Türk Klinik Biyokimya Derg 2023; 21(2): 110-118

Araştırma Makalesi / *Research Article*

https://doi.org/10.56615/tkbd.2023.14

Biochemical Markers in Determining the Risk of Intensive Care Unit Admission in COVID-19

COVID-19'da Yoğun Bakıma Yatış Riskinin Belirlenmesinde Biyokimyasal Belirteçler

Meltem Yardim[1] **Levent Deniz[2]** **Damla Kayalp[3]**

Nilüfer Celik[4] **Burcu Ulas Kahya [5]**

1 Department of Medical Biochemistry, Yerkoy State Hospital, 66900 Yozgat, Turkey

2 Department of Medical Biochemistry, Sorgun State Hospital, 66900 Yozgat, Turkey.

3 Department of Medical Biochemistry, Yozgat City Hospital, 66900 Yozgat, Turkey

4 Department of Biochemistry, Dr. Behcet Uz Children's Hospital, 35210 Izmir, Turkey

5 Department of Medical Oncology, Faculty of Medicine, Gazi University, Ankara, Turkey

Başvuru Tarihi / *Received:* 13 Mart 2023 Kabul Tarihi / Accepted: 18 Ağustos 2023

ABSTRACT

Aim: It was aimed to determine predictive markers for the need for intensive care unit (ICU) hospitalization in patients with coronavirus infection.

Material and Methods: This study was performed retrospectively from data of patients hospitalized with the diagnosis of Coronavirus 2019 (COVID-19) in Yerkoy State Hospital. A total of 170 patients with a laboratory diagnosis of coronavirus were included. Thorax computed tomography (CT) findings, hematologic data, liver and kidney function tests, lipid profiles, basal hormone data and some vitamin levels were assessed. Gender, age, and length of hospital stay were determined. The existence of an independent relationship between biochemical parameters and the risk of admission to the ICU was investigated by binary logistic regression analysis.

Yazışma adresi: Meltem Yardım

Department of Medical Biochemistry, Yerkoy State Hospital, 66900 Yozgat, Turkey

e-posta: meltem_yardim@hotmail.com.tr

Etik onay: Türkiye Cumhuriyeti Sağlık Bakanlığı ve Yozgat Bozok Üniversitesi Klinik Araştırmalar Etik Kurulu 18.06.2021tarih ve 2017-KAEK-189_2021.06.18_01 sayılı kurur kararı

Results: Mean age of participants was 69.12±13.72 years. 145 (85.3%) patients were discharged from the hospital with recovery, and 25 (14.7%) patients were referred to another hospital due to ICU needs. The median length of stay in the hospital was 5 (range 1-64) days. 143 (84.1%) patients had pathology in thorax CT. Length of stay in the hospital was significantly lower in referred patients than in non-ICU patients (p<0.001). Coronary artery disease (CAD) percentage was significantly higher in patients requiring ICU admission (p=0.010). We found no significant differences between non-ICU and ICU patients regarding age, sex, and CT findings. Platelet count (p=0.004) and monocyte percentage (p=0.018) were significantly lower, and Lactate Dehydrogenase (LDH) was significantly higher in patients requiring ICU p=0.007).

Conclusion: The increase in LDH, decrease in platelet and monocyte, and presence of concomitant CAD in patients hospitalized with the diagnosis of COVID-19 may alert physicians regarding the need for ICU.

Keywords: COVID-19; Intensive care unit; LDH; Hematological parameters.

ÖZET

Amaç: Korona virüs enfeksiyonu olan hastalarda yoğun bakım ünitesi (YBÜ) gereksinimi için prediktif belirteçlerin belirlenmesi amaçlandı.

Gereç ve Yöntem: Bu çalışma, Yerköy Devlet Hastanesi'ne koronavirüs tanısı ile yatırılan hastaların verilerinden retrospektif olarak yapılmıştır. Çalışmaya COVID-19 tanılı toplam 170 hasta dahil edildi. Toraks bilgisayarlı tomografi (BT), hematolojik veriler, karaciğer ve böbrek fonksiyon testleri, lipid profilleri, bazal hormon verileri ve bazı vitamin düzeyleri değerlendirildi. Cinsiyet, yaş ve hastanede kalış süreleri belirlendi. Biyokimyasal parametreler ile YBÜ yatış riski arasındaki bağımsız ilişkinin varlığı binary lojistik regresyon analizi ile araştırıldı.

