Middle Black Sea Journal of Health Science /
Mid Blac Sea J Health Sci
August 2022; 8(3): 432-439

RESEARCH ARTICLE
DOI: 10.19127/mbsjohs.1129139

The Prognostic Significance of Lactate Dehydrogenase Albumin Ratio in Elderly COVID-19 Patients

Gurkan Altuntas[1(ID)], Mumin Murat Yazici[1(ID)], Ali Celik[1(ID)] , Ozcan Yavasi[1(ID)]

[1]Department of Emergency Medicine, Training and Research Hospital, Recep Tayyip Erdogan University, Rize, Turkiye

Received: 10 June 2022, Accepted: 24 July 2022, Published online: 31 August 2022

Abstract

Objective: An acute respiratory disease caused by a novel coronavirus emerged in December 2019. This disease associated with the novel coronavirus quickly spread across the world, leading to significant fatalities. Reliable predictors of disease mortality and severity are therefore needed in order to decide on clinical follow-up or earlier clinical intervention. This study was performed around the hypothesis that the LDH/ALB ratio would yield more sensitive results in predicting the potential relationship between disease severity and mortality in patients with COVID-19 aged over 65.

Methods: COVID-19 patients aged over 65 presenting to a tertiary emergency department between August and October 2021, were investigated in this single-center, retrospective study. All patients over 65 presenting to the emergency department and diagnosed with COVID-19 were included. The study population was constituted following the application of the inclusion and exclusion criteria. Pulmonary involvement percentages and laboratory parameters were compared against patient mortality and thoracic tomography.

Results: The relationship between patients' lactate dehydrogenase/albumin ratios and mortality status was evaluated. The optimal cut-off value for the lactate dehydrogenase/albumin ratio in predicting mortality was 9.6 (AUC:0.815, sensitivity 75.9%, specificity 76.3%, p=0.001). The relationship between patients' lactate dehydrogenase/albumin ratios and severity of pulmonary involvement was also examined. The cut-off value for severe pulmonary involvement was 11.2 (AUC:0.946, sensitivity 93.6%, specificity 87.4%, p=0.001).

Conclusion: In conclusion, LDH/ALB ratio could be used to predict mortality and severity of pulmonary involvement in elderly COVID-19 patients.

Key words: *COVID-19, Elderly Patients, Lactate Dehydrogenase Albumin Ratio, Emergency Medicine*

Suggested Citation: Altuntas G, Yazıcı M M, Celik A, Yavasi O. The Prognostic Significance of Lactate Dehydrogenase Albumin Ratio in Elderly COVID-19 PatientsMid Blac Sea Journal of Health Sci, 2022;8(3):432-439.

Address for correspondence/reprints:

Gurkan Altuntas

Telephone number: +90 (505) 945 53 44

E-mail: gurkan_altuntas@hotmail.com

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by the novel severe acute respiratory virus coronavirus 2 (SARSCoV-2) first appeared in December 2019, and quickly spread across the world. A pandemic was declared on 11 March, 2020. By 23 January, 2022, the public health problem COVID-19 had infected approximately 340 million people worldwide and resulted in approximately 5 million deaths (1). The mortality rate is particularly high among patients over 65 and with comorbidities such as hypertension, chronic respiratory and heart disease, diabetes, kidney failure, and malignancy. For these reasons, various biomarkers are needed to predict disease severity and mortality in these patients (2,3).

Since it reflects the scale of cellular damage, serum lactate dehydrogenase (LDH) elevation has been linked to increased infection severity. Some studies have suggested that LDH levels can be employed as a prognostic factor in determining the severity of various infectious diseases (4,5). Low albumin (ALB) levels have been associated with multiple inflammatory disorders as a negative acute phase reactant. Although the pathogenesis is not fully understood, levels of ALB are thought to decrease due to the escape of ALB into the interstitial space as a result of increased capillary permeability (6,7). However, since serum ALB levels can also be low in conditions such as liver diseases and malnutrition, ALB measurement, together with other parameters, is recommended to yield more reliable results (8).

