristics and laboratory parameters were compared according to the presence of COVID-19 and mortality. Patients with COVID-19 were compared according to mortality and gender.

Results: The mean patient age was 74.7 ± 11.3 years. COVID-19 positivity was not associated with marked differences in laboratory values. Lung disease, bedridden status, worse renal function scores, and high C-reactive protein level was more often observed in non-survivors (p < 0.05). A decline in D-dimer level was more apparent in survivors; the increase in ferritin and neutrophil–lymphocyte ratio was more apparent in non-survivors (not significant). Among patients with COVID-19, women had higher mean platelet volume than men (p = 0.033). The rise in ferritin level was more pronounced in men, whereas the rise in neutrophil–lymphocyte ratio and platelet–lymphocyte ratio was higher in women.

Conclusion: In this geriatric cohort, chronic lung disease and bedridden status were the main determinants of mortality. Moreover, different patterns of inflammatory markers may help predict the severity of COVID-19.

Keywords: COVID-19, pneumonia, intensive care unit, morbidity, mortality, geriatrics

ÖZ

Amaç: Laboratuar parametreleri COVID-19’un şiddet ve mortalitesini ön görebilir. Pnömoni teşhisiyle iki yoğun bakım ünitesinde tedavi edilen hastalarda ilk kabulde ve 72 saat sonra elde edilen laboratuar bulguları ile mortalite ve morbidite arasındaki ilişiği inceledi.

Gereç ve Yöntem: Toplam 75 hastanın kayıtlarından (Mart-Mayıs 2020) gelen bilgiler geriye dönük incelendi. Hasta özellikleri ve laboratuar parametreleri COVID-19 ve mortalite varlığına göre karşılaştırıldı. COVID-19+ olan hastalar, mortalite ve cinsiyeti göre daha karşılaştırıldı.

Bulgular: Ortalama yaş 74.7±11.3 yıl idi. COVID-19 pozitifliği ile belirgin değişikliklerle ilişkili değildi. Akciğer hastalığı, yatağa bağlılık, kötü böbrek fonksiyon skorları ve yüksek CRP eks hastalarda daha yaygın idi (p<0.05). D-dimerde azalma sah kalanlarda daha belirgin idi; ferritin ve nötrofil/lenfosit oranları arasında daha görünür idi (opportistik olarak anlamlı değiş). COVID-19+ hastalar arasında ortalama platelet hacmi anlamlı olarak daha yüksek idi (p=0.033). Ferritin yüksekliği erkeklerde daha belirgin iken, nötrofil/lenfosit ve trombosit/lenfosit oranları kadınlarda daha yüksek sıaptı.

Sonuç: Bu geriatrik kohortta kronik akciğer hastalığı ve yatağa bağlılık mortalitenin temel belirleyicileri olarak sıaptı. Ayrıca inflamatur parankimlerde farklı paternleri de COVID-19’da hastalik şiddetini ön görülmese de yardımcı olabilir.

Anahtar Kelimeler: COVID-19, pnömoni, yoğun bakım ünitesi, morbidite, mortalite, geriatri
Introduction

An infectious disease caused by coronavirus emerged in Wuhan, China’s Hubei province, at the end of December 2019 and spread rapidly around the world. The World Health Organization (WHO) identified COVID-19 disease, which stands for 2019 coronavirus disease, in February 2020 (1). The virus that causes COVID-19 has been identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

In the literature, lymphopenia, increased C-reactive protein, ferritin, alanine and aspartate aminotransaminases and lactate dehydrogenase, prolonged prothrombin time, and increase in D-dimer, creatine phosphokinase and troponin levels have been reported in these patients (2-4). These changes in laboratory parameters have been associated with a poor prognosis (5-7). The course of COVID-19 disease is very similar to classic ARDS disease. However, some differences detected in the laboratory parameters of the patients suggest that the laboratory parameters at the hospitalization stage and after 72 hours can provide prediction about the severity and mortality of the disease (8). In order to test our hypothesis, we planned a retrospective study in which we examined the relationship between hospitalization and 72nd hour laboratory findings of patients who were followed up in our intensive care units with hypoxemia during the COVID-19 pandemic process with mortality and morbidity.

Materials and Methods

Patients

This study was conducted under following permissions of Scientific Research Platform of the Republic of Turkey Ministry of Health (Permit No: Leyla Kazancıoğlu-2020-05-20T12_40_44) and Recep Tayyip Erdogan University Non-invasive Clinical Research Ethics Committee (Date: 01/07/2020; Decision No: 2020/123). During the COVID-19 pandemic period, the patients we examined were followed up in our intensive care units with hypoxemia during the COVID-19 pandemic process with mortality and morbidity.

