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Research Paper: Predictive Value of Base Deficit, Serum Albumin, and C-reactive Protein/Albumin Ratio for Mortality in Severe Burn Patients

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ABSTRACT

Burn patients are at risk of serious complications, including sepsis, acute respiratory distress syndrome, and organ dysfunction, despite advancements in medical treatment. Early prediction and management of sepsis and acute inflammation and the identification of high-risk patients are crucial for the improvement of outcomes. This study aimed to evaluate the prognostic value of serum albumin, base deficit, and C-reactive protein (CRP)/albumin ratio (CAR) in severe burn patients.In a retrospective analysis of 195 patients with 20%-80% total body surface area (TBSA) burns admitted to the burn intensive care unit (ICU) at Velayat University Hospital from April 2018 to April 2021, serum albumin, base deficit, and CAR were measured upon admission.Significant differences were observed between survivors and non-survivors in terms of serum albumin levels (3.05±0.56 vs. 1.89±0.69 g/dL), base deficit (3.36±2.15 vs. 10.62±1.71 mmol/l), CRP (20.95±29.33 vs. 54.62±46.29 mg/L), CAR (7.73±11.52 vs. 36.80±35.59), and length of ICU stay (2.75±2.51 vs. 6.45±4.50) ($P<0.001$). Multivariate logistic regression indicated that unlike CRP, serum albumin levels ($P=0.045$), base deficit ($P=0.001$), and TBSA ($P=0.046$) were significantly associated with increased mortality.As evidenced by the obtained results, serum albumin, base deficit, and CAR are linked to adverse outcomes and may be valuable tools for risk stratification, identifying high-risk patients, and guiding early interventions in burn patients. Further research is needed to validate these findings and explore the underlying mechanisms.

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1. Introduction

Despite numerous advancements in the treatment of burn patients, resulting in improved prognosis, burns are still responsible for disability and high mortality [1, 2], accounting for about 180,000 deaths annually [3]. Burns can cause functional, aesthetic, and psychological difficulties [4] and activate local inflammatory responses [5]; therefore, the investigation of the factors predicting mortality and prognosis of burn patients is essential for accelerating clinical management [6]. Burns can cause local and systemic inflammation, affecting the wound healing process and hemodynamic changes on the skin, blood vessels, and components [7, 8] depending on the depth and total body surface area (TBSA) of injuries. The increase in extracellular fluid caused by major burns is also associated with increased vascular permeability and a decrease in serum albumin, accelerating the shock stage [5]. Hypoalbuminemia, which is defined as a decrease in serum albumin concentration of less than 2 g/dL is linked to an increase in TBSA, greater burn severity, and higher mortality [4]. it can cause complications related to increased extravascular fluid, such as edema, delayed healing, pulmonary lesions, increased susceptibility to sepsis, and death [9, 10]. In general, various markers can predict inflammation [11]. Considering that tissue hypoxia, albumin loss, and C-reactive protein (CRP) increase are observed in severe burns, investigating the relationship between CRP and albumin can lead to new perspectives on inflammatory response in the management of burn victims [12, 13]. CRP, which is widely used as a marker of inflammation, infection, and sepsis [14-16], is one of the oldest indicators of acute-phase response [17, 18] correlated with burn size and depth [19]. In addition, albumin level is recognized as an indirect inflammatory marker, and changes in the albumin level are reliable indicators of increased or decreased inflammation [11]. Moreover, CRP/alb (CAR) is an indicator of inflammation and sepsis, while it is a better indicator than albumin and CRP alone [20, 21]. Acute blood loss and direct injury cause loss of hemoglobin and oxygen delivery in burn patients [22], hypoxemia due to an increase in metabolism, and, on the other hand, a decrease in the capacity of oxygen delivery lead to tissue hypoxia and the production of lactic acid and metabolic acidosis [23, 24]. The metabolic acid-base disorder is a change in hydrogen ions directly resulting from the shift in HCO3; moreover, a decrease in HCO3 will increase hydrogen ions and produce metabolic acidosis [25]. In addition, deficiency in acid and base disrupts oxygen delivery to tissues [26] and, in severe cases, can lead to kidney, lung, and digestive system dysfunction [26, 27]. In burn injury, an elevated base deficit is a marker of global tissue acidosis resulting from impaired oxygenation [5]. Nonetheless, to the best of our knowledge, few studies have demonstrated the role of CRP, base deficit, and serum albumin level in sepsis and prognostic prediction in severe burns. In light of the aforementioned issues, the present study aimed to assess the predictive value of base deficit, serum albumin level, and CRP/Alb ratios for prognosis in severe burn patients.

