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HALP score as a new prognostic factor for Covid-19

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Abstract

Objective: This research aims to analyze the HALP. (hemoglobin, albumin, lymphocyte. platelet) score of.survivor-deceased Covid-19 patients.

Material and methods: 590 patients with. Covid-19 were. included. in. this. study. Patients. were. divided. into two groups as survivor (n:296) and deceased (n:294). Patient information was collected from the hospital online system. The Study was conducted retrospectively, and it aims to.investigate.the association.between HALP score and.mortality.in Covid-19.patients.

Results: In.the deceased group.the.mean.age was 71.32±10.9 (n:294) while in the survivor.group, it.was 59.97±16.2 (n:296) (p:0.000). 65,6% of the deceased group were.male, while 55% of survivor group were male (p<0.001). The median HALP score was 11,45 (1,00-1594,00) in the deceased group, while it was 23,58 (1,73-231,75) (p<0.001) in survivor group. Through our analysis,.we have found.that.the.HALP score.was associated with mortality, thus the.relationship.between 1/HALP.score.and.mortality was examined. While the median 1/HALP was 0.08 (0.01-1.00) in deceased group, it was 0.04 (0.01-0.58) in the survivor group. ROC (receiver. operating.characteristic) analysis was executed for determining the cut off value of 1/HALP. The cut.off.value of 1/HALP for mortality was 0,064 ((AUC: 0,724 (0,682-0,767); 67,3% Sensitivity, 67,0% Specificity; p<0.001)).

Conclusion: There is a meaningful correlation established between low HALP score and.mortality. in.Covid-19.patients. We.have reached the.conclusion that using HALP score.to. predict.mortality.in.Covid-19. patients might be useful.

Key words: HALP, Covid-19, ICU, mortality

Introduction

A.new.virus,.from the coronavirus family,.which. was called as Sars-Cov-2 in December 2019, led to the outbreak of a pandemic in March 2020. The disease due to this virus was defined as Covid-19 [1]. The pandemic, which affected approximately 613,972,905 people, has caused 6,516,982 deaths since its onset [2]. With the increasing significance of determining the Covid-19 prognosis, many new markers and scoring systems, in addition to well-known markers such as serum ferritin level, neutrophil lymphocyte ratio and d-dimer were found to successfully show the Covid-19 progression [3–5]. A relationship between low hemoglobin level and Covid-19 mortality was described, which is thought to be due to the lower oxygen carrying capacity in anemic patients, especially in elderly with comorbidities [6]. Similarly, a relationship.was.found.between.low. albumin.and Covid-19 mortality. A low albumin level increases the risk of mortality for Covid-19, regardless of other mortality-increasing characteristics such as age and comorbid situations [7]. The lymphocyte level can be found higher or lower in viral infections and, a significant relationship was depicted among low lymphocyte level and mortality in Covid-19 [8]. Thrombocytopenia is a well-known poor prognostic component in multi-organ failure, and an important parameter in Acute Physiology Score II, which is a widely used scoring system for detecting mortality [9].

The HALP score, is a mathematical formula produced from albumin, hemoglobin, lymphocyte

and platelet counts, which are frequently used as inflammation markers. This scoring system is used as a new prognostic factor especially for malignancies and was shown to be related with increased inflammation. The HALP score is computed with this equation: lymphocytes(/L).x.albumin(g/L).x.hemoglobin(g/L) / platelets.(/L) [10]. In addition to its use for determining inflammation, HALP.score.can also be.used as predictor. of.mortality in ischemic.stroke [11].

There are no other studies in the current literature depicting the association between the HALP score and Covid-19. The relationship between inflammatory processes and Covid-19 is well known, thus we aim.to investigate.relationship.between. Covid-19.and HALP score which is a novel inflammatory indicator.

Material and methods

Data.from.590.patients.with.Covid-19.from.15/03/2020 to 15/01/2021 in internal.medicine wards.and ICUs included study and analyzed retrospectively. Demographic information and laboratory findings were gathered from the hospital electronic system. Decision for ICU admission was made according to the Covid-19 guide by the.World.Health.Organization. According. to.these.guides, patients.with.confusion, PaO2/FiO2. <300, respiratory.rate ≥ .30/min, SpO2 <90% despite.5 L/min.oxygen. therapy, systolic.blood.pressure.<90 mmHg, mean.arterial. pressure <65 mmHg, acute.organ dysfunction such as.acute. bleeding diathesis,acute.kidney.injury,.impaired.acute.liver. function.tests,.immunosuppression.were.followed.up in the ICU [12]. Patients were described in two groups as deceased or survivor. Standard deviation and mean value were used for quantitative0values, whereas.percentages.and numbers were.used.to represent.qualitative.values. Shapiro-Wilk.was. used.for determining normality.distribution. For comparing the qualitative values, Chi-square test was used. Meanwhile, Mann-Whitney-U and Independent T.tests were executed for. quantitative.values according.to normality.distribution. HALP score was calculated using the laboratory data of patients.at hospital.admission. Due to the correlation between low HALP score and mortality, ROC analysis was performed to anticipate the functionality of 1/HALP level.for identifying. the severity of disease and mortality.separately. For.statistical.significance, p<0.05 was. accepted. IBM SPSS, Version 20.0 package. program.was performed for.execute statistical. analysis.