Patient characteristics (age, gender, GCS score, APACHE 2 score, arrest history before coming to ICU, comorbid diseases), pulmonary tomography findings, time from onset of symptoms to hospital admission, referral location, under what conditions intubation was performed, hospitalization time, intubation day and duration, duration of stay in ICU, respiratory parameters (respiratory rate, arterial oxygenation parameters, invasive mechanical ventilation settings), hemodynamic parameters (arterial blood pressure, pulse) and biochemistry, hemogram, coagulometry, arterial blood gas parameters, inflammation markers (CRP, D-dimer, ferritin, Neutrophil/Lymphocyte Ratio [NLR], Platelet/Lymphocyte Ratio [PLR]) of hospitalization day and 72nd hour were obtained from the hospital’s electronic database.

Biochemistry samples (including inflammatory and coagulation parameters) were evaluated with Beckman Coulter AUS800 (USA) automatic biochemistry analyzer, hemogram samples were evaluated with Mindray BC-6000 (China) automatic hemogram analyzer, and Arterial Blood Gas (ABG) samples were evaluated with Radiometer ABL800 FLEX (USA).

The patients were grouped and compared according to the parameters listed below.

Grouping by the presence of COVID-19 positivity

Nasopharyngeal swab samples (Additionally tracheal aspirate if intubated) were collected from all patients who were taken or planned to be taken to ICUs during the COVID-19 pandemic process. Total RNA was detected with the RNA isolation kit (PCR-Bio-Speedy COVID-19 RT-qPcr, Bioeksen, Turkey). Patients diagnosed with COVID-19 by Reverse Transcription Polymerase Chain Reaction were considered COVID-19 positive.

Patients who were found to be positive in the intensive care unit while the swab/aspirate sample taken outside the intensive care unit was negative, was also considered to be COVID-19 positive.

According to the above criteria, patients were divided into 2 groups as the COVID-19 positive pneumonia group (Group COVID-19+) and the COVID-19 negative pneumonia group (Group COVID-19 -).

Grouping by mortality

All patients were grouped as survivors and non-survivors according to the mortality that occurred during the ICU hospitalization period. Patients who were discharged from the ICU alive and died in the ward or at home during their follow-up were classified as survivors in grouping.
Grouping of COVID-19 positive patients

COVID-19 positive patients were grouped and compared according to mortality. In statistical analysis, COVID-19 positive patients were grouped and compared according to gender, since a significant difference was found only in terms of gender when compared according to the parameters of COVID-19 positive patients.

Statistical analysis

For statistical analysis, the data were evaluated with SPSS for Windows version 22 (SPSS, IBM, Chicago, IL, USA) software. The conformity of continuous variables to normal distribution was investigated by Kolmogorov-Smirnov test. Data conforming to normal distribution were given as mean ± standard deviation and compared using an independent t-test. Continuous variables not conforming to the normal distribution were given as median (interquartile width) and compared using the Mann-Whitney U test. Categorical data are given as numbers (%) and compared with the Fisher’s exact test. In the analyzes, p < 0.05 was considered statistically significant.

Results

Data of 75 patients were evaluated. (Figure 1). Patient characteristics were given separately in each comparison table. Briefly, the mean age of the COVID-19+ cases was 72.3 ± 10.5 years in the early geriatric group according to the WHO classification, and the mean age of the COVID-19 cases was 76.4 ± 11.6 years in the advanced age group according to the WHO classification, but there was no statistically significant difference (p = 0.121) between two groups. The duration between the onset of symptoms and hospital admission was longer in COVID-19+ patients (p = 0.01).

Comparison by the presence of COVID-19 positivity

Laboratory data taken on the day of hospitalization are given in Table 1. Briefly, no laboratory parameter obtained at the admission was statistically significantly different. However, D-dimer and erythrocyte distribution width were lower and ferritin was higher in COVID-19+ patients (p = 0.05, 0.044 and 0.044, respectively).

Comparison by mortality

The comparison of laboratory data according to mortality is given in Table 2. Briefly, APACHE II score was higher in non-survivors (p = 0.026). Non-survivors had worse renal function scores (p = 0.05); higher LDH values and white blood cell number (p = 0.054 and 0.041, respectively). Among the inflammatory markers, only CRP was significantly different (higher in non-survivors, p = 0.022) between groups. To note, the fall in D-dimer was more apparent in survivors; the increase in ferritin and neutrophil lymphocyte ratio was more apparent in non-survivors, although there was no statistical significance.