A limited number of studies have evaluated the LDH/ALB ratio as a prognostic factor in infectious diseases. In the present study, we hypothesized that the LDH/ALB ratio would be capable of use as a prognostic factor in patients with COVID-19. This study was performed around the hypothesis that the LDH/ALB ratio would yield more sensitive results in predicting the potential relationship between disease severity and mortality in patients with COVID-19 aged over 65.

METHODS

Study design

This single-center, retrospective study was performed with COVID-19 patients over 65 presenting to the emergency department (ED) of a tertiary training and research hospital in Turkey between August and October 2021. The data for elderly patients with diagnoses of COVID-19 confirmed by positive reverse transcription-PCR (RT-PCR) of nasopharyngeal swabs were retrieved from the hospital's electronic medical records and reviewed. Approval for the study was granted by the local ethical committee before the data were scanned (decision number 2022/22). The retrieved data contained only clinical information and included no personally identifiable information.

Inclusion criteria: Patients aged over 65, presenting to the emergency department, diagnosed with COVID-19, and not meeting the exclusion criteria were included in the study.

Exclusion criteria: Patients with active neoplasia, transferred from another institution, refusing diagnosis and treatment, with deficient information in the data record system, patients without thoracic computed tomography (CT), trauma patients or with hemolysis at laboratory tests were excluded.

The data retrieved included patients' demographic information, known comorbidities, routine laboratory tests during the diagnosis and treatment of COVID-19, thoracic computed tomography (CT) images, length of hospital stay, and discharge status. All patient data were calculated using laboratory and imaging findings at the time of presentation to the emergency department.

Pulmonary involvement was classified as a percentage following thoracic CT examinations. Accordingly, 0-25% involvement was classified as mild, 25%-50% as moderate, and greater than 50% as severe disease.

Endpoints

The primary endpoint of this study was the prognostic value of the LDH/ALB ratio in predicting mortality in elderly patients with COVID-19. The secondary endpoint was to determine the predictive power of the LDH/ALB ratio in differentiating patients with and without severe pulmonary involvement based on thoracic CT.

Statistical Analysis

All statistical analyses were performed on Jamovi v.1.6 software (Jamovi Project Computer Software, version 1.6. Sidney, Australia). Type 1 errors of 5% were applied in all analyses. According to the normality status, continuous variables were expressed as mean and standard deviation (SD) or median and interquartile ranges (IQR). The Shapiro-Wilk test and Q-Q plots were applied to evaluate whether or not data were normally distributed. Categorical data were presented as frequency (n) and percentage (%). According to the distribution pattern, continuous variables were compared using the t-test or Mann-Whitney U test. A receiver operating curve (ROC) was produced to determine the cut-off levels of the LDH/ALB ratio for mortality and severity of pulmonary involvement. Finally, sensitivity, specificity, likelihood ratios (+LR and -LR), positive and negative predictive values were calculated for the LDH/ALB ratio.

RESULTS

8187 patients presented to ED with suspected or diagnosed COVID-19 during the study period. Two hundred six patients were included in the study following application of the inclusion and exclusion criteria, 91 (44.2%) men and 115 (55.8%) women. The patient flow chart is shown in Figure 1. The median age of the patients was 77 (IQR 70-83) years, and the mortality rate in these patients was 26.2% (54/206). Analysis of thoracic CT revealed severe involvement in 31 (15%) cases. The characteristics of patients' demographics, medical history, and the data of the hospitalizations are shown in Table 1.