2. Materials and Methods

This retrospective study selected 195 patients with 20%-80% TBSA burns from the burn intensive care unit at Velayat Sub-Specialty Burn and Plastic Surgery Center in Guilan Province, Rasht, Iran. The inclusion criteria entailed burns covering 20%-80% of TBSA, thermal or chemical burns, hospitalization within 24 hours post-burn, a hospital stay of over seven days, and an age range of over 18 years. On the other hand, patients with liver diseases (cirrhosis and hepatitis), inflammatory conditions (e.g., osteoarthritis and inflammatory bowel disease), or other medical issues (e.g., acute pancreatitis, acute infection, myocardial infarction, malignancy, malnutrition, and nephrosis), history of sepsis during admission, and incomplete data were excluded. From April 2018 to April 2021, 538 patients were initially considered; however, 195 cases met the criteria for final analysis (Figure 1). Treatment and management adhered to relevant guidelines, including fluid resuscitation, nutritional support, surgery, inhalation injury management, and infection prevention and treatment. All patients underwent burn surgery (debridement and escharotomy on admission if needed, followed by advanced dressings, such as hydrogel, foam, and amnion membrane, and then mesh skin grafting) within 30 days post-burn. Patients were assessed using the Advanced Trauma Life Support index and received volume resuscitation following the Parkland Formula. Patients displaying signs of respiratory failure, potential airway injury, or decreased consciousness (Glasgow Coma Scale <9) were intubated for airway protection. Daily routine blood tests, including complete blood count, electrolytes, and albumin, were performed along with clinical reassessments. Patients were assigned to survived and non-survived groups, and serum albumin level, base deficit, and CRP/Alb ratio as predictors of mortality were measured at the time of admission, extracted from the Hospital Information System used for initial care and ongoing hospitalization. Severe burn injury in this study was defined as TBSA ≥20%.

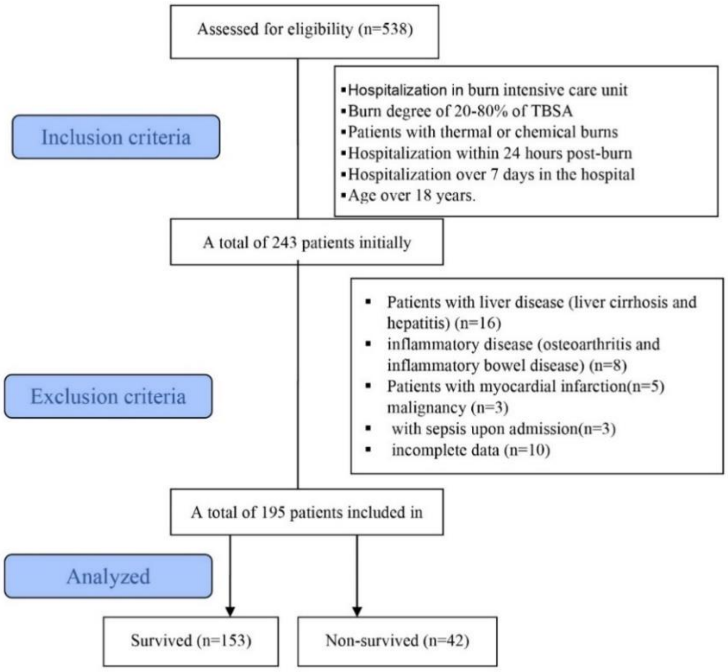

Figure 1. Flow chart demonstrating the patient enrollment

2.1. Statistical Methods

Descriptive statistics were reported as mean±standard deviation for continuous variables and frequencies with percentages for categorical variables. Multivariate logistic regression analysis was conducted to examine the relationships between variables. Independent Kruskal-Wallis and Mann-Whitney U tests were employed as appropriate for comparisons between groups. Spearman's Rho correlation coefficient was calculated to assess the correlation between continuous variables. All data were analyzed two-tailed, and a p-value of less than 0.05 was considered statistically significant for the aims of this paper. The data were analyzed in SPSS software (version 28).

