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Can the HALP score predict survival in severe COVID-19 pneumonia?

Original Study

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Abstract

Introduction. The coronavirus infection has caused a pneumonia pandemic worldwide. Our study aimed to determine the relationship between the HALP score and survival in patients monitored in the intensive care unit due to COVID-19 pneumonia.
Materials and Methods. Adult patients monitored in our hospital's COVID intensive care unit between 01.11.2020 and 30.11.2021 were retrospectively evaluated. The effect of the HALP score on survival was investigated with examinations.
Results. The death rate in the 103 patients included in the study was found to be 49.5% (n = 51). When evaluated in terms of patients' gender distribution and median age, no significant difference was observed between survivors and deceased patients (p = 0.20 and p = 0.96, respectively). Ferritin, CRP, LDH and fibrinogen levels were found significantly higher in the deceased patient group compared to the surviving patient group. The median value of the HALP score was significantly higher in the surviving patient group (9.35) compared to the deceased patient group (6.83) (p = 0.015). In the binary logistic regression analysis, HALP score, LDH, and CRP were found to be statistically significant risk factors for mortality.
Conclusion. As a result of our study, we believe that the HALP score could be a practical and easily accessible scoring method that can be used to predict survival in COVID-19 patients monitored in the intensive care unit.

Keywords

COVID-19 • HALP score • survival

1. Introduction

A new coronavirus infection started in the People's Republic of China at the end of 2019 and developed into a pneumonia pandemic. This pandemic has spread all over the world, causing a global pandemic [1]. The causative virus has been named "Severe Acute Respiratory Syndrome-Coronavirus-2" (SARS-CoV-2) by the World Health Organization (WHO), and the disease it causes is called corona virus disease 2019 (COVID-19) [2,3]. The latest data from the WHO reports that there are over 220 million cases and over 4.5 million deaths worldwide [4].

SARS-CoV-2 mainly spreads through respiratory droplets and close contact [5]. Hospitalization is required in 20% of infected patients [6]. Epidemiological studies have shown that 6–10% of patients develop a more severe form of COVID-19 and require admission to the intensive care unit (ICU) complicated by acute hypoxemic respiratory failure related to acute respiratory distress syndrome (ARDS) [7].

Severe COVID-19 pneumonia is often characterized by pulmonary inflammation. Cytokine storms involving the release of pro-inflammatory cytokines, which are life-threatening, can contribute to systemic organ failure observed in critically ill COVID-19 patients [8]. Inflammation has been found to be closely associated with the severity of COVID-19 [9]. Most patients admitted to the ICU require mechanical ventilation due to diffuse lung damage and ARDS. Many ICU reports have shown that COVID-19-associated ARDS leads to long-term mechanical ventilation and increased mortality, varying between 20-62% worldwide [10,7].

The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) score is an easily calculable indicator of systemic inflammation and nutritional status. It has also been proposed as a useful prognostic factor in many cancer patients. The HALP score is calculated with the following formula: hemoglobin (g/dL) x albumin (g/L) x lymphocytes (cell/L)/platelets (cell/L) [11]. The HALP score is a comprehensive index providing clues regarding the immune status as well as the nutritional status of the patients [12].

1.1. Objectives

Although the predictive value of the HALP score for mortality has been demonstrated in cancer patients [11], studies assessing its predictive value in COVID-19 patients are lacking. In our study, we aimed to evaluate the predictive value of the HALP score for survival in patients admitted to the ICU due to severe COVID-19 pneumonia.

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2. Materials and methods

2.1. Study design and case selection

In this retrospective study, we evaluated patients 18 years of age or older who were admitted to our hospital's COVID ICU due to COVID-19 pneumonia between November 1, 2020 and November 30, 2021. All data were recorded at the time of ICU admission, including socio-demographic characteristics, laboratory findings including whole blood count, coagulation parameters (fibrinogen, D-dimer), and biochemical parameters (albumin, ferritin, C-reactive protein [CRP]), comorbidities, mechanical ventilatory support, and outcomes.