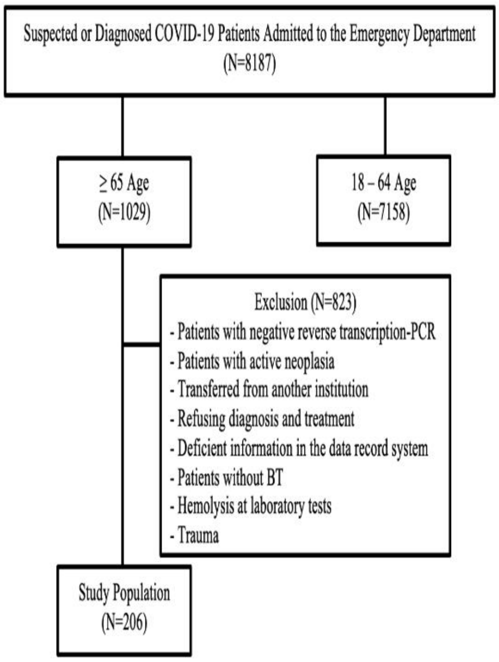

Figure 1. Flow Chart

The summary statistics of patients' laboratory values are shown in Table 2. The statistical analysis regarding mortality revealed that neutrophil, lymphocyte, platelet, sodium, AST, CRP, troponin T, D-dimer, fibrinogen, ferritin, LDH, ALB, creatinine, and the LDH /ALB ratio were significant predictors. In addition, WBC, neutrophil, ALT, AST, CRP, troponin T, D-dimer, fibrinogen, ferritin, LDH, and ALB were found statistically significant in differentiating patients with severe pulmonary involvement. The relationship between the LDH/ALB ratio and mortality was also evaluated. The median LDH/ALB ratio was higher in the non-surviving group than in the surviving group (12 (IQR 9.6-16.4) and 6.7 (IQR 5.1-9.4), respectively, p =0.001). The optimal cut off value of the LDH/ALB ratio to predict mortality was 9.6, exhibited a sensitivity of 75.9% and a specificity of 76.3% (Area under the curve; AUC, 0.815 (95% confidence interval (CI): 0.747-0.882, p =0.001).

Table 1. The Patients' Demographic Data, Comorbidities, and Lengths of Hospital Stay

		According to Mortality		According to Tomographic Involvement	
	All Patients (n=206)	**No Mortality (n=152)**	**Mortality (n=54)**	**Mild-Moderate Involvement (n=175)**	**Severe Involvement (n=31)**
Gender					
Male	91 (44.2%)	59 (28.7%)	32 (15.5%)	75 (36.4%)	16 (7.8%)
Female	115 (55.8%)	93 (45.1%)	22 (10.7%)	100 (48.5%)	15 (7.3%)
Age (Years)	77 (IQR 70-83)	76.5 (IQR 70-83)	79 (IQR 72.3-84.8)	77 (IQR 70-83)	80 (IQR 75.5-84)
Comorbidities					
Hypertension	145 (70.4%)	105 (51.0%)	40 (19.4%)	123 (59.7%)	22 (10.7%)
Diabetes	68 (33.0%)	46 (22.3%)	22 (10.7%)	56 (27.2%)	12 (5.8%)
CAD	52 (25.2%)	32 (15.5%)	20 (9.7%)	42 (20.3%)	10 (4.9%)
Stroke	21 (10.2%)	17 (8.3%)	4 (1.9%)	19 (9.2%)	2 (1.0%)
CHF	26 (12.6%)	13 (6.3%)	13 (6.3%)	23 (11.1%)	3 (1.5%)
CRF	31 (15.0%)	15 (7.3%)	16 (7.7%)	25 (12.1%)	6 (2.9%)
COPD	25 (12.1%)	17 (8.2%)	8 (3.9%)	21 (10.2%)	4 (1.9%)
Dementia	18 (8.7%)	10 (4.8%)	8 (3.9%)	16 (7.7%)	2 (1.0%)
Hepatitis B	2 (1.0%)	0 (0%)	2 (1.0%)	0 (0%)	2 (1.0%)
Immunodeficiency	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Length of Hospitalization (Days)	6 (IQR 0-11)	5 (IQR 0-11)	6.5 (IQR 3-12)	6 (IQR 0-10.5)	7 (IQR 3-18)

***CAD**: Coronary Artery Disease, **CHF**: Congestive Heart Failure, **CRF**: Chronic Renal Failure, **COPD**: Chronic Obstructive Pulmonary Disease, **IQR:** Interquartile Range*
***Note:** Normally distributed data are expressed as Mean ± SD (Min.-Max.), and abnormally distributed data as Median (IQR 25-75)*

In addition, patients' LDH/ALB ratios were higher in the group with severe tomographic involvement than in the non-severe group (median:16.3; IQR: 13.3-19.7, and 7; IQR: 5.3-9.7, respectively, p=0.001). The AUC value of the LDH/ALB ratio for predicting severe tomographic involvement was 0.946 (95% CI: 0.907-0.985, p =0.001). At a threshold value of 11.2 (sensitivity 93.6% and specificity 87.4%), the LDH/ALB ratio supports the detection of patients with severe tomographic involvement as an influential predictive factor.

