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PREDICTIVE RELEVANCE OF DIFFERENT CLINICAL AND LABORATORY FINDINGS FOR HIGHER MORTALITY IN PATIENTS WITH COVID-19 IN A SINGLE CENTER COHORT: NEUTROPHIL/LYMPHOCYTE RATIO, HIGH CRP, GGT AND CREATININE LEVELS ARE ASSOCIATED WITH HIGH MORTALITY

COVID-19'DA KLİNİK VE LABORATUVAR BULGULARININ MORTALİTE GÖSTERGESİ OLARAK DEĞERİ, TEK MERKEZ KOHORT ÇALIŞMASI, YÜKSEK NÖTROFİL/LENFOSİT ORANI, CRP, GGT, KREATİNİN DEĞERLERİ VE ARTMIŞ MORTALİTE RİSKİ

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ABSTRACT

Objective: Early detection of mortality risk is important in patients diagnosed with of coronavirus disease 2019 (COVID-19). Therefore, we aimed to evaluate the predictive value of different clinical and laboratory parameters in disease severity and mortality in patients with COVID-19.

Materials and Methods: Patients admitted to hospital with a diagnosis of COVID-19 were evaluated retrospectively. The patients' admission date, discharge date, intensive care transfer/death date, contact history, smoking, symptoms at the time admission, vital markers at admission, and laboratory parameters were recorded.

Results: The study included a total of 347 patients, of whom 168 (48.4%) were female. The mean age of the patients was 59.69±16.87 (14-97) years, while 40.9% (n=142) were aged over 65 years. Overall, 10.1% (n=35) of the patients required transfer to an intensive care unit and 8.4% (n=29) were deceased. When clinical parameters were evaluated at the time of admission, oxygen saturation was found to be lower in the group that died (79.51±6.95), compared to the survivors (88.78±6.11) (p<0.001). Additionally, male gender (p=0.05), advanced age (p<0.001),

ÖZET

Amaç: Koronavirüs hastalığı 2019 (COVID-19) tanısı ile takip edilen hastalarda mortalite riskinin erken tespiti önemlidir. COVID-19'da farklı klinik ve laboratuvar parametrelerin hastalık şiddeti ve mortalite göstergesi olarak değerinin saptanması hedeflenmiştir.

Gereç ve Yöntem: COVID-19 tanısı ile hastaneye yatırılan hastalar retrospektif olarak değerlendirilmiştir. Hastaların yatış tarihi, taburculuk tarihi, yoğun bakıma sevk ve ölüm tarihleri, başvuru sırasındaki semptomları, başvuru anındaki klinik ve laboratuvar parametreleri kaydedilmiştir.

Bulgular: Çalışmaya 168'i (%48,4) kadın olmak üzere toplam 347 hasta dahil edildi. Hastaların yaş ortalaması 59,69±16,87 (14-97) iken, %40,9'u (n=142) 65 yaşın üzerindeydi. Hastaların %10,1'i (n=35) yoğun bakım ünitesine transfer edildi ve %8.4'ü (n=29) öldü. Başvuru anındaki klinik paremetreler değerlendirildiğinde, oksijen saturasyonu ölen grupta (79,51±6,95) sağ kalanlara göre daha düşüktü (88,78±6,11) (p<0,001). Erkek cinsiyet (p=0,05), ileri yaş (p<0,001), pozitif PCR sonucu (p=0,036), şiddetli toraks BT tutulumu (p<0,001) ve en az bir komorbidite varlığı (p=0,003) mortalite grubunda daha fazlaydı. Çok değişkenli analizlerde

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positive PCR result (p=0.036), congestive heart failure (p=0.044), severe COVID-19 involvement on thorax CT (p<0.001), and presence of at least one comorbidity (p=0.003) were observed at a higher rate in the mortality group. In the multivariate analyses, increased values of the NLR (HR: 1.04, 95% CI: 1.00-1.08), creatinine (OR: 1.37, 95% CI: 1.13-1.66), CRP (=-0.18, OR: 0.98, 95% CI: 0.97-0.99), GGT (OR: 1.006, 95% CI: 1.001-1.012), age (OR: 5.67, 95% CI: 2.24-14.38), male gender (OR: 2.38, 95% CI: 0.98-5.75), and presence of any comorbidity (OR: 5.23, 95% CI: 2.08-13.13) were associated with mortality.

