IWJ WILEY

Predictive value of serum albumin and calcium levels in burn patients with *Pseudomonas aeruginosa* infection: A comprehensive analysis of clinical outcomes

Seyed Ashkan Haghighi Bardineh[1] | Heydar Ali Balou[2] |
Hadi Sedigh Ebrahim-Saraie[2,3] | Mohammadreza Mobayen[1] |
Mojdeh Esmailzadeh[1] | Samane Haghighi[4] | Arezoo Haghighi[5] |
Mahsa Sadeghi[1,3]

[1]Burn and Regenerative Medicine Research Center, Guilan University of Medical Sciences, Rasht, Iran

[2]Razi Clinical Research Development Unit, Razi Hospital, Guilan University of Medical Sciences, Rasht, Iran

[3]Department of Microbiology, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

[4]Institute of Theoretical and Translational Medicine, Semmelweis University, Budapest, Hungary

[5]Department of Pharmacology and Pharmacotherapy, Faculty of Pharmaceutical Sciences, Semmelweis University, Budapest, Hungary

Correspondence
Heydar Ali Balou, Razi Clinical Research Development Unit, Razi Hospital, Guilan University of Medical Sciences, Rasht, Iran.
Email: heydaralibalou@gmail.com

Mahsa Sadeghi, Burn and Regenerative Medicine Research Center, Guilan University of Medical Sciences, Rasht, Iran.
Email: mahsa_heris@yahoo.com

Abstract

In the ongoing challenge to reduce burn-associated mortality rates, this study explores the predictive capacity of clinical factors in burn patients, focusing on vitamin D, calcium, and serum albumin levels during hospitalisation in cases with *Pseudomonas aeruginosa* infection. Our research involves a comprehensive analysis of 100 burn patients, encompassing crucial clinical parameters such as the burn severity index, serum albumin, vitamin D, and calcium levels at admission. Data were meticulously entered into IBM Statistics SPSS software version 28 and subjected to statistical analysis. The study reveals an average patient age of 39.75 years and a notable 34% mortality rate. Additionally, the average lengths of hospital and intensive care unit (ICU) stays are determined to be 11.33 and 7.79 days, respectively. Significantly, a correlation between calcium and albumin variables and treatment outcomes is established, showcasing their potential to predict variable changes in patient mortality rates. Furthermore, a noteworthy association is observed between serum calcium levels and the duration of ICU hospitalisation. In conclusion, albumin and calcium variables emerge as sensitive and specific indicators for predicting outcomes in burn patients. Importantly, the independence of these factors from the physician's experience and diagnosis reduces human error and thus increases the accuracy of mortality prediction in this patient population.

Key Messages

- There was a significant relationship between serum albumin and calcium levels and treatment results in burn patients with *Pseudomonas aeruginosa* infection.
- Hypoalbuminemia is identified as a critical factor impacting adverse outcomes, particularly leading to prolonged stays in the intensive care unit (ICU).
- The vitamin D level in deceased patients was not significantly different from that of survivors.
- The study highlights the clinical relevance of serum albumin levels as independent predictors, reducing human error and enhancing accuracy in mortality prediction.

1 | INTRODUCTION

Burns are a devastating and prevalent public health concern, with over 90% of burn-related fatalities occurring in low-income countries.[1–3] Despite the high mortality rate, advances in burn treatment have significantly increased the chance of survival. However, the probability of death can be predicted by clinical factors.[4–6] Accurate assessment of the mortality risk in burn patients is crucial for predicting disease progression, reducing morbidity, optimising treatment strategies, and expediting clinical intervention.[1,4] Prognostic factors such as the Abbreviated Burn Severity Index (ABSI) include gender, age, Total Body Surface Area (TBSA), full-thickness injuries, and inhalation burns but do not include biochemical variables.[4] Severe burn injuries disturb immune and physiological responses, including inflammation, immunosuppression, reduced plasma levels of vitamin D and its carrier proteins (hypoalbuminemia), and calcium homeostasis derangements.[4,7,8] Clinical studies have established an association between low circulating vitamin D levels and adverse outcomes in burn patients, including increased susceptibility to infections, sepsis, pneumonia, prolonged hospital stays, recurrent ICU admissions, delayed wound healing, organ failure, escalated treatment costs, and higher mortality rates.[7,9,10] On the other hand, vitamin D is a hormone known for its role in calcium homeostasis.[11] Calcium derangement is associated with complications of severe trauma (including hypothermia, coagulopathy, and acidosis) and poorer outcomes in trauma patients. Studies have revealed a high prevalence of calcium disorders, particularly hypocalcaemia, in critically ill trauma patients, often presenting in an asymptomatic manner, hindering timely intervention.[12,13] Hypoalbuminemia, a common clinical