3. Results

A total of 195 patients were enrolled in this study. The basic and clinical characteristics of the patients are presented in Table 1. The mean age of patients was 39.81±14.23 years (age range of 16-70 years). The mean age scores for males and females were 38.53 and 46.09 years, respectively. A comparison of clinical characteristics between surviving and non-survived patients revealed a significant relationship between outcome and other clinical features, except the length of stay (LOS) (P=0.365). Analysis pointed to a higher TBSA and a prolonged ICU stay in non-survived patients. The laboratory study illustrated a lower serum albumin level (SAL), higher base deficit (BD), higher CRP, and higher CAR in deceased patients (P<0.001) (Table 2). Table 3 displays a significant relationship between laboratory parameters and TBSA. The mean BD, CRP, and CRP/Alb increased, and the mean SAL decreased with TBSA (P<0.001). Spearman's Rho test showed a significant and inverse relationship between the SAL with LOS

(P=0.025) and ICU stay (P=0.001). In addition, CRP/Alb demonstrated a significant and direct relationship with LOS (P=0.077) and ICU stay (P=0.001). CRP and BD were not significantly correlated with LOS; however, higher CRP and BD were associated with longer ICU stays (P=0.001) (Table 4). Furthermore, a multivariate model, which was created to establish predictors of mortality, showed that unlike CRP, increased BD (OR 5.401; P< 0.001), increased TBSA (OR 1.082; P=0.046), and decreased SAL (OR 10.375; P=0.045) are all significant risk factors for mortality in burn patient (Table 5).

Table 1. Basic and clinical characteristics of patients

Parameters	Number	Percentage
Gender		
Male	162	83.1%
Female	33	16.9%
Marital status		
Single	68	34.9%
Married	127	65.1%
Place of residence		
Urban	126	64.6%
Rural	69	35.4%
Cause of burn		
Scalds	36	18.5%
Thermal burn	78	40%
Contact burn	15	7.7%
Inhalation burn	59	30.3%
Chemical burn	7	3.6%
TBSA		
20-39%	134	68.7%
40-59%	28	14.4%
60-80%	33	16.9%
Burn degree		
Second degree	82	42.1%
Third degree	69	35.4%
Fourth degree	44	22.6%
Anatomical site of burn		
Head and neck	22	11.3%
Trunk	43	22.1%
Upper extremities	76	39%
Lower extremities	38	19.5%
Total body	16	8.2%
Mechanical ventilation		
Yes	50	25.6%
No	145	74.4%
Inhalation injury		
Yes	62	31.8%
No	133	68.2%
Outcome		
Discharge	153	78.5%
Death	42	21.5%
Total	195	100%

TBSA: total body surface area

Table 2. Clinical characteristics of patients associated with outcome

Parameters	Survived (n=153)	Non-survived (n=42)	*P*-value
TBSA	28.73±9.86	61.69±21.81	0.001*
LOS	8.58±5.24	7.86±4.95	0.365
ICU stay	2.75±2.51	6.45±4.50	0.001*
SAL	3.05±0.56	1.89±0.69	0.001*
BD	3.36±2.15	10.62±1.71	<0.001*
CRP	20.95±29.33	54.62± 46.29	<0.001*
CRP/Alb	7.73±11.52	36.80±35.59	0.001*

TBSA: total body surface area; LOS: length of stay; ICU: intensive care unit; SAL: serum albumin level; BD: base deficit; CRP: c-reactive protein; CRP/Alb: CRP to albumin ratio. P values were calculated by independent-samples Mann-Whitney U test. * $P < 0.05$.