Conclusions: Several clinical and laboratory parameters, such as advanced age, male gender, presence of any comorbidity, and NLR, GGT, CRP and creatinine levels at the time of admission can predict mortality in COVID-19 patients. These parameters obtained at the time of admission can contribute to the reduction of mortality through a closer clinical and laboratory follow-up in these patients.

Keywords: COVID-19, mortality, mortality risk factors, gamma-glutamyl transferase, neutrophil/lymphocyte ratio, SARS-CoV-2

artmış nötrofil/lenfosit oranı (HR: 1,04, %95 GA: 1,00-1,08), kreatinin (OR: 1,37, %95 CI: 1,13-1,66), CRP (=-0,18, OR: 0,98, 95) % GA: 0,97-0,99), GGT (OR: 1,006, %95 GA: 1,001-1,012), yaş (OR: 5,67, %95 GA: 2,24-14,38), erkek cinsiyet (OR: 2,38, %95 GA: 0,98 -5,75) ve komorbidite varlığı (OR: 5,23, %95 GA: 2,08-13,13) mortalite ile ilişkili bulundu.

Sonuç: COVID-19'da ileri yaş, erkek cinsiyet, komorbidite varlığı ve başvuru anındaki artmış NLR, GGT, CRP ve kreatinin değerleri gibi çeşitli klinik ve laboratuvar parametreler mortaliteyi öngörmede yardımcı olabilir. Başvuru anında elde edilen bu parametrelerle belirlenen hastaların daha yakın klinik ve laboratuvar takibi mortalitenin azaltılmasına katkı sağlayacaktır.

Anahtar Kelimeler: COVID-19, mortalite, mortalite risk faktörleri, gama-glutamil transferaz, nötrofil/lenfosit oranı, SARS-CoV-2

INTRODUCTION

In November 2019, a new coronavirus called "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) was identified in Wuhan, China (1, 2). Coronavirus disease 2019 (COVID-19) caused by the virus can lead to a wide clinical variability from mild diseases to acute respiratory failure and death (3). With the emergence of SARS-CoV-2 in Wuhan and its spread across the world, COVID-19 has become a global problem and resulted in the deaths of millions of people. Several risk factors, such as male gender, advanced age, and diabetes have been associated with high mortality in patients with COVID-19 in previous studies (4, 5). In addition, there have been some efforts to determine biomarkers that can indicate prognosis and mortality related to the disease. Laboratory parameters, such as lL-6, D-dimer, C-reactive protein (CRP), and absolute lymphocyte count are some of these biomarkers that have been found to have prognostic significance (4–6).

Neutrophil/lymphocyte ratio (NLR) can be easily calculated by dividing the absolute neutrophil count by the absolute lymphocyte count in routine blood tests and appears to be a useful biomarker because it is applicable in almost every laboratory. In a study by Liu et al., NLR was identified as an independent risk factor of mortality in patients followed up in hospital with a diagnosis of COVID-19, as well as other routine laboratory parameters (7).

In this study, we aimed to evaluate the prognostic importance of routine laboratory parameters and NLR in the prediction of severe disease and mortality in patients with COVID-19.

MATERIALS AND METHODS

Study design and participants

Patients over 18 years who presented to our hospital and received a probable or definitive diagnosis of COVID-19 between July 1, 2020 and October 1, 2020 were included in the study. Cases were defined according to the World Health Organization definitions (8). A positive result in the SARS-CoV-2 real-time reverse-transcription polymerase chain reaction (RT-PCR) test of a respiratory tract sample was defined as a definite diagnosis, while appearance consistent with viral pneumonia in thoracic computed tomography (CT) together with appropriate clinical findings was accepted as a probable case despite a negative SARS-CoV-2 RT-PCR test.

All the patients were treated with hydroxychloroquine and/or favipiravir. Dexamethasone 8 mg or equivalent was applied to patients with an oxygen saturation (SpO_2) of <90% at the time of admission and/or during follow-up. The patients who developed secondary bacterial infections were evaluated on daily rounds and treated with antibiotics, if necessary.

The study was approved by the local ethics committee of Agri Education and Research Hospital (Date: 11.12.2020, No: 29).

Data collection

Demographic data, accompanying diseases, laboratory and lung CT findings of the patients were retrospectively obtained from the hospital information system. For the patients who were transferred to other intensive care unit (ICU) centers, the mortality status was screened for using the National Death Notification System.