deficiency in burn patients, is independently associated with elevated risks of infectious complications, increased TBSA, greater burn severity, prolonged hospital stays, and increased mortality rates.[1,14] It also contributes to renal failure, edema, delayed recovery, pulmonary lesions, and enhanced susceptibility to sepsis. Therefore, vitamin D, calcium, and albumin levels are potential prognostic markers of burn severity and outcomes. Identifying these biochemical indicators is clinically essential for predicting disease progression, guiding management strategies, optimising treatment interventions, and reducing the risk of complications and mortality.[1] A limited number of studies have evaluated the role of these biochemical factors in the metabolism and outcome of patients with severe burns.[10,15] Given that *Pseudomonas* species are prevalent bacteria in hospital infections, particularly in the ICU,[16] this study aims to determine the relationship between the concentrations of vitamin D, calcium, and serum albumin upon admission and the complications and mortality outcomes in burn patients with *Pseudomonas aeruginosa* infection.

2 | METHODS

2.1 | Research design and methodology

We conducted a retrospective cross-sectional study on burn patients in an educational and treatment center in the North of Iran from March 2019 to March 2022. Our study included all hospitalised burn patients aged 18 years or older with *P. aeruginosa* infection. Data were extracted and recorded from the patient's medical records using a data collection form. The inclusion criteria were second/third-degree burns and TBSA>20%. All subjects

were those whose vitamin D, calcium, and albumin levels were measured upon admission. Normal values of 25(OH)D serum are >20 ng/mL (50 nmol/L). Serum 25(OH)D values >200 ng/mL (500 nmol/L) are defined as toxic. Normal serum calcium and albumin levels are also considered 8.1–10.4 mg/dL and 3.5–4.5 mg/dL, respectively.[17–19] Any patient with an infection before the burn injury, patients who had received vitamin D supplementation before entry, or patients whose records did not have sufficient information to analyse the variables were excluded from the study. There was no missing data. The investigated variables were age, sex, length of stay (LOS), length of stay in ICU, burn site, infection site, inhalation burn, TBSA, burn grade, and outcome. The results of laboratory tests such as vitamin D, calcium, and albumin during admission to the burn department were also examined.

2.2 | Statistical analysis

The results were presented as mean values and standard deviation (SD). The normality of the data was checked using the Kolmogorov–Smirnov test. Also, the Manne Whitney U-test was performed to compare quantitative variables. The chi-square or Fisher's exact test was used to compare categorical variables. Logistic regression analysis assessed the association between mean laboratory markers and outcomes, including mortality and hospital days, reporting odds ratios (ORs), and 95% confidence intervals (CIs). Data analysis and statistical analysis were done using SPSS 28.0. A value of $p \leq 0.05$ was considered statistically significant for all tests.

2.3 | Ethics statement

Ethical approval for this study (IR.GUMS.REC.1401.062) was provided by the Regional Ethics Committee of Guilan University of Medical Sciences, Rasht, Iran on May 18, 2022.