Comparison of COVID-19+ patients by mortality

There were a total of 31 COVID-19+ patients, including 10 survivors (32.2%) and 21 non-survivors (67.7%). The data of these patients are given in Table 3. Briefly, there was no statistically significant difference. However, the increase in ferritin, NLR and TLR was more pronounced in non-survivors, but the difference was not statistically significant.

Comparison of COVID-19+ patients by gender

Laboratory data of these patients are given in Table 4. In summary, gender distribution was equal. Women had lower Glasgow coma scores (p = 0.056) and higher mean platelet volume (p = 0.033). The rise in ferritin was more pronounced in men, whereas the rise in NLR and TLR was higher in women, but the difference was not statistically significant.

Discussion

In this descriptive, retrospective cohort study, in which we examined the effects of clinical and laboratory data of 75
## Table 1. Patient characteristics and laboratory values according to COVID-19 positivity

|                                      | COVID-19 - (n=44) | COVID-19 + (n=31) | p     |
|--------------------------------------|-------------------|-------------------|-------|
| **Patient characteristics**          |                   |                   |       |
| Age, years                           | 76.4±11.6         | 72.3±10.5         | 0.121 |
| Male gender, n (%)                   | 27 (61.4%)        | 16 (51.6%)        | 0.546 |
| Exitus, n (%)                        | 30 (68.2%)        | 20 (64.5%)        | 0.931 |
| Glasgow Coma Score                   | 8.5 (3.0 - 13.2)  | 9.0 (6.0 - 15.0)  | 0.360 |
| Apache2 score at the day of hospitalization | 24.4±10.1       | 23.1±9.6          | 0.576 |
| History of cardiac arrest before reaching the hospital, n (%) | 10 (22.7%)       | 3 (9.7%)          | 0.246 |
| Congestive heart failure, n (%)      | 12 (27.3%)        | 7 (22.6%)         | 0.849 |
| Hypertension, n (%)                  | 32 (72.7%)        | 21 (67.7%)        | 0.834 |
| Diabetes Mellitus, n (%)             | 9 (20.5%)         | 9 (29.0%)         | 0.561 |
| Chronic Obstructive Lung Disease, n (%) | 13 (29.5%)      | 4 (12.9%)         | 0.157 |
| Bedridden due to serebrovascular disease, n (%) | 10 (22.7%)      | 4 (12.9%)         | 0.439 |
| COVID19 signs present in thorax computerized tomography, n (%) | 23 (52.3%)       | 20 (64.5%)        | 0.413 |
| Duration between onset of symptoms until admission to hospital, days | 2.0 (1.0 - 2.0)  | 2.0 (1.0 - 4.5)  | 0.010 |
| Days in hospital until admission to ICU, days | 0.0 (0.0 - 1.2) | 0.0 (0.0 - 2.0)  | 0.359 |
| Day of intubation                    | 1.0 (1.0 - 1.0)   | 1.0 (1.0 - 1.0)   | 0.617 |
| Duration of intubation, days         | 8.0 (2.8 - 13.5)  | 7.0 (2.0 - 26.0)  | 0.645 |
| Length of stay in ICU, days          | 8.5 (3.0 - 18.2)  | 7.0 (5.0 - 26.5)  | 0.649 |
| FiO2, %                              | 54.7±13.0         | 62.7±23.8         | 0.064 |
| PEEP, cmH2O                          | 8.2±2.9           | 9.6±3.8           | 0.105 |
| Systolic arterial blood pressure, mmHg| 130.0 (101.0 - 170.0) | 128.0 (128.0 - 128.0) | 0.932 |
| Diastolic arterial blood pressure, mmHg | 80.0 (55.5 - 90.0) | 72.0 (72.0 - 72.0) | 0.924 |
| Pulse, beats/min                     | 106.2±31.5        | 92.0±32.6         | 0.678 |
| **Biochemistry parameters**          |                   |                   |       |
| Glucose, mg/dL                       | 150.0 (129.2 - 201.5) | 147.0 (127.2 - 191.0) | 0.972 |
| Urea, mg/dL                          | 78.0 (57.0 - 126.2) | 47.0 (35.0 - 77.0) | 0.019 |
| Creatinine, mg/dL                    | 1.2 (0.9 - 1.9)   | 1.0 (0.7 - 1.4)   | 0.027 |
| eGFR                                  | 44.0 (33.2 - 72.0) | 56.0 (44.0 - 89.0) | 0.077 |
| Albumin, g/dL                        | 32.4±8.5          | 32.6±4.9          | 0.927 |
| Total bilirubin, mg/dL               | 0.8 (0.5 - 1.3)   | 0.8 (0.6 - 1.3)   | 0.729 |
| Direct bilirubin, mg/dL              | 0.2 (0.1 - 0.3)   | 0.2 (0.1 - 0.3)   | 0.613 |
| ALT, U/L                             | 21.5 (14.0 - 69.8) | 25.5 (14.0 - 42.2) | 0.269 |
| AST, U/L                             | 32.0 (24.0 - 102.0) | 40.0 (26.5 - 69.0) | 0.268 |
| GGT, U/L                             | 35.5 (19.2 - 59.0) | 26.5 (20.2 - 46.5) | 0.716 |
| LDH, U/L                             | 344.5 (235.8 - 567.2) | 303.0 (256.5 - 463.5) | 0.596 |
| Creatine kinase, mg/dL               | 59.5 (54.2 - 191.2) | 85.5 (68.2 - 113.2) | 0.508 |
| **Complete blood count parameters**  |                   |                   |       |
| White blood cells, 10^9/L            | 12.8 (9.0 - 15.7)  | 11.5 (6.7 - 13.1)  | 0.113 |
| Lymphocyte number, 10^9/L            | 0.8 (0.5 - 1.3)   | 0.9 (0.5 - 1.2)   | 0.725 |
| Monocyte number, 10^9/L              | 0.6 (0.3 - 0.8)   | 0.4 (0.3 - 0.7)   | 0.657 |
Table 1. Continued