The patients' admission date, discharge date, ICU transfer/death date, contact history, smoking, symptoms during admission, vital markers at admission, complete blood count, urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, lactate dehydrogenase (LDH), creatine kinase (CK), D-dimer, ferritin, troponin and CRP values, the highest values of ferritin and CRP and the lowest lymphocyte count during the follow-up, and lymphocyte count at discharge were recorded. Hydroxychloroquine, favipiravir and steroid use for the treatment of COVID-19 and antibiotic use for the treatment of secondary infections were also noted. In thorax CT, cases with ground glass densities of over three foci or greater than 3 cm diameter or the presence of consolidation were classified as moderate pneumonia, and those with the involvement of all lobes in both lungs and at least three lesions larger than 3 cm in diameter were classified as severe pneumonia (9).

Statistical analysis

All the data were analyzed using the Statistical Package for the Social Sciences (SPSS) software package for Windows (v 21.0; IBM, Armonk, NY, USA). Individual and aggregated data were summarized using descriptive statistics, including mean, standard deviation and median (min-max) values, frequency distributions and percentages. The normality of data distribution was verified with the Kolmogorov-Smirnov test. Comparison of the variables with a normal distribution was performed with Student's t-test. Variables which were not normally distributed were compared between the groups using the Mann Whitney U and Kruskal-Wallis tests. Evaluation of categorical variables was performed with the chi-square test. Correlation analysis was performed using the Pearson or Spearman test according to the normality of data distribution. p values of <0.05 were considered statistically significant.

RESULTS

Demographic features

The study included a total of 347 patients, of whom 168 (48.4%) were women. The mean age of the patients was 59.69±16.87 (14-97) years, while 40.9% (n=142) were over 65 years. Of the patients, 30.8% (n=107) had a history of

Table 1: Baseline clinical features of the patients hospitalized with COVID-19

	Clinical variables	Number (n)	Percent (%)
Gender	Male	179	51.5
	Female	168	49.5
Age (year)	<65	205	59
	≥65	142	41
PCR status	Negative	96	27.6
	Positive	251	72.3
ICU admission	No	312	90
	Yes	35	10
Tobacco use	Absent	307	89
	Present	30	11
HT	Absent	200	57.7
	Present	147	42.3
DM	Absent	258	74.4
	Present	89	25.6
COPD/asthma	Absent	281	81
	Present	66	19
Coronary artery disease	Absent	297	85.6
	Present	50	14.4
Malignancy	Absent	344	99.2
	Present	3	0.8
Acute renal failure	Absent	340	98
	Present	7	2
Hydroxychloroquine treatment	Absent	184	53.1
	Present	163	46.9%
Favipiravir treatment	Absent	100	28.8%
	Present	247	71.2%

PCR: Polymerase chain reaction, ICU: Intensive care unit, HT: Hypertension, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease

contact with a positive COVID-19 case and 72% (n=250) had a positive COVID-19 RT-PCR test. The most common complaint was fatigue/myalgia at a rate of 71.2% (n=247), followed by cough (59.4%), shortness of breath (53.6%), fever (36.0%), and headache (18.4%). When the risk factors of the patients were evaluated, the presence of at least one comorbidity was observed in 13.8% (n=48) of the patients. The baseline clinical and laboratory parameters of the patients are summarized in Table 1.

Overall, 10.1% (n=35) of the patients required transfer to ICU and 8.4% (n=29) died. When the clinical parameters were evaluated at the time of admission, oxygen saturation was found to be lower in the mortality group (79.51±6.95) compared to the survivors (88.78±6.11) (p<0.001). In the univariate analysis, male gender (p=0.054), advanced age (p<0.001), a positive PCR result (p=0.036), congestive heart failure (p=0.044), severe COVID-19 involvement in thorax CT (p<0.001), and presence of at least one comorbidity (p=0.003) were observed at a significantly higher rate among the patients that developed mortality. The comparison of the clinical and laboratory parameters of the patients is presented in Table 2.

Laboratory parameters at the time of admission

There was a statistically significant increase in the leukocyte, neutrophil and NLR values among the patients who were deceased (p=0.03, 0.03, and 0.001, respectively). Furthermore, the serum urea (p<0.001), creatinine (p<0.001), LDH (p<0.001), AST (p<0.001), ALT (p=0.02), GGT (p=0.046), D-dimer (p=0.002) and troponin (p<0.001) values were significantly higher in the mortality group compared to the survivors. Additionally, the mortality group had increased CRP (104.2 vs 57.6 mg/L; p=0.001) and ferritin (589.5 vs 375.0 ng/mL) levels but lower lymphocyte (0.95 vs 1.4x109/L) values (p=0.001, <0.001, and =0.001, respectively) (Table 2).