3 | RESULTS

During the study period, 100 hospitalised burn patients met the criteria for entering this study. Most patients (80 cases, 80%) were male, and 20 (20%) were female. The age range of the patients was from 20 to 86 years (mean age: 39.97 ± 15.37 years). The average burn percentage (TBSA) of all patients was 48.20 ± 24.87. The average length of stay in the hospital (LOS) and the intensive care unit (ICU-LOS) were 11.33 ± 5.96 days

and 7.79 ± 4.95 days, respectively. 88% of patients were in the ICU for 1–20 days. 68% of patients had inhalation injuries, and death was observed in 34% of all patients. Wound infection (66%), lung infection (9%), and urinary tract infection (8%) were the most common hospital infections observed, respectively. Seventeen percent of patients had other infections. The results of the analysis of quantitative variables based on treatment outcomes are presented in Table 1. There was no significant difference between the average age of the patients in the surviving and deceased groups (p-value = 0.095). In comparison, there was a significant relationship between the average percentage of burns (TBSA), the LOS, the ICU-LOS, and the number of surgeries (the ratio of the graft to the percentage of burns) with the mortality of patients. The patients of the deceased group had an average percentage of burns and a more extended hospitalisation period (p-value = 0.000). Table 2 shows the comparison results of the average length of hospitalisation based on the level of the examined markers. Among the three laboratory markers measured, there was only a significant difference between the average ICU hospitalisation duration in the two groups of patients with low and normal albumin (p-value = 0.043). The results of multivariable logistic regression for mortality status in patients showed a significant relationship between calcium and albumin variables and the outcome. These variables were able to predict the variable changes in the mortality rate in patients (Table 3). The vitamin D level in deceased patients was not significantly different from that of survivors. The sensitivity and specificity were obtained as 90.9 and 58.8, respectively.

4 | DISCUSSION

Our study delves into the predictive value of serum albumin and calcium levels in burn patients with *P. aeruginosa* infection. The analysis of 100 patients revealed a significant correlation between these variables and treatment outcomes, emphasising their potential as sensitive indicators for predicting variable changes in patient mortality rates. Notably, serum calcium levels were also associated with the duration of ICU hospitalisation. These findings underscore the clinical relevance of albumin and calcium as independent predictors, mitigating human error and enhancing mortality prediction accuracy. The observed male predominance among burn patients aligns with existing literature, emphasising the recognised risk factor of the male gender for burn incidents.[20–22] Compared to some reports, the higher mortality rate in our study may be attributed to the elevated average TBSA among participants.[4,23] Importantly,

TABLE 1 Characteristics of the burn injuries in 100 patients (Analysis of quantitative variables).

	Survived (Total No = 66)	**Died (Total No = 34)**	**p-value**
Age (mean)	13.06 ± 37.08	19.12 ± 44.94	0.095
Body surface burned (%)	11.41 ± 35.33	25.00 ± 73.18	0.000
ICU-LOS*	3.71 ± 4.27	4.87 ± 7.71	0.000
LOS	6.93 ± 10.12	5.35 ± 11.95	0.026
Graft ratio to TBSA	0.25 ± 0.41	0.20 ± 0.18	0.000

*88% of patients were in the ICU for 1–20 days.

TABLE 2 Results related to comparison of the mean for LOS and ICU-LOS based on Lab markers status.

Lab marker	Variable	Lab marker status		Test statistics[a]	Sig.
		Normal	**Abnormal**		
Vitamin D	LOS	13.75 ± 5.39	11.12 ± 5.99	842	0.145
	ICU-LOS	6.88 ± 5.38	5.32 ± 4.35	437	0.378
Calcium	LOS	13.31 ± 7.29	10.95 ± 5.65	798	0.233
	ICU-LOS	4.50 ± 5.30	5.62 ± 4.25	502	0.108
Albumin	LOS	9.30 ± 3.46	11.56 ± 6.15	389	0.486
	ICU-LOS	2.90 ± 2.88	5.72 ± 4.49	274	0.043

[a]Independent-samples Mann–Whitney U-test.

TABLE 3 Multivariate logistic regression results for mortality status in patients.