Exclusion criteria included age less than 18 years of age, patients with heart failure, coexisting comorbidities or systemic conditions that might affect the components of the HALP score (severe anemia, chronic liver disease/renal failure, etc.).

COVID-19 was diagnosed based on clinical manifestations and a positive PCR test [13]. Severe COVID-19 pneumonia was defined as the presence of objective radiographic findings consistent with COVID-19 pneumonia, characterized by bilateral diffuse infiltrations accompanied by an oxygen saturation of less than 90% in the air room, and a PaO_2/FiO_2 of less than 300 mmHg [14].

Treatment of COVID-19 severe pneumonia during ICU stay comprised medical treatment and invasive (IMV) or non-invasive (NIMV) mechanical ventilation. Availability of extracorporeal membrane oxygenation support (ECMO) was excessively limited at our institution during the COVID-19 pandemic.

The HALP score was measured at the time of admission to the ICU and its association with mortality during ICU stay was analyzed.

2.2. Statistical analysis

IBM SPSS version 23.0 software package was used for the analysis of data. The Kolmogorov-Smirnov test was used to test the normality of variables. Variables showing normal distribution were expressed as mean ± standard deviation, and variables not showing normal distribution as median values (minimum-maximum). Categorical variables were expressed as numbers and percentages. Normally distributed variables were compared using the independent t-test. Those that did not show normal distribution were compared using the Mann–Whitney U test. Comparisons between groups for categorical variables were made with the Pearson chi-squared test. Binary logistic regression analysis was performed to determine risk factors for mortality, using the Backward (Wald) method. The level of significance was set as $p < 0.05$.

3. Results

A total of 103 patients (58 males, 45 females) were included in the study. The average age of the patients was 70 ± 10.6 years. The sociodemographic and clinical characteristics and laboratory findings of the patient group are summarized in Table 1.

Eighty-seven patients (84.5%) had comorbidities; the most common of these were hypertension (53.4%), diabetes mellitus (31.1%), lung diseases (28.2%), and cardiac diseases (25%). During the ICU stay, 46 patients (44.7%) received NIMV and 57 patients (55.3%) received IMV. The median HALP score was 8.0 (1.5–60.0). During the ICU stay, mortality occurred in 51 patients (49.5%).

Patients who survived and who died from COVID-19 were similar with respect to age, gender, and the presence of comorbidities (Table 1).

The average stay in the intensive care unit for patients undergoing NIMV (non-invasive mechanical ventilation) was significantly lower (8.8 ± 6.3 days) compared to those undergoing IMV (invasive mechanical ventilation) (13.3 ± 7 days) ($p = 0.001$). The median HALP score was found to be 7.88 (1.45–56.30) in patients undergoing IMV and 7.99 (2.27–59.97) in patients undergoing NIMV, with no significant difference between the groups ($p = 0.91$). Mortality rates were significantly higher in patients undergoing IMV ($p < 0.001$) (Table 1).

Median values of ferritin, CRP, LDH and mean fibrinogen values were significantly higher in the deceased patient group compared to the surviving patient group ($p = 0.014$, $p < 0.001$, $p = 0.001$, $p = 0.032$, respectively) (Table 1). The median values of albumin and lymphocytes were significantly higher in the surviving patient group ($p = 0.006$ and $p = 0.002$, respectively) (Table 1).

Median D-dimer values were found to be similar between the surviving and deceased patient groups (3.01 and 3.02, respectively) ($p = 0.88$) (Table 1).

Median ALT and AST values were found to be similar between the surviving and deceased patient groups ($p = 0.739$, $p = 0.395$, respectively) (Table 1).