Table 3. Clinical characteristics of patients associated with total body surface area

Parameters	TBSA			*P* value
	20-39% (n=134)	40-59% (n=28)	60-80% (n=33)	
SAL	3.21±0.43	2.31±0.31	1.53±0.28	<0.001*
BD	3.29±2.42	6.24±2.54	10.43±2.50	<0.001*
CRP	17.90± 29.43	32.93±23.70	66±44.60	<0.001*
CRP/Alb	5.96±10.74	14.84±11.84	45.88±34.77	<0.001*

TBSA: total body surface area; SAL: serum albumin level; BD: base deficit; CRP: c-reactive protein; CRP/Alb: CRP to albumin ratio. P-values were calculated by independent-samples Kruskal-Wallis's test. * $P < 0.05$

Table 4. Correlation Between Laboratory Parameters and Length of Stay in hospital and intensive care unit

Parameters	LOS		ICU stay	
	Correlation Coefficient	P-value	Correlation Coefficient	P-value
SAL	- 0.16	0.025*	- 0.507	0.001*
BD	0.027	0.706	0.467	0.001*
CRP	0.127	0.077	0.390	0.001*
CRP/Alb	0.145	0.043*	0.450	0.001*

LOS: length of stay; ICU: intensive care unit; SAL: serum albumin level; BD: base deficit; CRP: c-reactive protein; CRP/Alb: CRP to albumin ratio. P values were calculated by Spearman's Rho test. * $P< 0.05$

Table 5. Multivariate logistic regression model for risk factors of death

Variable	B	Exp(B)	95% CI		P-value
			Lower	Upper	
TBSA	0.099	1.082	0.989	1.184	0.046*
CRP	0.001	1.001	0.974	1.028	0.948
SAL	2.339	10.375	0.952	113.082	0.045*
BD	1.687	5.401	2.286	12.761	0.001*
ICU	0.212	1.237	0.964	1.586	0.094
Constant	24.554	-	-	-	0.001

TBSA: total body surface area; ICU: intensive care unit; SAL: serum albumin level; BD: base deficit; CRP: c-reactive protein; B: unstandardized regression coefficient; Exp(B): odds ratio. P values were calculated by Multivariate logistic regression. * $P< 0.05$

4. Discussion

As a common trauma, burns are responsible for significant morbidity and mortality, especially in low- and middle-income countries. The identification of predictive clinical and laboratory factors can help improve the quality of care and reduce the physical and economic burden. According to the results, 162 (83.1%) patients were male, 33 (16.9%) were female, and the mean age of all patients was 39.81±14.23 years. Consistent with the results of the present study, 70.6% of patients in the study by Aghakhani et al. were male, and their mean age was 34.72 ± 20.26 years [28]. Like in other Third World countries, burns are more common at older ages [29, 30]. The analysis of the causes of burns revealed that the most common causes were thermal injuries (40%). in a previous study, we pointed out that most burns were caused by thermal injuries, such as flames and explosions. Flames were also cited as the most common cause of burns in other studies [30-32]. As evidenced by the obtained results, 31.8% of patients suffered inhalation injuries, and 25.6% required mechanical ventilation. Aghakhani et al. reported that 1.5% of patients had an inhalation injury [28]. The higher rate of inhalation injury in our study is probably due to the evaluation of patients with >20% TBSA admitted to the ICU. The mean TBSA of patients was 35.83%, and there was a significant difference between the mean TBSA of deceased and surviving patients, with deceased patients having a higher mean TBSA (P<0.05). In agreement with this finding, Güldoğan et al. reported that TBSA, the need for mechanical ventilation, and the length of hospital stay were significantly correlated with mortality rate [33]. The evaluation of LOS revealed that the mean LOS was 8.43 days [28]. In studies conducted in the United States [34] and Hong Kong [35], the LOS values were 8 and 9 days, respectively. All of these data are in line with the present study. In this study, the mean LOS scores in deceased and surviving patients were 7.86 and 8.85 days, respectively, and no significant difference was found between these two groups in mean LOS. The results highlighted that patients stayed in the ICU for an average of 3.55 days. The mean scores of ICU LOS for deceased and surviving patients were 6.45 and

