Investigation of Biochemical Blood Parameters of COVID-19 Patients Short (running) title: Biochemical Blood Parameters of COVID-19 Patients

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Abstract

Objectives: In this study, it was aimed to investigate the effect of biochemical blood values on the course of the disease. Material and Methods: This is a retrospective study. For the treatment of COVID-19, clinical features and biochemical test parameters of 243 patients who applied to Malatya Training and Research Hospital in Malatya province of Turkey between 03 March and 31 December 2021 were used. Results: In the regression analysis performed in patients with Covid, glucose, urea, ALP, LDH, albumin, calcium and potassium levels were found to be effective on the severity of the disease. Conclusion: Biochemical parameters can be used as clinical findings to predict the diagnosis and course of COVID-19.

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There is no conflict of interest in the study

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ABSTRACT

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Keywords: Covid-19, Biochemical, Biomarker, Pandemic.

INTRODUCTION

The global epidemic known as the coronavirus disease (COVID-19) was first seen in 2019 in Wuhan, China (1). This recently discovered epidemic still continues to spread worldwide as a severe and contagious disease

(2). Coronavirus Disease 2019 (COVID-19) has a variable clinical presentation from asymptomatic to severe illness leading to death (3).

Studies are continuing to develop effective treatments in the fight against COVID-19 (4-10). Although there are many new treatment options available to combat COVID-19, the success rate varies. For this reason, laboratory tests; It plays an important role in predicting the severity and course of the disease and in determining the appropriate treatment (11).

Although studies in the literature have broadly defined the clinical features of COVID-19, the evaluation of changes in the most common biochemical parameters reported in patients with COVID-19 is still not fully determined (2). At the same time, it is seen that there are certain differences in the results due to the different designs of the studies and insufficient sample sizes (11).

Since the biochemical changes of the blood play an important role in predicting the condition and prognosis of the patients, guiding the treatment and even evaluating the curative effect, there is a need to obtain more convincing results about the biochemical (11-14). In this study, it was aimed to evaluate the changes in biochemical parameters of COVID-19 patients according to clinical features.

METHOD

Data Collecting

This is a retrospective study. For the treatment of COVID-19, clinical features and biochemical test parameters of 243 patients who applied to Malatya Training and Research Hospital in Malatya province of Turkey between 03 March and 31 December 2021 were used. Data were obtained from Malatya Training and Research Hospital patient registration automation. The study was approved by the Malatya Training and Research Hospital Ethics Review Board (Approval Number: 23536505-000-13874).

Statistical Analysis

In the study, descriptive statistics and categorical variables were shown as numbers and percentages, and continuous variables as median (minimum-maximum). The chi-square test was used to examine the relationship between two independent categorical variables. The Mann-Whitney U test was used to test the significance of the difference between the means of two non-parametric variables. Diagnostic test performances of biochemical blood parameters were tested by ROC analysis. Multivariate logistic regression analysis was performed to evaluate the independent factors that were statistically significant. Statistical analyzes were performed using "IBM SPSS Statistics (Version 25.0) for Windows and Jamovi (Version 2.3) for Windows software".

FINDINGS

In the study, there is a significant relationship between the discharge/ex statues of the patients and their age(X^2 =25,09,p <0.05), chronic disease (X^2 =32,84p <0.05) and duration of hospitalization (X^2 =23,41 p <0.05). There is no significant relationship between gender and discharge/ex (X^2 =2,37,p >0.05) (Table 1).

Table 1. Comparison of Ex and Discharge Status of Patients According to Demographic Variables

Categories	Discharge	Ex	X^2	p
Age				
<65	100 (93,7)	7 (6,5)	25,09	0,00*?>?
65	91 (66,9)	45 (33,0)		
Gender				
Female	80 (74,0)	28 (29,5)	2,37	0,12
Male	111 (82,2)	24 (17,7)		
Chronic Disease				
Yes	37 (54,4)	31 (45,5)	32,84	0,00*

Categories	Discharge	Ex	X^2	p
No	154 (88)	21 (12)		
Duration of Hospitalization				
<10	134 (87,5)	19(12,4)	23,41	0,00*?>?
10	50 (60,2)	33(39,7)		

*p <0.05 significant diffrence, Chi Square.

The significance of the difference between ex and discharge was tested with the Mann-Whitney U test. As a result of the analysis, statistically significant differences were found between ex and discharge. According to the results, Glucose, Urea, Creatinine, AST, ALP, LDH, CK, T. Bilirubin, D. Bilirubin, Sodium, Potassium and CRP values, mean age and hospital stay were higher in patients with ex. Protein, Albumin and Calcium values were found to be lower (Table 2).

