

Effect of vitamin D on clinical outcomes in patients with thermal injury

Sepide Pirdastan¹ | Marjan Mahdavi Roshan² | Mohammadreza Mobayen¹ |
Reza Asadzadegan¹ | Mohammad Ebrahim Ghafari³ |
Seyed Amirhossein Mazhari⁴ | Mahsa Sadeghi¹  |
Parissa Bagheri Toolaroud^{1,5} | Hamidreza Alizadeh Otaghvar⁶ 

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

²Cardiovascular Disease Research Center, Department of Cardiology, Heshmat Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

³Department of Biostatistics and Epidemiology, Faculty of Health, Qom University of Medical Sciences, Qom, Iran

⁴Student Research Committee, Azerbaijan Medical University, Baku, Azerbaijan

⁵Health Information Management Research Center, Kashan University of Medical Sciences, Kashan, Iran

⁶Trauma and Injury Research Center, Iran University of Medical Sciences, Tehran, Iran

Correspondence

Reza Asadzadegan, Burn and Regenerative Medicine Research Center, Guilan University of Medical Sciences, Rasht, Iran.
Email: reza.asadzadegan@gmail.com

Hamidreza Alizadeh Otaghvar, Trauma and Injury Research Center, Iran University of Medical Sciences, Tehran, Iran.
Email: h.otaghvar1360@gmail.com

Abstract

Evaluating complications and mortality risks in burn patients is crucial for effective treatment planning and improving survival rates. This study investigated the relationship between the serum vitamin D level and the clinical outcomes of adult burns patients. This was a prospective cohort of adult patients hospitalized due to thermal burns at a burn centre in the north of Iran. Based on the level of 25 hydroxyvitamin D measured upon admission, patients were divided into two groups of patients with sufficient 25 hydroxyvitamin D level and insufficient 25 hydroxyvitamin D level. Descriptive statistics were used for baseline demographics. Univariate analysis was conducted using Mann–Whitney U, Chi-square, independent samples, and Fisher's exact tests. A multivariate logistic regression was performed to adjust for the effects of confounding variables. Statistical analyses were conducted using SPSS 28.0 software. A total of 220 patients were included in the study. The average total body surface area burned was 30.52 ± 9.34 . Patients with insufficient vitamin D levels had longer hospital stays (12.53 vs. 11.45) and longer stays in the intensive care unit (ICU) (3.32 vs. 2.40) than those with appropriate vitamin D levels. Participants with insufficient vitamin D levels exhibited a numerically higher incidence of infections than those with adequate levels ($p < 0.05$). The multivariate regression found that vitamin D deficiency levels were associated with increased

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infection rates and prolonged hospital stay. This study suggests that vitamin D deficiency is a significant risk factor for adverse clinical outcomes in burn patients. Further research is needed to confirm these associations and to explore potential interventions to optimize vitamin D status in this patient population.

KEYWORDS

burns, sepsis, thermal injury, trauma, vitamin D

Key Messages

- Patients with insufficient vitamin D levels had longer hospital stays (12.53 vs. 11.45) and longer stays in the intensive care unit (ICU) (3.32 vs. 2.40) than those with appropriate vitamin D levels.
- Participants with insufficient vitamin D levels exhibited a numerically higher incidence of infections than those with adequate levels ($p < 0.05$).
- This study suggests that vitamin D deficiency is a significant risk factor for adverse clinical outcomes in burn patients.

1 | INTRODUCTION

Burn injuries represent a significant public health concern due to their extreme severity and disabling nature. Burn deaths are estimated at 260 000 people annually, more than 90% of which occur in low-income countries.¹⁻³ Evaluating markers of complications and risk of death in burn patients is essential for planning and improving treatment measures, reducing clinical complications and increasing the chance of survival.^{1,4,5} Usually, biochemical variables are not used as prognostic factors in burn patients. Meanwhile, important metabolic changes occur even in 10% burns (TBSA = 10%).⁶ Vitamin D deficiency is frequent in critically ill patients, including those who have suffered burns.^{7,8} A clinical study recently reported that most burn patients (79.6%) had vitamin D deficiency at admission.⁹ Severe burn damage can cause a decrease in vitamin D and the proteins that carry it.⁷ This is of concern because vitamin D has wide-ranging biological effects on the body and may affect short-term and long-term outcomes in these patients.⁷ Vitamin D stimulates wound healing and enhances immunity through vitamin D receptors in B and T lymphocytes, monocytes and macrophages.⁸ In addition, vitamin D levels are associated with the biomechanical properties of hypertrophic scars. Therefore, vitamin D is a critical nutrient in burn care.⁸ The literature on hypovitaminosis D and its clinical consequences in adult burn patients is limited.⁷ However, some studies have shown that low vitamin D levels in critically ill patients can be associated with negative outcomes such as infection and sepsis, increased length of hospitalization, wound healing time, organ failure and increased mortality risk.^{7,9-17} Some studies also reported no

association between vitamin D deficiency and outcomes such as length of hospitalization, sepsis and mortality.¹⁸⁻²⁰ Although vitamin D levels following severe burns can decrease due to prolonged hospitalization and lack of supplementation, however, in some of these studies, the low vitamin D status most likely reflects pre-injury 25 hydroxy-vitamin D (25(OH)D) levels in the population and is not a consequence of burns.⁷ Due to the lack of standard comparative studies and contradictory findings, whether vitamin D deficiency can be used as a predictor of mortality has not yet been determined. Therefore, this study investigated the relationship between the vitamin D level at admission and the outcome in burn patients.