Variable	Beta coefficient	Exp(B)	95% CI		p-value
			Lower	**Upper**	
Vitamin D	−0.048	0.953	0.872	1.042	0.292
Calcium	−1.086	0.338	0.138	0.826	0.017
Albumin	−2.861	0.058	0.013	0.243	0.001
Constant	15.585	–	–	–	0.001

our findings highlight hypoalbuminemia's significant impact, particularly on prolonged ICU stays, emphasising its role as a prognostic indicator for adverse outcomes. While conflicting reports exist in the literature regarding the effect of serum albumin levels on patient outcomes, our study contributes to the growing body of evidence supporting its relevance.[1,4,14,24–27] The inverse relationship between calcium concentration and mortality in critically ill patients, especially those with infectious complications, reflects the findings of several studies.[12,13,15,28–31] However, inconsistencies between studies may result from methodological variations and patient characteristics.[32,33] Despite the widely reported association between low vitamin D levels and adverse outcomes in critically ill patients, our study did not identify a significant relationship with burn patient outcomes.[34–37] This finding aligns with other studies reporting conflicting results and underscores the need for further investigation through rigorous research and more extensive clinical trials.[38–40] Our study proposes

the incorporation of albumin and calcium concentrations as objective biochemical markers to predict outcomes in burn patients, complementing the ABSI. Using such markers could enhance reliability and simplicity in predicting results, bypassing the limitations of subjective data and observer error. However, caution is advised due to study limitations, including its single-center design, retrospective nature, and relatively small sample size. Future research should prioritise multi-center, prospective studies with more extensive, diverse populations. Additionally, conflicting literature on vitamin D in burn outcomes requires further exploration through more extensive clinical trials. While serum albumin and calcium exhibit promise as prognostic markers, their clinical implementation warrants validation through well-designed trials focusing on standardisation and generalizability. Continuous research efforts are crucial for refining the predictive value of these biomarkers, advancing clinical care, and improving outcomes for burn patients.

5 | LIMITATIONS

This single-center study in North Iran, reliant on retrospective data, may lack universal applicability due to population-specific characteristics, introducing potential selection bias and incomplete records. The inclusion of only 100 burn patients limits generalizability, emphasising the need for larger sample sizes to enhance statistical power and result reliability. Additionally, the focus on *P. aeruginosa* infection in burn patients may limit direct applicability to other infection types, necessitating further research for broader insights into different infectious contexts.

6 | RECOMMENDATION FOR FUTURE STUDIES

Future studies could investigate the underlying mechanisms through which serum albumin and calcium levels affect outcomes in burn patients. Understanding the molecular and physiological pathways involved will contribute to a more comprehensive understanding of their prognostic significance. It is also recommended to investigate the effect of different types of infections on the outcomes of burn patients by considering a wider range of microbial factors. To increase the generalizability of the findings, it will be beneficial to conduct multicentre studies including different populations and environments. This approach can help to validate observed correlations and identify potential changes in different groups of patients.

7 | CONCLUSION

Our study highlights the predictive value of serum albumin and calcium in burn patients with *P. aeruginosa* infection. The observed link to adverse outcomes, including mortality, suggests their potential utility in predicting patient outcomes. Study limitations such as single-center design, retrospective nature, and a small sample size underscore the need for caution. Future research should pursue multi-center, prospective studies with more extensive, diverse populations. Conflicting literature on vitamin D in burn outcomes requires further investigation through more extensive clinical trials. While serum albumin and calcium show promise as prognostic markers, their clinical implementation requires validation through well-designed trials emphasising standardisation and generalizability. In essence, ongoing research is crucial for refining the predictive value of these biomarkers, advancing clinical care, and improving outcomes for burn patients.

ORCID
Heydar Ali Balou https://orcid.org/0009-0003-8739-2632
Mahsa Sadeghi https://orcid.org/0000-0001-5765-5647