In the correlation analysis, NLR was slightly positively correlated with age (r=0.173, p=0.001) and CRP (r=0.106, p=0.049) and moderately negatively correlated with SpO_2 (r=-0.437, p<0.001). A mild negative correlation was observed between CRP and SpO_2 (r=-0.152, p=0.005) and a moderate positive correlation between CRP and GGT (r=0.325, p<0.001). There was no correlation between the remaining clinical and laboratory parameters.

Evaluation of risk factors for mortality

In the multivariate analyses (forward logistic regression method), increased NLR [odds ratio (OR): 1.034, 95% confidence interval (CI): 1.003-1.066], advanced patient age (OR: 1.097, 95% CI: 1.054-1.14), presence of any comorbidity (OR: 12.74, 95% CI: 3.36-48.3), male gender (OR: 3.48, 95% CI: 1.28-9.47), and high creatinine (OR: 1.37, 95% CI: 1.13-1.66), CRP (=0.018, OR: 1.018, 95% CI: 1.005-1.032) and GGT (OR: 1.006, 95% CI: 1.001-1.012) levels were associated with mortality (Table 3). Although the serum ferritin, BUN, ALT, AST, D-dimer and troponin levels were higher in the mortality group according to the univariate analysis, none of these parameters were associated with mortality in the multivariate analysis.

DISCUSSION

In this study, the rates of ICU admission (10.1%) and mortality (8.4%) were found to be lower compared to previous studies. In a study by Liu et al. including 245 patients, the mortality rate was reported to be 13.4% (7), and in a multicenter study with 1,859 patients, it was determined as 11.1% (10).

Several risk factors associated with a severe disease course and high mortality have been previously described in patients with COVID-19. In a multicenter retrospective study, several parameters such as age, number of comorbidities, cancer history, shortness of breath, change of consciousness, radiological involvement, and elevated laboratory parameters (NLR, LDH, and direct bilirubin) were included in risk scoring to evaluate the risk of progression to critical illness in patients hospitalized with COVID-19. It was stated that this scoring, performed at the time of hospital admission, could predict progression to critical illness (11). In a study conducted in China, advanced age, male gender, and hypertension were found to be associated with mortality (12). Similarly, in another study with 3,988 patients, advanced age, male gender, and the presence of chronic obstructive pulmonary disease and diabetes mellitus as comorbidities were identified as risk factors for higher mortality (13). Similarly, in the current study, older age, presence of at least one comorbidity, and male gender were associated with higher mortality.

When the laboratory parameters were evaluated, NLR, serum CRP and ferritin levels were higher among the mortality group than the survivors. NLR and increased inflammatory markers and their association with poor prognosis have also been defined in many diseases, such as liver cirrhosis and cerebrovascular events and malignancy (14-18). Additionally, it has been reported that NLR can be used as a supporting finding for the pneumonia severity score in patients followed up with a diagnosis of pneumonia in terms of infectious diseases (19). Neutrophils, along with lymphocytes, play an important role in the response to viral infections (20). Patients diagnosed with COVID-19 who have a high neutrophil count at the time of admission have an up to eight-fold higher risk of progression to severe disease (21). More than one mechanism contributes to the occurrence of lymphopenia in COVID-19. SARS-CoV-2 can cleave lymphocytes by attaching to angiotensin-converting enzyme (ACE) receptors expressed by lymphocytes. The cytokine storm that occurs with the increase in inflammatory mediators can trigger lymphocyte apoptosis. In addition, cytokine acti-

Table 2: Comparison of the clinical and laboratory parameters between the patients with and without mortality