2 | METHODS

2.1 | Study design and data collection

This prospective cohort study was conducted for 6 months, from March 2022 to September 2022, at Velayat Hospital, a burn care and plastic surgery centre affiliated with Guilan University of Medical Sciences, Rasht, Iran. Patients between 18 and 89 years old who presented with extensive burns (total body surface area [TBSA] > 20%) were gradually included in the study (consecutive sampling). Only thermal burns were considered. Patients who received vitamin D supplements before admission, pregnant women and cancer patients were excluded from the study. On the day of hospitalization, the serum concentration of 25(OH)D was measured by the ELISA method by spectrophotometry. According to Endocrine Society guidelines, vitamin D sufficiency is defined as a cutoff point equal to or higher than 30 ng/

mL of 25(OH)D.²¹ Patients with sufficient vitamin D were compared with those with insufficient vitamin D concentrations. Also, other information related to each patient regarding age, sex, length of stay (LOS), length of stay in the intensive care unit (ICU-LOS), ventilator use, TBSA percentage, BMI, presence of infection, cardiovascular complications, number of surgeries and outcome (discharge/death) was obtained by a nurse as part of a routine admission assessment. Based on the equation

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2 (\sigma_1^2 + \sigma_2^2)}{(d)^2},$$

and using the standard deviations of 19.5 (vitamin D insufficient level group) and 9.75 (vitamin D sufficient level group) from the previous study,²² with $d = 7.5$ and $\alpha = 0.05$, a minimum of 110 patients for both case and control groups was required. Thus, a total sample size of 220 cases (110 patients in each case and control group) were determined. The sampling method was accessible, and the patients were grouped according to gender, age, percentage of burns and inhalation injury.

2.2 | Statistical analysis

The data distribution was shown as frequency, mean and standard deviation. The normality of the data was checked using the Kolmogorov–Smirnov test or the Shapiro–Wilk test. The Chi-square test was used to compare proportions. There were no missing data. The Mann–Whitney *U*-test was used to compare parametric variables without normal distribution, and the independent *t*-test was used to

compare variables with normal distribution. A multivariate logistic regression was performed to adjust for the effects of confounding variables and determine whether vitamin D adequacy was a predictor of mortality and infection in burn patients. SPSS® V28.0 statistical package was used to perform all the analyses. A *p*-value <0.05 was considered statistically significant.

2.3 | Ethical approval

The study protocol was approved according to the Declaration of Helsinki and the Ethics Committee of Guilan University of Medical Sciences, Rasht, Iran (IR.GUMS.REC.1400.223).

3 | RESULTS

3.1 | Patients

The study population's demographic data are summarized in Table 1. The study population comprised 220 patients with thermal burns: 110 (50%) were categorized in the group with inadequate vitamin D levels and another 110 patients (50%) with adequate vitamin D levels ($p > 0.05$). Baseline characteristics were similar between groups. Patients had few comorbidities in both groups. The mean age of the patients was 42.47 ± 14.76 years, with a predominance of male participants (80.45%).

TABLE 1 Comparison of baseline characteristics between patients with insufficient and adequate vitamin D levels.

| Variables | Adequate vitamin D (n=) | Insufficient vitamin D (n=) | <i>p</i> -value |
|---------------------------------|-------------------------|-----------------------------|-----------------|
| Age, median years | 44.07 ± 11.46 | 42.30 ± 15.10 | 0.661 |
| Gender, <i>n</i> (%) | | | |
| Male | 93 (52.5) | 84 (47.5) | 0.175 |
| Female | 17 (39.5) | 26 (60.5) | |
| BMI, mean kg/m ² | 23.73 | 25.20 | 0.127 |
| Weight, mean kg | 74.46 | 78.65 | 0.231 |
| Smoking | 37 (33.6) | 34 (30.9) | 0.665 |
| Alcohol consumption | 6 (5.5) | 11 (10.0) | 0.207 |
| Drug abuse | 52 (47.3) | 47 (42.7) | 0.554 |
| Inhalation injury, <i>n</i> (%) | 18 (16.4) | 13 (11.8) | 0.333 |
| Burn size, median %TBSA (IQR) | 26.60 ± 10.13 | 30.62 ± 9.28 | 0.688 |
| Comorbidities, <i>n</i> (%) | | | |
| HTN | 2 (12.5) | 9 (33.3) | 0.32 |
| CAD | 1 (12.5) | 0 (0) | 0.58 |
| Diabetes | 1 (12.5) | 13 (33.3) | 0.26 |

3.2 | Clinical outcomes

Patients with inadequate vitamin D levels had longer hospital stays (12.53 vs. 11.45 days) and longer stays in the intensive care unit (3.32 vs. 2.40 days) than those with sufficient vitamin D levels. A significant difference in infection rates was observed between the two groups; patients with insufficient vitamin D levels showed a higher incidence of infections when contrasted with individuals with an adequate level ($p < 0.001$). The group with insufficient vitamin D had a higher mortality rate, but this difference did not have statistical significance (3.6% vs. 0%, $p = 0.122$) (Table 2).

