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ORIGINAL RESEARCH

The utility of hemoglobin, albumin, lymphocyte and platelet (HALP) score in predicting mortality among COVID-19 patients: a preliminary study

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Abstract

Several scoring systems are used to predict critical care requirements in coronavirus disease 2019 (COVID-19) patients. This study aims to determine the relationship between the hemoglobin, albumin, lymphocyte, and platelet (HALP) scores and in-hospital mortality for COVID-19 patients who visited the emergency department (ED). This retrospective study included patients over 18 years of age. Data were scanned into a digital information system of the hospital. The area under the receiver operating characteristic (ROC) curve and the area under the curve (AUC) were used to measure each discriminant cutoff value to predict mortality. A total of 458 patients were included in this study. The mean age of the patients was 72 years, and 216 (47.2%) patients were women. ROC analysis was performed to examine the predictive power of the HALP score in predicting mortality in COVID-19 patients, with an AUC of 0.720 (95% confidence interval: 0.676–0.761), a Youden index of 0.357, and a p value of 0.001. As a result of the statistical analysis, it was determined that the HALP score was statistically significant in the prediction of mortality in COVID-19 patients ($p < 0.001$). In this study, we found that the HALP score could be a good predictor of in-hospital mortality among COVID-19 patients.

Keywords

COVID-19; HALP score; Mortality

1. Introduction

Coronavirus disease 2019, which is termed COVID-19, is caused by severe acute respiratory syndrome coronavirus 2 and is a contagious respiratory disease [1]. Since 11 March 2020, when the World Health Organization (WHO) declared a pandemic, more than 500 million people have been infected, and more than six million have died worldwide [2]. Although the pandemic seems to have been brought under control through the vaccines that have been developed against COVID-19, new waves of infections are still reported in many countries [3].

At the peak of the pandemic, most emergency departments (EDs) and hospitals experienced similar challenges. Most health systems came to the point of collapse because facilities were having problems, such as the number of beds in the intensive care unit (ICU) and number of ventilators being exhausted, and the facilities were no longer able to meet the healthcare demands [4]. Therefore, the early detection of patients with a possible serious COVID-19 infection and at high risk of death can reduce the pressure on medical services and ensure that medical resources are used more efficiently.

Various scoring systems and algorithms have been developed to predict critical care requirements among COVID-19 patients [5]. An ideal scoring system should include data that can be easily recorded and calculated, should be able to distinguish critical patients from other patients, and should be applicable in all populations [6].

It has been stated that malnutrition in patients with COVID-19 has negative effects on the immune system, which can adversely affect the prognosis [7]. The hemoglobin, albumin, lymphocyte, and platelet (HALP) scores are indices that aim to evaluate the nutritional and immune systems of patients [8]. In the literature, studies have shown that a low HALP score could be used to predict mortality in patients with malignancy [9, 10].

The goal of this study was to examine the relationship between the HALP score and in-hospital mortality among COVID-19 patients who visited the ED and were admitted to the hospital.

2. Methods

This retrospective observational study was carried out in the ED of Kartal Dr. Lütfi Kırdar City hospital between 01 January 2022, and 01 June 2021.

All COVID-19 patients aged over 18 years who were ad-

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mitted to the ED between 01 January 2022, and 01 June 2022, were included in the study. The diagnosis of COVID-19 was determined based on the World Health Organization (WHO) guidelines. This study includes only patients who had positive results in the real-time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) test of nasal and pharyngeal swab samples. The exclusion criteria were as follows: patients with negative reverse transcription-polymerase chain reaction test results, patients with hematological malignancies, patients who were transferred from another hospital, patients who died in the ED, and patients in whom the HALP score could not be measured.

The data of all the patients obtained at the time of initial admission to the ED were recorded in a pre-created dataset. The medical records of the patients were examined digitally, and age, sex, body temperature, heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate, comorbid diseases, laboratory parameters, inpatient or intensive care unit admission, and HALP score were recorded in the dataset. The HALP score was measured using the following formula: hemoglobin (g/L) $\times$ albumin (g/L) $\times$ lymphocyte (/L)/platelet (/L) [8]. Hematological tests were performed using an autoanalyzer (Sysmex XN-1000, Sysmex Corporation, Kobe, Japan), and biochemical tests were performed with an automated biochemical analyzer (Cobas e801, Roche Diagnostics, Mannheim, Germany).

In this study, we aimed to examine the relationship between the HALP score and in-hospital mortality among COVID-19 patients. The in-hospital mortality rate was the primary outcome of the study.