Table 2. Comparison of Measurements by Discharge and Ex Condition

	Discharge	Ex	U	p
	M(Min-Max)	M(Min-Max)		
Age	64(21-93)	79(55-93)	2514,0	0,00*
Duration of Hospitalization	7(0-52)	12(1-65)	3155,0	0,00*
GLUCOSE	118,0(28,0-54,0)	156,8(16,0-476,0)	2928,0	0,00*
UREA	40,(0,57-338,0)	109,3(11,0-405,0)	1310,5	0,00*
CREATININE	0,81(0,37-107,0)	1,4(0,3-7,5)	2666,5	0,00*
AST	29,0(12,0-122,0)	43,0(11,0-2898,0)	3064,5	0,00*
ALT	29,9(6,0-264,0)	24,5(3,0-942,0)	4455,5	0,26
ALP	78,0(32,0-338,0)	99,0(35,0-514,0)	3321,0	0,00*
GGT	41,0(5,0-408,0)	55,5(12,0-669,0)	4428,5	0,23
LDH	293,0(26,0-1087,0)	555,0(234,0-4151,0)	1503,0	0,00*
CK	69,9(0,5-88,0)	143,0(25,0-4002,1)	3116,0	0,00*
CK-MB	17,8(0,5-88,0)	17,8(0,9-103,0)	4167,5	0,07
T.BILIRUBIN	0,57(0,12-15,89)	0,8(0,2-15,0)	2804,5	0,00*
D.BILIRUBIN	0,13(0,02-8,67)	0,3(0,06-9,1)	2001,5	0,00*
PROTEIN	6,2(4,1-8,13)	5,4(3,4-7,3)	2357,5	0,00*
ALBUMIN	3,3(1,9-4,7)	2,3(0,9-4,2)	1356,0	0,00*
CALCIUM	8,7(2,5-11,0)	7,2(1,7-15,2)	2660,0	0,00*
PHOSPHORUS	3,21(1,4-10,3)	3,2(1,5-15,6)	4616,0	0,43
SODIUM	139,0(124,0-188,0)	141,0(3,0-164,0)	3538,0	0,00*
POTASIUM	4,45(3,2-515,0)	4,9(2,2-8,2)	3950,5	0,02*
CHLORINE	103,8(91,0-148,0)	103,8(94,0-121,0)	4794,0	0,70
CRP	1,5(0,0-247,0)	12,5(0,1-37,7)	1248,0	0,00*

*p <0.05 significant diffrence, Mann-Whitney U., M: Median

The COVID-19 diagnostic test performances of the biochemical blood values that were significant in the comparison analyzes of the discharge and Ex group were tested with ROC analysis. In the literature, an AUC of 0.5 suggests no discrimination (i.e., ability to diagnose patients with and without the disease or condition based on the test), 0.7 to 0.8 is considered acceptable, 0.8 to 0.9 is considered excellent, and more than 0.9 is considered outstanding (15, 16). Accordingly, among the "area under the ROC Curve (AUC)" values, Urea (AUC=0.868), LDH (AUC=0.849), Albumin (AUC=0.863) and CRP(AUC=0.874) values can be considered excellent. The highest significant AUC value was obtained for CRP (AUC=0.874) (Table 3).

Table 3. Diagnostic Performance of Biochemical Blood Parameters

n=243	AUC (95% CI)	*p*	Cut-off	Sensitivity (%)	Specificity (%)	PPV(%)	NPV (%)
GLUCOSE	0,705(0,62-0,78)	0,00	[?] 128	80,77	59,69	35,29	91,94
UREA	0,868(0,80-0,93)	0,00	[?] 52	86,54	69,11	43,27	94,96
CREATININE	0,732(0,63-0,82)	0,00	[?] 1,03	69,23	74,35	42,35	89,87
AST	0,691(0,60-0,77)	0,00	[?] 40	55,77	73,82	36,71	85,98
ALP	0,666(0,57-0,75)	0,00	[?] 82	73,08	57,07	31,67	88,62
LDH	0,849(0,79-0,90)	0,00	[?] 344	86,54	64,92	40,18	94,66
CK	0,686(0,60-0,76)	0,00	[?] 161,45	42,31	87,43	47,83	84,77
T.BILIRUBIN	0,718(0,63-0,80)	0,00	[?] 0,69	61,54	71,73	37,21	87,26
D.BILIRUBIN	0,798(0,73-0,86)	0,00	[?] 0,2	69,23	76,44	44,44	90,12
PROTEIN	0,763(0,68-0,84)	0,00	[?] 5,1	44,23	95,29	71,88	86,26
ALBUMIN	0,863(0,80-0,91)	0,00	[?] 2,7	69,23	82,72	52,17	90,8
CALCIUM	0,732(0,64-0,82)	0,00	[?] 6,7	48,08	90,58	58,14	86,5
SODIUM	0,644(0,54-0,74)	0,00	[?] 141	55,77	70,68	34,12	85,44
POTASIUM	0,602(0,49-0,70)	0,02	[?] 4,84	53,85	73,82	35,9	85,45
CRP	0,874(0,81-0,93)	0,00	[?] 4,28	88,46	71,2	45,54	95,77