2.75 days, respectively, and a significant difference was found between these two groups in the mean LOS. In a study by Pavoni et al. in Italy, patients were hospitalized in the ICU for 23 days, and the mean LOS in the ICU for deceased patients was 31 days [36]. This discrepancy can be ascribed to different inclusion criteria. In addition, Shupp et al. found that patients with sepsis and higher TBSA stayed longer in the hospital, especially in the ICU [37]. The mean SAL of patients was 2.80 g/dL. The mean SAL scores in deceased and surviving patients were 1.89 and 3.05, respectively, and there was a significant difference between these two groups (P=0.05). Aguayo-Becerra et al. indicated that a SAL <2 g/dL was associated with mortality with high sensitivity and specificity. In the stated study, SAL proved to be a reliable prognostic factor upon admission and an indicator of mortality in patients with severe burns [38]. This association is probably due to the relationship of SAL with the patient's nutritional status and the weakening of the immune system, leading to such complications as sepsis, which is one of the leading causes of death [39]. In addition, a study by Roham et al. unveiled that SAL was significantly higher in survivors than deceased patients one week after discharge. The mentioned study found that the higher the degree of burn, the lower the albumin level; nonetheless, SAL and age showed no significant relationship with LOS [40]. In another study by Megahed et al., the mean SAL was 3.33±0.44 g/dL upon admission, 2.85±0.54 g/dL after three days, and 2.46±0.67 g/dL after one week. The stated research, consistent with the present study, demonstrated that SAL can be used as an independent variable to predict mortality in these patients [5]. Several studies have pointed to an association between SAL as a predictor of nutritional status in patients with such conditions as malignancies and burns leading to deterioration of nutritional status and LOS [41, 42]. The present study demonstrated an inverse and significant relationship between SAL and LOS, particularly in the ICU, consistent with previous studies (P=0.05). the analysis of arterial blood gas samples revealed a mean BD of 4.92 mEq/L. The mean BD scores in deceased and surviving patients were 10.62 and 3.36 mEq/L, respectively (P=0.05). In line with the results of the present study, Fitzwater et al. found that deceased patients had a greater BD in the first 24 and 48 hours after admission. In addition, a BD of ≥6 mEq/L was shown to be associated with a higher mortality rate [43]. Megahed et al. reported that BD, hypoalbuminemia, and anemia could be used as independent risk factors for the prediction of mortality [5]. The increase in BD is due to metabolic acidosis, which is one of the consequences of the loss of RBCs leading to impaired blood flow and cardiac activity that occurs in severe burn injuries. In addition, acidosis can lead to urinary, respiratory, gastrointestinal tract dysfunction, and increased mortality [44, 45]. The present study highlighted a significant and direct association between BD and TBSA (P=0.05). nevertheless, there was no significant association between BD and LOS. Consistent with the current research, in the study by Cochran et al., BD showed no significant association with the likelihood of acute respiratory distress syndrome, sepsis, the need for mechanical ventilation, and LOS [46]. CRP is closely related to the body's inflammatory state, and elevated CRP levels have been found in such conditions as burns, infections, ischemia, and trauma. Previous studies on patients admitted to the intensive care unit have demonstrated that elevated serum CRP levels are directly related to increased organ failure and mortality [47]. Given that serum CRP levels increase rapidly 2- to 12-fold in the normal pathophysiology of burn and its blood level remains high between 90 and 270 days, using this marker to predict burn-related sepsis and mortality remains controversial [48, 49]. In the present study, the mean CRP level was 28.20 mg/L, and there was a significant association between the two groups of patients who died and those who survived (54.62 and 20.95 mg/L, respectively) (P = 0.05). Gulhan et al. showed that a serum CRP level > 6 mg/L is a risk factor for developing sepsis in pediatric burns [50] . Maile et al. pointed out that CRP levels were associated with TBSA in both genders and that higher CRP levels in women were associated with higher LOS, possibly due to the association of infection, sepsis, and increased LOS with CRP [51]. CRP/Alb ratio reflects both inflammatory and nutritional status. This is important since while CRP is linked to systemic inflammation, it may be a confounding factor in burn patients. It might be misleading due to chronic inflammation, a part of the physiologic response to burn