Clinical and laboratory findings (mean±SD)	Total n=347	Non-mortality group n=318 (91.6%)	Mortality group n=29 (8.4%)	p-value
Body temperature (°C)	36.83±0.73	36.83±0.74	36.84±0.65	0.666
Oxygen saturation (SpO_2)	88.00±6.69	88.78±6.11	79.51±6.95	**<0.001**
Systolic BP (mmHg)	119.08±14.89	118.87±14.67	122.10 ±17.08	0.233
Diastolic BP (mmHg)	72.76±10.58	72.76±10.56	72.75±10.98	0.585
Hemoglobin (g/L)	13.69±0.87	13.70±1.91	13.52±1.46	0.279
Platelet (x10^9/L)	193.86±80.33	196.06±82.05	170.40±54.01	0.136*
WBC count (x10^6/L)	7.40±8.97	7.25± 9.24	9.05±4.89	**0.032***
Neutrophil count (x10^9/L)	5.44±0.54	5.27±5.45	7.34±4.87	**0.030***
Lymphocyte count (x10^9/L)	1.36±0.765	1.40±0.78	0.95±0.46	**0.001***
Neutrophil/lymphocyte ratio	5.72±8.78	5.23±8.40	11.03±11.06	**<0.001***
BUN (mg/dL)	46.26±34.46	43.34±31.40	78.27±48.56	**<0.001***
Creatinine (mg/dL)	1.18±1.03	1.13±1.01	1.66±1.06	**<0.001***
Glucose (mg/dL)	135.21±62.96	133.41±59.59	154.53±92.24	0.123*
AST (U/L)	38.29±33.60	33.89±17.36	86.59±88.92	**<0.001***
ALT (U/L)	30.21±28.49	27.94±18.75	55.07±73.14	**0.023***
GGT (IU/L)	49.83±62.28	47.37±53.88	76.72±119.00	**0.046***
LDH (mg/dL)	313.12±146.00	299.26±123.10	465.22±255.80	**<0.001***
CRP (mg/L)	61.53±85.12	57.63±87.29	104.20±34.79	**<0.001***
Ferritin (ng/mL)	329.60±335.80	305.82±317.90	589.52±415.50	**<0.001***
D-dimer (µg/mL)	0.70±1.16	0.70±1.21	0.76±0.64	**0.021***
Troponin (ng/l)	32.54±333.7	9.36±30.17	285.82±1135.40	**<0.001***
	Clinical variables	**Patients alive n (%)**	**Patients exitus n (%)**	**p-value (Odds ratio)**
Gender (n, %)	Male Female	159 (50.0%) 159 (50.0%)	20 (69.0%) 9 (31.0%)	**0.054**
Age (years) (mean±SD)	59.7±16.9	58.34±16.4	74.5±14.4	**<0.001***
Age (n, %)	<65 year ≥65 year	198 (62.3%) 120 (37.7%)	7 (24.1%) 22 (75.9%)	**<0.001 (15.9)**
PCR (n, %)	Negative Positive	93 (29.2%) 225 (70.8%)	3 (10.7%) 25 (89.3%)	**0.03 (4.74)**
Intensive care unit (n, %)	No Yes	302 (95.0%) 16 (5.0%)	10 (34.5%) 19 (65.5%)	**<0.001**
Tobacco use (ever) (n, %)	Absent Present	280 (88.1%) 36 (11.3%)	27 (93.1%) 2 (6.9%)	0.617
Hypertension (n, %)	Absent Present	186 (58.5%) 132 (41.5%)	14 (48.3%) 15 (51.7%)	0.287
Diabetes mellitus (n, %)	Absent Present	236 (74.2%) 82 (25.8%)	22 (75.9%) 7 (24.1%)	0.846
COPD/asthma (n, %)	Absent Present	260 (81.8%) 58 (18.2%)	21 (72.4%) 8 (27.6%)	0.220
Coronary artery disease (n, %)	Absent Present	274 (86.2%) 44 (13.8%)	23 (79.3%) 6 (20.7%)	0.225
Malignancy (n, %)	Absent Present	315 (99.1%) 3 (0.9%)	29 (100.0%) 0 (0.0%)	0.769
CT findings (n, %)	Moderate involvement Severe involvement	229 (73.4%) 83 (26.6%)	9 (31.0%) 20 (69.0%)	**<0.001**
Any comorbidity (n, %)	Absent Present	280 (88.1%) 38 (11.9%)	19 (65.5%) 10 (34.5%)	**0.003 (11.3)**

BP: Blood pressure, WBC: White blood cell, BUN: Blood urea nitrogen, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, GGT: Gamma-glutamyl transferase, LDH: Lactate dehydrogenase, CRP: C-reactive protein, PCR: Polymerase chain reaction, COPD: Chronic obstructive pulmonary disease, CT: Computer tomography, SD: Standard deviation, p<0.05 statistically significant,
*: Mann-Whitney U test=Mortality-Non-mortality

Table 3: Multivariate analysis of mortality-associated factors with the forward logistic regression method

Variables	Bj	OR	95% CI	p-value
Neutrophil/lymphocyte ratio (NLR)	0.033	1.034	**1.003-1.066**	***0.03****
Age (years)	0.093	1.097	**1.054-1.14**	***<0.001****
Gender (male)	1.25	3.48	**1.28-9.47**	***0.015****
Any comorbidity	2.55	12.74	**3.36-48.3**	***<0.001****
Creatinine (mg/dL)	0.314	1.37	**1.13-1.66**	***0.001****
CRP (mg/L)	0.018	1.018	**1.005-1.032**	***0.008****
GGT (IU/L)	0.006	1.006	**1.001-1.012**	***0.022****
Constant	-10.211	0.00		***<0.001****