Bulgular: Hastaların ortalama yaşı 69,12±13,72 yıl idi. 145 (%85,3) hasta şifa ile hastaneden taburcu edildi, 25 (%14,7) hasta ise yoğun bakım ihtiyacı nedeniyle başka bir hastaneye sevk edildi. Hastanede ortalama kalış süresi 5 (1-64) gündü. 143 (%84,1) hastada toraks BT'de patoloji saptandı. Hastanede kalış süresi, sevk edilen hastalarda taburcu edilen hastalara göre anlamlı olarak daha düşük saptandı (p<0,001). Koroner arter hastalığı (KAH) yüzdesi yoğun bakım gereksinimi olan hastalarda anlamlı olarak yüksekti (p=0,010). Yoğun bakım gereksinimi olan ve olmayan hastalar arasında yaş, cinsiyet ve BT bulguları açısından anlamlı fark bulunmadı. Trombosit sayısı (p=0,004) ve monosit yüzdesi (p=0,018) YBÜ gereksinimi olan hastalarda anlamlı olarak düşük, Laktat Dehidrogenaz (LDH) anlamlı olarak yüksekti (p=0,007).

Sonuç: COVID-19 tanısı ile yatırılan hastalarda LDH artışı, trombosit ve monositte azalma ve eşlik eden KAH varlığı yoğun bakım ihtiyacı açısından uyarıcı olabilir.

Anahtar Kelimeler: COVID-19; Yoğun bakım ünitesi; LDH; Hematolojik parametreler.

INTRODUCTION

SARS-CoV-2 is a viral pathogen that enters the systemic circulation and secondary target organs through different receptors after infecting the lungs, which is the main target organ, via the alveolo-capillary membrane. The disease may progress with simple upper respiratory tract infection findings, or it may lead to fatal cardiorespiratory disease. For this reason, the need for an intensive care unit (ICU) may arise at any time in patients diagnosed with COVID-19 (1). However, we do not yet have a biomarker to predict the ICU need of patients with coronavirus.

Approximately 5-6% of patients hospitalized with a laboratory-confirmed diagnosis of COVID-19 infection need an ICU. However, it is very difficult to predict which patients initially hospitalized for simple COVID-19 symptoms will need an ICU. Male patients with cardiovascular pathology, diabetes, and hypertension are more likely to attend the ICU. It is known that patients with chronic obstructive pulmonary disease and those using angiotensin-converting enzyme inhibitors have an increased ICU risk. It is known that approximately half of the patients with COVID-19, hospitalized with the diagnosis of acute respiratory distress (ARDS)

need ICU. Thorax CT data is another parameter used to determine ICU admission. However, there may be patients who need ICU even though there is no significant lung involvement in CT, and some cases with lung involvement in CT may not need ICU (2-5).

Due to the systemic nature of COVID-19 disease, lung, heart, kidney, liver, and bone marrow involvement may occur. Depending on the involved organ, different pathologies can be detected in laboratory parameters and radiological findings. Although the history of smoking, hypertension, coronary artery disease (CAD), heart failure and obstructive pulmonary disease keeps the physician awake to admit the patient to the ICU, approximately half of the patients do not have a history of additional pathology. Therefore, there is a need for simple and reproducible markers to predict the need for ICU admission. This study was conducted retrospectively on hospitalized patients admitted to a public hospital, without an ICU, with symptoms and were laboratory confirmed to have COVID-19 (6-8).

In this study, it was aimed to evaluate the difference in terms of chronic diseases, demographic data, and laboratory tests between patients with and without intensive care need hospitalized with the diagnosis of COVID-19 in our hospital. In addition, it was aimed to determine the predictive values of the factors affecting the need for intensive care.