| Parameter                                      | COVID-19 - (n=44)            | COVID-19 + (n=31)          | p      |
|------------------------------------------------|------------------------------|----------------------------|--------|
| Neutrophil number, 103/uL                      | 10.6 (7.7 - 13.3)            | 9.0 (5.3 - 11.6)           | 0.126  |
| Red blood cell mass, 10/uL                      | 4.0 (3.6 - 4.4)              | 4.1 (3.7 - 4.4)            | 0.628  |
| Hemoglobin, g/dL                                | 11.3±2.1                     | 11.9±2.2                   | 0.310  |
| Hematocrit, %                                   | 34.6±6.8                     | 35.2±6.7                   | 0.579  |
| Mean corpuscular volume, fL                      | 88.4±6.1                     | 88.7±4.5                   | 0.833  |
| Platelets, 103/uL                               | 225.0 (191.0 - 269.0)        | 217.0 (165.8 - 316.5)      | 0.986  |
| Mean platelet volume, fL                         | 9.8±1.1                      | 9.9±1.5                    | 0.678  |
| Red cell distribution width (SD), fL             | 49.1±6.3                     | 45.9±6.5                   | 0.048  |
| Red cell distribution width (CV), %             | 16.0±2.4                     | 14.8±2.3                   | 0.044  |
| **Coagulometry parameters**                     |                              |                            |        |
| Prothrombin time, sec                           | 20.1±8.9                     | 17.5±5.2                   | 0.229  |
| International normalized ratio                  | 1.50±0.7                     | 1.3±0.4                    | 0.219  |
| PT%                                            | 68.4±25.4                    | 76.0±23.8                  | 0.273  |
| Fibrinogen, mg/dL                               | 419.3±190.9                  | 476.4±138.8                | 0.528  |
| **Arterial blood gas values**                   |                              |                            |        |
| pH                                             | 7.3±0.1                      | 7.3±0.2                    | 0.223  |
| pCO₂, mmHg                                      | 52.3±17.5                    | 44.5±15.5                  | 0.123  |
| pO₂, mmHg                                       | 70.5 (36.4 - 86.1)           | 82.2 (52.1 - 105.0)        | 0.241  |
| sO₂, %                                         | 75.7±26.9                    | 86.8±14.7                  | 0.108  |
| Lactate, mmol/L                                 | 2.0 (1.6 - 3.5)              | 1.7 (1.2 - 3.0)            | 0.279  |
| **Inflammation markers**                        |                              |                            |        |
| C-reactive protein, mg/L                        |                              |                            |        |
| Day of admission to ICU                         | 87.0 (15.2 - 163.0)          | 90.5 (15.0 - 128.2)        | 0.991  |
| 72th hour                                       | 118.0 (82.0 - 206.0)         | 116.5 (85.5 - 178.2)       | 0.854  |
| D-dimer, μg FEU/mL                              | 3.7 (1.6 - 4.7)              | 3.4 (2.2 - 4.2)            | 0.824  |
| Day of admission to ICU                         | 2.6 (2.0 - 6.6)              | 1.5 (0.8 - 2.3)            | 0.050  |
| Ferritin, ng/mL                                 | 67.2 (25.5 - 219.6)          | 56.7 (22.3 - 177.0)        | 0.684  |
| Day of admission to ICU                         | 187.0 (95.9 - 257.0)         | 850.0 (319.0 - 897.5)      | 0.044  |
| Neutrophil/Lymphocyte ratio                     |                              |                            |        |
| Day of admission to ICU                         | 10.7 (7.4 - 20.8)            | 8.5 (4.5 - 16.6)           | 0.176  |
| 72th hour                                       | 9.7 (6.7 - 20.8)             | 14.8 (9 – 25.4)            | 0.305  |
| Platelet/Lymphocyte ratio                       | 284.3 (162.7 - 457.1)        | 269.6 (118.5 - 511.6)      | 0.671  |
| Day of admission to ICU                         | 262 (142 - 451)              | 315 (269 - 422)            | 0.352  |