To perform statistical analysis, SPSS v. 25.0 software package (SPSS Inc., Chicago, IL, USA) and MedCalc ver. 12.5 (MedCalc Software Ltd, Ostend, Belgium) were used. Descriptive statistics are presented as the mean and standard deviation values and percentage distribution. The relevance of the data to the normal distribution was cross-checked with the Kolmogorov-Smirnov test. ROC curve analysis was used to determine the cutoff values of the HALP score in predicting mortality. Youden J index was used to obtain the optimal cut-off value, and related sensitivity, specificity, positive predictive, and negative predictive values were given. The significance level was accepted as $p < 0.05$.

3. Results

The study was completed with 458 patients who met the inclusion criteria. The main characteristic findings of the patients are presented in Table 1. To compare their various characteristics, the patients were categorized into two groups: survivors and nonsurvivors. In order of frequency, the most common comorbidities among the patients were hypertension, diabetes mellitus, and cardiovascular diseases. The statistical analysis revealed that the hemoglobin, platelet, and albumin levels and the mean HALP score of the nonsurvivor group were statistically significantly lower than those of the survivor group ($p = 0.007$, $p = 0.004$, $p < 0.001$, and $p < 0.001$, respectively).

To examine the predictive power of the HALP score for predicting mortality, ROC analysis was performed. The AUC value was measured as 0.720 (95% Confidence Interval (CI): 0.676–0.761), the Youden index was measured as 0.357, and the p value was measured as 0.001. As a result, it was determined that the HALP score was statistically significant in the prediction of mortality in COVID-19 patients ($p < 0.001$) (Table 2, Fig. 1).

4. Discussion

In this retrospective cohort study, we investigated the prognostic value of the HALP score in patients with COVID-19 and found that a lower HALP score at the time of admission to the ED was correlated with in-hospital mortality.

The HALP score is used as an index of immune and nutritional status. Nutrition is one of the factors that determines the immune response, and good nutrition plays an important role in a favorable immune response. It has been shown that COVID-19 results in a poorer outcome in elderly and obese patients with a poor nutritional status [11].

This study might be the first in the literature to examine the relationship between the mortality status of COVID-19 patients and HALP scores. The HALP score includes four variables: hemoglobin, albumin, lymphocytes, and platelets. There are studies that have examined the prognostic role of each variable in COVID-19 patients.

Previous studies have shown that critically ill patients have reduced hemoglobin levels [12]. In a study conducted with 733 COVID-19 patients, it was reported that anemia at the time of admission could be used to predict in-hospital mortality [13]. Bellmann-Weiler *et al.* [14] emphasized that the presence of anemia at admission was an independent mortality predictor in 259 COVID-19 patients.

Albumin, a protein synthesized in the liver, provides plasma oncotic pressure and plays a role in the transport of endogenous and exogenous substances. In the presence of nutritional problems, sepsis, severe trauma, malignancy, and severe inflammation, low albumin levels can be observed due to increased vascular permeability [15]. It has been shown that hypoalbuminemia is associated with mortality in critically ill patients [16]. In a study conducted in Italy, the data of 319 COVID-19 patients were examined, and when the patients were divided into survivor and nonsurvivor groups, the nonsurvivor group was determined to have lower albumin levels at the time of admission [17]. In a meta-analysis of 11 studies, it was emphasized that COVID-19 patients with low albumin levels at admission were likely to have a more severe disease course [18].

In studies conducted during the early stages of the pandemic, it has been reported that patients who died due to COVID-19 had lower lymphocyte counts than those who survived [19]. Although the cause of low lymphocyte levels in COVID-19 cannot yet be fully explained, various hypotheses have been proposed to explain this finding. First, lymphocyte infiltration and sequestration may occur in the lungs, gastrointestinal tract, or lymphoid tissues. Second, in COVID-19, increased proinflammatory cytokines, such as interleukin-6, may induce further lymphocyte reduction [20]. In a meta-analysis covering the data of 3099 patients from 23 studies, lymphopenia at admission was found to be related to poor outcomes in COVID-19 patients [21]. In the current study, we attribute the lack of a

TABLE 1. Baseline characteristics of the patients.