MATERIAL AND METHODS

Approval for this study was obtained from the Ministry of Health of the Republic of Turkey and the Clinical Research Ethics Committee of Yozgat Bozok University (Date: 18.06.2021 and Decision Number: 2017-KAEK-189_2021.06.18_01).This retrospective study was performed by recording and subsequently analyzing the medical data from the files of patients hospitalized with the diagnosis of COVID-19 in Yerköy State Hospital. A total of 170 patients with a laboratory diagnosis of COVID-19 who were hospitalized in Yerkoy State Hospital between 1 December 2020 and 31 May 2021 were included in the study. Of these, 86 were female and 84 were male patients aged between 19 and 98 years. Real-time reverse transcription polymerase chain reaction (RT-PCR) positivity was accepted for diagnosing COVID-19. Patients younger than 18 years of age, pregnant and clinically diagnosed with COVID-19 without PCR confirmation were excluded from the study. Patients' age, gender, length of hospital stays, comorbidities, need for intensive care, survival and thorax CT, and laboratory data were obtained and recorded retrospectively from patient files and the hospital information management system. The results of laboratory tests driven at the time of the patients' first application were evaluated. One hundred seventy patients with demographic and laboratory data were separated into two groups: those who needed intensive care (n = 25) and those who did not (n = 145). Age, gender, comorbidities and laboratory tests of these groups were statistically analyzed and compared. C-reactive protein (CRP), urea, creatinine, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), LDH, Alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), total protein, albumin, creatine kinase (CK) concentrations were measured with Beckman Coulter AU 680 (Beckman Coulter, Inc., Brea, CA, USA) device, complete blood count (CBC) parameters (WBC, PLT, RBC, HGB, HCT, MPV, RDW, NEU%, LYM%, MONO%) were measured with ABX Pentra DX 120 (Horiba Medical, Montpellier, France) device. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated by dividing the neutrophil value in the complete blood count by the lymphocyte value and dividing the platelet value by the lymphocyte value, respectively. Serum ferritin, vitamin B12, 25-Hydroxy Vitamin D [25(OH) D], Thyroid-Stimulating Hormone (TSH), free thyroxine (FT4) concentrations were measured with chemiluminescence immunoassay method on the ADVIA Centaur XP immunoassay analyzer (Siemens Healthineers, Erlangen, Germany). Patients with dyspnea and respiratory distress, respiratory rate ≥ 30/min, PaO2/FiO2 < 300, increased oxygen demand in the follow-up,

SpO2 < 90% or PaO2 < 70 mmHg despite 5 L/min oxygen therapy, hypotension (systolic blood pressure< 90 mmHg, more than 40 mmHg decrease from normal systolic blood pressure, mean arterial pressure<65 mmHg, tachycardia>100/min), acute kidney injury, development of acute organ dysfunction such as acute liver function tests, confusion, acute bleeding diathesis, immunosuppression, Troponin elevation and arrhythmia were accepted as intensive care referral criteria.

Statistical Analysis

The Shapiro-Willk test was used to determine whether the continuous variables were normally distributed. Continuous data were exhibited as mean and standard deviation or median (25^{th} and 75^{th} percentile), and discrete data as the ratio (per cent). Between groups, analysis of the continuous variables was performed with the Student's t-test or Mann-Whitney U test, depending on the normality of distribution. Between groups, analysis of the categorical variables was performed with the Chi-square test. Binary logistic regression analysis was performed to identify factors independently associated with admission to the ICU. The diagnostic performance of the laboratory parameters was assessed using Receiver Operating Characteristic (ROC). Using Youden's index, optimal cut-off values for the laboratory parameters were determined. All analysis were performed on IBM SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism 8.0 software (GraphPad Software, San Diego, California, USA). P significance level was accepted as <0.05.

RESULTS

In our study, we included 170 COVID-19-positive patients (86 females and 84 males) with a mean age of 69.12 ± 13.72 (19-98) years. 145 (85.3%) patients were discharged from the hospital with recovery, and 25 (14.7%) patients were referred to another hospital due to intensive care unit need. The median length of stay in the hospital was 5 (range 1-64) days. Although 143 (84.1%) patients had viral pneumonia findings compatible with COVID-19 on thorax CT, none of the cases were mortal. Duration of stay in the hospital was significantly lower in patient referred with the need of ICU than in the discharged patients (p<0.001). CAD percentage (p=0.010) was significantly higher in the ICU patients than in the non-ICU patients (Figure 1). We found no significant differences between ICU and non-ICU patients regarding age, sex, CT findings and other comorbidities. Platelet count (p=0.004) and monocyte percentage (p=0.018) were significantly lower in the ICU patients than in the non-ICU patients (Figure 2a-2b). LDH (p=0.007) was significantly higher in the ICU patients than in the non-ICU patients (Figure 2c). We found no significant differences between ICU and non-ICU patients regarding other laboratory measurements (Table 1).