The median HALP score was 9.35 (2.27–59.97) in the surviving patient group and 6.83 (1.45–17.80) in the deceased patient group. The difference between the groups was found to be statistically significant ($p = 0.015$). The mortality rate among all patients was 49.5% ($n = 51$). The characteristics of the patients monitored in the ICU are given in Table 1.

We conducted a binary logistic regression analysis by including variables found to be statistically significant in univariate analysis (albumin, lymphocytes, ferritin, fibrinogen, CRP, HALP score, and LDH) to predict mortality. In the model (Omnibus test $p < 0.001$), HALP score, LDH, and CRP were found to be statistically significant risk factors for mortality. An increase of one unit in CRP increased mortality by 1.012 times, an increase of one unit in LDH increased mortality by 1.003 times, and an increase of one unit in the HALP score decreased mortality by 0.89 times (Table 2).

Table 1. General characteristics of patients who received intensive care and survived or deceased

		Survival	Non-survival	P value
Patients, n		52	51	
Gender n (%)	Male	30 (57.7)	28 (54.9)	0.203
	Female	22 (42.3)	23 (45.1)	
Age (years) median (min-max)		65.40 (38-90)	69.71 (27-93)	0.960
Comorbidity n (%)	Yes	46 (52.8)	41 (47.2)	0.258
	No	6 (37.5)	10 (62.5)	
Number of comorbidity median (min-max)		1(0-4)	2(0-4)	0.857
Mechanical ventilation n (%)	NIMV	45 (86.5)	1 (2)	< 0.001
	IMV	7 (13.5)	50 (98)	
HALP score median (min-max)		9.35 (2.27-59.97)	6.83 (1.45-17.80)	0.015
Hemoglobin (g/dL) median (min-max)		11,9 (8.2-15.2)	12.24 (8.8-15.1)	0.48
Albumin (μL) median (min-max)		32.33 (13-41)	30.18 (18-37)	0.006
Lymphocytes (μL) median (min-max)		875.12 (200-3900)	574.51 (200-1700)	0.002
Platelet ($10^3/mm^3$) median (min-max)		295 (97-673)	282 (56-715)	0.48
Ferritin (ng/mL) median (min-max)		375.44 (5.4-1500)	517.82 (57-1500)	0.014
Fibrinogen (mg/dl) mean±SD.		462.75±131.60	522.02±144.66	0.032
D-dimer (ng/mL) median (min-max)		3.01 (0.15-25)	3.02 (0.15-33.02)	0.88
CRP (mg/L) median (min-max)		85.06 (2-228)	127.14 (8-211)	< 0.001
ALT (IU/L) median (min-max)		25(6-197)	25(7-122)	0.739
AST (IU/L) median (min-max)		33(9-194)	38(10-133)	0.395
LDH (U/L) median (min-max)		406 (148-1575)	540 (251-1005)	0.001

NIMV: Non-invasive mechanical ventilation, IMV: İnvasive mechanical ventilation, CRP: C-reactive protein, ALT: Alanine aminotransferase, AST: aspartate aminotransferase, LDH: Lactate dehydrogenase

Table 2. Evaluation of mortality with binary logistic regression analysis

	p value	OR	95% CI for OR	
			Lower	Upper
LDH	0.015	1.003	1.001	1.005
CRP	0.002	1.012	1.005	1.020
HALP score	0.002	0.883	0.817	0.954

Model Summary: Nagelkerke R square:0.34 ; Hosmer Lemeshow Test Chi Square:14.210 p:0.076
OR: Odds ratio, CI: Confidence interval

4. Discussion

COVID-19 continues to be a significant health problem causing deaths worldwide every day [15]. Patients with severe symptoms require admission to the intensive care unit for close monitoring and mechanical ventilation support [16]. Critical cases may include severe pneumonia and acute respiratory distress syndrome (ARDS), pulmonary thromboembolism, and cardiac and neurological complications [17].