PPV: "Positive predictive value"; NPV: "Negative predictive value"

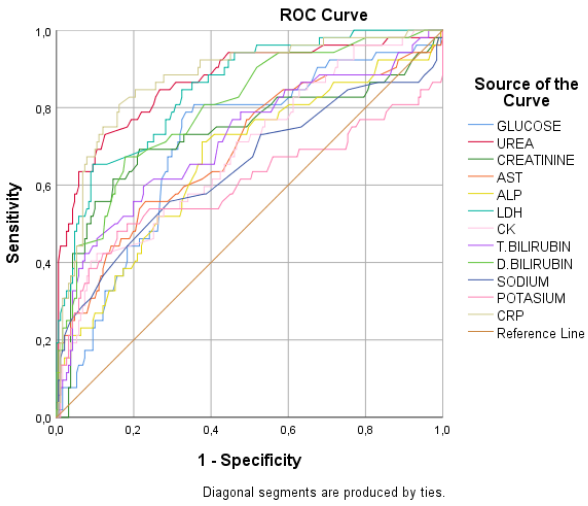

Figure 1. Curves of biochemical blood parameter of COVID-19 patients who were died

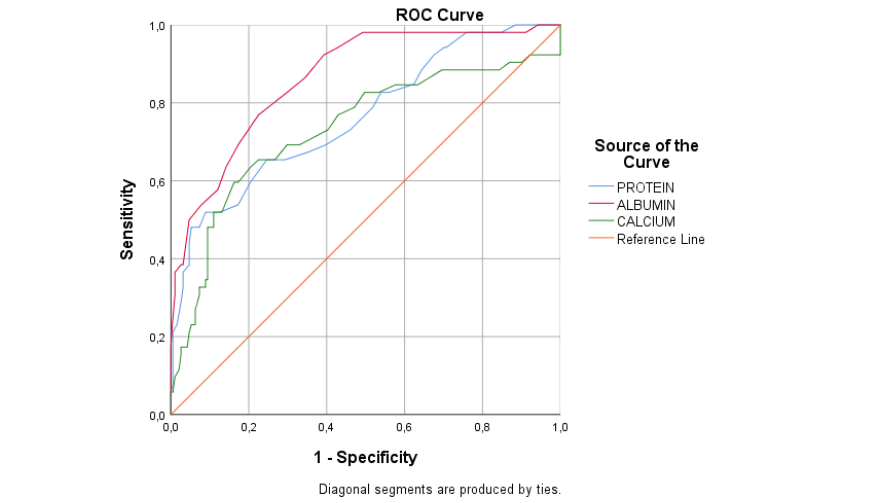

Figure 2. Curves of biochemical blood parameter of COVID-19 patients who were died

Biochemical blood parameters found to be significant as a result of univariate analyzes were included in the multivariate logistic regression model. First, VIF (Variance Inflation Factor) analysis was performed to detect multiple linear correlation. VIF is calculated to determine the degree of relationship of an independent variable with other independent variables (17). If VIF is greater than or equal to 10, there is a multicollinearity problem (18-20). In the study, the VIF value of T. Bilirubin and D. Bilirubin parameters was found to be above 10. T. Bilirubin and D. Bilirubin were removed from the model and the model was re-established. The result of the established multivariate logistic regression analysis model, the mean increases in Glucose (OR:1.01, p <0.05), Urea (OR:1.03,p <0.05), ALP (OR:1.01, p <0,05), LDH (OR: 1.01, p <0.05) parameters were found to increase the risk of death. On the other hand the mean increases in Albumin (OR:0,22, p <0,05), Calcium (OR:0,73,p <0,05) and Potasium (OR:0,38, p <0,05) parameters were found to decrease the risk of death (Table 4).