ICU: intensive care unit; FiO₂: fraction of inspired oxygen; PEEP: positive end-expiratory pressure; eGFR: estimated glomerular filtration rate; ALT: alanine aminotransferase; ASALT: aspartate amino transferase; GGT: gama glutamil transferaz; LDH: lactate dehydrogenase; pCO₂: partial pressure of carbon dioxide; PO₂: partial pressure of oxygen; sO₂: oxygen saturation.
# Table 2. Patient characteristics and laboratory values according to mortality

| Patient characteristics                                      | Survivors (n=22) | Non-survivors (n=53) | p   |
|--------------------------------------------------------------|------------------|----------------------|-----|
| **Patient characteristics**                                  |                  |                      |     |
| Age, years                                                   | 74.0±12.5        | 75.0±10.8            | 0.720|
| Male gender, n (%)                                           | 10 (45.5%)       | 33 (62.3%)           | 0.279|
| COVID19 positivity, n (%)                                    | 10 (45.5%)       | 21 (39.6%)           | 0.834|
| Glasgow Coma Score                                          | 10.5±4.2         | 8.3±4.8              | 0.068|
| Apache2 score at the day of hospitalization                 | 19.7±8.4         | 25.6±9.9             | 0.016|
| History of cardiac arrest before reaching the hospital, n (%)| -                | 13 (24.5%)           | 0.026|
| Congestive heart failure, n (%)                             | 6 (27.3%)        | 13 (24.5%)           | 1.000|
| Hypertension, n (%)                                          | 15 (68.2%)       | 38 (71.7%)           | 0.979|
| Diabetes Mellitus, n (%)                                     | 7 (31.8%)        | 11 (20.8%)           | 0.469|
| Chronic Obstructive Lung Disease, n (%)                     | 4 (18.2%)        | 13 (24.5%)           | 0.768|
| Bedridden due to cerebrovascular disease, n (%)             | 3 (13.6%)        | 11 (20.8%)           | 0.693|
| COVID19 signs present in thorax computerized tomography, n (%)| 14 (63.6%)       | 29 (54.7%)           | 0.649|
| Duration between onset of symptoms until admission to hospital, days | 2.4±1.9         | 2.5±2.1              | 0.794|
| Days in hospital until admission to ICU, days               | 1.4±2.0          | 1.1±2.5              | 0.676|
| Day of intubation                                            | 1.5±2.2          | 1.4±1.1              | 0.748|
| Duration of intubation, days                                | 17.1±23.7        | 11.4±11.6            | 0.205|
| Length of stay in ICU, days                                 | 17.7±21.5        | 13.2±16.1            | 0.318|
| FiO₂, %                                                      | 54.3±17.4        | 59.5±18.9            | 0.266|
| PEEP, cmH₂O                                                  | 8.6±3.1          | 8.8±3.5              | 0.806|
| Systolic arterial blood pressure, mmHg                       | 130.0±30.0       | 132.2±46.6           | 0.941|
| Diastolic arterial blood pressure, mmHg                      | 73.3±15.3        | 74.6±25.7            | 0.941|
| Pulse, beats/min                                             | 87.7±18.6        | 111.4±32.1           | 0.267|
| **Biochemistry parameters**                                  |                  |                      |     |
| Glucose, mg/dL                                               | 156.2±65.0       | 172.1±61.6           | 0.332|
| Urea, mg/dL                                                  | 61.5±45.4        | 92.1±52.8            | 0.024|
| Creatinine, mg/dL                                            | 1.0±0.4          | 1.7±1.1              | 0.012|
| eGFR                                                         | 69.6±28.6        | 51.2±27.4            | 0.013|
| Albumin, g/dL                                                | 32.6±7.6         | 31.1±5.6             | 0.393|
| Total bilirubin, mg/dL                                       | 0.9±0.5          | 1.0±0.7              | 0.623|
| Direct bilirubin, mg/dL                                      | 0.2±0.2          | 0.3±0.3              | 0.148|
| ALT, U/L                                                     | 130.3±405.9      | 107.2±225.8          | 0.766|
| AST, U/L                                                     | 153.7±495.1      | 161.7±335.7          | 0.938|
| GGT, U/L                                                     | 66.2±107.0       | 83.3±135.2           | 0.636|
| LDH, U/L                                                     | 308.6±123.6      | 494.1±376.8          | 0.054|
| Creatine kinase, mg/dL                                       | 173.4±127.2      | 157.2±275.4          | 0.904|
| **Complete blood count parameters**                          |                  |                      |     |
| White blood cells, 103/uL                                    | 9.8±4.0          | 13.0±6.3             | 0.041|
| Lymphocyte number, 103/uL                                    | 0.9±0.5          | 1.2±1.3              | 0.347|
## Table 2. Continued