The cut-off values of the LDH/ALB ratio for mortality and severe tomographic involvement and a receiver operating curve (ROC) analysis are shown in Table 3 and Figure 2.

Table 2. Patients' Laboratory Indices

		According to Mortality			According to Tomographic Involvement		
	All Patients (n=206)	**No Mortality (n=152)**	**Mortality (n=54)**	**P Value**	**Mild-Moderate Involvement (n=175)**	**Severe Involvement (n=31)**	**P Value**
WBC (10^3/uL)	7 (IQR 5.4-9.4)	6.9 (IQR 5.5-8.6)	8.4 (IQR 4.7-11.4)	0.106	6.9 (IQR 5.4-8.7)	9 (IQR 5.7-10.9)	**0.034**
Neutrophil (10^3/uL)	5 (IQR 3.6-7.4)	4.8 (IQR 3.6-6.5)	6 (IQR 3.6-9.9)	**0.020**	4.9 (IQR 3.4-6.6)	6.7 (IQR 4.4-9.2)	**0.010**
Lymphocyte (10^3/uL)	1.1 (IQR 0.8-1.6)	1.2 (IQR 0.8-1.7)	0.8 (IQR 0.6-1.2)	**0.001**	1.1 (IQR 0.8-1.6)	0.9 (IQR 0.5-1.4)	0.174
Platelet (10^3/uL)	179 (IQR 139-243)	185 (IQR 147-252)	165 (IQR 114-211)	**0.015**	176 (IQR 140-244)	181 (125-220)	0.343
Sodium (mmol/L)	135 (IQR 132-137)	136 (IQR 133-137)	134 (IQR 130-137)	**0.037**	136 (IQR 133-137)	134 (IQR 127-138)	0.080
Potassium (mmol/L)	4.3 ± 0.5 (2.7-6.3)	4.3 ± 0.5 (2.7-5.4)	4.4 ± 0.7 (2.7-6.3)	0.100	4.3 ± 0.5 (2.7-5.4)	4.4 ± 0.8 (2.7-6.3)	0.520
Chlorine (mmol/L)	101(IQR 98-104)	101 (IQR 98-103)	101 (IQR 97.3-104)	0.765	101 (IQR 98-103)	101 (IQR 95-105)	0.727
ALT (U/L)	18.5 (IQR 14-31)	18 (IQR 14-28)	20 (IQR 13.3-32.5)	0.646	17 (IQR 13-27)	31 (IQR 21.5-48.5)	**0.001**
AST (U/L)	28.5 (IQR 20-46.8)	27 (IQR 19-41)	43 (IQR 26.3-61)	**0.001**	27 (IQR 19-40)	52 (IQR 43.5-105)	**0.001**
CRP (mg/L)	96 (IQR 29.3-164)	74 (IQR 20.9-131)	151 (IQR 79.3-195)	**0.001**	77 (IQR 24-139)	168 (IQR 96-225)	**0.001**
Troponin T (ng/L)	14.2 (IQR 6.7-35.5)	10.5 (IQR 5-22.1)	35.8 (IQR 18.9-145)	**0.001**	13 (IQR 5.9-29)	35 (IQR 19.5-101)	**0.001**
D-Dimer (µg/mL)	0.6 (IQR 0.3-1)	0.5 (IQR 0.3-0.9)	0.8 (IQR 0.4-2.1)	**0.009**	0.5 (IQR 0.3-0.9)	1 (IQR 0.5-2.4)	**0.001**
Fibrinogen (mg/dL)	489 (IQR 398-594)	478 (IQR 391-556)	546 (IQR 441-676)	**0.002**	478 (IQR 391-569)	579 (IQR 503-699)	**0.001**
Ferritin (ng/mL)	545 (IQR 270-1103)	440 (IQR 213-851)	967 (IQR 409-1601)	**0.001**	481 (IQR 256-960)	997 (IQR 470-1507)	**0.009**
LDH (U/L)	264 (IQR 205-369)	241 (IQR 196-320)	394 (IQR 307-512)	**0.001**	245 (IQR 198-333)	488 (IQR 442-647)	**0.001**
ALB (g/L)	35.4 ± 4.2 (24-45)	36.3 ± 4.2 (24-45)	32.9 ± 2.9 (24-40)	**0.001**	36 ± 4.2 (24-45)	32.3 ± 2.8 (24-36)	**0.001**
Creatine (mg/dL)	1.1 (IQR 0.8-1.5)	1 (IQR 0.8-1.3)	1.4 (IQR 1.1-2.1)	**0.001**	1.1 (IQR 0.9-1.5)	1.3 (IQR 0.8-1.7)	0.685
LDH/ALB Ratio	7.9 (IQR 5.5-10.9)	6.7 (IQR 5.1-9.4)	12 (IQR 9.6-16.4)	**0.001**	7 (IQR 5.3-9.7)	16.3 (IQR 13.3-19.7)	**0.001**