	Survivor group		Nonsurvivor group		Total		
	Mean n	SD %	Mean n	SD %	Mean n	SD %	*p*
Gender							0.048
Female	140	50.9	76	41.5	216	47.2	
Male	135	49.1	107	58.5	242	52.8	
Age (years)	68.9	15.3	76.6	9.9	72.0	13.9	0.001
Systolic blood pressure (mmHg)	126.5	17.9	127.4	25.7	126.9	21.3	0.66
Diastolic blood pressure (mmHg)	71.6	11.2	71.1	14.8	71.4	12.7	0.66
Pulse (beats/min)	85.1	15.2	95.6	20.6	88.3	18.2	0.001
Respiratory rate (min)	22.5	5.8	27.6	8.3	24.4	7.2	0.001
Body temperature (°C)	36.7	0.7	36.9	0.8	36.8	0.8	0.09
Chronic obstructive pulmonary disease	16	11.3	23	19.3	39	14.9	0.07
Diabetes mellitus	68	44.4	46	37.7	114	41.5	0.26
Hypertension	96	58.9	63	50.4	159	55.2	0.15
Congestive heart failure	12	8.6	25	21.9	37	14.6	0.003
Coronary artery disease	31	21.5	21	18.4	52	20.2	0.54
Chronic renal failure	9	6.3	21	18.8	30	11.8	0.002
White blood cell (10^9/L)	7.6	4.0	10.2	5.5	8.6	4.8	0.001
Lymphocyte (10^9/L)	1.1	0.6	0.7	0.3	0.9	0.5	0.37
Hemoglobin (g/dL)	12.6	1.9	12.0	2.3	12.3	2.1	0.007
Platelet (10^9/L)	220.3	93.8	238.8	99.6	227.6	96.4	0.04
Blood urea nitrogen (mg/dL)	46.7	31.9	81.3	58.7	60.4	47.6	0.001
C-reactive protein (mg/dL)	87.6	73.0	120.7	87.8	100.6	80.7	0.048
Albumin (g/L)	34.3	4.9	31.8	6.4	33.3	5.7	0.001
Aspartate aminotransferase (IU/L)	42.4	30.9	77.4	322.6	56.3	205.1	0.07
Alanine aminotransferase (IU/L)	30.8	23.8	46.8	170.5	37.2	109.2	0.12
Creatinine (mg/dL)	1.18	2.63	1.74	1.71	1.40	2.32	0.01
Admission status							0.001
Inpatient unit	255	91.7	75	41.0	330	71.6	
Intensive care unit	23	8.3	108	59.0	131	28.4	
HALP score	25.1	18.8	13.6	11.2	20.5	17.1	0.001

SD: standard deviation, HALP: hemoglobin, albumin, lymphocyte, and platelet.

TABLE 2. Predictive performance of the HALP score for mortality in patients with COVID-19.

	AUC	Cutoff	Sensitivity	Specificity	+LR	−LR	PPV	NPV	Youden index
HALP score	0.720 (0.676–0.761)	<16.7	74.7	60.9	1.9	0.4	56.2	77.7	0.357

HALP: hemoglobin, albumin, lymphocyte, and platelet, AUC: area under the curve, LR: likelihood ratio, PPV: positive predictive value, NPV: negative predictive value.