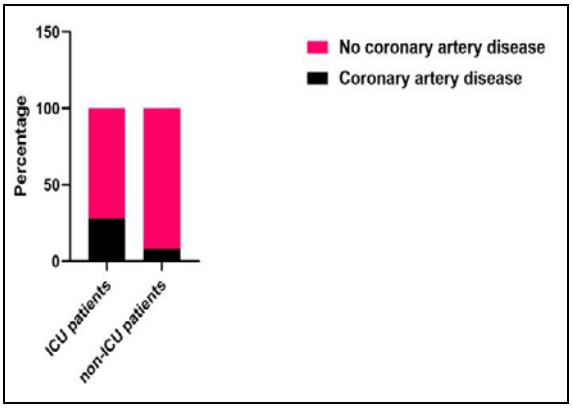

Figure 1. Coronary artery disease percentage regarding patient outcome.

Multiple logistic regression analysis revealed that CAD [odds ratio (95% CI)=4.723 (1.243-17.951), p=0.023], low platelet count [odds ratio (95% CI)= 0.993 (0.987-0.999),p=0.030], low monocyte percentage [odds ratio (95% CI)= 0.823 (0.696-0.974),p=0.023] and high LDH [odds ratio (95% CI)=1.006 (1.002-1.010),p=0.005] were independently associated with admission to ICU after adjusted with age, sex and presence of COVID-19 compatible thorax CT findings (Table 2).

Table 1. Summary of patients' characteristics and laboratory measurements regarding outcome

		Outcome		
	Total (n=170)	**Non-ICU patients (n=145)**	**ICU patients (n=25)**	**p**
Age (years)	69.12 ± 13.72	68.83 ± 13.75	70.84 ± 13.69	0.500
Sex				
Female	86 (50.6%)	75 (51.7%)	11 (44.0%)	0.619
Male	84 (49.4%)	70 (48.3%)	14 (56.0%)	
CT findings				
COVID-19 compatible	143 (84.1%)	119 (82.1%)	24 (96.0%)	0.133
No pneumonia	27 (15.9%)	26 (17.9%)	1 (4.0%)	
Length of stay in hospital, days	5 (3 - 7)	5 (4 - 8)	3 (2 - 5)	**<0.001**
Mortality	0 (0.0%)	0 (0.0%)	0 (0.0%)	N/A
Comorbidities	119 (70.0%)	102 (70.3%)	17 (68.0%)	1.000
Hypertension	87 (51.2%)	72 (49.7%)	15 (60.0%)	0.460
Diabetes mellitus	49 (28.8%)	44 (30.3%)	5 (20.0%)	0.415
Coronary artery disease	19 (11.2%)	12 (8.3%)	7 (28.0%)	**0.010**
Cerebrovascular accident	5 (2.9%)	5 (3.4%)	0 (0.0%)	1.000
Hyperlipidemia	35 (20.6%)	31 (21.4%)	4 (16.0%)	0.729
Asthma	12 (7.1%)	10 (6.9%)	2 (8.0%)	0.691
COPD	23 (13.5%)	19 (13.1%)	4 (16.0%)	0.751
Other	27 (15.9%)	20 (13.8%)	7 (28.0%)	0.082
RBC($x10^6/\mu L$)	4.68 ± 0.61	4.67 ± 0.63	4.76 ± 0.54	0.492
Hemoglobin (g/dL)	13.26 ± 1.89	13.21 ± 1.88	13.55 ± 1.98	0.412
Hematocrit (%)	40.79 ± 5.45	40.62 ± 5.35	41.74 ± 5.99	0.344
RDW (%)	14.17 ± 1.89	14.22 ± 1.96	13.86 ± 1.38	0.381
Platelet ($x10^3/\mu L$)	245.64 ± 109.17	252.86 ± 113.54	203.80 ± 66.60	**0.004**