__WBC:__ White Blood Cell, __ALT__: Alanine Transaminase __AST__: Aspartate Transaminase __CRP__: C-reactive protein __LDH__: Lactate dehydrogenase, __ALB:__ Albumin __IQR:__ Interquartile Range
__Note:__ Normally distributed data are expressed as mean ± SD (Min.-Max.) and abnormally distributed data as median (IQR 25-75) values
__Note 2:__ Student's t-test was used for normally distributed data and the Mann Whitney U test for abnormally distributed data.

Table 3. The Cut-off Values of the LDH/ALB Ratio for Mortality and Severe Tomographic Involvement

	LDH/ALB Ratio for Mortality	**LDH/ALB Ratio for Severe Tomographic Involvement**
AUC ± SD	0.815 ± 0.034	0.946 ± 0.020
95% CI	0.747-0.882	0.907-0.985
Cut-off	9.6	11.2
Sensitivity (%)	75.9 (62.4-86.5)	93.6 (78.6-99.2)
Specificity (%)	76.3 (68.8-82.8)	87.4 (81.6-92.0)
+ LR	3.2 (2.3-4.4)	7.44 (5.0-11.1)
- LR	0.32 (0.2-0.5)	0.07 (0.02-0.3)
PPV (%)	53.3 (45.2-61.1)	56.9 (46.9-66.3)
NPV (%)	89.9 (84.6-93.5)	98.7 (95.2-99.7)
Accuracy (%)	76.2 (69.8-81.9)	88.4 (83.2-92.4)
P Value	0.001	0.001

__LDH:__ Lactate Dehydrogenase, __ALB:__ Albumin, __AUC:__ Area Under the Curve, __SD:__ Standard Deviation, __LR:__ Likelihood Ratio, __PPV:__ Positive Predictive Value, __NPV:__ Negative Predictive Value, __CI:__ Confidence Interval

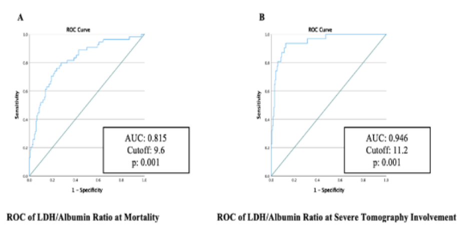

Figure 2. ROC Curve and Cutoff Value of Lactate Dehydrogenase/Albumin Ratio at Mortality and Severe Tomography Involvement

DISCUSSION

COVID-19 disease remains a significant public health problem that has led to more than 5 million deaths worldwide. Consequently, an essential part of health service resources was set aside to fight the pandemic. Reliable markers of disease severity and mortality are therefore needed in terms of efficient use of health service resources and for earlier clinical intervention and predicting patient outcomes (9).

The present study investigated the relationship between the LDH/ALB ratio and mortality and severe pulmonary involvement in patients with COVID-19 disease. The results show that the LDH/ALB ratio can be evaluated as a prognostic marker during laboratory evaluation at initial presentation to the ED. ROC analysis revealed an AUC of 0.815 (cut-off: 9.6) with a sensitivity of 75.9 and a specificity of 76.3 (+LR: 3.2, -LR: 0.32) in mortality prediction. Furthermore, the LDH/ALB ratio showed better accuracy in identifying severe pulmonary involvement with an AUC of 0.946 (cut-off: 11.2; sensitivity: 93.6%, specificity: 87.4%, +LR: 7.44, -LR: 0.07). These results showed that this ratio could be combined with other laboratory parameters to predict mortality and might be useful for ruling out severe pulmonary involvement.