Results

Mean.age.of deceased group.was 71.32±10.9 (n:294) and.the.mean.age. for.the.survivor group.was.59.97±16.2 (n:296) (p<0.001). 65,6% of the deceased group were.male,. and 55% of the survivor.patients.were male (p<0.001) (Table1). Regarding comorbid diseases, the frequency of coronary.artery. disease,.hypertension,.congestive.heart.failure.and.diabetes was higher in deceased patients, which was statistically.significant (Table 1). While.the.mean .CRP level of deceased.patients.was 140.0±97.4 mg/L, this.level.was 67.3±68.5 mg/L in the survivor patients (p<0.001). Median procalcitonin level was 0.67 (0.02-100) ng/dl in the deceased group, and it was.0.1 (0.01-100). ng/dl (p<0.001) in the survivor.group. When ferritin level was examined, the median ferritin was 855,00 (6,69-40002,00) µg/L in the deceased group, while it was 289,00 (1,90-6321,00) µg/L in the survivor group (p<0.001). The mean.LDH level was 521,00 (126,00-10056,00) U/L in the deceased group, and 4319,00 (118,00-1196,00) U/L (p<0.001) in the survivor.group. The.difference.between.positive acute phase.reactants.between the deceased and.the survivor.group was also statistically. significant (Table 1).

When.the.albumin level.was examined,.the mean albumin level.of the deceased group and survivor.group were 28,70±4,63 g/L and 33,49±5,62 mg/dl (p<0.001) respectively. Median lymphocyte level was 0,57 (0,06-8,74) k/uL in the deceased group, and 0,85 (0,11-4,87) k/uL (p:0.006) in the survivor.group. Mean thrombocyte level.was 201,24±93,89 k/uL in the deceased group, and 208,09±88,99 k/uL (p:0.363) in.the survivor group. The.difference between.thrombocyte level in deceased and survivor group was.not statistically significant (Table 1).

Median HALP score was 11,45 (1,00-1594,00) in the deceased group, while this ratio was 23,58 (1,73-231,75) (p<0.001) in the survivor group. Since a low.HALP.score was correlated with.high mortality,.we investigated the relationship.

Table 1 Demographics and comparison of laboratory findings in deceased and survivor patients.

Age	Deceased	Survivor	P
	71.32 ±10.92 (n:294)	59.97±16.24 (n:296)	<0,001
Gender (n)	M:193 (%65.6) F:101 (%34.4)	M:165 (%55.9) F:130 (%44.1)	<0,001
Comorbidities			
Diabetes Mellitus	108 (%36,6)	81 (%27,5)	0,019
Hypertension	172 (%58,3)	138 (%46,7)	0,005
Chronic Kidney Failure	40 (%13,6)	26(%8,7)	0,067
Coronary artery disease	83(%28,2)	49 (%16,5)	0,001
Congestive Heart Failure	48 (%16,3)	18(%6,0)	<0,001
Laboratory findings			
CRP	140,60±97,48	69,52±68,80	<0,001
Procalcitonin	0,67 (0,02-100,00)	0,1 (0,01-100,00)	<0,001
Ferritin	855,00 (6,69-40002,00)	289,00 (1,90-6321,00)	<0,001
LDH	521,00 (126,00-10056,00)	319,00 (118,00-1196,00)	<0,001
Hemoglobin	12,07±2,09	12,51±1,87	0,006
Albumin	28,70±4,63	33,49±5,62	<0,001
Lymphocyte	0,57 (0,06-8,74)	0,85 (0,11-4,87)	0,006
Thrombocyte	201,24±93,89	208,09±88,99	0,363
HALP	11,45 (1,00-1594,00)	23,58 (1,73-231,75)	<0,001
1/HALP	0,08 (0,01-1,00)	0,04(0,01-0,58)	<0,001

Table 2 ROC curve for estimate mortality in Covid-19.

Parameter	AUC %95 Cl	Cut-off	Sensitivity %	Specificity %	P
1/HALP	0,724 (0,682-0,767)	0,064	67,3	67,0	p<0.001

between.1/HALP.and.mortality. While the median 1/HALP was 0.08 (0.01-1.00) in the deceased group, it was 0.04 (0.01-0.58) in the survivor group (p<0.001) (Table 1). A Roc.analysis was used for.determining the cut.off. value.of 1/HALP, and the sensitivities, specificities, cut.off.values, and area.under.the curve. were.calculated. Cut off.value.of 1/HALP for mortality. was calculated as 0,064 ((AUC: 0,724 (0,682-0,767); 67,3% Sensitivity,. 67,0% Specificity. p<0.001) (Table 2). (Figure1).