MPV (fl)	9.21 ± 1.01	9.19 ± 1.05	9.36 ± 0.75	0.418
WBC ($x10^3/\mu L$)	6.4 (5.0 - 9.0)	6.5 (5.0 - 8.4)	5.9 (4.9 - 9.4)	0.860
Lymphocyte (%)	18.48 ± 9.69	18.70 ± 10.01	17.23 ± 7.64	0.486
Monocyte (%)	9.72 ± 3.59	9.94 ± 3.70	8.45 ± 2.62	**0.018**
Neutrophil (%)	69.71 ± 11.20	69.15 ± 11.50	72.99 ± 8.77	0.113
Lymphocyte ($x10^3/\mu L$)	1.05 (0.79 - 1.37)	1.05 (0.8 - 1.37)	1.09 (0.71 - 1.33)	0.911
Monocyte ($x10^3/\mu L$)	0.59 (0.44 - 0.86)	0.59 (0.44 - 0.88)	0.51 (0.44 - 0.72)	0.258
Neutrophil ($x10^3/\mu L$)	4.35 (3.32 - 6.79)	4.42 (3.36 - 6.55)	4.23 (3.28 - 7.73)	0.743
Platelet to lymphocyte ratio (PLR)	210.31 (154.59 - 322.23)	216.67 (159.14 - 327.01)	177.38 (146.13 - 245.65)	0.131
Neutrophil to lymphocyte ratio (NLR)	4.12 (2.59 - 6.76)	4.06 (2.47 - 6.76)	4.42 (3.18 - 6.53)	0.514
Urea(mg/dL)	41.6 (29.8 - 60.1)	41.5 (30.05 - 59.2)	48.1 (28.8 - 70.3)	0.572
Creatinine(mg/dL)	0.94 (0.72 - 1.24)	0.92 (0.71 - 1.22)	0.99 (0.79 - 1.42)	0.219
AST(U/L)	33 (23 - 44)	32 (23 - 44)	34.5 (26.5 - 45)	0.309
ALT(U/L)	25 (17 - 38)	25 (16 - 38)	31 (17 - 41)	0.553
LDH(U/L)	348.05 ± 124.41	337.63 ± 122.96	412.43 ± 115.95	**0.007**
ALP(U/L)	74 (56 - 93)	74 (57 - 93)	73 (53 - 82)	0.733
GGT(U/L)	30 (21 - 51)	30 (21 - 48)	39.5 (23 - 58.5)	0.262
Total protein(g/dL)	6.77 ± 0.62	6.78 ± 0.63	6.68 ± 0.57	0.502
Albumin(g/dL)	3.44 ± 0.36	3.46 ± 0.38	3.38 ± 0.28	0.344
CK(U/L)	98 (63 - 147)	98 (62 - 142)	115 (72 - 164)	0.308
CRP (mg/L)	74.70 (30.10 - 110.30)	74.70 (28.60 - 110.30)	71.25 (34.45 - 106.45)	0.945
Ferritin(ng/mL)	253.0 (108.5 - 516.1)	251.4 (92.9 - 481.4)	351.3 (238.45 - 843.4)	0.077
Vitamin D (ng/mL)	11.90 (8.89 - 17.26)	11.90 (8.92 - 17.47)	10.75 (8.30 - 13.36)	0.479
TSH (mU/L)	1.13 (0.54 - 1.67)	1.15 (0.45 - 1.77)	1.01 (0.77 - 1.42)	0.941
FT4(ng/dL)	1.11 ± 0.26	1.11 ± 0.28	1.07 ± 0.16	0.690
Vitamin B12(pg/mL)	406.68 ± 188.07	419.24 ± 197.03	328.80 ± 89.95	0.160