LDH, an important enzyme in glycolysis, plays a vital role in the conversion of lactate to pyruvate in cells, and its levels rise following tissue breakdown. Higher serum LDH levels have been linked to several diseases, including malignancies, infectious diseases, and liver diseases (10,11). Since LDH is also present in lung tissue, LDH level elevation may be expected in association with pneumonia in patients with severe COVID-19 infection (9).

The levels of various markers also decrease in infectious diseases together with the emerging inflammatory response. Although the mechanisms responsible for hypoalbuminemia in COVID-19 have not been fully elucidated, this is thought to derive from increased vascular permeability and a shortened ALB half-life. Decreased ALB levels have been associated with poor outcomes (12,13). However, since there may be variability in levels in various comorbid conditions, we think that the combined use of these two markers may yield more accurate results than their use alone.

In literature, a few studies have investigated whether the LDH/ALB ratio is a prognostic factor for infectious conditions. Jeon et al. reported that the LDH/ALB ratio could be employed as an independent predictor of in-hospital mortality in patients with infection followed-up in the intensive care department, citing 81.5% sensitivity and 41.2% specificity (8). Yan et al. reported that the LDH/ALB ratio was significant in determining the risk of post-stroke pneumonia in patients undergoing acute ischemic stroke (AUC: 0.762 (95% CI, 0.737-0.786) (14). In the study by Lee et al., they found that the LDH/ALB ratio could be an independent prognostic factor for in-hospital mortality in patients with lower respiratory tract disease (15).

To the best of our knowledge, the present study is the first to investigate the prognostic significance of the LDH/ALB ratio in elderly patients with COVID-19 and its usefulness in predicting the severity of pulmonary involvement. Various biomarkers have been compared against CT involvement levels in patients with COVID, and their diagnostic significance has been discussed. Serin et al. compared CT involvement status with the LDH/lymphocyte ratio and concluded that this was of diagnostic value in COVID-19 disease, with 76.4% sensitivity and 59.60% specificity (4). Tan et al. reported correlation between CRP and thoracic CT findings (16).

Limitations

There are some limitations of this study. The first one is the nature of the single-center investigation that limits the generalize our results. Second, due to the study design, it included elderly patients with various comorbid conditions. We think that LDH and ALB values may vary depending on the underlying disease. Therefore, we employed the LDH/ALB ratio to obviate this. Finally, our data represent those at initial presentation to hospital, and LDH and ALB levels during hospitalization were not included. We think that further studies are now needed to investigate this subject, which we consider to be of considerable importance, in greater detail.

CONCLUSION

The LDH/Albumin ratio calculated from the LDH and Albumin levels routinely measured within laboratory parameters can be used to predict mortality and severity of pulmonary involvement in elderly COVID-19 patients. The LDH/ALB ratio appears to be useful as an initial prognostic indicator as it shows a good AUC for elderly COVID-19 patients. We think that our study will shed light on future studies for infective diseases.

Ethics Committee Approval: Ethics committee approval was received for this study from the Clinical Research Ethics Committee of Recep Tayyip Erdogan University Faculty of Medicine (ethics committee date and no: 2022/22).

Peer-review: Externally peer-reviewed.

Author Contributions: Author Contributions: Concept: G.A, M.M.Y, Design: G.A, M.M.Y, A.C, Literature search: G.A, A.C, O.Y, Data Collection and Processing: M.M.Y, A.C, Analysis or Interpretation: G.A, O.Y, A.C, Writing: G.A, M.M.Y, A.C.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The author declared that this study hasn't received no financial support.