REFERENCES

1. Bandeira NG, Barroso MVV, Matos MAA, et al. Serum albumin concentration on admission as a predictor of morbidity and mortality in patients with burn injuries. *J Burn Care Res*. 2021; 42(5):991-997.
2. Mobayen M, Torabi H, Bagheri Toolaroud P, et al. Acute burns during the COVID-19 pandemic: a one-year retrospective study of 611 patients at a referral burn centre in northern Iran. *Int Wound J*. 2023;20:3204-3211.
3. Eftekhari H, Sadeghi M, Mobayen M, et al. Epidemiology of chemical burns: an 11-year retrospective study of 126 patients at a referral burn centre in the north of Iran. *Int Wound J*. 2023;20:2788-2794.
4. Aguayo-Becerra OA, Torres-Garibay C, Macías-Amezcua MD, et al. Serum albumin level as a risk factor for mortality in burn patients. *Clinics*. 2013;68:940-945.
5. Toolaroud PB, Nabovati E, Mobayen M, et al. Design and usability evaluation of a mobile-based-self-management application for caregivers of children with severe burns. *Int Wound J*. 2023;20:2571-2581.
6. Rangraz Jeddi F, Nabovati E, Mobayen M, et al. A smartphone application for caregivers of children with severe burns: a survey to identify minimum data set and requirements. *J Burn Care Res*. 2023;44:irad027.
7. Al-Tarrah K, Hewison M, Moiemen N, Lord JM. Vitamin D status and its influence on outcomes following major burn injury and critical illness. *Burns Trauma*. 2018;6:6.
8. Jha S, Goyal P, Bhattacharya S, Baranwal S. Calcium homeostasis comparison in thermal burn patients–early tangential excision and grafting versus conservative management. *Ind J Plastic Surg*. 2020;53(3):381-386.
9. Cho YS, Seo CH, Joo SY, Ohn SH. The association between vitamin D levels and burn factors in different burn types. *Burns Trauma*. 2020;8:8.
10. Mohammadi AA, Shafaeipour A. Evaluation of vitamin D3 and calcium deficiency after recovery from extensive burn. *World J Plastic Surg*. 2021;10(1):60-65.

11. Zavala S, Larson J, O'Mahony M, Rech M. Impact of insufficient admission vitamin D serum concentrations on sepsis incidence and clinical outcomes in patients with thermal injury. *Burns*. 2020;46(1):172-177.

12. Kronstedt S, Roberts N, Ditzel R, et al. Hypocalcemia as a predictor of mortality and transfusion. A scoping review of hypocalcemia in trauma and hemostatic resuscitation. *Transfusion*. 2022;62:S158-S166.

13. Sanaie S, Mahmoodpoor A, Hamishehkar H, et al. Association between disease severity and calcium concentration in critically ill patients admitted to intensive care unit. *Anesth Pain Med*. 2018;8(1):e57583.

14. Sung J, Bochicchio GV, Joshi M, et al. Admission serum albumin is predicitve of outcome in critically ill trauma patients. *Am Surg*. 2004;70(12):1099-1102.

15. Cornelius BG, Clark D, Williams B, et al. A retrospective analysis of calcium levels in pediatric trauma patients. *Int J Burns Trauma*. 2021;11(3):267-274.

16. Hasannejad-Bibalan M, Sadeghi M, Hemmati H, et al. A two-year study of microbiological characteristics of intravascular catheter-related bloodstream infections at Razi hospital, Iran. *New Zealand J Med Lab Sci*. 2021;75(3):202-205.

17. von Domarus C, Brown J, Barvencik F, Amling M, Pogoda P. How much vitamin D do we need for skeletal health? *Clin Orthop Relat Res*. 2011;469:3127-3133.

18. Chen J-M, Wu T-Y, Wu Y-F, Kuo K-L. Association of the serum calcium level with metabolic syndrome and its components among adults in Taiwan. *Arch Endocrinol Metab*. 2023;67:e000632.

19. Akirov A, Masri-Iraqi H, Atamna A, Shimon I. Low albumin levels are associated with mortality risk in hospitalized patients. *Am J Med*. 2017;130(12):1465.

20. Duke J, Wood F, Semmens J, et al. A study of burn hospitalizations for children younger than 5 years of age: 1983–2008. *Pediatrics*. 2011;127(4):e971-e977.

21. Geyik MF, Aldemir M, Hosoglu S, Tacyildiz HI. Epidemiology of burn unit infections in children. *Am J Infect Control*. 2003; 31(6):342-346.

22. Santucci S, Gobara S, Santos C, Fontana C, Levin A. Infections in a burn intensive care unit: experience of seven years. *J Hospital Infect*. 2003;53(1):6-13.