*: statistically significant at p<0.05. OR: Odds ratio, CI: Confidence interval, CRP: C-reactive protein, GGT: Gamma-glutamyl transferase, Bj: Regression coefficient

vation impairs lymphocyte proliferation and turnover by affecting lymphoid organs (22). In a previous study, it was shown that a decrease in the CD8+ T lymphocyte count and interleukin (IL)-6 was a good prognostic marker of mortality in patients with COVID-19 (23). On the other hand, the functional capacity of lymphocytes decreases with the decrease in the number of lymphocytes, especially in COVID-19 cases with a severe clinical course (24). It has been observed that COVID-19 progresses more severely in patients with a high NLR value (11, 20, 25). In a study by Liu et al. evaluating 245 patients, NLR was found to be an independent risk factor associated with high mortality, especially among men (7). In another observational study with 1,859 COVID-19 patients, mortality was found to have a significant correlation with increased NLR, low platelet count and high creatine and D-dimer values (10). We also observed a significant association between NLR and mortality in our study.

In this study, although several clinical and laboratory parameters, such as severe thorax CT findings, leucocyte and neutrophile counts, and ferritin, CRP, creatinine, ALT, AST, GGT, LDH and troponin levels were higher, lymphocyte levels were lower among the mortality group in the univariate analysis, only advanced age, presence of any comorbidity, and higher NLR, CRP, creatinine and GGT values were determined to be associated with high mortality in the multivariable analysis. This is consistent with previous studies reporting an association between high mortality in COVID-19 and higher ferritin, CRP and D-dimer levels reflecting a greater inflammatory response (26, 27). Additionally, we determined that the correlation between low SpO_2 with CRP and NLR was also compatible with the association between these two parameters and high mortality in our study.

Liver test abnormalities are more frequently observed in severe cases of COVID-19. Liver injury and liver enzyme abnormalities in COVID-19 may be multifactorial and result from the direct pathogenic effects of the virus, adverse drug reactions, higher systemic immune response (cytokine storm), and hypoxia in these patients (28). Elevation of the GGT level and the organ infiltration of IL-6-producing cells are the defining characteristics for patients with the severe COVID-19 (29, 30). In a study by Zhang et al., CRP and NLR were correlated with high GGT levels (29). In our study, CRP but not NLR was correlated with GGT, which is consistent with the above-mentioned study. Higher GGT levels at admission, as well as other liver enzymes have been associated with mortality and ICU admission among COVID-19 patients (31). Furthermore, GGT has been found to be a useful biomarker when combined with other laboratory parameters in COVID-19 (32). The biliary epithelium expresses the ACE-2 receptor, which is the known as the binding site of SARS-CoV-2, while the expression in hepatocytes is possibly much lower, which is consistent with increased GGT rather than transaminase levels among the patients with COVID-19 in our study (33). In addition to GGT elevation, an increased creatinine level has also been associated with poor prognosis and may be an independent risk factor of in-hospital death in patients with COVID-19 (34). Furthermore, higher BUN and/or creatinine levels and NLR are independent predictors of severe disease and higher mortality in patients with COVID-19, which is also in agreement with our findings (35). Liver and kidney dysfunction reflecting multiorgan involvement in COVID-19, possibly due to the direct effect of the SARS-CoV-2 virus or cytokine storm can contribute to the higher mortality associated with the disease.

In conclusion, in COVID-19, at risk patients can be identified in the early period with several simple clinical and laboratory parameters. This evaluation, performed at the time of admission, can contribute to the reduction of mortality through a closer clinical and laboratory follow-up. The hospital mortality rate can be reduced by determining high-risk patients at admission, which would

also facilitate early appropriate treatment in these patients. Controlled prospective studies with larger patient populations are needed to confirm the prediction of mortality in patients with COVID-19.

Limitations of our study

Important limitations of our study are its retrospective observational design and the absence of a control group. The patient group included in our study population may not reflect all COVID-19 patients due to the hospitalization of more severe cases, and this may have caused a bias.

Ethics Committee Approval: This study was approved by the Ethical Committee of the Agri Education and Research Hospital (Date: 11.12.2020, No:29)

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