COPD: Chronic obstructive pulmonary disease; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; LDH: Lactate dehydrogenase; ALP: Alkaline phosphatase (ALP); GGT: gamma-glutamyl transferase (GGT);CK: Creatine kinase; CRP:C-reactive protein; TSH:Thyroid-Stimulating Hormone; free thyroxine (FT4).Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to the normality of distribution and as frequency (percentage) for categorical variables.

LDH performed the highest area under the curve (AUC) value with 0.693 (95% confidence interval [CI]=0.616–0.762), presenting 69.6% of sensitivity and 67.6% of specificity at a cut-off value of 374, p<0.001. Monocyte percentage performed the AUC value of 0.625 (95% CI= 0.548–0.698), presenting 72.0% sensitivity and 56.6% specificity at a cut-off value of 8.90, p=0.024. Platelet count performed the AUC value of 0.620 (95% CI= 0.543–0.693), presenting 92.0% sensitivity and 37.2% specificity at a cut-off value of 269, p=0.026 (Table 3).

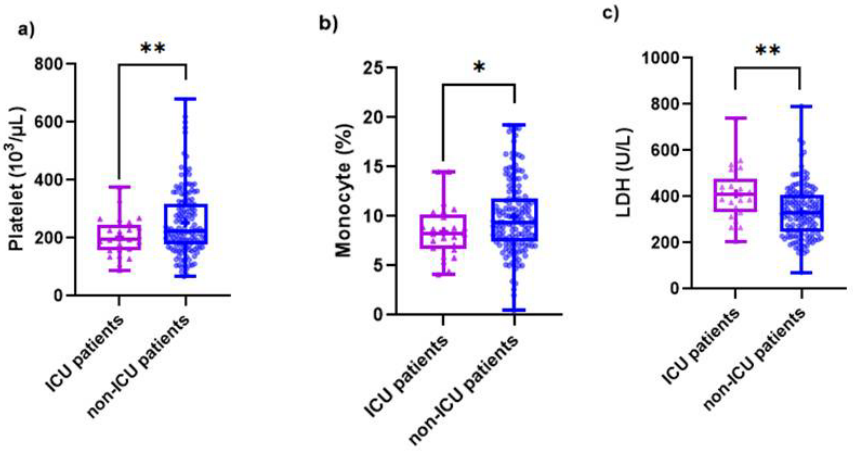

Figure 2. a) Platelet count (x10³/μL) (mean ± standard deviation), **b)** Monocyte (%), **c)** LDH (U/L)(mean ± standard deviation) regarding outcome.
(*p<0,05 **p<0,01).

Table 2. Factors independently associated with admission to ICU, multiple logistic regression analysis.

	β coefficient	Standard error	P	Exp(β)	95.0% CI for Exp(β)	
Age(years)	0.002	0.020	0.933	1.002	0.964	1.041
Sex, Male	0.354	0.536	0.510	1.424	0.498	4.074
Pathological CT findings	1.973	1.122	0.079	7.195	0.798	64.841
Coronary artery disease	1.553	0.681	**0.023**	4.723	1.243	17.951
Platelet (x10³/μL)	-0.007	0.003	**0.030**	0.993	0.987	0.999
Monocyte (%)	-0.195	0.086	**0.023**	0.823	0.696	0.974
LDH (U/L)	0.006	0.002	**0.005**	1.006	1.002	1.010
Constant	-2.922	2.019	0.148	0.054		

LDH: Lactate dehydrogenase; CI: Confidence Interval; Nagelkerke R^2=0.277

Table 3. Receiver operating curve analysis of laboratory parameters in identifying admission to ICU

Parameter	Cutoff	AUC (95% CI)	Sensitivity	Specificity	p
LDH (U/L)	≥374	0.693 (0.616-0.762)	69.6%	67.6%	**<0.001**
Monocyte (%)	≤8.90	0.625 (0.548-0.698)	72.0%	56.6%	**0.024**
Platelet (x10³/μL)	≤269	0.620 (0.543-0.693)	92.0%	37.2%	**0.026**

LDH: Lactate dehydrogenase; AUC: area under the curve; CI: Confidence Interval.

DISCUSSION

We have insufficient predictive markers to determine whether patients hospitalized for palliative purposes due to SARS-CoV-2 need ICU or not. ICU referral is often considered due to deterioration of the patient's general condition and deterioration of respiratory functions. However, sometimes it may be too late for the ICU when the patient presents symptoms. Therefore, delay in ICU referral can be prevented if these patients are followed up with the help of predictive biomarkers (9-11).

In the multivariable regression analysis, we found that age, sex, and pathological thorax CT findings were not predictive in the referral of patients to ICU. In the regression analysis for other comorbidities, the presence of CAD independently affected referral to ICU (1-3). In the multivariable analysis of hematological parameters, low platelet and monocyte and increased LDH independently affected referral rates for ICU (1-4). In addition to the presence of CAD, the change in LDH, platelet and monocyte was determined as an independent factor determining the referral of patients to a higher institution, regardless of age, gender and CT data. The absence of age and sex predictive value may be due to the small number of patients and heterogeneity. It should be a predictive marker for the ICU, as advancing age will lead to damage to the alveolar-capillary membrane (6-8). However, age and sex may seem ineffective due to changes in patients' lifestyles, body mass indexes, eating habits and frequency of going to health check-ups. If the number of cases had been higher, both age and male gender might have appeared as independent parameters for referral to ICU.

We found no significant association between changes in other hematological parameters, liver enzymes, renal function test changes and referral to the ICU. However, considering that the deterioration in kidney and liver functions occurs later, we find it useful to interpret the findings of these organs as early or late. Similarly, it is appropriate to interpret the tomographic changes in the lung, which is the main target organ of the virus, as early and late-stage findings and to talk about its predictive value accordingly (4-7).