| Parameter                                      | Survivors (n=22) | Non-survivors (n=53) | p    |
|------------------------------------------------|------------------|----------------------|------|
| Monocyte number, 10³/µL                        | 0.4±0.2          | 0.7±0.5              | 0.028|
| Neutrophil number, 10³/µL                      | 8.4±3.8          | 11.0±5.6             | 0.061|
| Red blood cell mass, 10³/µL                    | 4.0±0.6          | 4.0±0.8              | 0.953|
| Hemoglobin, g/dL                               | 11.6±2.0         | 11.5±2.2             | 0.882|
| Hematocrit, %                                  | 34.9±6.3         | 35.0±6.9             | 0.980|
| Mean corpuscular volume, fL                    | 88.3±4.6         | 88.6±5.8             | 0.862|
| Platelets, 10³/µL                              | 238.3±87.7       | 246.0±106.1          | 0.779|
| Mean platelet volume, fL                       | 9.6±1.1          | 9.9±1.3              | 0.509|
| Red cell distribution width (SD), fL           | 45.8±5.6         | 48.6±6.7             | 0.111|
| Red cell distribution width (CV), %            | 14.8±2.2         | 15.7±2.4             | 0.167|
| Coagulometry parameters                        |                  |                      |      |
| Prothrombin time, sec                          | 15.3±2.5         | 20.6±8.6             | 0.022|
| International normalized ratio                 | 1.1±0.2          | 1.6±0.7              | 0.024|
| PT%                                            | 86.2±19.1        | 65.7±24.7            | 0.005|
| Fibrinogen, mg/dL                              | 422.8±204.6      | 476.7±115.8          | 0.605|
| Arterial blood gas values                      |                  |                      |      |
| pH                                             | 7.3±0.1          | 7.3±0.1              | 0.744|
| pCO₂, mmHg                                     | 56.2±15.2        | 45.9±16.9            | 0.069|
| pO₂, mmHg                                      | 72.1±73.4        | 82.2±42.5            | 0.568|
| sO₂, %                                         | 74.9±23.6        | 82.9±22.3            | 0.300|
| Lactate, mmol/L                                | 2.4±1.5          | 3.3±3.3              | 0.409|
| Inflammation markers                           |                  |                      |      |
| C-reactive protein, mg/L                       |                  |                      |      |
| Day of admission to ICU                        | 52 (9 - 103)     | 95.5 (42 – 194.5)    | 0.022|
| 72th hour                                      | 107 (82 - 158)   | 123 (84 - 225)       | 0.205|
| D-dimer, µg FEU/mL                             | 3.9 (2.1 - 4.9)  | 3.2 (1.9 – 3.8)      | 0.469|
| Day of admission to ICU                        | 2 (1.2 - 2.3)    | 2.3 (1.2 – 7.3)      | 0.201|
| Ferritin, ng/mL                                | 245 (187 - 410)  | 118 (109 - 177)      | 0.667|
| 72th hour                                      | 258 (139-996)    | 418 (160 - 726)      | 0.554|
| Neutrophil/Lymphocyte ratio                    |                  |                      |      |
| Day of admission to ICU                        | 10.8 (7 - 17)    | 9.2 (5.5 - 19.7)     | 0.642|
| 72th hour                                      | 7.7 (6 – 15.2)   | 16 (9.9 – 26.9)      | 0.074|
| Platelet/Lymphocyte ratio                      |                  |                      |      |
| Day of admission to ICU                        | 298 (161 - 500)  | 255 (148 - 489)      | 0.594|
| 72th hour                                      | 209.5 (157.5 - 282) | 185 (144 - 269) | 0.665|