Mortality rates in critically ill patients with COVID-19 are between 11–61% [18]. Differences in mortality in ICU patients can be attributed to patient demographics, suitability of the ICU, and differences in admission policies. Of the 103 patients admitted to our study, 51 had died. The mortality rate of 49.5% has been assessed as consistent with literature data.

Respiratory support with IMV is a cornerstone of critical care medicine. The need to initiate IMV in patients admitted to

the ICU due to severe COVID-19 pneumonia is one of the most important predictive factors of mortality [19]. Similarly, in our study, mortality was found to be significantly higher in patients who underwent IMV.

There are studies showing that older age and male gender are associated with higher mortality in COVID-19 patients [20,21]. In our study, while the average age of the deceased patients was higher, no significant difference was found between the groups. In the study conducted by Ciceri et al., male gender was not identified as a significant risk factor for the mortality of COVID-19 patients [22]. Similarly, in our study, no significant difference was found between the groups in terms of male gender.

In a study conducted on COVID-19 patients monitored in intensive care, the number of comorbidities observed in the group of surviving patients [2(1-4)] was found to be significantly lower than in the group of deceased patients [3(2-4)] [19]. In our study too, while fewer comorbidities were found in the group of surviving patients, no significant difference was found between them. We foresee that this situation can be explained by differences in the severity of comorbidities and differences in treatment and control status. In our study, as in another study, hypertension and diabetes mellitus were identified as the most common comorbidities in patients admitted to the hospital with COVID-19 [23].

Ferritin, as an inflammation marker, has been evaluated in intensive care patients due to severe COVID-19 pneumonia. In studies conducted, despite elevated levels of ferritin, no significant difference was found between the groups of deceased and surviving patients [24,7]. In our study, however, ferritin levels were found to be significantly higher in the group of deceased patients. This result provides us with information that the levels of inflammation at the time of the patients' admissions are correlated with the severity of the disease.

In patients with COVID-19 pneumonia, high fibrinogen and d-dimer levels are commonly observed [25]. In our study, the fibrinogen and d-dimer levels of our patients were high, consistent with the literature. Fibrinogen values were significantly higher in the group of deceased patients. While d-dimer values were higher in the group of deceased patients, no significant difference was found between them.

CRP plays a significant role in inflammatory processes. High CRP levels have been associated with the severity of COVID-19 disease [26]. In the study of Martinot et al., high CRP levels in cases of COVID-19 were evaluated as one of the independent factors associated with both ICU admission and mortality [27]. In our study too, CRP levels were found to be significantly higher in the group of deceased patients. Additionally, CRP was identified as a significant risk factor in predicting mortality.

LDH is released from cells when cytoplasmic membranes are damaged [28,29]. LDH increases lactate production, leading to an increase in immunosuppressive cells and inhibition in cytolytic cells [30]. In the meta-analysis involving 4,203 patients by Zyang et al., it was stated that elevated LDH predicted ICU admission, mortality, and ARDS [31]. In our study, in accordance with the literature, LDH levels were significantly higher in the group of deceased patients compared to surviving patients. Furthermore, LDH was determined as a significant risk factor in terms of predicting mortality.

The HALP score is used as an indicator of systemic inflammation and nutritional status. This score is composed of hemoglobin, albumin, lymphocyte, and platelet values, which are widely used biomarkers in daily practice. A high HALP score has been associated with survival [11,32,33].