Table 4. Evaluation of Risk Factors Affecting Ex with Multivariate Logistic Regression Analysis

	B	B	OR(95% CI
GLUCOSE	0,01	1,01(1,00-1,01)	1,01(1,00-1,0
UREA	0,03	1,03(1,01-1,05)	1,03(1,01-1,0
CREATININE	-0,01	1,00(0,90-1,10)	1,00(0,90-1,1
AST	0,00	1,00(0,99-1,00)	1,00(0,99-1,0
ALP	0,01	1,01(1,00-1,01)	1,01(1,00-1,0
LDH	0,01	1,01(1,00-1,01)	1,01(1,00-1,0
CK	0,00	1,00(1,00-1,00)	1,00(1,00-1,0
PROTEIN	0,06	1,06(0,46-2,44)	1,06(0,46-2,4
ALBUMIN	-1,51	0,22(0,06-0,89)	0,22(0,06-0,8
CALCIUM	-0,31	0,73(0,57-0,93)	0,73(0,57-0,9
SODIUM	-0,02	0,98(0,91-1,06)	0,98(0,91-1,0
POTASIUM	-0,98	0,38(0,16-0,86)	0,38(0,16-0,8
CRP	0,00	1,00(0,98-1,02)	1,00(0,98-1,0
Observed Overall Percentage: 92,6	Observed Overall Percentage: 92,6	Observed Overall Percentage: 92,6	Observed O

DISCUSSION

In the study, age, chronic illness, length of stay and biochemical blood parameters of the patients were evaluated separately and their effects on the risk of death were investigated. In our study, the mortality rate of patients [?]65 was found to be higher. Similarly, Ergenc et al. (21) found that patients with [?]65 deaths had a higher mortality rate. In the study of Teker et al. (22), found that the course of COVID-19 disease worsened with age and deaths increased. . Unver-Ulusoy et al. (23) found that 68.8% of the patients hospitalized in the intensive care unit were 65 years and older. According to the information reported by the US Centers for Disease Control and Prevention (CDC), the mortality rate observed in [?]65 patients is higher (24). It is thought that weakened immune functions in elderly patients predispose to infection (25). Therefore, it is thought that the mortality rate may be higher in patients over 65.

In our study, it is seen that the mortality rate is higher in patients with chronic diseases. Wang et al. (26) reported that elderly people are at higher risk for chronic diseases and infections, and that mortality due to COVID-19 increases in those with hypertension and coronary heart disease. Reyes-Sánchez et al. (27) in his study on adults who tested positive for COVID-19 in Mexico, revealed that chronic diseases may be associated with the severity of COVID-19 and deaths. Considering the information in the literature, it is seen that the state of chronic illness can be used as a leading parameter in estimating the course of the disease.

In our study, it was concluded that the risk of death from COVID-19 did not differ significantly by gender. However, it is seen that there are different results in the literature. The effect of gender on the risk of COVID-19 and death was investigated by Doerre and Doblhammer (28). In the study, it was determined that the mortality rate in men was 2 times higher than that in women. Unver-Ulusoy et al. (23) found that men have a higher risk of death. Peckham et al. (29) found that male patients were almost three times more likely to be admitted to the intensive care unit than females and had higher mortality rates. Considering the results in the literature, it can be said that men are in the disadvantaged group in deaths caused by COVID-19.

The hospitalization time of the patients who died was found to be higher. According to Rozman et al. (30), the probability of being discharged within the first 7 days after hospitalization was 36.5%, while the probability of dying in the same period was 7.9%. On the 21st day, the probability of being discharged increased to 72.9%, while the probability of death increased to 14.4%. da Costa Sousa et al. (31) revealed that a longer hospital stay may be related to age. More comprehensive studies are needed to explain the relationship between length of stay and death.

In our study, the diagnostic power of biochemical blood parameters of COVID-19 patients was investigated. Among the biochemical parameters included in the study, the AUC values of Urea, LDH, Albumin and CRP were found to be high (0.8-0.9). Among these parameters, the highest AUC value belongs to CRP. Logistic regression analysis was performed to understand the effect of biochemical parameters on the risk of death. The increase in Glucose, Urea, ALP and LDH values increased the risk of death; It was observed that the increase in Albumin, Calcium and Potassium values decreased the risk of death. In the study of Ergenç et al. (21), WBC, procalcitonin, troponin, ferritin, monocytes, INR, LDH, AST, ALT, MVC and PLT values were found to be higher in the old ex. Ferrari et al. (32) stated that simple hematological tests can be used in the diagnosis of COVID-19 in developing countries where RT-PCR testing is limited.

Strength and Limitation of the Study

The biggest strength of this study is the high sample size and the use of various biochemical blood values.

The major limitation of this study is that it is a retrospective study with its own limitations.

Conflict of Interest

There is no conflict of interest

Financial Support

No financial support

Patient Consent

It is a study that does not require patient consent.

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