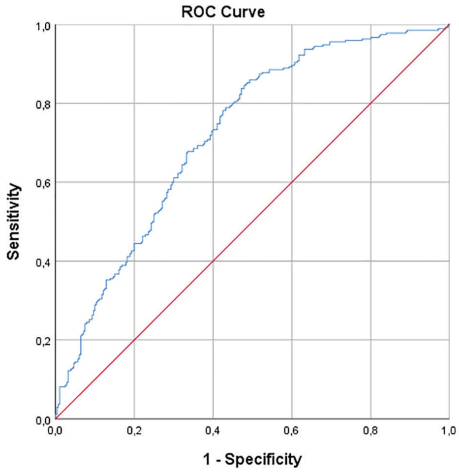

Figure 1 - ROC curve for estimate mortality in Covid-19.

Discussion

It is well-known that increased positive acute phase reactants are related with.increased mortality.and.severity. of Covid-19. Many studies and reviews in current literature has shown that increased CRP, LDH, and procalcitonin levels. were.related with high Covid-19 morbidity and mortality [13,14]. Similarly, in our study, increased CRP, LDH,.and. procalcitonin.levels. were associated with increased mortality in deceased.group (p<0.001, p<0.001, p<0.001). SARS-Cov-2 virus is known to impact red blood cell membrane (RBC) and hemoglobin oxygen affinity. It is also assumed that the adaptation mechanism of RBCs in compliance with the oxygen demand is impaired as well [15]. Additionally, the inflammatory indicators and the rate.of.mortality were higher in Covid-19.patients with low hemoglobin levels [16,17]. In a.retrospective.cohort study conducted on.222.patients diagnosed with Covid-19, the mean. hemoglobin.level was 11.1 g/dl.in patients with severe disease compared to 12.8 g/dl in non-severe patients [18]. In our group of patients, the mean hemoglobin level of deceased patients was 12.07±2.09, and 12.51±1.87 in survivor patients (p:0.006). In some other studies, a positive association was shown between increased ferritin levels due to inflammatory iron mechanism, the length.of.stay in hospital, the need for ICU, and the need for mechanical ventilators [19,20]. Similarly, in.our.study, we also found a positive association between the increased serum ferritin and mortality (p<0.001).

Albumin is a plasma colloid that has a critical function in preserving the intravascular oncotic pressure and the carriage of some substances in the plasma. It is also a well known negative acute phase reactant which decreases in inflammatory processes, nutritional deficiencies, and in conditions such as cirrhosis given that it is synthesized from the liver [21]. It is believed that ARDS condition in Covid-19 worsens due to the extravasation of the intravascular volume caused by low albumin, which also causes deterioration of kidney and gastrointestinal system functions [22]. In line with the current literature, we demonstrated a the strong correlation between low albumin and.mortality. in Covid-19.patients (p<0.001).

Lymphopenia is commonly.seen.in Covid-19.patients, almost up to 85% of the.patients.who. are.severely ill [23]. In a meta-analysis.of 23 studies,.lymphopenia was linked with the development of ARDS and the increased need for ICU [24]. In Covid-19, lymphopenia develops rapidly after infection, which is believed to be due to lymphocyte sequestration [25]. In another meta-analysis conducted with 71 studies, a relationship was found between lymphopenia and increased mortality [26]. Similar to the recent literature findings, we also pointed out a significant correlation between low lymphocyte level and mortality (p:0.006).

The platelets are an important component of the primer coagulation system. Even though they do not play a part in the inflammatory process, approximately 40% of severely ill Covid-19 patients have thrombocytopenia [27]. One meta-analysis.of 17.studies and 3481 patients. showed that a low (<150000) platelet count was associated with poorer outcomes [28]. In our. study,.no statistically.significant result was.found. between thrombocyte level and.mortality.

The HALP.score.is a newly introduced scoring.system that.is.calculated.as hemoglobin x albumin x lymphocyte / platelet. The first study in the literature on the HALP scoring system outlined the relationship between low HALP level and poor prognosis in 820 locally advanced colorectal cancer patients in 2016 [29]. Similarly, some studies showed that there was an inverse relationship between survival in bladder cancer and HALP.score, which is also an.independent risk factor.for predicting nephrectomy in renal cell carcinoma. It was also stated that the HALP score is a powerful tool to determine the inflammatory state in these patients [30,31]. Furthermore, in another study implemented on 1337 patients diagnosed with acute ischemic stroke, a positive correlation between low HALP score, and re-stroke and mortality was discovered [11]. According to a study investigating the relationship between inflammation and HALP score, although no correlation existed between the HALP score and prognosis of ANCA-positive vasculitis patients, a low HALP score could be partially useful for initial diagnosis [32]. In the study that we have established, a significant correlation was evident between low HALP score and mortality (p<0.001).

Conclusion

As a result, a significant correlation was found between a low HALP score and mortality in Covid-19. We strongly believe that HALP.score.could.be.a.useful.parameter to determine mortality in Covid-19 patients.

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