injuries. Therefore, CRP does not always correlate directly with mortality risk in burn injuries [16]. In addition, serum albumin levels can serve as a sensitive biomarker and a prognostic factor of burn injuries [52]. However, some studies have demonstrated that albumin supplementation has only limited effects on burn patient outcomes, and serum albumin levels alone cannot accurately predict mortality [53]. Therefore, we chose to utilize the CRP/Alb ratio, which offers a more comprehensive assessment by considering both the inflammatory and nutritional status. This approach is further supported by several research studies demonstrating the strong predictive value of CRP/Alb ratio for various conditions, especially those involving inflammation in their pathophysiology [54, 55]. The results of the present study pointed to a significant difference between the two groups in the mean CRP/Alb level, being higher in deceased patients (P=0.05). Recent studies have increasingly highlighted the predictive value of CRP/Alb ratio in predicting mortality, outcomes, and severity across various diseases, such as metabolic syndrome and COVID-19 [56, 57]. For instance, in patients with aneurysmal subarachnoid hemorrhage, higher CRP/Alb ratios were closely linked to disease severity and poor outcomes at three months, with better predictive value and accuracy than traditional markers, such as serum glucose and albumin alone [58]. In a similar vein, in 2022, OZCAN et al. demonstrated that the CRP/Alb ratio is an independent risk factor for six-month mortality in acute pulmonary embolism patients, strongly correlating to the Pulmonary Embolism Severity Index [59]. In addition, in 2022, Jang et al. found that in neurocritically ill patients suffering from acute stroke, the CRP/Alb ratio was a reliable predictor of in-hospital mortality, showing comparable efficacy to CRP levels alone with better predictive value for mortality than albumin alone [60]. Although few articles explore the value of CRP/Alb ratio among several diseases, its predictive value for determining burn injury outcomes has not been well-studied. In patients with severe burn injuries, sepsis, which is a life-threatening condition, is one of the significant causes of mortality. In 2021, Yu et al. demonstrated the CRP/Alb ratio as a predictor of sepsis and a prognostic factor in patients with severe burns. TBSA and CRP/Alb were two independent risk factors for sepsis in severe burns. A higher CRP/Alb ratio (≥1.66) upon admission was associated with the development of sepsis and higher mortality 30 days after burn [16]. We also showed a significant and direct association between CRP and TBSA (P=0.05); nonetheless, no relationship was observed between CRP and LOS. Meanwhile, a substantial and direct association was detected between CRP/Alb ratio and LOS and ICU (P=0.05). Our study contributes to the growing literature on the prognostic significance of CRP/Alb ratio in severe burn patients. Our research offers several unique strengths, unlike previous studies that may have focused on specific patient populations or outcomes. First, we investigated the relationship between CAR and TBSA, offering insights into the potential impact of burn severity on prognostic significance of CAR. Second, our analysis of the association between CAR and LOS in ICU and hospital provides valuable information for clinical decision-making and resource allocation. Finally, by including both septic and non-septic patients, our study offers a broader perspective on the predictive value of CAR, regardless of sepsis status. These findings contribute a more comprehensive understanding of the role of CAR in burn injury outcomes and support its potential as a valuable prognostic marker.

5. Conclusion

Patients with severe burn injuries often experience a drop in serum albumin levels and an increase in the CRP/Alb ratio, which can cause significant physiological changes in cellular function associated with burn patient outcomes. Utilizing these indicators systematically could assist in the identification of patients at higher risk.

Ethical Considerations

Compliance with ethical guidelines

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Authors'contributions

SR, and AS: contributed to the study design. ASh, and NR: collection of the data. EKL: performed the data analysis. MM: interpreted the data. SM, EGhN, and PBT: contributed to the manuscript writing. All authors read and approved the final manuscript.

Conflict of Interests

Each author has contributed substantially to the conception and design of the study or acquisition of data or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content. Each author observed and approved the contents of the submitted manuscript. None of the authors has any personal or financial conflicts of interest.

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