ICU: intensive care unit; FiO₂: fraction of inspired oxygen; PEEP: positive end-expiratory pressure; eGFR: estimated glomerular filtration rate; ALT: alanine aminotransferase; AST: aspartate amino transferase; GGT: gama glutamil transferaz; LDH: lactate dehydrogenase; pCO₂: partial pressure of carbon dioxide; PO₂: partial pressure of oxygen; sO₂: oxygen saturation.
patients with a diagnosis of pneumonia in our ICUs during the COVID-19 pandemic period, on mortality and morbidity, we determined some patient characteristics and laboratory parameters showing morbidity and mortality.

It has been reported that mostly middle-aged and older adults are affected by COVID-19 infection and the mortality rate of older adults is higher (10-13). In a report by the Chinese Center for Disease Control and Prevention, case fatality rates were reported as 8 and 15%, respectively, among those aged 70-79 years and those aged 80 and over (10). In a study conducted in the United Kingdom, the risk of death among patients aged 80 and over was found to be 20 times that of patients aged 50-59 years (13). In the United States, 67% of 2449 patients diagnosed with COVID-19 during February-March 2020 were over the age of 45; the mortality rate is higher in elderly individuals; It has been reported that 80% of the deaths occur in people aged 65 and over (14). In our study, there was no association between mortality and age. However, it is important to note that >80% of our patients are above 65 years of age. Comparison according to mortality showed that comorbidities such as hypertension, congestive heart failure and diabetes mellitus were as prevalent in survivors as mortal cases. It is interesting to note that mortal cases presented with more frequent chronic obstructive lung disease or bedridden status due to cerebrovascular disease. We are in opinion that in this geriatric patient cohort, these two conditions, able to pronounce the severity of oxygenation defect and thrombotic complications, were major determinants of the negative outcome.

COVID-19+ disease can occur in healthy individuals of all ages; however, hospitalization was observed in the elderly group, often accompanied by comorbidities. In a study of 355 patients who died due to COVID-19 infection in Italy, the average number of pre-existing comorbidities was 2.7; there was no concomitant disease in only 3 patients' history (15). In our region, between March and April 2020, mortality rates were higher in patients with COVID-19+ pneumonia in the early geriatric age group. When Table 1 was examined,
it was found that the frequency of comorbidity was lower in the COVID-19+ group, but when Table 3 was examined, the frequency of comorbidity was generally higher in patients with a mortal course regardless of the COVID-19 diagnosis. It was striking that the frequency of DM was higher in survivors; we believe that this is due to the non-severity of DM disease in our cohort of patients. We noted that only diabetes mellitus was more prevalent in COVID19 + patients. The rest were similar; except chronic obstructive lung disease and bedridden status, which were lower. With these results, we thought that the presence of comorbidities in the geriatric age group are not associated with susceptibility to COVID19 infection. However, given the lower mortality rate among the COVID19 + patients in our cohort compared to the current literature, we may presume that the lack of comorbidities may decrease the severity of COVID19 infection.

Among the laboratory parameters studied, d-dimer was found to be higher in patients with COVID-19- on the day of hospitalization. In the follow-up, at the 72nd hour, it was found to be higher in cases with mortality. With these results, we believe that d-dimer is a marker that is not specific to COVID-19 disease and persistently high values may show mortality at the 72nd hour.

In the literature, mortality has been reported to be higher in men compared to women (16-18). In a meta-analysis (including 77,392 patients), COVID-19 patients had significantly higher morbidity, severity and mortality in men compared to women (19). In our study, it was found that the mortality rate was higher in male gender, but there was no statistically significant difference. On the other hand, differences in MPV and NLO values depending on gender were remarkable. MPV and NLO, which are unconventional parameters used in mortality and morbidity monitoring, are also provide information about cardiovascular complications and inflammation (20-23). MPV value was found to be higher than normal in all our patients, and we observed that this elevation was significant only in COVID-19+ female patients. We found that patients with COVID-19 had lower NLR and

| Table 4. Comparison of COVID-19+ patients according to gender |
|---------------------------------------------------------------|
|                  | Male (n=16) | Female (n=15) | p     |
| Age, years       | 70±8.9      | 74.8±11.9     | 0.210 |
| Exitus, n (%)    | 12 (75%)    | 9 (60%)       | 0.470 |
| Glasgow Coma Score | 11.1±4.9   | 7.9±4         | 0.056 |
| Apache2 score at the day of hospitalization | 22.5±10.7 | 23.8±8.6 | 0.714 |