When previous studies were assessed, it was observed that parameters such as thorax CT findings, CRP, ferritin, NLR and PLR were important in ICU hospitalization and mortality in COVID-19 (9-11). The fact that no significant difference was observed in our study may be related to the low sample size and the assessment of test results at the first admission. In addition, the reason of the short hospitalization period in patients who required ICU is that, they referred to another center with ICU after approximately 3 days after hospitalization while other patients continue to be hospitalized at our in-patient service.

When the LDH results were compared, it was observed that the results were statistically significant. According to the ROC analysis performed for LDH results, the cut-off value was≥374 U/L, sensitivity was %69.6, and specificity was %67.6. Values above the cut-off value ≥374 U/L were found to be significantly associated with the need for intensive care. Similar results have been found in previous studies. Han Y. et al. evaluated the clinical and laboratory data of 107 patients with COVID-19 and compared the patients with severe clinical status with the patients who were not clinically severe and reported the serum LDH cut-off value as 344.5 U/L (sensitivity 68.8%, specificity 96.9%) as predictive for severe clinical condition (12). In another study conducted by Poggiali E. et al., the relationship between LDH values and respiratory failure in 123 patients with COVID-19 admitted to the emergency department was examined and it was stated that high LDH concentrations at the time of admission were an independent risk factor for the detection of severe COVID-19 cases and mortality (13).In the binary logistic regression analysis, we observed that the increase in LDH concentrations independently increased the risk of intensive

care hospitalization in COVID-19 patients. The increase in LDH concentrations was thought to be evidence of the virus moving from the lung to the systemic circulation and initiating early liver damage.

Another result we found in our study is that the rate of monocyte (%) decreased significantly in patients requiring intensive care. Considering the studies in the literature, it has been stated that severe COVID-19 pneumonia is associated with cytokine storm and excessive activation of monocytes and macrophages. Monocytes are cells that play an important role in phagocytosis, cytokine production, antigen presentation, and other immune function processes. Circulating monocytes infiltrate peripheral tissues during inflammation and differentiate into macrophages or dendritic cells (14,15). In the literature, data on the number of monocytes in COVID-19 infection are limited and there are conflicting results. An increase in the number of monocytes has been reported in some studies. In some other studies, it was stated that there was a decrease in the number of monocytes (16-18). Kilercik et al., compared hematological parameters between surviving and non-surviving patients with COVID-19 and reported that there was a significant difference in the number of monocytes and the rate of monocytes (%) decreased significantly with the severity of the disease. They associated the decrease in monocytes (%) with the selective recruitment of monocytes in the lungs during the development of ARDS (19).

Consistent with the literature, platelet count was significantly decreased in patients requiring intensive care in our study. In a meta-analysis that evaluated nine studies in patients with COVID-19 and included 1779 cases, 399 (22.4%) of which were severe, a decreased platelet count was observed in severe patients (20). Platelet counts may have decreased due to the possibility of disseminated intravascular damage due to widespread organ involvement in the COVID-19 infection. Similarly, depending on the prevalence of infection, one of the reasons for the deterioration in adaptive immunity maybe a decrease in the number of monocytes. It is an expected finding that the need for ICU increases in the presence of CAD. The affinity of the virus for the myocardium may have increased the referral rates for the ICU by exacerbating already defective cardiac function (8,21-23).

The limitation of our study is that it was conducted retrospectively in a single center, and the number of cases was limited. Since D-dimer and procalcitonin parameters could not be measured in our hospital, these parameters could not be evaluated in terms of intensive care requirements.

CONCLUSION

As a result, the increase in LDH, decrease in platelet and monocyte count, and the presence of concomitant CAD in patients hospitalized with COVID-19 infection should alert the physician regarding the patient's need for ICU. When changes are detected in biochemical and hematological parameters, the physician should be prepared to refer and manage the patient to a higher institution.

CONFLICT OF INTERESTS None

REFERENCES

1. Celik O, Saglam A, Baysal B, Derwig IE, Celik N, Ak M, et al. Factors preventing materno-fetal transmission of SARS-CoV-2. Placenta 2020;97:1-5.
2. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. China Medical Treatment Expert Groupfor Covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708-20.
3. Huang C, Wang Y, Li X,Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395 (10223):497-506.
4. Myers LC, Parodi SM, Escobar GJ, Liu VX. Characteristics of hospitalized adults with COVID-19 in an integrated health care system in California. JAMA 2020;323(21):2195-8.

