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

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

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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 ilişkiyi inceledik.
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 cinsiyete göre de karşılaştırıldı.
Bulgular: Ortalama yaş 74.7±11.3 yıl idi. COVID-19 pozitifliği laboratuar değerlerinde belirgin değişikliklerle ikişkili değildi. Akciğer hastalığı, yatağa bağımlılık, kötü böbrek fonksiyon skorları ve yüksek CRP eks hastalarda daha yaygın idi ($p<0.05$). D-dimerde azalma sağ kalanlarda daha belirgin idi; ferritin ve nötrofil/lenfosit oranı ölenlerde daha görünür idi (istatistiksel olarak anlamlı değil). COVID-19+ hastalar arasında ortalama platelet hacmi anlamlı olarak daha yüksekti ($p=0.033$). Ferritin yüksekliği erkeklerde daha belirgin iken, nötrofil/lenfosit ve trombosit/lenfosit oranları kadınlarda daha yüksek saptandı.
Sonuç: Bu geriatrik kohortta kronik akciğer hastalığı ve yatağa bağımlılık mortalitenin temel belirleyicileri olarak saptandı. Ayrıca inflamatuar belirteçlerin farklı paternleri de COVID-19'da hastalık şiddetinin ön görülmesine 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 followed up in the intensive care units with the diagnosis of pneumonia between 19 March and 20 May 2020 were diagnosed according to WHO's provisional guide dated 28 January 2020 (9). Because the study ws designed as a retrospctive cohort study, informed consent from the patients was waived. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

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 werelower 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 ($p=0.016$). A history of cardiac arrest before reaching the hospital was only seen 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 differencewas not statisticallysignificant.

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

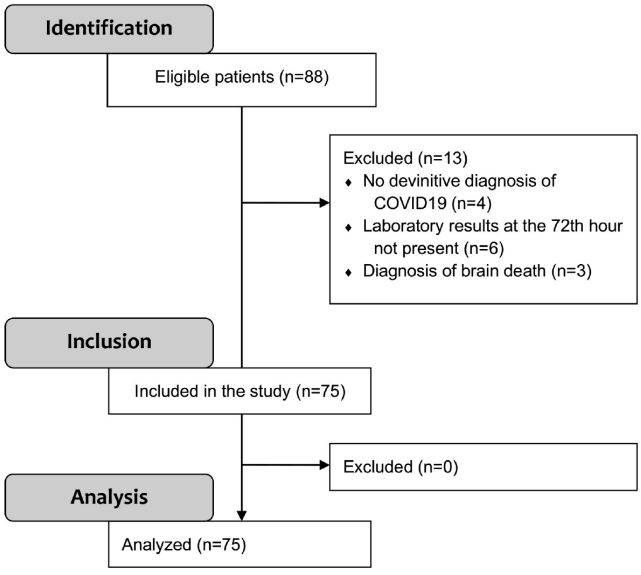

Figure 1.

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, cmH_2O	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 blodd cells, 103/uL	12.8 (9.0 - 15.7)	11.5 (6.7 - 13.1)	0.113
Lymphocyte number, 103/uL	0.8 (0.5 - 1.3)	0.9 (0.5 - 1.2)	0.725
Monocyte number, 103/uL	0.6 (0.3 - 0.8)	0.4 (0.3 - 0.7)	0.657

Table 1. Continued			
	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	35.5±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	1.5±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
pCO_2, mmHg	52.3±17.5	44.5±15.5	0.123
pO_2, mmHg	70.5 (36.4 - 86.1)	82.2 (52.1 - 105.0)	0.241
sO_2, %	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			
Day of admission to ICU	3.7 (1.6 - 4.7)	3.4 (2.2 - 4.2)	0.824
72th hour	2.6 (2.0 - 6.6)	1.5 (0.8 - 2.3)	0.050
Ferritin, ng/mL			
Day of admission to ICU	67.2 (25.5 - 219.6)	56.7 (22.3 - 177.0)	0.684
72th hour	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			
Day of admission to ICU	284.3 (162.7 - 457.1)	269.6 (118.5 - 511.6)	0.671
72th hour	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; 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.

Table 2. Patient characteristics and laboratory values according to mortality			
	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 serebrovascular 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
FiO_2, %	54.3±17.4	59.5±18.9	0.266
PEEP, cmH_2O	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 blodd 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			
	Survivors (n=22)	**Non- survivors (n=53)**	**p**
Monocyte number, 103/uL	0.4±0.2	0.7±0.5	0.028
Neutrophil number, 103/uL	8.4±3.8	11.0±5.6	0.061
Red blood cell mass, 10/uL	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/uL	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
pCO_2, mmHg	56.2±15.2	45.9±16.9	0.069
pO_2, mmHg	72.1±73.4	82.2±42.5	0.568
sO_2, %	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
72^{th} hour	107 (82 - 158)	123 (84 - 225)	0.205
D-dimer, µg FEU/mL			
Day of admission to ICU	3.9 (2.1 - 4.9)	3.2 (1.9 – 3.8)	0.469
72^{th} hour	2 (1.2 - 2.3)	2.3 (1.2 - 7.3)	0.201
Ferritin, ng/mL			
Day of admission to ICU	245 (187 - 410)	118 (109 - 177)	0.667
72^{th} 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
72^{th} 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
72^{th} 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.

Table 3. Comparison of COVID-19+ patients according to mortality			
	Survivors (n=10)	Non-survivors (n=21)	p
Age, years	71±13.9	73±8.8	0.637
Male gender, n (%)	4 (%25)	12 (%75)	0.458
Glasgow Coma Score	10.5 (8 - 14.8)	9 (6 - 15)	0.666
Apache2 score at the day of hospitalization	23 (15 - 26.8)	26 (13 - 31)	0.433
Complete blood count parameters			
Mean platelet volume, fL	9 (8.7 - 10.1)	10.2 (9 - 11.2)	0.098
Inflammation markers			
C-reactive protein, mg/L			
Day of admission to ICU	112.5 (38 - 141.8)	87 (11.8 - 113)	0.441
72th hour	138 (84 - 226)	116 (87.5 - 176.5)	0.749
D-dimer, µg FEU/mL			
Day of admission to ICU	3.7 (2.4 - 4.4)	3.2 (2.6 - 3.9)	0.881
72th hour	2 (0.6 - 3)	1.2 (0.8 - 2.2)	0.779
Ferritin, ng/mL			
Day of admission to ICU	150 (38 - 419.6)	257 (122 - 277.0)	0.684
72th hour	418 (220 - 602)	890.5 (858 - 1203)	0.100
Neutrophil/Lymphocyte ratio			
Day of admission to ICU	8.4 (5.4 - 11.7)	8.5 (4.4 - 18.4)	0.722
72th hour	8.9 (7.5 - 10.2)	16.4 (10.6 - 32.5)	0.266
Platelet/Lymphocyte ratio			
Day of admission to ICU	327 (218- 489)	200 (113 - 512)	0.360
72th hour	324.5 (316 - 333)	313 (240 - 487)	0.874

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. Howeverit 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,

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
Inflammation markers			
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

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

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 retrospctive 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., İ.B., Analysis or Interpretation: L.K., A.Ö., As.Ö., Literature Search: B.E., H.K., A.H., İ.B., Ş.B., T.E., Writing: L.K., A.H.

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