Anemia is a common condition encountered in intensive care patients. A prospective study involving 5,925 patients monitored in intensive care reported that lower hemoglobin levels were associated with higher morbidity and mortality [34]. In a meta-analysis evaluating COVID-19 patients, it was observed that anemia was associated with short-term mortality risk [35]. Albumin is a negative acute phase reactant marker used in assessing nutritional status and indicates protein levels in the blood. In a meta-analysis conducted by Paliogiannis et al., it was shown that serum albumin concentrations were significantly lower in severe COVID-19 patients compared to those with mild disease [36]. Inflammation leads to an increase in the number of neutrophils and platelets, along with a decrease in lymphocyte count [37]. In a meta-analysis involving COVID-19 patients, it was concluded that a low lymphocyte count is associated with mortality [38]. In COVID-19, a slight decrease in platelet count, as well as platelet activation and aggregation abnormalities, can occur. Nevertheless, a published article found that platelet counts are not a predictor of COVID-19 mortality [39]. The HALP score is an integration of these four parameters mentioned above. There are studies in the literature showing that the HALP score is associated with prognosis in cancer patients [33,40]. Another study suggested that the HALP score could be a strong indicator for acute ischemic stroke (11). In our study, the HALP score was significantly higher in the group of surviving patients with severe COVID-19. Our results reveal that the HALP score correlates with prognosis in patients with severe COVID-19 pneumonia. We determined that a low HALP score is a significant risk factor in terms of mortality.

As a result of our study, we believe that the HALP score could be a practical and easily accessible scoring method that can be used to predict survival in COVID-19 patients monitored in the intensive care unit. Additionally, the tests for CRP and LDH could also be significant risk factors in predicting mortality. For this reason, we believe that the evaluation of the HALP score at the hospital admission could be used in predicting the prognosis of severe COVID-19 patients who require intensive care.

Our study had some limitations. Firstly, we had a limited number of patients in our study, which could affect the power

of the study to detect an existing effect. Secondly, this was a retrospective observational study and there might be unmeasured confounding factors that could have affected the result of our study. We only obtained the number of hemoglobin, albumin levels, lymphocyte count, and platelet count at admission, but we did not present the dynamic change of the HALP score at different stages. Therefore, multicenter cohort studies are still needed to validate the findings.

Authors' Contribution

Study design: F.E., M.Ç.; Data collection: M.Ç., S.U.; Statistical analysis: H.Ç., N.S.; Data interpretation: M.Ç., F.E.,N.S.; Manuscript preparation: M.Ç., H.Ç.; Literature search: M.Ç., S.U.

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Conflict of interest

There is no conflict of interest.

Ethics approval

Ethics Committee approval has been granted. The name of the committee and the number of the decision: Balikesir University Clinical Research Ethics Committee Decision number: 2022/14.

References

[1] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020; 323: 1061-1069.

[2] Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, Si HR, Zhu Y, Li B, Huang CL et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020; 579: 270-273.

[3] Jiang F, Deng L, Zhang L, Cai Y, Cheung CW, Xia Z. Review of the Clinical Characteristics of Coronavirus Disease 2019 (COVID-19). J Gen Intern Med. 2020; 35: 1545-1549.

[4] https://data.who.int/dashboards/covid19/deaths?n=c (Accessed December 2022)

[5] Zhou M, Zhang X, Qu J. Coronavirus disease 2019 (COVID-19): a clinical update. Front Med. 2020; 14: 126-135.

[6] Varghese GM, John R, Manesh A, Karthik R, Abraham OC. Clinical management of COVID-19. Indian J Med Res. 2020; 151:401-410.

[7] Oliveira E, Parikh A, Lopez-Ruiz A, Carrilo M, Goldberg J, Cearras M, Fernainy K, Andersen S, Mercado L, Guan J et al. ICU outcomes and survival in patients with severe COVID-19 in the largest health care system in central Florida. PLoS One. 2021; 16: e0249038.

[8] Panigrahy D, Gilligan MM, Huang S, Gartung A, Cortés-Puch I, Sime PJ, Phipps RP, Serhan CN, Hammock BD. Inflammation resolution: a dual-pronged approach to averting cytokine storms in COVID-19? Cancer Metastasis Rev. 2020; 39: 337-340.

[9] Gong J, Dong H, Xia QS, Huang ZY, Wang DK, Zhao Y, Liu WH, Tu SH, Zhang MM, Wang Q, Lu FE. Correlation analysis between disease severity and inflammation-related parameters in patients with COVID-19: a retrospective study. BMC Infect Dis. 2020; 20: 963.