**Complete blood count parameters**

- **Mean platelet volume, fL**: 9.4±1.4; 10.6±1.4; 0.033
- **C-reactive protein, mg/L**
  - Day of admission to ICU: 98 (35.5 - 119.5); 86 (17.7 - 127.5); 0.917
  - 72th hour: 104 (86 - 179); 138 (86.5 - 176); 0.977
- **D-dimer, µg FEU/mL**
  - Day of admission to ICU: 5.9 (5.2 - 6.6); 3.2 (1.8 - 3.8); 0.127
  - 72th hour: 1.6 (0.5 - 2.3); 1.5 (1.1 - 2.5); 0.859
- **Ferritin, ng/mL**
  - Day of admission to ICU: 118 (32 - 410); 100 (44 - 256); 0.698
  - 72th hour: 896 (882 - 899); 510 (269.5 - 788); 0.273
- **Neutrophil/Lymphocyte ratio**
  - Day of admission to ICU: 15.9 (4.9 - 21.2); 7.4 (4.4 - 9.8); 0.178
  - 72th hour: 12.9 (10.4 - 20.3); 19.4 (7.9 - 32.5); 0.828
- **Platelet/Lymphocyte ratio**
  - Day of admission to ICU: 382 (117 - 539); 181 (144.4 - 318); 0.265
  - 72th hour: 297 (240 - 333); 454.5 (339 - 712); 0.104
TLR values on the day of hospitalization, however values at the 72nd hour was higher (albeit not statistically significant). This difference was only seen in women. With these results, we think that the high MPV values, late increase or persistency in high NLR and TLR values may be used as indicators of COVID-19 disease and mortality in women.

In a study comparing severe and moderate COVID-19 patients, RDW-CV, RDW-SD values among the morphological parameters were found to be higher in the severe COVID-19 patient group (24). In another study, it was predicted that the increase in RDW value within the first 72 hours after hospitalization in patients with severe sepsis and septic shock may be associated with adverse clinical outcomes (25). In our cohort of patients, RDW-SD and RDW-CV values were higher on the day of hospitalization, similar to d-dimer, in COVID-19-patients and in patients with a mortal course. We believe that the reason for this situation is due to the lower mortality among our COVID-19+ patients.

This retrospective cohort study has many limitations. First of all, the limited number of patients may have affected the statistical significance of the results. Secondly, mortality in COVID-19+ patients was lower than reported in reports published at similar periods, making the markers difficult to interpret. As stated above, it was concluded that parameters such as d-dimer, NLO, and MPV are markers specific to mortality rather than COVID-19. However, it should be kept in mind that all patients admitted to the ICU during the period when patient data are collected were potentially approached as COVID-19+, and all of them were given hydroxychloroquine, favipiravir, azithromycin and similar antibiotics in accordance with the relevant guidelines. In addition, according to the data obtained in this period, the guidelines and treatment scheme were updated frequently. Considering that some patients who started treatment with COVID-19+ were determined to be COVID-19- and the treatments were terminated, it is obvious that it will be difficult to evaluate the effects of empirical antibiotherapy on laboratory parameters in a retrospective study. Finally, the diversity of pneumonia agents in COVID-19-patients and bacterial superinfection agents observed in all COVID-19+ patients may also have caused the difference in biochemical parameters.

Conclusion

As a result, the patient cohort we followed up in the ICU with the diagnosis of pneumonia during the COVID-19 pandemic period consisted of the geriatric age group with comorbidities. In this patient group, we believe that male gender and high d-dimer values measured at 72nd hour are determinative for mortality, and the high MPV value in women and NLR value in men can be used as indicators of COVID-19 disease and mortality.

Ethics

Ethics Committee Approval: Approval for the study (decision no: 2020/123, date: 23.06.2020) was obtained from Recep Tayyip Erdoğan University Faculty of Medicine’s Ethics Committee.

Informed Consent: Because the study we designed as a retrospective cohort study, informed consent from the patients was waived.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: L.K., Ş.B., Design: L.K., B.E., A.Ö., T.E., Data Collection and Process: L.K., B.E., H.K., A.Ö., T.K., As.Ö., I.B., Analysis or Interpretation: L.K., A.Ö., As.Ö., Literature Search: B.E., H.K., A.Ö., I.B., Ş.B., T.E., Writing: L.K., A.H.

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