5. Wang Y, Lu X, Li Y, Chen H, Chen T, Su N, et al. Clinical course and outcomes of 344 intensive care patients with COVID-19. Am J Respir Crit Care Med 2020;201(11):1430-4.
6. Ferrario CM, Jessup J, Chappell MC, Averill DB, Brosnihan KB, Tallant EA, et al. Effect of angiotensin-converting enzyme inhibition and angiotensin II receptor blockers on cardiac angiotensin-converting enzyme 2. Circulation. 2005;111(20):2605-10.
7. Carenzo L, Costantini E, Greco M, Barra FL, Rendiniello V, Mainetti M, et al. Hospital surge capacity in a tertiary emergency referral centre during the COVID-19 outbreak in Italy. Anaesthesia 2020;75(7):928-34.
8. Celik O, Celik N, Aydin S, Baysal B, Aydin S, Saglam A, et al. Combating sars-cov-2 through lipoxins, proteasome, caveolin and nuclear factor-κb pathways in non-pregnant and pregnant populations. Cell Mol Biol (Noisy-le-grand) 2020;66(3):221-9.
9. Qu R, Ling Y, Zhang YH, Wei LY, Chen X, Li XM, et al. Platelet-to-lymphocyte ratio is associated with prognosis in patients with coronavirus disease-19. J Med Virol2020;92(9):1533-41.
10. Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. Int Immunopharmacol 2020;84:106504.
11. 11.Orhan B, Deniz L, Saglam ZA, Eren G, Inal BB. The effect of diagnostic value of biochemical parameters on mortality in COVID-19 patients. Med Science 2022;11(4):1511-5.
12. 12.Han Y, Zhang H, Mu S, Wei W, Jin C, Tong C, et al. Lactate dehydrogenase, an independent risk factor of severe COVID-19 patients: a retrospective and observational study. Aging (Albany NY) 2020;12(12):11245-58.
13. Poggiali E, Zaino D, Immovilli P, Rovero L, Losi G, Dacrema A, et al. Lactate dehydrogenase and C-reactive protein as predictors of respiratory failure in CoVID-19 patients. Clin Chim Acta2020;509:135-8.
14. Pence BD. Severe COVID-19 and aging: are monocytes the key? GeroScience 2020;42:1051-61.
15. Gómez-Rial J, Rivero-Calle I, Salas A, Martinón-Torres F. Role of monocytes/macrophages in Covid-19 pathogenesis: implications for therapy. InfectDrug Re- sist 2020;13:2485-93.
16. Zhou Y, Fu B, Zheng X, Wang D, Zhao C, Qi Y, et al. Pathogenic T-cells and inflammatory monocytes incite inflammatory storms in severe COVID-19 patients. Natl Sci Rev 2020;7(6):998-1002.
17. Pirsalehi A, Salari S, Baghestani A, Sanadgol G, Shirini D, Baerz MM, et al. Differential alteration trend of white blood cells (WBCs) and monocytes count in severe and non-severe COVID-19 patients with in a 7-day follow-up. Iran J Microbiol 2021;13(1):8-16.
18. Sanchez-Cerrillo I, Landete P, Aldave B, San- chez-Alonso S, Sanchez-Azofra A, Marcos-Jimenez A, et al. Differential redistribution of activated monocyte and dendritic cell subsets to the lung as- sociates with severity of COVID-19. medRxiv 2020:10.1101/2020.05.13.20100925.
19. Kilercik M, Demirelce Ö, Serdar MA, Mikailova P, Serteser M. A newhaematocytometricindex: Predicting severity and mortality risk value in COVID-19 patients. PLoSOne 2021;16(8):e0254073.
20. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. Clin Chim Acta 2020;506:145-8.
21. D'Ecclesiis O, Gavioli C, Martinoli C, Raimondi S, Chiocca S, Miccolo C, et al. Vitamin D and SARS-CoV2 infection, severity and mortality: A systematic review and meta-analysis. PLoS One 2022;17(7):e0268396.
22. Melenotte C, Silvin A, Goubet AG, Lahmar I, Dubuisson A, Zumla A, et al. Immune responses during COVID-19 infection. Oncoimmunology 2020;9(1):1807836.
23. Mattioli F, Piva S, Stampatori C, Righetti F, Mega I, Peli E, et al. Neurologic and cognitive sequelae after SARS-CoV2 infection: Different impairment for ICU patients. J Neurol Sci 2022;432:120061.