REFERENCES

1. World Health Organization (WHO). COVID-19 pandemic data in the world. https://covid19.who.int (accessed on 23/January/2022).
2. Korkusuz R, Karandere F, Senoglu S, Kocoglu H, Yasar KK. The prognostic role of D-dimer in hospitalized COVID-19 patients. Bratisl Lek Listy. 2021;122(11):811-815. doi.org /10.4149/BLL_2021_129.
3. Centers for Disease Control and Prevention. People WhoAre at Higher Risk for Severe Illness. 2020; https://www.cdc.gov/coronavirus/2019-ncov/need- extra-precautions/people-at-higher-risk.html. Accessed April 8, 2020.
4. Serin I, Sari ND, Dogu MH, Acikel SD, Babur G, Ulusoy A, et all. A newparameter in COVID-19 pandemic: initial lactate dehydrogenase (LDH)/Lymphocyte ratio for diagnosis and mortality. J Infect Public Health. 2020 Nov;13(11):1664-1670. doi.org/10.1016/j.jiph.2020.09.009.
5. Wang B, Chen G, Cao Y, Xue J, Li J, Wu Y. Correlation of lactate/albumin ratio level to organ failure and mortality in severe sepsis and septic shock. J Crit Care. 2015 Apr;30(2):271-5. doi.org/10.1016/j.jcrc.2014.10.030.
6. Soeters PB, Wolfe RR, Shenkin A. Hypoalbuminemia: Pathogenesis and Clinical Significance. JPEN J Parenter Enteral Nutr. 2019; 43(2): 181- 193. doi.org/10.1002/jmv.26003.
7. Huang J, Cheng A, Kumar R, Fang Y, Chen G, Zhu Y, et all. Hypoalbuminemia predicts the outcome of COVID-19 independent of ageandco-morbidity. J MedVirol. 2020 Oct;92(10):2152-2158. doi.org/10.1097/MD.0000000000027538.
8. Jeon SY, Ryu S, Oh SK, Park JS, You YH, Jeong WJ, et all. Lactate dehydrogenase to albumin ratio as a prognostic factor for patients with severe infection requiring intensive care. Medicine (Baltimore). 2021 Oct 15;100(41):e27538. doi.org/10.1002/jpen.1451.
9. Henry BM, Aggarwal G, Wong J, Benoit S, Vikse J, Plebani M, et al. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. Am J Emerg Med. 2020;38(9):1722-1726. doi.org/10.1016/j.ajem.2020.05.073.
10. Wu MY, Yao L, Wang Y, Zhu XY, Wang XF, Tang PJ, et all. Clinical evaluation of potential usefulness of serum lactate dehydrogenase (LDH)

in 2019 novel coronavirus (COVID-19) pneumonia. Respir Res. 2020 Jul 6;21(1):171. doi.org/10.1186/s12931-020-01427-8.

11. Aday U, Boyuk A, AkkoC H. The prognostic significance of serum lactate dehydrogenase-to-albumin ratio in colorectal cancer. Ann Surg Treat Res. 2020 Sep;99(3):161-170. doi.org/10.4174/astr.2020.99.3.161.

12. Wu MA, Fossali T, Pandolfi L, Carsana L, Ottolina D, Frangipane V, et all. Hypoalbuminemia in COVID-19: assessing the hypothesis for underlying pulmonary capillary leakage. J Intern Med. 2021 Jun;289(6):861-872. doi.org/10.1111/joim.13208.

13. Paliogiannis P, Mangoni AA, Cangemi M, Fois AG, Carru C, Zinellu A. Serum albumin concentrations are associated with disease severity and outcomes in coronavirus 19 disease (COVID-19): a systematic review and meta-analysis. Clin Exp Med. 2021 Aug;21(3):343-354. doi.org/10.1007/s10238-021-00686-z.

14. Yan D, Huang Q, Dai C, Ren W, Chen S. Lactic Dehydrogenase to Albumin Ratio Is Associated With the Risk of Stroke-Associated Pneumonia in Patients With Acute Ischemic Stroke. Front Nutr. 2021 Sep 16;8:743216. doi: 10.3389/fnut.2021.743216.

15. Lee BK, Ryu S, Oh SK, Ahn HJ, Jeon SY, Jeong WJ, et all. Lactate dehydrogenase to albumin ratio as a prognostic factor in lower respiratory tract infection patients. Am J Emerg Med. 2022 Feb;52:54-58. doi: 10.1016/j.ajem.2021.11.028.

16. Tan C, Huang Y, Shi F, Tan K, Ma Q, Chen Y, et all. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. J Med Virol. 2020 Jul;92(7):856-862. doi.org/10.1002/jmv.25871.