[10] Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA. 2020; 323: 2052–2059.

[11] Tian M, Li Y, Wang X, Tian X, Pei LL, Wang X, Zhang L, Sun W, Wu J, Sun S et al. The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score is Associated With Poor Outcome of Acute Ischemic Stroke. Front Neurol. 2021; 11: 610318.

[12] Zhai B, Chen J, Wu J, Yang L, Guo X, Shao J, Xu H, Shen A. Predictive value of the hemoglobin, albumin, lymphocyte, and platelet (HALP) score and lymphocyte-to-monocyte ratio (LMR) in patients with non-small cell lung cancer after radical lung cancer surgery. Ann Transl Med. 2021; 9: 976.

[13] T.C. Sağlık Bakanlığı.Turkey Country Assessment. https://covid19.saglik.gov.tr/Eklenti/39551/0/covid-19rehberigenelbilgilerepidemiyolojivetanipdf.pdf

[14] T.C. Sağlık Bakanlığı.Turkey Country Assessment. https://covid19.saglik.gov.tr/Eklenti/43095/0/covid-19rehberieriskinhastayonetimivetedavi-12042022pdf.pdf

[15] World Health Organization. WHO Coronavirus (COVID-19) Dashboard. https:// covid19.who.int (accessed July 24, 2022)

[16] Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, Holden KA, Read JM, Dondelinger F, Carson G et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. Br Med J. 2020; 369:m1985.

[17] Kenny G, Mallon PW. COVID-19 clinical presentation and therapeutic considerations. Biochem Biophys Res Commun. 2021; 538: 125-131.

[18] Liu S, Yao N, Qiu Y, He C. Predictive performance of SOFA and qSOFA for in-hospital mortality in severe novel coronavirus disease. *Am J Emerg Med*. 2020; 38: 2074–2080.

[19] Kukoč A, Mihelčić A, Miko I, Romić A, Pražetina M, Tipura D, Drmić Ž, Čučković M, Ćurčić M, Blagaj V et al. Clinical and laboratory predictors at ICU admission affecting course of illness and mortality rates in a tertiary COVID-19 center. Heart Lung. 2022; 53: 1-10.

[20] Gallo Marin B, Aghagoli G, Lavine K, Yang L, Siff EJ, Chiang SS, Salazar-Mather TP, Dumenco L, Savaria MC, Aung SN et al. Predictors of COVID-19 severity: a literature review. Rev Med Virol. 2021; 31: e2146.

[21] Figliozzi S, Masci PG, Ahmadi N, Tondi L, Koutli E, Aimo A, Stamatelopoulos K, Dimopoulos MA, Caforio ALP, Georgiopoulos G. Predictors of adverse prognosis in COVID-19: a systematic review and meta-analysis. Eur J Clin Invest. 2020; 50: e13362.

[22] Ciceri F, Castagna A, Rovere-Querini P, De Cobelli F, Ruggeri A, Galli L, Conte C, De Lorenzo R, Poli A, Ambrosio A et al. Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy. Clin Immunol. 2020: 217: 108509.

[23] Beigmohammadi MT, Amoozadeh L, Rezaei Motlagh F, Rahimi M, Maghsoudloo M, Jafarnejad B, Eslami B, Salehi MR, Zendehdel K. Mortality Predictive Value of APACHE II and SOFA Scores in COVID-19 Patients in the Intensive Care Unit. Can Respir J. 2022: 5129314.p.8.

[24] Umeh C, Tuscher L, Ranchithan S, Watanabe K, Gupta R. Predictors of COVID-19 Mortality in Critically Ill ICU Patients: A Multicenter Retrospective Observational Study. Cureus. 2022; 14: e20952.

[25] Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. Blood. 2020; 135: 2033–2040.