23. Romero LM. Valor Pronostico del Nivel de Albumina Serica Inicial en los Pacientes Quemados.

24. Pérez-Guisado J, de Haro-Padilla JM, Rioja LF, DeRosier LC, De La Torre JI. Serum albumin levels in burn people are associated to the total body surface burned and the length of hospital stay but not to the initiation of the oral/enteral nutrition. *Int J Burns Trauma*. 2013;3(3):159-163.

25. Cooper AB, Cohn SM, Zhang HS, et al. Five percent albumin for adult burn shock resuscitation: lack of effect on daily multiple organ dysfunction score. *Transfusion*. 2006;46(1):80-89.

26. Investigators SS. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *New Eng J Med*. 2004; 350(22):2247-2256.

27. Dubois M, Heylbroeck C, Deroy P, Bracco D, Burns K, Sirdar E. Administration of albumin in burn patients: a systematic review. *J Burn Care Res*. 2007;28:S102.

28. Chen L-R, Yang B-S, Chang C-N, Yu C-M, Chen K-H. Additional vitamin and mineral support for patients with severe burns: a nationwide experience from a catastrophic color-dust explosion event in Taiwan. *Nutrients*. 2018;10(11):1782.

29. Zhang Z, Xu X, Ni H, Deng H. Predictive value of ionized calcium in critically ill patients: an analysis of a large clinical database MIMIC II. *PLoS ONE*. 2014;9(4):e95204.

30. Dey S, Karim HMR, Yunus M, Barman A, Bhattacharyya P, Borthakur MP. Relationship of on admission hypocalcaemia and illness severity as measured by APACHE-II and SOFA score in intensive care patients. *J Clin Diagn Res*. 2017;11(3):UC01.

31. Egi M, Kim I, Nichol A, et al. Ionized calcium concentration and outcome in critical illness. *Crit Care Med*. 2011;39(2): 314-321.

32. Steele T, Kolamunnage-Dona R, Downey C, Toh C-H, Welters I. Assessment and clinical course of hypocalcemia in critical illness. *Crit Care*. 2013;17(3):1-10.

33. Zivin JR, Gooley T, Zager RA, Ryan MJ. Hypocalcemia: a pervasive metabolic abnormality in the critically ill. *Am J Kidney Dis*. 2001;37(4):689-698.

34. Krajewski A, Piorun K, Maciejewska-Markiewicz D, et al. 25-hydroxycholecalciferol concentration is associated with protein loss and serum albumin level during the acute phase of burn injury. *Nutrients*. 2020;12(9):2780.

35. de Haan K, Groeneveld A, de Geus HR, Egal M, Struijs A. Vitamin D deficiency as a risk factor for infection, sepsis and mortality in the critically ill: systematic review and meta-analysis. *Crit Care*. 2014;18(6):1-8.

36. Upala S, Sanguankeo A, Permpalung N. Significant association between vitamin D deficiency and sepsis: a systematic review and meta-analysis. *BMC Anesthesiol*. 2015;15(1):1-11.

37. Blay B, Thomas S, Coffey R, Jones L, Murphy CV. Low vitamin D level on admission for burn injury is associated with increased length of stay. *J Burn Care Res*. 2017;38(1):e8-e13.

38. Ala-Kokko TI, Mutt SJ, Nisula S, et al. Vitamin D deficiency at admission is not associated with 90-day mortality in patients with severe sepsis or septic shock: observational FINNAKI cohort study. *Ann Med*. 2016;48(1–2):67-75.

39. Ratzinger F, Haslacher H, Stadlberger M, et al. 25 (OH) D and 1, 25 (OH) D vitamin D fails to predict sepsis and mortality in a prospective cohort study. *Sci Rep*. 2017;7(1):1-10.

40. Vosoughi N, Kashefi P, Abbasi B, Feizi A, Askari G, Azadbakht L. The relationship between vitamin D, clinical outcomes and mortality rate in ICU patients: a prospective observational study. *J Res Med Sci*. 2016;21:21.