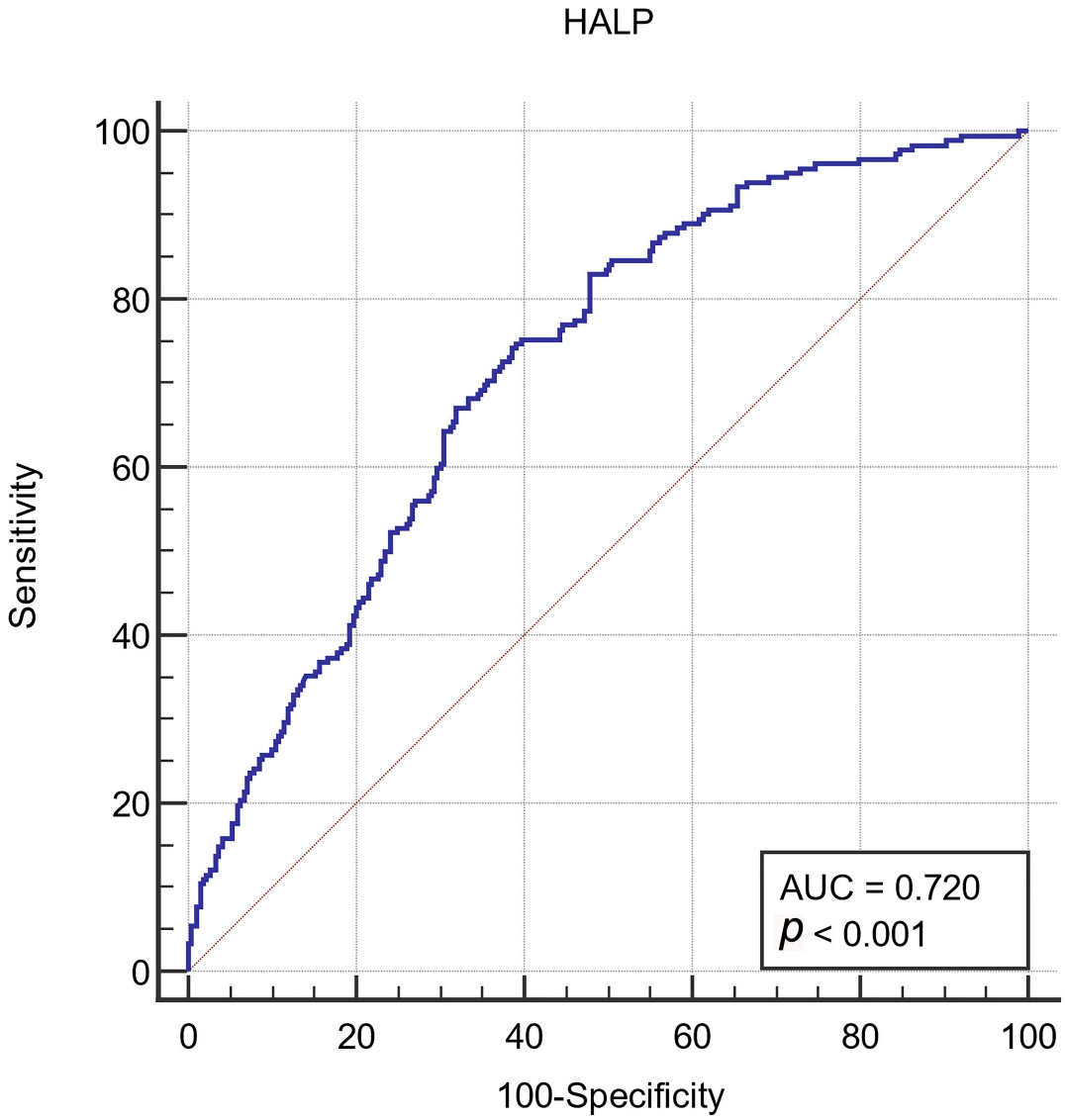

FIGURE 1. Receiver operating characteristic curve of the HALP score in predicting in-hospital mortality among patients with COVID-19. HALP: hemoglobin, albumin, lymphocyte, and platelet; AUC: area under the curve.

significant relationship between the survivor and nonsurvivor groups in terms of the lymphocyte count to our relatively small sample size.

There are articles that have examined the relationship between platelet count, the last variable of the HALP score, and COVID-19. In studies conducted in China during the first period of the pandemic, it has been stated that 12–36.2% of COVID-19 patients had thrombocytopenia [22, 23]. In a study from Wuhan, COVID-19 patients were categorized into platelet count groups of (0, 50], (50, 100], (100–150], and (150–), and the mortality rates of these groups were determined as 92.1%, 61.2%, 17.5%, and 4.7%, respectively [24].

Since there is currently no study that has examined the relationship between the HALP score and COVID-19 in the literature, we were not able to compare the results of our study. However, the hemoglobin, albumin, and platelet counts, which are variables of the HALP score, were also found to be low in our study, and these results are in agreement with the results in the literature.

5. Conclusions

This study has certain limitations. First, it had a single-center retrospective design. Second, only the hemoglobin, albumin, lymphocyte, and platelet counts, which are variables of the HALP score that were obtained at the time of presentation to the ED, were evaluated, and dynamic changes were not investigated. Multicenter prospective studies are needed to adapt the results of our study to the general population.

Although the number of daily cases due to COVID-19 has decreased, deaths due to the disease still occur on a daily basis in various parts of the world. These patients are usually first seen by an emergency physician in the ED. Therefore, it is important for emergency physicians to identify critically ill patients in the early period. In this study, we found that low HALP scores at admission were associated with in-hospital mortality in patients with COVID-19. Although the HALP score has been studied mostly in cancer patients, future studies will perhaps investigate the combination of the HALP score with other scores and obtain clearer information about the

prognosis of various diseases.

AUTHOR CONTRIBUTIONS

HA, MK and RA—contributed to the study conception and design; HA and RA—contributed to the data analysis and interpretation; MK and RA—contributed to the manuscript drafting; HA, MK and RA—are the guarantors of the study. All authors approved the final article.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Institutional Review Board of Kartal Dr. Lütfi Kırdar City Hospital (2022/514/228/24, date: 30 June 2022), which waived the need for informed consent owing to its retrospective nature.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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