In a multivariate regression analysis, after adjusting for confounding variables such as age, TBSA and comorbidities, vitamin D deficiency remained independently associated with increased infection rates and longer hospital stays. Nonetheless, no statistically significant association was detected between vitamin D deficiency and mortality.

4 | DISCUSSION

A deficiency in vitamin D has been linked to higher infection rates, prolonged hospitalization and increased mortality among critically ill individuals.^{23–25} These adverse outcomes could be attributed to the finding that the synthesis of 1,25-dihydroxy (OH)₂ vitamin D within immune cells derived from circulating 25-OH vitamin D. As a result of this process, the antibacterial activities increase by inducing the production of cathelicidin and other antimicrobial peptides.^{26–28} Therefore, this study investigated the relationship between the vitamin D level at admission and the outcome in burn patients.

The majority of the participants were male. Men are more likely to work in dangerous jobs, which may explain why they experience burns more frequently than women.²⁹ Our results showed that patients with

insufficient vitamin D levels had a prolonged hospital LOS and longer ICU-LOS than those with adequate vitamin D levels. Furthermore, individuals with inadequate vitamin D levels who needed mechanical ventilation showed a tendency towards an extended period of mechanical ventilation, and this difference between the two groups had statistical significance. A recent retrospective study by Blay et al. compared 318 burn patients with low vitamin D and sufficient vitamin D. Patients with low vitamin D concentrations had prolonged stays in hospital and intensive care units and a trend towards more ventilator days and increased complications.⁹ These findings suggest that vitamin D deficiency may be associated with recovery and hospitalization duration.

One of the study's considerable results was the significant difference in infection rates between individuals with inadequate and adequate vitamin D levels. Infection incidence was statistically greater in patients with vitamin D deficiency. The association between vitamin D deficiency and increased infection rates remained significant even after adjusting for confounding variables, highlighting the potential clinical relevance of addressing vitamin D status in burn patients to mitigate infection risk. This observation aligns with previous studies claiming that vitamin D helps regulate immune system activity and may contribute to a lower risk of infections.³⁰

Our study did not identify a significant difference in inpatient mortality between the groups. This result is consistent with a previous study.³⁰ While it seems that burn patients with sufficient vitamin D experience better results than those with insufficient levels,^{13,24,25} it remains uncertain whether the provision of vitamin D supplementation would enhance these outcomes. Moreover, it is unclear whether this impact on results would be more significant in patients with extensive burns or whether the degree of vitamin D deficiency influences. However, it is important to note that the study may be underpowered to detect such differences, given the relatively small sample size. Larger studies or meta-analyses

TABLE 2 Comparison of outcomes between patients with insufficient and adequate vitamin D levels.

| Variables | Adequate vitamin D ($n = 110$) | Insufficient vitamin D ($n = 110$) | p -value |
|---------------------------------|----------------------------------|--------------------------------------|------------|
| Hospital LOS, median days (IQR) | 11.45 (SD = 3.32) | 12.53 (SD = 3.69) | 0.023 |
| ICU-LOS | 2.40 (SD = 1.14) | 3.32 (SD = 1.43) | 0.013 |
| ICU admission, n (%) | 20 (18.2) | 49 (44.6) | <0.001 |
| Operations, mean | 4.75 (SD = 4.83) | 4.24 (SD = 3.50) | 0.371 |
| Mechanical ventilation, n (%) | 0 (0) | 7 (6.4) | 0.014 |
| Discharge Status | | | |
| Mortality, n (%) | 0 (0) | 4 (3.6) | 0.122 |
| Infection, n (%) | 26 (23.6) | 95 (86.4) | <0.001 |

may provide more definitive insights into the relationship between vitamin D status and mortality in this context.

4.1 | Clinical Implications

The findings of this study underscore the potential clinical significance of assessing and addressing vitamin D status in patients with thermal burn injuries. Strategies to prevent or correct vitamin D deficiency could be considered part of the overall care plan for these patients, aiming to reduce infection risk and potentially shorten hospital LOS.

4.2 | Limitations and future research

The study may have limited generalizability as it focuses on patients with thermal injuries. Therefore, the findings may not directly apply to a broader population with different injuries or medical conditions.

5 | CONCLUSION

This study suggests that vitamin D deficiency is a significant risk factor for adverse clinical outcomes in burn patients. Further research is needed to confirm these associations and to explore potential interventions to optimize vitamin D status in this patient population.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data supporting this study's findings are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This research was approved by the Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1400.223).

ORCID

Mahsa Sadeghi  <https://orcid.org/0000-0001-5765-5647>
Hamidreza Alizadeh Otaghvar  <https://orcid.org/0009-0000-3620-0977>

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