[26] Li L, Zhang S, He B, Chen X, Wang S, Zhao Q. Risk factors and electrocardiogram characteristics for mortality in critical inpatients with COVID-19. Clin Cardiol. 2020; 43: 1624–1630.

[27] Martinot M, Eyriey M, Gravier S, Bonijoly T, Kayser D, Ion C, Mohseni-Zadeh M, Camara S, Dubois J, Haerrel E et al. Predictors of mortality, ICU hospitalization, and extrapulmonary complications in COVID-19 patients. Infect Dis Now. 2021; 51: 518-525.

[28] Han Y, Zhang H, Mu S, Wei W, Jin C, Tong C, Song Z, Zha Y, Xue Y, Gu G. Lactate dehydrogenase, a risk factor of severe COVID-19 patients: A Retrospective and Observational Study. Aging (Albany NY). 2020; 12: 11245-11258.

[29] Kuang ZS, Yang YL, Wei W, Wang JL, Long XY, Li KY, Tong CY, Sun Z, Song ZJ. Clinical characteristics and prognosis of community-acquired pneumonia in autoimmune disimmunocompromised host: a retrospective observational study. World J Emerg Med. 2020; 11: 145–151.

[30] Ding J, Karp JE, Emadi A. Elevated lactate dehydrogenase (LDH) can be a marker of immune suppression in cancer: Interplay between hematologic and solid neoplastic clones and their microenvironments. Cancer Biomark. 2017; 19: 353–356.

[31] Zhang JJY, Lee KS, Ang LW, Leo YS, Young BE. Risk Factors for Severe Disease and Efficacy of Treatment in Patients Infected With COVID-19: A Systematic Review, Meta-Analysis and Meta-Regression Analysis. Clin Infect Dis. 2020; 71: 2199-2206.

[32] Peng D, Zhang CJ, Tang Q, Zhang L, Yang KW, Yu XT, Gong Y, Li XS, He ZS, Zhou LQ. Prognostic significance of the combination of preoperative hemoglobin and albumin levels and lymphocyte and platelet counts (HALP) in patients with renal cell carcinoma after nephrectomy. BMC Urol. 2018; 18: 20.

[33] Jiang H, Li H, Li A, Tang E, Xu D, Chen Y, Zhang Y, Tang M, Zhang Z, Deng X et al. Preoperative combined hemoglobin, albumin, lymphocyte and platelet levels predict survival in patients with locally advanced colorectal cancer. Oncotarget. 2016; 7: 72076–72083.

[34] Sakr Y, Lobo S, Knuepfer S, Esser E, Bauer M, Settmacher U, Barz D, Reinhart K. Anemia and blood transfusion in a surgical intensive care unit. Crit Care. 2010; 14: R92.

[35] Zuin M, Rigatelli G, Quadretti L, Fogato L, Zuliani G, Roncon L. Prognostic Role of Anemia in COVID-19 Patients: A Meta-Analysis. Infect Dis Rep. 2021; 13: 930-937.

[36] 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; 21: 343-354.

[37] Zhang Y, Chen B, Wang L, Wang R, Yang X. Systemic immune-inflammation index is a promising noninvasive marker to predict survival of lung cancer: A meta-analysis. Medicine (Baltimore). 2019; 98: e13788.

[38] Taylor EH, Marson EJ, Elhadi M, Macleod KDM, Yu YC, Davids R, Boden R, Overmeyer RC, Ramakrishnan R, Thomson DA et al. Factors associated with mortality in patients with COVID-19 admitted to intensive care: a systematic review and meta-analysis. Anaesthesia. 2021;76: 1224-1232.

[39] Amgalan A, Othman M. Hemostatic laboratory derangements in COVID-19 with a focus on platelet count. Platelets. 2020; 31: 740–745.

[40] Yilmaz M. Is There Predictive Significance of HALP Score in Metastatic RCC Patients Treated with Nivolumab? EJMI. 2021; 5: 33-38.